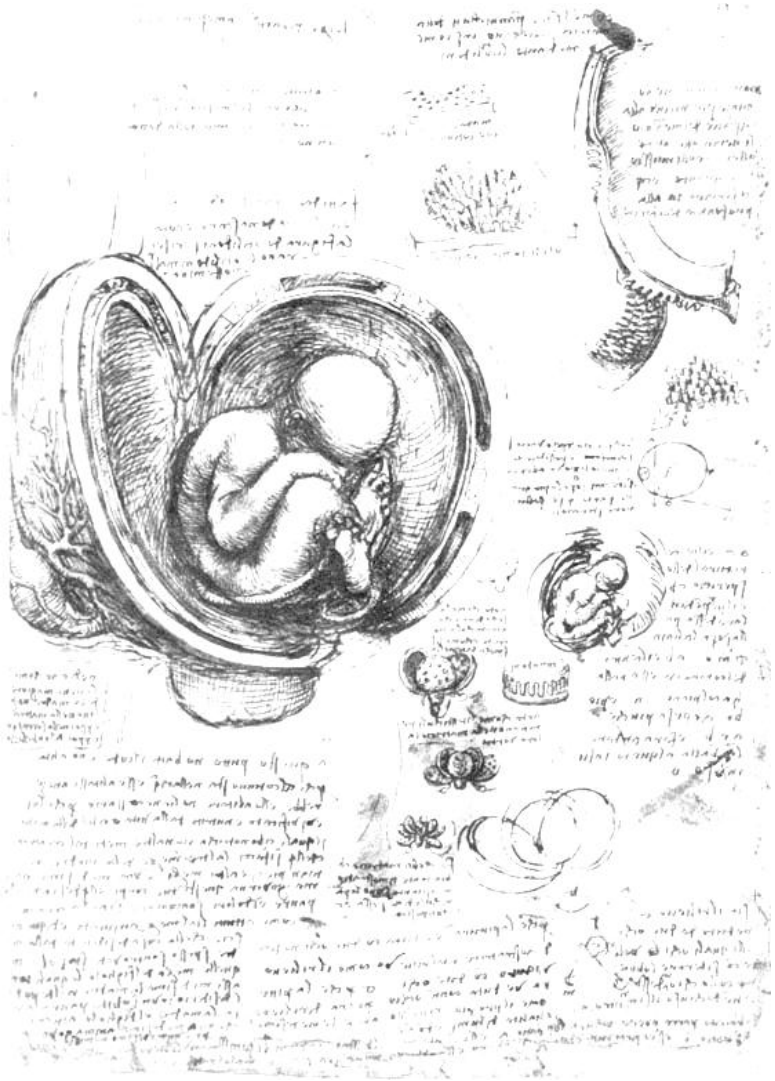
Volume XIX, Nr. 1, 2013, Timişoara, Romania
ISSN 2065-376X

MEDICINE IN EVOLUTION



CENTER OF PROMOTING HEALTH EDUCATION AND MOTIVATION FOR PREVENTION IN DENTISTRY
CENTER FOR CONTINUOUS MEDICAL EDUCATION

http://umft.ro/newpage/medicineinevolution

Journal edited with the support of

Printed at: WALDPRESS, Timisoara,
17 Brandusei Street,
Phone/Fax: 0040256422247

Edited at: EUROSTAMPA, Timisoara
26, Revolutiei 1989 Street,
Phone: 0040256204816

EDITORIAL BOARD

CONTENTS

ARTICLES

CRISTIAN MORNOS, HANS-JURGEN JAHRAUS, CRISTIAN OANCEA, ELENA ARDELEANU, LUCIAN PETRESCU, ADINA IONAC, SORIN PESCARIU

SPECKLE TRACKING ECHOCARDIOGRAPHY, A MODERN TECHNIQUE FOR LEFT VENTRICULAR DEFORMATION ANALYSIS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION.....1

GEORGE PUENEA, DAN NEMES, LILIANA CATAN, ELENA AMARICAI, DANIEL POPA, LAVINIA BUSESCU, ROXANA BALACESCU

CCUPATIONAL CHRONIC LOW BACK PAIN IN YOUNG ACTIVE ADULTS - A NEW COMPLEX AND NONINVASIVE ASSESSMENT METHOD……11

HANS-JURGEN JAHRAUS, CRISTIAN MORNOS, CRISTIAN OANCEA, ELENA ARDELEANU, LUCIAN PETRESCU

THE INFLUENCE OF TREATMENT WITH BOSENTAN AND SILDENAFIL ON MYOCARDIAL DEFORMATION PARAMETERS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION.....18

ALINA FEILER, MARIA MOGOŞEANU, IOANA ZOSIN

AN INTERDISCIPLINARY APPROACH IN THE DIAGNOSIS OF GRAVES OPHTHALMOPATHY GENERAL REVIEW.....26

RADU PETROMAN, DAN NEMEŞ, MIHAI DRĂGOI, DANIEL POPA, DAN SURDUCAN

BENEFITS OF SPECIFIC EARLY DIAGNOSIS AND TREATMENT IN INFLAMMATORY RHEUMATIC DISEASES.....32

CLARA MATEI, MIRCEA TAMPA, SIMONA-ROXANA GEORGESCU, ISABELA SARBU, RODICA-MARIANA ION, CAROLINA CONSTANTIN, MONICA NEAGU

THE ROLE OF PORPHYRIN PRECURSOR-BASED PHOTODYNAMIC THERAPYIN DERMATOLOGY.....38

MIRCEA TAMPA,CLARA MATEI, SIMONA-ROXANA GEORGESCU, VASILE BENEA, ISABELA SARBU, RODICA-MARIANA ION, CAROLINA CONSTANTIN, MONICA NEAGU, SANDA POPESCU

5-AMINOLEVULINIC ACID PHOTODYNAMIC THERAPY IN THE TREATMENT OF CUTANEOUS SQUAMOUS CELL CARCINOMA IN SITU (BOWEN'S DISEASE).....45

I. GYALAI, M. TOMESCU, O. ANCUȘA

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PAROXISMAL ATRIAL FIBRILLATION PATIENTS WITHOUT STRUCTURAL CARDIAC DIDEASE, WITH AND WITHOUT ARTERIAL HYPERTENSION.....51

LOREDANA DUMITRAȘCU, MIHAELA ADINA DUMITRACHE, CRISTIAN COMES, IRINA DONCIU, RUXANDRA MORARU

COMMON AND PROFFESIONAL LANGUAGE IN ORAL HEALTH EDUCATION…….....57

PAULA BICOV, DAN NEMES, LILIANA CATAN, ELENA AMĂRICĂI, DANIEL POPA

COMPREHENSIVE APPROACH OF THE PERIARTICULAR SOFT TISSUE INJURIES OF THE KNEE.....63

ANDREEA DAN, ȘERBAN NEGRU, IZABELLA ȘARGAN, RADU DAN

FOLFOX4 – A THERAPEUTIC OPTION IN COLORECTAL LIVER METASTASES…….....69

RADU DAN, ANDREEA DAN, OCTAVIAN CREȚU, LAURENȚIU SIMA, ȘERBAN NEGRU

PATHOLOGICAL COMPLETE REMISSION IN RECTO SIGMOID CANCER PATIENT WITH LIVER METASTASES AFTER XELOX/BEVACIZUMAB TREATMENT - A CASE REPORT.....73

VALERIA MOCANU, ROMULUS TIMAR, MIHNEA MUNTEANU, BOGDAN TIMAR, RALUCA HORHAT, ADINA BUCUR , VIOREL SERBAN

DRY-EYE SYNDROME IN PATIENTS WITH TYPE 2 DIABETIC MELLITUS.....77

MELINDA ONEŢ, ANGELA CODRUŢA PODARIU, RAMONA AMINA POPOVICI, RODICA JIANU, RUXANDRA SAVA-ROŞIANU, ROXANA OANCEA

CAMOUFLAGE THERAPY IN CLASS II ANGLE ANOMALIES -APLICABILITY AND LIMITATIONS.....84

ALI FAHS, ANCA TEMELCEA, DANIELA MĂNUC

RELATIONSHIP BETWEEN AESTHETIC MOTIVATION AND PREFERENCES FOR ORTHODONTIC TREATMENT.....92

MATEESCU TEODORA, ALINA ANGLITOIU, PODARIU ANGELA, RAMONA AMINA POPOVICI, MOJSE MARCEL, ROXANA OANCEA, RUXANDRA SAVA ROSIANU, DANIELA JUMANCA

THE EFFECT OF INTERDISCIPLINARY TREATMENT ON MAXILLARY COMPRESSION CAUSED BY ORAL BREATHING….....99

RAMONA AMINA POPOVICI, ANGELA CODRUTA PODARIU, MOJSE MARCEL, ROXANA OANCEA, RUXANDRA SAVA ROSIANU, GALUSCAN ATENA, MELINDA ONET, ALEXANDRA SABINA PODARIU

CLINICAL TRIAL EVALUATING THE EFFECTIVENESS OF RAPID MAXILLARY EXPANSION TECHNIQUE (RME) TO RESOLVE UPPER MAXILLARY COMPRESSION ASSOCIATED WITH ORAL BREATHING….....104

EZATOLLAH AGHAJANI, ANCA TEMELCEA

EVALUATION OF SURGICAL-ORTHODONTIC TREATMENT ON PALATALLY IMPACTED CANINES…….....109

ŞERBAN ROŞU

MANDIBULAR BODY FRACTURE IN PATHOLOGICAL BONE TREATED BY RECONSTRUCTION WITH NONVASCULARIZED BONE GRAFT HARVESTED FROM ILIAC CREST- CASE REPORT.....113

CÂNDEA ADRIAN, TOPALĂ FLORIN, ROMÎNU MIHAI

THE MARGINAL AND INTERNAL FIT OF ALL-CERAMIC INLAY-RETAINED FIXED PARTIAL DENTURES MADE WITH THE LAVA SYSTEM.....117

CRISTIAN IRIMIA, CRISTINA PĂDURARIU

CASE REPORT: RIDGE AUGMENTATION USING RETROMOLAR REGION.....125

BILAL TAKOUZLI, CRISTIAN IRIMIA, TIBERIU NIŢĂ

INFECTIOUS COMPLICATIONS FOLLOWING SURGICAL REMOVAL OF LOWER WISDOM TEETH.....129

BELAL NIJIM, CRISTIAN IRIMIA, OCTAVIAN DINCĂ

PREVALENCE OF ORAL PREMALIGNANT LESIONS.....134

CHRISTINA MIHAI, LAURENŢIU GONTARIU, DIANA GOLEA, ALEXANDRU-ANDREI ILIESCU, ANDREI ILIESCU

COMPARATIVE STUDY BETWEEN KERR FILE NEEDLES USE FROM STAINLESS STEEL OR NICKEL-TITANIUM ALLOY AND PROTAPER CUTTERS USED IN MANUAL WIDENING OF ROOT CANALS WITH DIFFERENT DEGREES OF CURVATURE.....139

KRALEV CAROLINE, OANA VELEA, DERBAN PAULA, ONISEI DAN, ONISEI DOINA

THE PERIODONTAL RISK FACTOR IN THE MANAGEMENT OF PERIODONTAL DISEASE.....147

LUCIEN RECLARU, LAVINIA ARDELEAN, LAURA CRISTINA RUSU

SURFACE CONDITION INFLUENCE ON GALVANIC CORROSION.....152

OTILIA CORNELIA BOLOS, CRISTINA MARIA BORTUN, ANCA SILVIA VÂLCEANU

A CRITICAL REVIEW UPON SOME PROPERTIES OF THE RESINS USED IN COMPLETE DENTURES TECHNOLOGY.....157

DANIELA JUMANCA, ATENA GALUSCAN, ANGELA PODARIU, ROXANA OANCEA, RAMONA POPOVICI, RUXANDRA SAVA-ROSIANU

THERAPEUTIC OPTIONS FOR DENTAL-MAXILLARY ABNORMALITIES IN PATIENTS WITH ORAL BREATHING.....164

ROXANA OANCEA, ANGELA CODRUȚA PODARIU, RAMONA AMINA POPOVICI, RUXANDRA SAVA-ROȘIANU, JUMANCA DANIELA, MELINDA ONEȚ

SCHOOL TEACHERS' ABILITIES IN THE DETECTION OF DENTAL CARIES -A PILOT STUDY.....169

JIANU ALEXANDRU, ONISEI DOINA, STRATUL STEFAN-IOAN

CURRENT METHODS FOR IMAGISTIC EVALUATION OF ADULT PATIENTS WITH PERIODONTAL DISEASE UNDERGOING ORTHODONTIC TREATMENT - A REVIEW PART I: COMBINED ORTHODONTIC - PERIODONTAL TREATMENT CONSIDERATIONS.....174

MARIA SUCIU, MINODORA ANDOR, CARMEN CRISTESCU, LIANA DRAGAN, LIANA SUCIU, MIRELA TOMESCU

CORRELATION OF PLASMA LEVELS OF ASYMMETRIC DIMETHYLARGININE WITH CAROTID INTIMA - MEDIA THICKNESS IN HYPERTENSIVE PATIENTS WITH ENDOTHELIAL DYSFUNCTION.....179

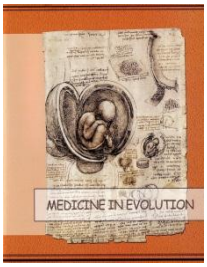
MINODORA ANDOR, MARIA SUCIU, LIANA DRAGAN, LAVINIA VLAIA, MIRELA VOICU, LIANA SUCIU, RALUCA GRADINARU, MIRELA TOMESCU

CORRELATION ANALYSIS BETWEEN BIOCHEMICAL, FUNCTIONAL AND STRUCTURAL MARKERS OF ENDOTHELIUM DAMAGE IN PATIENTS WITH ESSENTIAL HYPERTENSION.....188

LIANA SUCIU, MIRELA TOMESCU, CARMEN CRISTESCU, MARIA SUCIU, MIRELA VOICU, RALUCA GRĂDINARU

PHARMACOECONOMICS EVALUATION AS A MEANS OF MANAGING THE HEALTH CARE SYSTEM 198

SPECKLE TRACKING ECHOCARDIOGRAPHY, A MODERN TECHNIQUE FOR LEFT VENTRICULAR DEFORMATION ANALYSIS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION



CRISTIAN MORNOS[1], HANS-JURGEN JAHRAUS[1], CRISTIAN OANCEA[1], ELENA ARDELEANU[1], LUCIAN PETRESCU[1], ADINA IONAC[1], SORIN PESCARIU[1]

[1]University of Medicine and Pharmacy "Victor Babes" Timisoara, Romania

ABSTRACT

Introduction: Speckle tracking echocardiography represents a modern method recently introduced into the clinical practice, able to provide information that until now could not be obtained by conventional echocardiography.
Aim of the study: This study aims to analyze the role of speckle tracking echocardiography in evaluation of the left ventricle (LV) function in patients presenting pulmonary arterial hypertension (PAH).
Material and method: We analyzed two groups of patients: group 1 including 35 patients with PAH clinically and echocardiographically diagnosed and group 2 including 40 patients of the same age and gender, without any clinical or echocardiographic evidence of cardiac disease.
Results: Speckle tracking echocardiography, able to identify the subclinical changes in LV function, shows a significant reduction of the longitudinal global strain (VSε) in patients presenting PAH. The presence of an elevated systolic pressure in the pulmonary artery (SPPA) also influences the myocardial rotation, too. The left ventricular torsion (LVtor) and left ventricular twist (LVtw) were significantly lower in group 1 compared to group 2. These latter changes are due to the impairment of LV apical rotation, while the basal rotation is not affected.
Conclusions: The obtained data advocates for using the speckle tracking technique in assessing the impact of pulmonary arterial hypertension on the left ventricular dynamics.
Key words: *speckle tracking echocardiography, pulmonary arterial hypertension*

Correspondence to

Dr. Hans-Jurgen Jahraus,
Drd. University of Medicine and Pharmacy "Victor Babes" Timisoara, Romania.
Adress: Calea Al. Ioan Cuza Nr. 10, Timisoara,
tel. 0726160080,
e-mail: jrgenjahraus@yahoo.de

INTRODUCTION

Speckle tracking echocardiography represents a modern method recently introduced into the clinical practice, able to provide information that until now could not be obtained by conventional echocardiography[1-3]. It allows the analysis of extremely important parameters which characterize left ventricular (LV) function: the longitudinal myocardial deformation and rotation of the LV respectively. The method involves digital storing of bi-dimensional echocardiographic images, and subsequently post-processing them, using a specialized computer program/software. The longitudinal myocardial deformation can be expressed as a physical parameter called "strain", defined as the ratio of length variation ($l - l_0$) under the influence of a force, and initial length (l_0) [4-6], being expressed as a percentage: strain (ε) = $(l - l_0)/ l_0 = \Delta t/ l_0$, where l = final length, l_0 = initial length, v = final velocity, v_0 = initial speed, Δt = the analyzed time interval.

The pulmonary arterial hypertension (PAH) is a complex pathology with an often unfavorable prognosis. Therefore, obtaining data on the subclinical deterioration of ventricular function is extremely important. In the early stage of PAH there is a marked increase of pressure in the pulmonary artery, but the LV function is relatively normal. The most important hemodynamic change in PAH is the increase of resistance to the pulmonary blood flow. In evolving, the cardiac output will be reduced progressively, pressure in the pulmonary artery growing continuously. Initially, the pulmonary arteries may respond to vasodilators, but as the disease advances, the increased pulmonary vascular resistance becomes stable. The pulmonary capillary pressure remains normal until the final stages, when there is tendency to rise as response to the poor diastolic filling of LV, caused by alteration of interventricular septum configuration. The lung functions are usually normal in the primitive PAH, but sometimes a slight restrictive dysfunction may appear. Hypoxemia, which occurs frequently, is probably due to the discrepancy of ventilation–perfusion, aggravated by a low cardiac output.

AIM OF THE STUDY

This study aims to analyze the role of speckle tracking echocardiography in evaluation of the LV function in patients with PAH.

MATERIAL AND METHOD

We analyzed two groups of patients in the Echocardiography Laboratory of the Institute of Cardiovascular Diseases in Timisoara during November 2008 - March 2012:

- group 1 including 35 patients with PAH clinically and echocardiographically diagnosed (systolic pressure in pulmonary artery ≥ 36 mmHg), in sinusal rhythm, but who had normal LV systolic function (translated by documenting a ejection fraction of LV ≥ 50% determined by biplane planimetric method);
- group 2 including 40 patients of the same age and gender, without any clinical or echocardiographic evidence of cardiac disease, with systolic pressure in the pulmonary artery <36 mmHg, with normal systolic function of both LV and right ventricle (RV) due to transthoracic echocardiography.

Exclusion criteria were represented by: inadequate echocardiographic window, paced (electro-stimulated) rhythm, significant disorders of the left heart (valvulopathy, high blood pressure,

coronary disease) which can cause secondary PAH.

In all the enrolled patients a full clinical examination was performed. The walked distance in an interval of 6 minutes, on flat ground (6-minute walk test) was determined, too. The symptoms severity was evaluated on the basis of subjective assessment of the patient, including the case in the WHO functional classification/ New York Heart Association[7-8].

The arterial saturation of O_2 was determined in the enrolled patients by collecting the arterial blood by puncture either at the level of radial artery or the femoral artery in compliance with aseptic measures. The arterial blood was analyzed using a digital analyzer to determine Astrup parameters in a maximum time of 1 minute.

The surface electrocardiogram was also performed according to the recommended technique, the conventional transthoracic echocardiography as well as the tissular Doppler, using the echocardiographic system Vivid 7 GE. Doppler echocardiography allows accurate estimation of the systolic pressure in the pulmonary artery (SPPA) and by this it enables the diagnosis confirmation and grading of PAH severity.

The speckle tracking method requires adequate software and allows simultaneous analysis of multiple myocardial points of interest. The images recorded by the conventional technique were digitally stored and subsequently analyzed off-line using the PC software EchoPac Dimension (GE Medical). To obtain the global longitudinal strain of LV (LVε) it was necessary to register the two-dimensional images at the level of the three apical planes (apically 2 chambers, apically 3 chambers and apically 4 chambers) in a LV model including 17 segments. The LVε value was obtained by calculating the arithmetic average of the longitudinal strain of all 17 LV segments[9].

Speckle tracking allows both the analysis of longitudinal deformation and torsion, and respectively the myocardium rotation of LV in transverse plane. The bi-dimensional cardiac cycles using the QRS complex as trigger were purchased from the level of two incidence planes of the parasternal short axis: a basal plan as circular as possible, which meets the mitral valve, and a second apical plan, distally from the papillary muscles (these not being included in the image) also as circular as possible[5,6]. At the level of each plan three cardiac cycles recorded in post-expiratory apnea were stored, at a frame rate of 70-100 Hz, for further analysis. The counter-clockwise rotation of the myocardium was defined as positive, while clockwise rotation was defined as negative if we look at the cord from the apex. Thus, two other parameters can be calculated: LV twist and torsion. LV twist (LVtw) is represented by the net difference between the apical rotation and the basal one of LV for each time of the cardiac cycle. The program does not allow the determination of LV twist if there are significant variations between the heart rate of different cardiac cycles. In this study the maximum difference between the apical rotation and the basal one was used. LV torsion (LVtor) is obtained by dividing LV twist by the telediastolic longitudinal diameter of LV determined from incidence apically 4 chambers, according to the studies published previously[1,6].

For the statistical analysis the specialized software SPSS 11.5 (SPSS Inc., Chicago, IL, USA) and NCSS 2004 (NCSS, Kaysville, UT, USA) was used. The numerical variables are presented as mean ± standard deviation (SD) and compared using the t-student test or the analysis of variance. The categorical variables are presented as absolute values or percentage and compared using the χ^2 test. The correlation between the different echocardiographic parameters was determined by the Pearson correlation coefficient. A p value lower than 0.05 was considered as being significant statistically. The study was approved by the Ethics Committee of the Institute; all the patients expressed their agreement on the participation.

RESULTS

Out of the 51 patients in sinusal rhythm addressed for transthoracic echocardiography and identified as presenting PAH and normal LV systolic function, only 35 could be included in the group of patients with SPPA ≥ 36 mmHg (group 1). The other patients were excluded due to the exclusion criteria: inadequate echocardiographic window (6 patients), paced rhythm (1 patient), significant left heart disease (valvulopathy, high blood pressure, coronary disease) that can cause secondary PAH (9 patients). PAH etiology was represented by lung disease (22 patients), pulmonary embolism (9 patients) and congenital malformation respectively (4 patients).

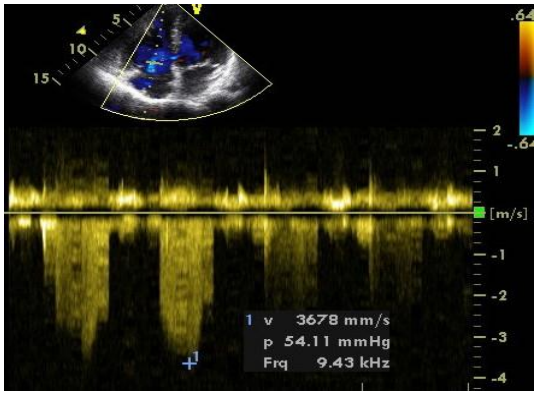
For setting up group 2, 43 voluntary patients of the same age and gender, without clinical or echocardiographic evidence of cardiac disease, with systolic pressure in pulmonary artery <36 mmHg, with normal systolic function both of the LV and RV at transthoracic echocardiography were analyzed. Three patients were excluded because of the inappropriate echocardiographic window.

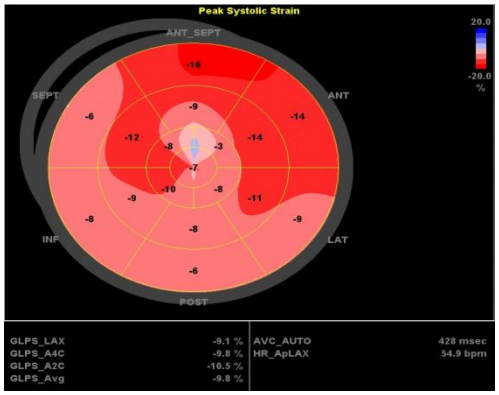
The basic characteristics of the analyzed groups are presented in Table 1. The average age of patients in group 1 was 41 ± 9 years, and estimated SPPA of 52 ± 16 mmHg; in group 2 the mean age was 38 ± 11 years, and SPPA only of 24 ± 10 mmHg ($p<0.001$). A percentage of 48% of the patients in group 1 had severe PAH (defined in the current study as a value of SPPA over 60 mmHg). There were no statistically significant differences in terms of age, gender, body mass index, mean blood pressure between the two groups (each $p > 0.05$).

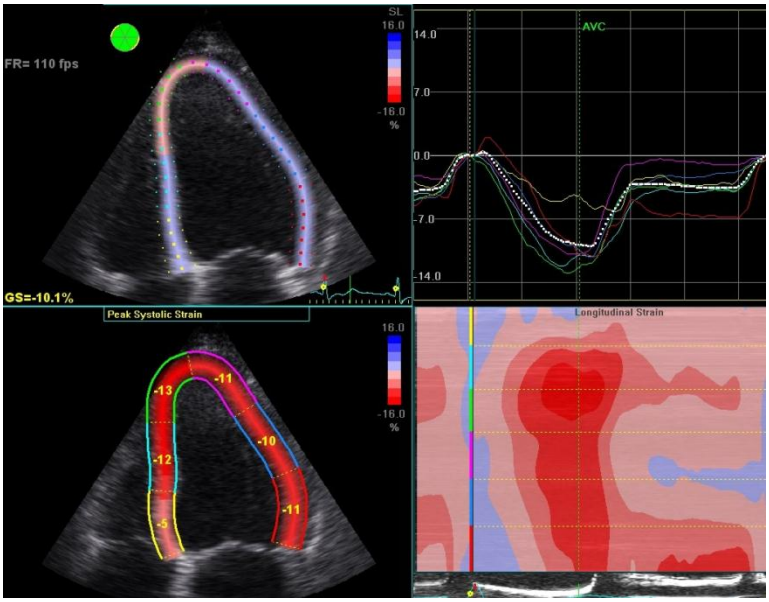
Table 1. The basic characteristics of the analyzed groups (data are presented as average ± SD or number (%)).

Characteristics	Group 1 (n=35)	Group 2 (n=40)	p
Average age (years)	41 ± 9	38 ± 11	0.85
Gender female	19 (54%)	22 (55%)	0.80
Body mass index (kg/m²)	28 ± 4	24 ± 5	0.56
Heart rate, beats/minute	91 ± 12	77 ± 15	0.02
Average blood pressure (mmHg)	95 ± 13	98 ± 16	0.27
Functional class NYHA I	7 (20%)	0	
Functional class NYHA II	14 (40%)	0	
Functional class NYHA III	9 (25.7%)	0	
Functional class NYHA IV	5 (14.3%)	0	
6-minute walk test (m)	446 ± 76	590 ± 54	0.001
Arterial saturation O_2 (%)	91 ± 7	98 ± 1	<0.001
SPPA (mmHg)	52 ± 16	24 ± 10	<0.001
SPPA >60 mmHg	17 (48%)	0	

In group 1, 5 patients (14.3%) were classified as NYHA functional class IV, 9 (25.7%) in NYHA class III, 14 patients presented NYHA functional class II (40%) and in the first class there were recorded only 7 patients (20%). The 6-minute walk test and saturation arterial of O_2 were significantly lower in patients of the group 1 (446 ± 76 vs 590 ± 54, $p = 0.001$, respectively 91 ± 7 vs 98 ± 1%, $p <0.001$).


1 v 3678 mm/s
p 54.11 mmHg
Frq 9.43 kHz
[m/s]


Peak Systolic Strain
ANT_SEPT
SEPT
ANT
INF
LAT
POST
GLPS_LAX -9.1 %
GLPS_A4C -9.8 %
GLPS_A2C -10.5 %
GLPS_Avg -9.8 %
AVC_AUTO 428 msec
HR_ApLAX 54.9 bpm


FR= 110 fps
GS=-10.1%
Peak Systolic Strain
AVC
Longitudinal Strain

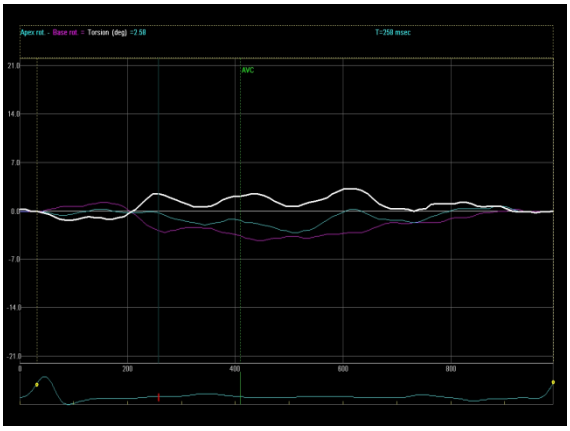

AVC

Fig. 1. Echocardiographic study performed in a patient with pulmonary arterial hypertension and normal ejection fraction of the left ventricle (group 1).

Considering the echocardiographic parameters, the obtained data are extremely interesting (Table 2). LV ejection fraction (LVEF), although normal, is significantly reduced in patients having PAH compared to the healthy volunteers lot (56 ± 4.5 vs. 71 ± 9.5%, p <0.001). Instead there are no statistically significant differences in the case of LV dimensions between the groups 1 and 2 (telediastolic diameter LVTDD: 3.3 ± 1.1 vs. 3.6 ± 1.2 mm/m^2, p = 0.75; telediastolic volume LVTDV: 78 ± 21 vs 72 ± 24 ml/m^2, p = 0.37; telesistolic volume LVTSV: 34 ± 14 vs 29 ± 12 ml/m^2, p = 0.29). Neither in the case of the tissular Doppler parameters, its wave respectively (the longitudinal systolic velocity of mitral ring) and the E/Ea (E=maximum early diastolic velocity of transmitral flow, Ea=maximum early diastolic velocity of mitral ring), no significant differences between the two groups were found (10.7 ± 3.53 vs 9.8 ± 3.7, p =0.13, respectively 7.51 ± 3.83 vs. 6.8 ± 3.5, p =0.21).

Table 2. Echocardiographic parameters of the analyzed groups (data are presented as average ± SD or number (%)).

Characteristics	Group 1 (n=35)	Group 2 (n=40)	p
SPPA (mmHg)	52 ± 16	24 ± 10	<0.001
DPPA (mmHg)	35 ± 8	14 ± 7	<0.001
Ejection fraction LV (%)	56 ± 4.5	71 ± 9.5	<0.001
LVTDD (mm/m^2)	3.3 ± 1.1	3.6 ± 1.2	0.75
LVTDV(ml/m^2)	78 ± 21	72 ± 24	0.37
LVTSV (ml/m^2)	34 ± 14	29 ± 12	0.29
TAPSE (mm)	15 ± 6	34 ± 14	<0.01
Sa_{tr} (cm/s)	8.3 ± 3.7	16.8 ± 5.6	<0.001
E (cm/s)	78 ± 17	110 ± 29	0.04
Ea (cm/s)	10.4 ± 2.7	16.7 ± 7.2	0.03
E/Ea	7.51 ± 3.83	6.8 ± 3.5	0.21
LVtor (°/cm)	1.4 ± 0.8	3.1 ± 1.8	<0.01
LVtw (°)	7.3 ± 6.2	14.2 ± 7.6	<0.01
LV apical rotation (°)	1.82 ± 0.96	5.76 ± 3.2	0.04
LV basal rotation (°)	-5.2 ± 3.6	-6.50 ± 4.8	0.23
LVε (%)	-8.76 ± 4.67	-16.03 ± 4.2	0.02

DPPA= dyastolic pressure in the pulmonary artery, Sa_{tr} = maximum systolic velocity of the free extremity of the tricuspid ring; TAPSE = maximum amplitude of the apical displacement of tricuspid annulus in systole

Speckle tracking echocardiography, a new technique able to identify the subclinical changes in LV function, shows a significant reduction of the longitudinal global strain (VSε) in patients presenting PAH: -8.76±4.67% in group 1 vs. -16.03±4.2% in group 2, p=0.02. The presence of an elevated SPPA also influences the myocardial rotation, too. The left ventricular torsion LVtor and LVtw were significantly lower in group 1 compared to group 2 (1.4±0.78°/cm vs. 3.07±1.8°/cm, p<0.01, and respectively 7.3±6.18° vs. 14.2±7.6°, p<0.01). These latter changes are due to the impairment of LV apical rotation (group 1: 1.82±0.96° vs. group 2: 5.76±3.2°, p<0.05), while the basal rotation is not affected (-5.2±3.6° in group 1 vs -6.50±4.8° in group 2, p=0.23).

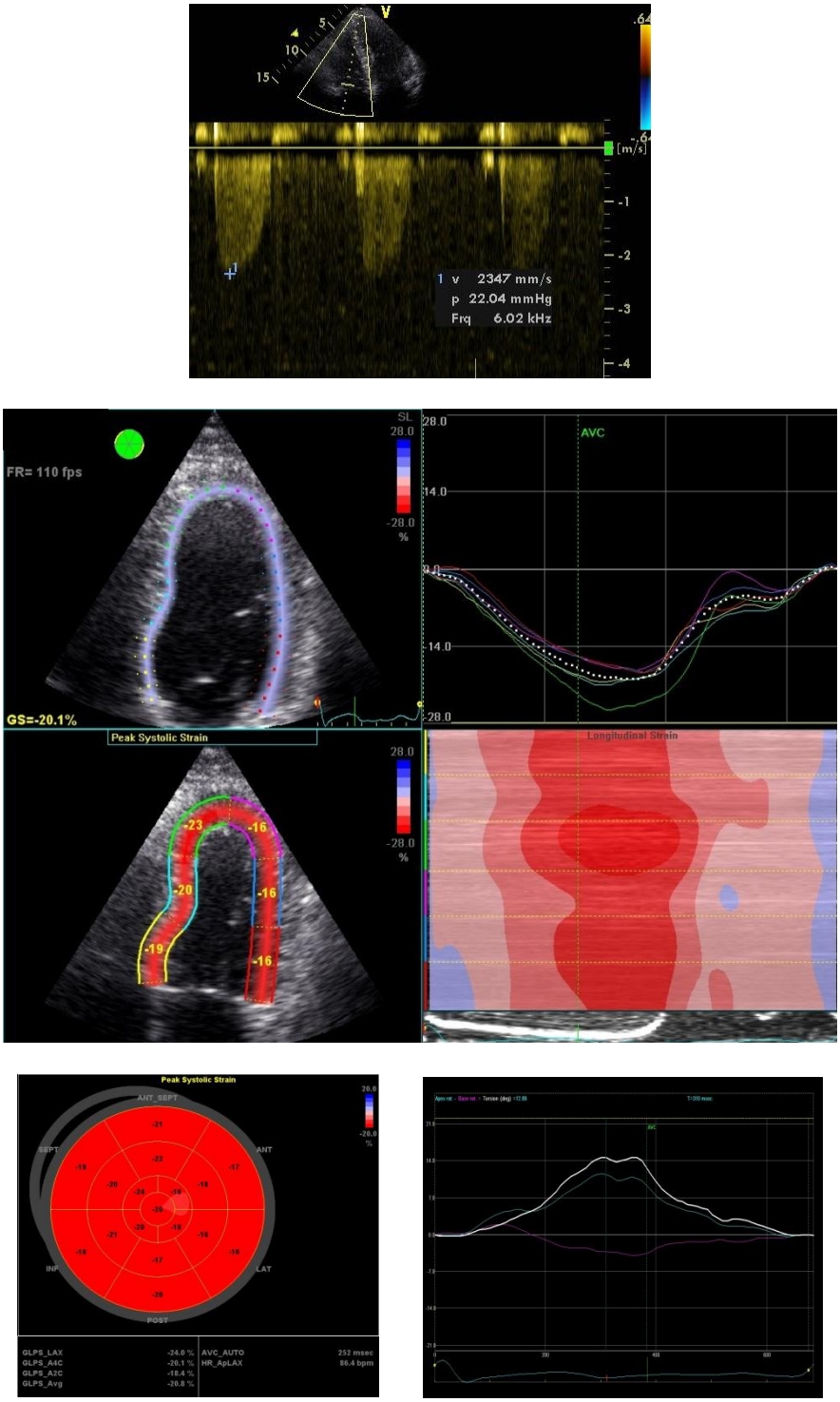


Fig. 2. Echocardiographic study performed in a patient without clinical or echocardiographic evidence of heart disease and normal systolic function of the left and right ventricles (group 2).

Simple linear regression documents a statistically significant inverse correlation between the LVtor and LVtw with SPPA estimated at echocardiograph (r =-0.63, p<0.01, and respectively = -0.52, p<0.01). We also found a statistically significant linear correlation between the 6-minute walk test and arterial saturation of O_2 on one hand and echocardiographically estimated SPPA at on the other hand (r = -0.67, p=0.026, and respectively = -0.58, p=0.032).

DISCUSSIONS

The study documents the impact which PAH development has on both the patient's clinical condition, with significant reduction of his functional capacity, on the laboratory data, with reducing of arterial saturation of O_2 and echocardiographic parameters respectively. Speckle tracking echocardiography documents the important damage of the longitudinal deformation and of LV torsion in patients with PAH, even if the LVEF is apparently preserved. This study illustrates the reduction of global longitudinal strain, of apical rotation, of twist and torsion of the left ventricular myocardium.

PAH represents a complex pathology affecting patients of any age, the prognosis being mostly unfavorable. The decrease in the functional capacity of the patient with PAH has been reported in numerous studies published in the last decade[8,10,11,12], thus the results obtained in this study were not a surprise. In the analyzed group of patients with PAH, the distance covered during the 6-minute walk test was significantly lower compared to the group of healthy individuals. The decrease of the functional capacity is also illustrated by the inclusion of PAH patients into different groups on the basis of NYHA functional classification: 5 patients (14.3%) were classified in NYHA functional class IV, 9 (25.7%) in class III, 14 patients in NYHA functional class II (40%) and only 7 patients (20%) in class I.

The transthoracic echocardiography is an excellent tool for detecting the patients with clinical suspicion of pulmonary hypertension, for confirmation of PAH, for grading its severity and the assessment of consequences upon the size and function of both ventricles. It currently represents the most widely used noninvasive imaging method for evaluating the patients with PAH, both in the initial stage, and in series, for the assessment of the disease progression, of the prognosis and response to treatment[11]. The clinical echo is closely related to the impaired function of the RV documented in our study by the impressive decreasing in velocity and amplitude of the systolic displacement of tricuspid ring. Recent studies have shown that the systolic velocity of the tricuspid ring significantly correlates with RV systolic function (estimated by measuring the change fraction of RV area). It is considered that a maximum systolic velocity <11.5 cm/s expresses with a sensitivity of 90% and a specificity of 85% a systolic dysfunction of the RV[13]. Echocardiographic techniques increasingly complex have been developed recently, allowing identifying the myocardial dynamic changes before the occurrence of the symptoms or altering the parameters from the conventional echocardiography. Two such techniques are represented by tissular Doppler imaging and speckle tracking respectively. Tissular Doppler echocardiography has emerged as a complementary method to the standard echocardiography, being able to evaluate the velocity of myocardial segments and other cardiac structures as well.

The speckle tracking technique has been implemented more recently in the medical practice, based on a two-dimensional image recognition of so called "speculums" (basically a fingerprint of the miocardic wall), and over time, tracking the movement of each identified point, throughout the cardiac cycle. Although in most patients with PAH the LV ejection fraction is normal (≥ 50%) suggesting a preserved systolic function of LV, the analysis of global longitudinal strain (longitudinal systolic deformation of the entire myocardium) shows the reduction of the maximum value in patients presenting PAH compared to the group of patients without any clinical and paraclinical signs of heart disease. Carefully assessing LVEF, we can still notice that in absolute value, this parameter, although kept within physiological limits, is lower in patients presenting SPPA>36 mmHg compared to the patients without PAH or other heart problems. Not only the longitudinal systolic function of LV is affected, but also the dynamics in transverse plane. In the analyzed groups, the LV twist (represented by the net difference between

the apical and basal rotation of LV for each moment of the cardiac cycle) and LV torsion[1,6] (obtained by dividing the LV twist to the LV longitudinal telediastolic diameter determined from incidence apically 4 chambers) were significantly lower in the group of patients with PAH compared to the group of healthy patients. The simple linear regression documents statistically significant inverse correlation between LVtw and respectively LVtor on one hand, and SPPA on the other hand. In other words, the torsion and twist of LV are much altered as the PAH is more severe. The LV apical rotation reduction represents a major determining factor involved in reducing LV torsion, the rotation of basal section not being modified in comparison to the healthy individuals group. These data are in agreement with the results obtained by Song's team, who, analyzing patients with interatrial septal defect, shows that the mere presence of congenital cardiac malformation does not have any influence on the LV rotation, but only the presence of PAH causes a reduction in myocardial twist of LV[14]. In this study the value of SPPA influenced linearly the LV twist value, too. Not the same results were obtained by Ramani et al in a recent study comparing patients with PAH without impaired LV systolic function and a group of healthy volunteers. In the PAH group, the basal rotation was significantly influenced by the presence of some increased pressional values at the level of pulmonary arterial circulation[15].

Despite the relatively small number of patients enrolled in this study some significant statistical data were obtained. We deliberately did not use more laborious and more difficult to measure in daily practice echocardiographic parameters for screening the patients (maximum ratio of strain/postsistolic strain, flow of pulmonary veins, Valsalva maneuver etc.). The patients with ectopic or multifocal atrial tachycardia, atrial fibrillation/atrial flutter, inadequate echocardiographic window, paced rhythm, significant left heart disease (valvulopathy, high blood pressure, coronary disease) that can cause secondary PAH, were not included in the study. The results obtained should be applied with the reserves of rigor to these categories of patients.

CONCLUSIONS

The data obtained in our study advocates for using the speckle tracking technique in assessing the impact of pulmonary arterial hypertension on the left ventricular dynamics. This modern technique documents the reduction of the global longitudinal strain, apical rotation, twist and torsion of the LV myocardium in patients presenting PAH. The method allows the analysis of longitudinal deformation and respectively of LV rotation, but requires digital storing of two-dimensional images and post-processing by means of dedicated software.

REFERENCES

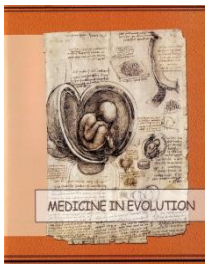
1. Notomi Y, Lysyansky P, Setser RM, Shiota T, Popovic ZB, Martin-Miklovic MG, Weaver JA, Oryszak SJ, Greenberg NL, White RD, Thomas JD. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. J Am Coll Cardiol 2005; 45 (12): 2034–2041.

2. Helle-Valle T, Crosby J, Edvardsen T, Lyseggen E, Amundsen BH, Smith HJ, Rosen BD, Lima JA, Torp H, Ihlen H, Smiseth OA. New noninvasive method for assessment of left ventricular rotation: speckle tracking echocardiography. Circulation 2005; 112 (20): 3149–3156.

3. Teske AJ, De Boeck BW, Melman PG, Sieswerda GT, Doevendans PA, Cramer MJ. Echocardiographic quantification of myocardial function using tissue deformation imaging, a guide to image acquisition and analysis using tissue Doppler and speckle tracking. Cardiovascular Ultrasound 2007; 5: 27.

4. Marwick TH. Measurement of strain and strain rate by echocardiography: ready for prime time? J Am Coll Cardiol 2006;47(7):1313-27.
5. Wang J, Khoury DS, Yue Y, Torre-Amione G, Nagueh SF. Left ventricular untwisting rate by speckle tracking echocardiography. Circulation 2007; 116 (22): 2580–2586.
6. Van Dalen BM, Vletter WB, Soliman OI, ten Cate FJ, Geleijnse ML. Importance of transducer position in the assessment of apical rotation by speckle tracking echocardiography. J Am Soc Echocardiogr 2008; 21 (8): 895–898.
7. Saggar R, Saggar R, Aboulhosn J, Belperio JA, Zisman DA, Lynch JP 3rd. Diagnosis and hemodynamic assessment of pulmonary arterial hypertension. Semin Respir Crit Care Med. 2009;30(4):399-410. .
8.Elliot C, Kiely DG. Pulmonary hypertension: diagnosis and treatment. Clin Med. 2004; 4(3):211-5.
9. Wang J, Khoury DS, Yue Y, Torre-Amione G, Nagueh SF. Preserved left ventricular twist and circumferential deformation, but depressed longitudinal and radial deformation in patients with diastolic heart failure. Eur Heart J 2008; 29(10):1283-1289.
10. Rubin J.L. Diagnostic and management of Pulmonary Arterial Hypertension: ACCP Evidence Based Clinical Practice Guideline. Chest 2004; 126:7-10S.
11. Galie N, Torbicki A, Barst R et al. Guidelines of diagnoses and treatment of pulmonary arterial hypertension. European Heart Journal 2004; 25:2243-2278.
12.Galie N, Simonneau G, ¨Pulmonary Hypertension¨ in ¨The ESC Textbook of Cardiovascular Medicine¨, ed. John Camm A, Luscher TF, Serruys PW, Blackwell Publiching 2006, p 759-782 .
13.Bleeker GB, Steendijk P, Holman ER, et al. Assessing right ventricular function: the role of echocardiography and complementary technologies. Heart 2006 ; 92;19-26.
14. Song J, Li C, Tong C, Yang H, Yang X, Zhang J, Deng Y. Evaluation of left ventricular rotation and twist using speckle tracking imaging in patients with atrial septal defect. J Huazhong Univ Sci Technolog Med Sci. 2008;28(2):190-3.
15. Ramani GV, Bazaz R, Edelman K, López-Candales A. Pulmonary hypertension affects left ventricular basal twist: a novel use for speckle-tracking imaging. Echocardiography. 2009;26(1):44-51.

OCCUPATIONAL CHRONIC LOW BACK PAIN IN YOUNG ACTIVE ADULTS - A NEW COMPLEX AND NONINVASIVE ASSESSMENT METHOD



GEORGE PUENEA[1], DAN NEMES[1,2], LILIANA CATAN[1], ELENA AMARICAI[1], DANIEL POPA[1], LAVINIA BUSESCU[2], ROXANA BALACESCU[2,]

[1]University of Medicine and Pharmacy "Victor Babes", Timisoara, [2]City University Emergency Hospital, Timisoara, -Rehabilitation and Rheumatology Department

ABSTRACT

Introduction:

During recent years, lumbosacralgia has become increasingly frequent among young active adults, having a strong impact upon their daily activities and social life. ***Aim of the study:*** *Early identification of lumbosacral symptoms in young active adults, using a non-invasive and affordable method (ActiGraph), correlated to specific assessment functional (Lesquene index) and life quality (Health Status Questionnaire - SP12-HSQ12) indicators, as well as of the causes leading to the above symptoms.*

Material and method:

Throughout one year, between 05.2010-04.2011, 94 patients aged between 25-45 years, 64 males and 30 females, diagnosed with lumbosacralgia by mechanical causes were monitored. The 94 patients were classified into 3 homogeneous groups and differentiated therapy was applied for each group: group 1 – complex therapy with drugs + lumbosacral orthesis, group 2 – same as group 1 + periodical rehabilitation treatment: 3 cures of 10 daily sessions every 6 months, group 3 – same as group 2 + home adapted kinesiotherapy programme. Each patient was subjected to 6 complex assessments: initial, at 2 weeks, at 6, 6.5, 12 and 12.5 months, respectively, before and after each therapy cure, consisting of: comprehensive clinical examination, daily activity assessment using the Lesquene functional index, life quality assessment by use of the SP12-HSQ12 questionnaire and an innovative, noninvasive method – ActiGraph – which accurately evaluates pain and functional parameters.

Results:

Mechanical lumbosacralgia in young, active adults is linked to the number of daily working hours, and the therapeutic success depends on the early identification of symptoms and on case management.

Conclusions:

Patients with mechanical lumbosacralgia who received complex drug treatment associated to specific, sustained, long term rehabilitation, experienced a significant improvement of the assessed parameters and of life quality, implicitely.

Key words: *lumbosacralgia, young active adult, assessment, life quality*

Correspondence to

Dr. George Puenea; Victor Babes University of Medicine and Pharmacy, Timisoara, România,
Telephone number: 0722438747;
Email: george.puenea@cardinalmed.ro

INTRODUCTION

Lumbosacralgia is defined as the lumbar pain and discomfort of mechanical causes, with or without irradiation into the lower limb, generated by diseased tissue and/or vertebral structures (discs, ligaments, vertebral peduncles) (1,2,3,4,5,6,7).

During recent years, lumbosacralgia has become increasingly frequent among young, active adults, having a strong impact on their daily activities and social life.

The lumbosacral syndrome causes physical and mental discomfort, being a frequent cause of working incapacity, studies showing that around 80-85% of the population develop at least one low back pain episode at some moment in life (5,6,7).

.

The diagnosis of lumbosascralgia is a complex one involving clinical, functional and medical imaging techniques.

Chronic occupational lumbosacralgia in young adults is closely related to the number of daily working hours, number of years of sustained activity, the type of activity, and therapeutic success depends on early diagnosis, treatment complexity and patient compliance.

In the absence of an appropriate, early, sustained and complex treatment coming after an accurate diagnosis and thorough assessment, the evolution of these diseases is unfavorable, leading to various degrees of invalidity

AIM

1. Early identification of lumbosacralgia symptoms in young, active adults, using a noninvasive and affordable method (ActiGraph), correlated to specific functional (Lesquene index) and life quality (Health Status Questionnaire - SP12-HSQ12) assessment indicators;

2. Identifying the causes leading to lumbosacralgia in young, professionally active adults, with work capacity, life quality and, last but not least, social life impairment;

3. Highlighting the role of specific medical rehabilitation associated to complex, early and sustained drug therapy for functional recovery and increased life quality in young patients with occupational lumbosacralgia;

4. Elaboration of individualized, sustained rehabilitation programmes, including a home adapted kinesiotherapy programme, allowing a significant change in the management of patients with occupational chronic lumbosacralgia, with the increase in their life quality by family, social and professional integration and, implicitly, with the decrease of social and economic costs.

MATERIAL AND METHOD

Throughout one year, between 05.2010-04.2011, 94 patients aged between 25-45 years, 64 males and 30 females, diagnosed with mechanical lumbosacralgia were monitored.

The 94 patients were divided into 3 homogeneous groups according to patient compliance and differentiated therapy was applied for each group:

-group 1- 34 patients received a complex combination of drugs (analgesics: Piafen 500mg/day, Gabapentin 300mg/day; NSAI: Celebrex 200mg/day, Meloxicam 15mg/day, Ketoprofen 200mg/day; myorelaxants: Mydocalm 150mg/day) in repeated cures with additional lumbosacral orthesis, where required (back brace);

-group 2- 31 patients, same treatment as for group 1 + periodic medical rehabilitation treatment: 3 cures of 10 daily sessions at every 6 months (initial, at 6 and 12 months, respectively), consisting of manual massage, electrotherapy and kinesiotherapy, the objectives being: pain relief, improved posture, body alignment, and functionality and reeducation in performing occupational and daily activities; (fig.1)

Fig. 1. Specific kinesiotherapy (1a-f. Kinesiotherapy 1g-h. analgesic electrotherapy, 1i. Relaxing massage,) – personal colection; patient consent.

-group 3-29 patients, same therapy as for group 2 + individually adapted home kinesiotherapy. Each patient underwent 6 complex assessments: initial (before implementing the treatment plan) , at 2 weeks (after drug therapy - group 1 and first 10 rehabilitation sessions – group 2 and 3), at 6 months (before the second cure of therapy), at 6.5 months (after the second cure of therapy), at 12 months (before the 3rd cure of therapy) and at 12.5 months (after the 3rd cure of therapy), consisting of: comprehensive clinical examination, assessment of daily activity by use of the Lesquene functional index (we scored as: 0= no disfunctionality, 1-4=mild impairment, 5-7=moderate impairment, 8-10=severe impairment, 11-13=high severity of impairment, ≥14 = extremely high severerity of impairment), life quality assessment using the Health Status Questionnaire: SP12-HSQ12 (we scored as: 0= no impairment, 1-7=slight impairment, 8-13=moderate impairment, 14-18=severe impairment, 19-24=very severe impairment, ≥25 = extreme severity of impairment) and an innovative, noninvasive method using an ActiGraph:

-which is worn line a wrist watch for 24 hours while the subject normally attends the usual daily activities

-by which we were able to assess, out of the multiple parameters determined by the device, the degree of pain after a day's work with long-lasting postures and/or physical activity, depending on the number of awakenings/night.

Physical Activity Research

General data

The ActiGraph (fig.2) is essential to the physical therapist providing rehabilitation treatment to help assess level of pain, strength, range of motion, endurance and gross motor function. The ActiGraph can be worn during physical therapy sessions or at home to determine if outpatient rehabilitative exercises and activities are improving the patient's endurance and function.

The ActiGraph is an ideal tool for physical activity, sports, and fitness research. The ActiGraph objectively measures and records the amount and intensity of activity and counts the number of steps taken over a given period of time. Algorithms have been provided to ActiGraph by prominent university groups that convert the collected

data into calories (Kcals) and MET's (Metabolic Equivalents) for adults and children.

The ActiGraph can determine sleep latency, amount of sleep, number and duration of awakenings, and overall sleep efficiency. The ActiGraph can be used in clinical applications to objectively determine the patient's sleep hygiene and as a tool aiding in the diagnosis and treatment of insomnia, circadian-rhythm disorders, and other sleep disorders. The ActiGraph can also be worn on the ankle to aid in the detection of restless leg syndrome (RLS) and periodic limb movement disorder (PLMD).

Technology

The GT1M activity monitor accurately and consistently measures and records time varying accelerations ranging in magnitude from approximately 0.05 to 2.5 G's. The accelerometer output is digitized by a twelve-bit (12) Analog to Digital Converter (ADC) at a rate of thirty times per second (30 Hertz). Once digitized, the signal passes through a digital filter that band-limits the accelerometer to the frequency range of 0.25 to 2.5 Hz. This frequency range has been carefully chosen to detect normal human motion and to reject changing accelerations within the pass band. Each sample is summed over a user specified interval of time called an 'epoch'.

The ActiLife desktop analysis software program is compatible with the ActiGraph GT1M and the Research version of the ActiTrainer. ActiLife allows the user to initialize the ActiGraph in a number of different operating modes and select epochs ranging from 30 times per second (raw mode) to 4 minutes.

The collected data is stored in ASCII format for simple access and compatibility with other analysis programs (e.g. SPSS & SAS). ActiLife contains several basic macros which use the ASCII data to generate a summary file, a caloric file, and a data table.

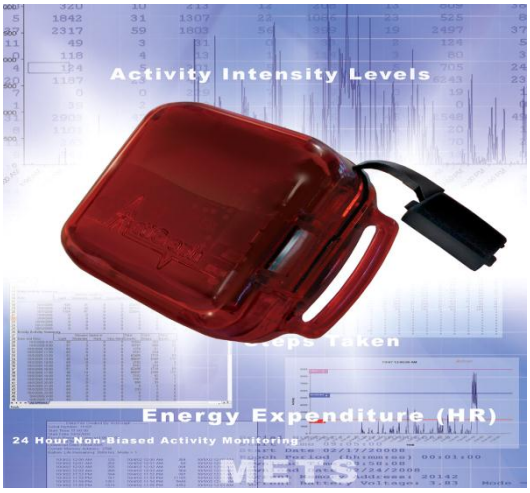


Fig.2 ActiGraph (8)

RESULTS

-Complex evaluation methods revealed a better evolution in group 3 as compared to groups 1 and 2 and of group 2 as compared to group 1, both in intermediate (at 6 and 6.5 months) and at the end of the cure (at 12 and 12.5 months), despite the fact that initially the complete clinical examination and functional indicators as well as life quality and parameters measured by the ActiGraph were similar in all three groups; (graphs 1,2,3 and table I)

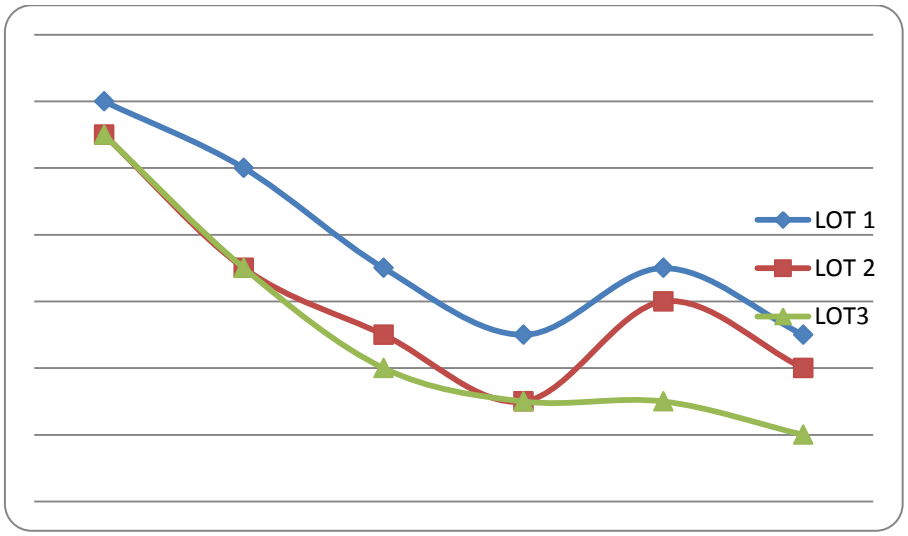
-In all three groups, favorable results were obtained at the end of each of the three therapeutic cures (2 weeks after the initial moment – at the end of cure 1, at 6.5 months – at the end of cure 2 and at 12.5 months – at the end of cure 3). (graphs 1,2,3 and table I)

Table I. Comparative results of the average values of the assessed parameters/group

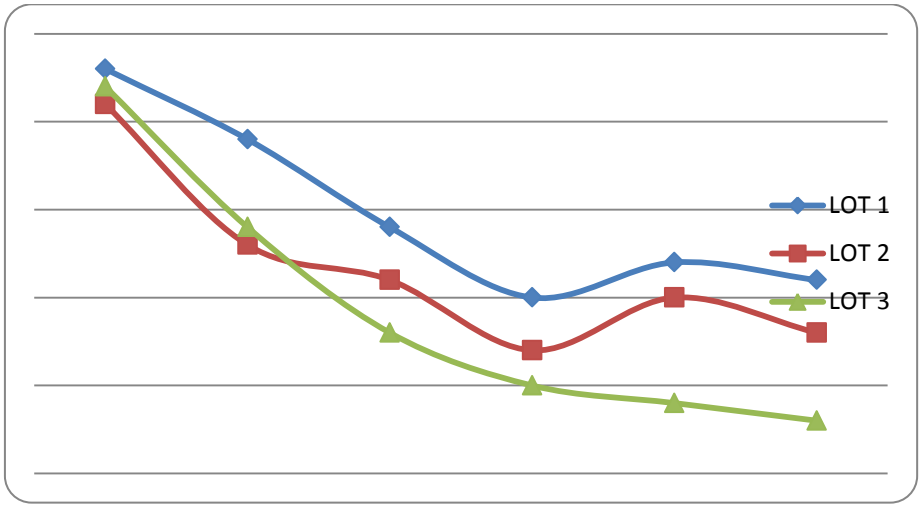
PARAMETERS	GROUP 1	GROUP 2	GROUP 3
Lesquene 0	12	11	11
Lesquene 0.5	10	7	7
Lesquene 6	7	5	4
Lesquene 6.5	5	3	3
Lesquene 12	7	6	3
Lesquene 12.5	5	4	2
SP12-HSQ12 0	23	21	22
SP12-HSQ12 0.5	19	13	14
SP12-HSQ12 6	14	11	8
SP12-HSQ12 6.5	10	7	5
SP12-HSQ12 12	12	10	4
SP12-HSQ12 12.5	11	8	3
AGrph.–Awakenings 0	19	18	19
AGrph.–Awakenings 0.5	15	11	10
AGrph.–Awakenings 6	13	8	5
AGrph.–Awakenings 6.5	10	5	3
AGrph.–Awakenings 12	12	7	2
AGrph.–Awakenings 12.5	10	5	2

Legend: SP12-HSQ12- Health Status Questionnaire; AGrph.– ActiGraph.

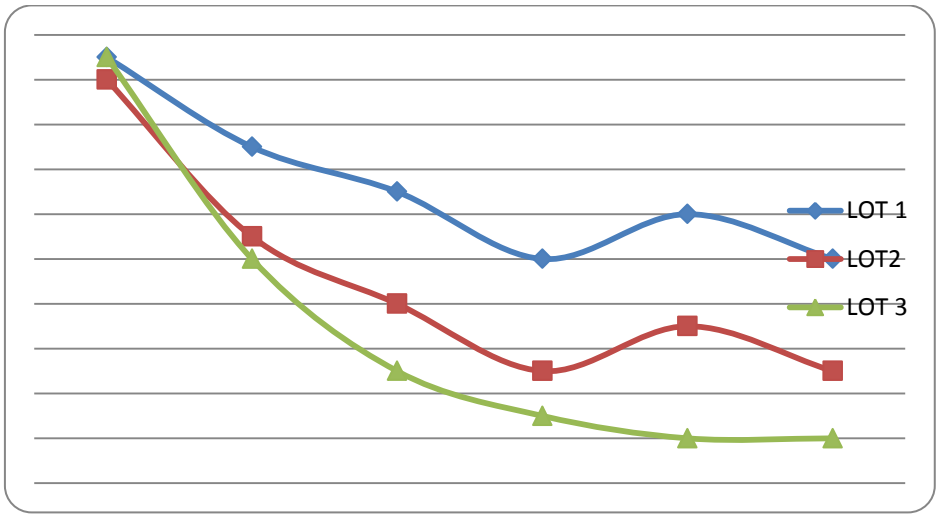
Graph 1. – Comparative results of Lesquene index average values/group



Graph 2. – Comparative results of the SP12-HSQ12 questionnaire average values/group



Graph 3. – Comparative results of average values obtained for ActiGraph-measured awakenings/night/group



CONCLUSIONS

Patients with mechanical lumbosacralgia who received a complex drug therapy combined with specific, sustained, long term medical rehabilitation, including a home-adapted kinesiotherapy programme, after a comprehensive, innovative, noninvasive assessment correlated to daily activity indicators, manifested a significant improvement of the assessed parameters and of their life quality, implicitly.

In order to contribute to therapeutic success, we support the need for all lumbosacralgia patients to wear a lumbosacral orthesis (back brace) during occupational or daily activities.

REFERENCES

-Burton A K, Balague F, Cardon G, Eriksen H R, Henrotin Y, Lahard A, Leclerc A, Muller G, van der Beek A J. European Guidelines for Prevention in Low Back Pain, 2009. www.backpaineurope.org.

-Hallett Whitman H, Clauw D J, Beary J F. Low Back Pain, in Paget S A et all (editors), Hospital for Special Surgery manual of rheumatology and outpatient orthopedic disorders: diagnosis and treatment 5th Ed, Lippincott Williams & Wilkins, 2008: 144-152.

-Bojincă Violeta. Durerea lombară joasă, în Ionescu R (coord), Esenţialul în reumatologie, Editura Amaltea, Bucureşti, 2006: 542-557.

-Hills E C. Mechanical Low Back Pain, 2006. www.emedicine.com.

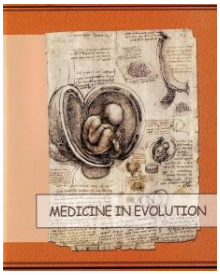
-Datta D, Mirza S K, White A A. Low Back Pain, in Harris D E Jr et all (editors), Kelley's textbook of rheumatology 7th Ed, W.B. Saunders Company, 2005: 588-600.

-Speed Cathy. Low Back Pain. BMJ, 2004, 328: 1119-1121.

-Karnath B. Clinical Signs of Low Back Pain. Hospital Physician, 2003; 56: 39-44.

-ActiGraph Applications- www.theactigraph.com

THE INFLUENCE OF TREATMENT WITH BOSENTAN AND SILDENAFIL ON MYOCARDIAL DEFORMATION PARAMETERS IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION



HANS-JURGEN JAHRAUS[1], CRISTIAN MORNOS[1], CRISTIAN OANCEA[1], ELENA ARDELEANU[1], LUCIAN PETRESCU[1]

1.University of Medicine and Pharmacy "Victor Babes", Timisoara

ABSTRACT

Introduction: Pulmonary arterial hypertension (PAH) represents a severe condition, with progressive evolution to death due to the deterioration of pulmonary circulation and of the right ventricular function (RV).
Aim of the study: This study aims to analyze the impact of Bosentan and Sildenafil treatment upon myocardial deformation in patients with PAH.
Material and method: We analyzed a lot of 38 patients with PAH. At the inclusion in the study, a first set of data was obtained including the clinical examination, surface electrocardiogram, pulmonary X-ray, standard biological samples, transcutaneous arterial saturation of O_2, 6-minute walk test as well as right cardiac catheterization and speckle tracking analysis. Once completed the clinical and paraclinical tests within the evaluation protocol of the PAH patients, the treatment with Bosentan and/or Sildenafil was initiated according to the treating pulmonologist's decision.
Results: The group of patients was monitored at an interval of 3 months. After 9 months a full revaluation was performed. At a total of 17 patients (44.7%) it was necessary a readjustment of the initial treatment. At the end of the 9 months of monitoring, 15 patients were administrated monotherapy with Bosentan (39.5%), 16 patients were treated with Sildenafil (42.1%), and 7 patients received a combination of Bosentan and Sildenafil (18.4%).
Conclusions: Speckle tracking imaging performed at enrollment in the study and then after 9 months from the treatment initiation, documents beneficial effects of Sildenafil and/or Bosentan even on LV function.
Keywords: *pulmonary arterial hypertension, Bosentan, Sildenafil, speckle tracking analysis*

Correspondence to

Dr. Mornos Cristian,
Victor Babes" University of Medicine and Pharmacy Timisoara ,Gh. Adam str. Nr. 13 a,
tel: 0256207355,
e-mail: mornoscristi@yahoo.com

INTRODUCTION

Pulmonary arterial hypertension (PAH) represents a severe disease, with progressive evolution to death due to the deterioration of pulmonary circulation and of the right ventricle function (RV).
Although pulmonary hypertension may develop as a primary disorder, in most cases it is secondary, being the expression of a hemodynamic alteration of various etiologies and with different pathogenic mechanisms, whose diagnosis and treatment raise multiple problems.

The pulmonary hypertension is defined as an increasing of the pulmonary arterial pressure > 25 mmHg at rest or > 30 mmHg at effort[1-3]. Death usually occurs by RV insufficiency or sudden death; usually in patients being in an advanced stage of the disease. Since the conventional therapy has not given the expected results, in the recent years there have been introduced a number of new drugs acting in different ways[4-7]: nitric oxide (Sildenafil), endothelin (Bosentan) or prostacyclin (Epoprostenol, Treprostinil, Iloprost). Although the optimal doses are not yet fully established, a number of studies being in progress, there have already been published numerous clinical studies which suggest the combination of two or even three drugs proven to reduce the systolic pressure in the pulmonary artery (SPPA)[8-11], with the advantage of reducing pulmonary arterial pressure by exerting action on multiple pathways simultaneously.

AIM OF THE STUDY

The present study aims to analyze the impact which the optimal therapy initiation has with this modern medication on myocardial deformation in patients with PAH.

MATERIAL AND METHOD

We analyzed a group of 38 patients with PAH proposed for treatment with Sildenafil and/or Bosentan, in 2008-2012.
Inclusion criteria were represented by the following conditions:
1. The presence of PAH with one of the following etiologies: idiopathic/ familial; associated with connective tissue disease (scleroderma, systemic lupus erythematosus, rheumatoid polyarthritis, connective tissue mixed disease, Sjogren syndrome); associated with congenital heart defects of interatrial or interventricular septal defect type, persistent arterial ductus and severe evolution of these toward Eisenmenger syndrome; of thrombo embolic cause with no indication of thromboendarterectomy or with persistent PAH after thromboendarterectomy;
2. Patients with PAH who are in the functional class NYHA II - IV;
3. Patients in which the right cardiac catheterism highlights an average pressure in pulmonary artery (APPA) > 35 mm Hg and SPPA > 45 mmHg, pulmonary capillary pressure <15 mmHg;
4. Patients whose distance at the 6-minute walk test performed initially is > 100 m and <450 m.
Exclusion criteria were represented by: inadequate echocardiographic window; PAH determined by obstructive or interstitial chronic pulmonary disease (except PAH associated with connective tissue diseases); portal hypertension; sleep apnea severe syndrome; electrostimulated (paced) rhythm.
At the inclusion in the study, a first set of data was obtained including the clinical examination, surface electrocardiogram, pulmonary X-ray, standard biological samples, transcutaneous arterial saturation of O_2, the 6-minute walk test as well as the right cardiac catheterism. **A full clinical examination** was performed to all the enrolled patients. Also in all patients it was determined the walked distance in a time of 6-minute, on flat ground (6-minute walk test). The severity of symptoms was evaluated based on subjective assessment of the patient, with including of the case in the functional classification WHO/ New York Heart

Association[12-15]: NYHA functional class I: no symptoms (fatigue or suffocation); NYHA functional class II: no symptoms at rest, but symptoms in moderate physical activity; NYHA functional class III: without symptoms at rest, but symptoms in mild physical activity (dressing, bathing, walking, etc.); NYHA functional class IV: symptoms are present at rest, too.

In all the enrolled patients there was performed the **surface electrocardiogram** and standard postero-anterior **thoracic radiography**, according to the recommended techniques. The **conventional transthoracic echocardiography** was performed as well as the tissular Doppler.

Doppler echocardiography allows accurate estimation of the SPPA and, thereby, it enables the diagnosis confirmation and grading of severity of PAH according to current guidelines.

Speckle tracking analysis requires adequate software and allows simultaneous analysis of the longitudinal deformation and of the myocardium torsion of the left ventricle (LV). The images recorded by the conventional technique were digitally stored and subsequently analyzed off-line using the software program EchoPac PC Dimension (GE Medical).

Speckle tracking allows both the analysis of longitudinal deformation and torsion or rotation of the LV myocardium in the transverse plane.

In all the enrolled patients there was performed **the determination of arterial saturation of O_2** using the transcutaneous method and by blood collection.

In all the analyzed patients there was drawn venous blood from antecubital vein to determine hemoleucogram (blood count), transaminases, seric bilirubin, international normalized ratio, serum creatinine, serum ionogram. Afterwards these analyzes were monitored monthly.

The right cardiac catheterism was performed using as an approaching way the femoral vein. The invasive pressures were measured directly using some multipurpose catheters attached to a pressure transducer (Cordis Corporation, Miami, FL). Diagnosis of PAH was confirmed by right cardiac catheterism, invasive technique which documented the existence of an average pulmonary arterial pressure (APAP) over 25 mmHg as well as a pulmonary vascular resistance higher than 3 Wood units.

Once completed, the clinical and paraclinical tests within the evaluation protocol of the patients with PAH, it was initiated the **treatment with Bosentan and/or Sildenafil** according to the treating pulmonologist's decision. The other drugs already included in the patient's treatment were given further if they din not have any contraindications to Bosentan or Sildenafil.

Thus Bosentan (Tracleer®; Actelion Pharmaceuticals, South San Francisco, CA, USA) was initiated with a dose of 2×62.5 mg/day per os, after 4 weeks the dose was increased to 2×125 mg to all patients in which there was not noticed increased hepatic enzymes.

In the case of Sildenafil (Revatio®; Pfizer, New York, NY, USA) the treatment was initiated at a dose approved by FDA for the treatment of PAH with 3×20 mg/day per os. Following pulmonologist's indication, if after the first month, the results were not as expected, it was decided either to increase initial drug dosage, or the combination with the second.

The group of patients was monitored by the pulmonologist at an interval of 3 months (surface electrocardiogram, pulmonary X-ray, standard biological samples, arterial transcutaneous saturation of O_2, 6- minute walk test, conventional echocardiography and tissular Doppler). After 9 months a full reassessment was performed including clinical examination, surface electrocardiogram, pulmonary X-ray, standard biological samples, arterial transcutaneous saturation of O_2, 6- minute walk test and complete transthoracic echocardiography (conventional, tissular Doppler and speckle tracking). The right cardiac catheterism was not repeated, this not being a part of the standard monitoring protocol for patients with PAH. In case of damage during the study, the medication was readapted by the treating physician.

For the statistical analysis there were used specialized software SPSS 11.5 (SPSS Inc., Chicago, IL, USA) and NCSS 2004 (NCSS, Kaysville, UT, USA). Numerical variables are presented as average value ± standard deviation (DS) and compared using the t-Student or analysis of variations. The treatment effects after 9 months were compared with data at baseline using the test

t-pair. An inferior P value at 0.05 was considered as being significant statistically. The study was approved by the Ethics Committee of the institution where the research was conducted; all the patients agreed to the inclusion in this study.

RESULTS

Out of the 52 patients presenting PAH, only 38 could be included in the group of analyzed patients. The other patients were excluded due to exclusion criteria: inadequate echocardiographic window (6 patients) and PAH caused by chronic obstructive pulmonary disease (8 patients).
The etiology of PAH in the studied group was represented by: idiopathic PAH / familial (12 patients), PAH associated with connective tissue disease (4 patients), PAH associated with congenital heart defects (18 patients); due to thromboembolic cause with no indication of thromboendarterectomy or persistent PAH after thromboendarterectomy (4 patients).
The average age of patients with PAH was 56 ± 17 years, SPPA determined invasively by 73 ± 8 mmHg, APPA by 55 ± 11 mmHg and pulmonary vascular resistance of 12 ± 5 Wood units.
A total of 37 patients were receiving loop diuretics and/or spironolactone (97.4%), 18 (47.4%) acenocoumarol, 14 patients (36.8%) calcium channel blockers (diltiazem or verapamil), 6 (15.8 %) were treated with digoxin, 2 (5.3%) received ivabradine and 12 patients (32%) other drugs. 6-minute walk test shows a value of 358 ± 76 m at baseline inclusion in the study, and arterial saturation of O_2 90 ± 6%. Regarding the functional class, 13 patients (34.2%) were classified in the NYHA functional class IV, 15 (39.5%) in NYHA class III, 10 patients had NYHA functional class II (26.3%).

Table 1. Echocardiographic parameters of the analyzed group at the time of enrollment in the study (data are presented as average ± DS or number (%)).

Characteristics	**Value**
Systolic pressure in pulmonary artery SPPA estimated (mmHg)	70 ± 11
Diastolic pressure in pulmonary artery estimated DPPA (mmHg)	37 ± 8
Ejection fraction LV (%)	59 ± 8
Telediastolic diameter of left ventricle TDDVS (mm/m²)	3.5 ± 0.9
Telediastolic volume of left ventricle TDVLV (ml/m²)	75 ± 18
Telesystolic volume of left ventricle TSVLV (ml/m²)	32 ± 12
Maximum amplitude of apical displacement of tricuspid ring in systole (mm)	14 ± 5
Left atrial volume (ml)	41 ± 12
Left ventricle torsion LVtor (°/cm)	1.5 ± 0.7
Left ventricle twist LVtw (°)	7.4 ± 4.5
Apical rotation of LV (°)	1.86 ± 0.91
Basal rotation of LV (°)	-5.4 ± 3.8
Global longitudinal strain of left ventricle LVε (%)	-8.9 ± 4.8

At a total of 17 patients (44.7%) was required readjustment of the initial treatment. Among the patients included in study, at the end of the 9 months of monitoring, a number of 15 were administrated monotherapy with Bosentan (39.5%), 16 patients were treated with Sildenafil (42.1%) and 7 patients received a combination of Bosentan and Sildenafil (18.4%).
The average dose administered was 60 mg/day for treatment with Sildenafil and 110 mg/day for Bosentan respectively

Table 2. The evolution of parameters tracked during the treatment with Sildenafil and/or Bosentan (data are presented as average ± deviație standard deviation SD).

Characteristics	**Enrollment**	**3 months**	**6 months**	**9 months**
Heart rate (beats/minute)	92 ± 14*	87 ± 15	84 ± 13	81 ± 12
NYHA functional class	3.2 ± 0.6*	2.9 ± 0.9	2.8 ± 0.7	2.6 ± 0.7
6-minute walk test (m)	358 ± 76*	385 ± 67	376 ± 71	391 ± 69
Arterial saturation O_2 (%)	90 ± 6*	91 ± 5	93 ± 6	93 ± 5
Systolic pressure in pulmonary artery SPPA estimated (mmHg)	70 ± 11	65 ± 14	67 ± 12	63 ± 13
Diastolic pressure in pulmonary artery DPPA estimated (mmHg)	37 ± 8	34 ± 10	34 ± 9	33 ± 9
Ejection fraction LV (%)	59 ± 8	61 ± 9	63 ± 12	65 ± 14
Telediastolic volume of left ventricle TDVLV (ml/m^2)	75 ± 18	73 ± 16	77 ± 19	76 ± 18
Maximum amplitude of apical displacement of tricuspid ring in systole (mm)	14 ± 3*	16 ± 5	17 ± 4	18 ± 4
Torsion of left ventricle LVtor (°/cm)	1.5 ± 0.7*	-	-	2.1 ± 0.5
Twist of left ventricle LVtw (°)	7.4 ± 4.5	-	-	8.8 ± 3.7
Apical rotation LV(°)	1.86±0.91	-	-	2.21±0.84
Basal rotation LV (°)	-5.4 ± 3.8*	-	-	-7.5 ± 3.1
Longitudinal global strain of left ventricle LVε (%)	-8.9 ± 4.8*	-	-	-10.2 ± 6.5

* $p < 0.05$ vs value at 9 months.

Speckle tracking imaging performed at enrollment in the study and subsequently after 9 months of treatment initiation has documented the beneficial effects of Sildenafil and/or Bosentan even on function of LV assessed by the analysis of myocardial deformation and rotation.

During monitoring there were not recorded any deaths in the analyzed group. A total of 15 patients (39.5%) were re-hospitalized due to right heart insufficiency decompensation during the 9 months of watching-up. Also, there have been no major adverse effects after the initiation of treatment with Sildenafil and/or Bosentan. Two patients who received the combination of Sildenafil with Bosentan (28.5%) showed an increasing in transaminases and in seric bilirubin, but these were resolved without dosage adjustment after about a week.

In patients who received monotherapy, it was not observed a significant increase of transaminases or seric bilirubin. All patients, in whom Sildenafil was associated with Bosentan, presented a minor headache and skin rush, but these side effects resolved within a few days without the need for dose modification. No patient described suggestive symptoms for arterial hypotension and neither were recorded any syncopal episodes during the monitoring of patients with PAH. Therefore, it was not necessary to discontinue the medication or dose reduction in none patient with PAH enrolled in this study.

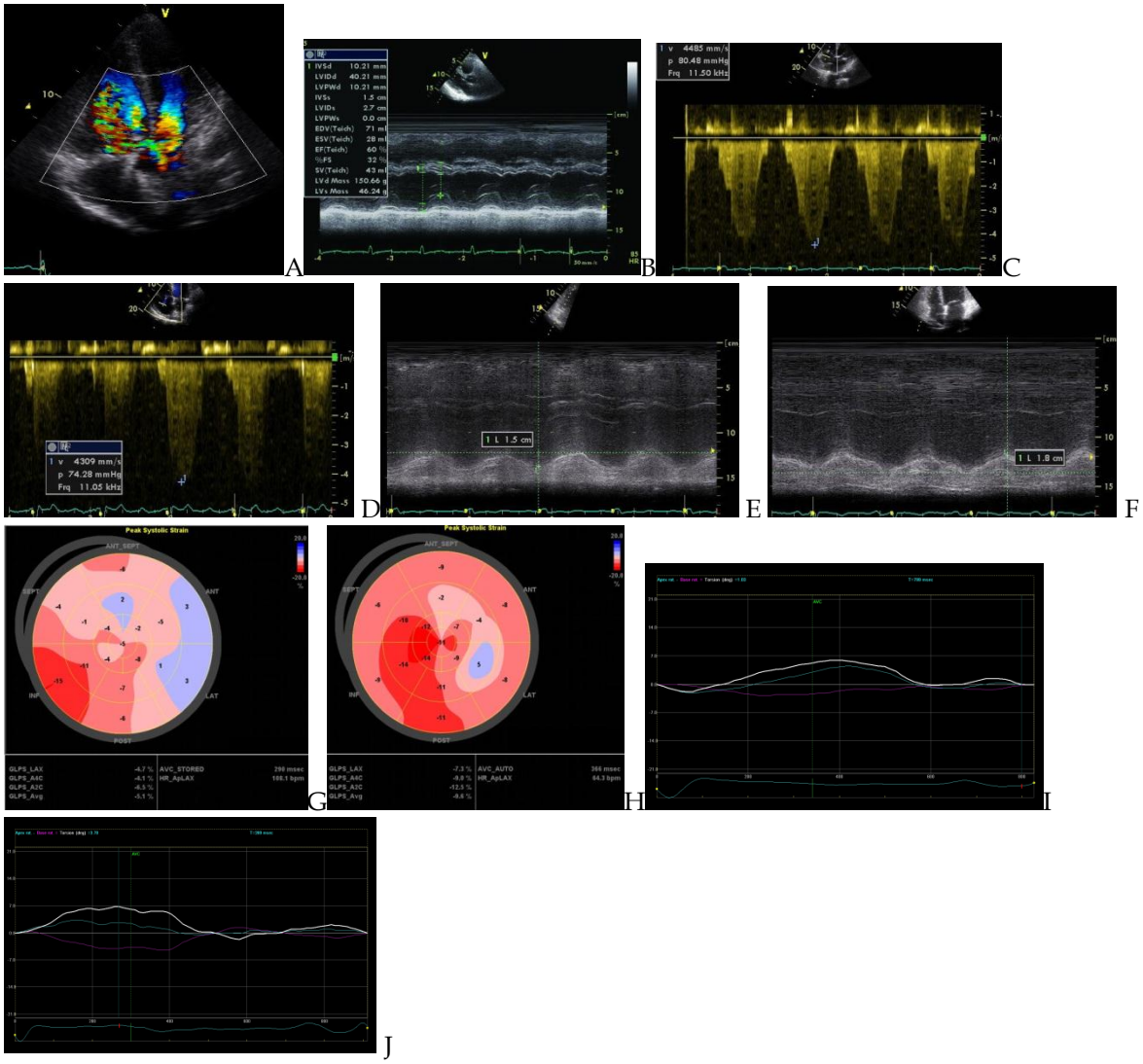


Fig. 1. Comparative echocardiographic study (at enrollment and after 9 months of treatment with Sildenafil and/or Bosentan) in a patient with arterial pulmonary hypertension consecutive to a perimembranous interventricular septal defect. ***A.*** *Transthoracic echocardiography, incidence apical 4 chambers, image 2D with color Doppler overlaid; the image highlights the septal interventricular defect with shunt left – right.* ***B.*** *Parasternal long axis incidence, section in mode M at the level of left ventricle; it can be observed the dilation of right ventricle and paradoxical motion of interventricular septum.* ***C.*** *Flow of tricuspid regurgitation recorded in Doppler continuously at enrollment in the study* ***(C)*** *and respectively after 9 months of treatment* ***(D)****, which allows the estimation of systolic pressure in pulmonary artery.* ***E.*** *Maximum amplitude of displacement of mitral annulus in systole recorded from apical incidence 4 chambers mode M at enrollment in the study* ***(E)*** *and respectively after 9 months of treatment* ***(F)****.* ***G.*** *The global longitudinal strain of left ventricle obtained through speckle tracking analysis at enrollment in the study* ***(G)*** *and respectively after 9 months of treatment* ***(H). I.*** *Torsion of LV obtained through speckle tracking analysis at enrollment in the study* ***(I)*** *and respectively after 9 months of treatment (J).*

DISCUSSION

The present study documents that, in patients with arterial pulmonary hypertension, the initiation of an appropriate medical treatment has a beneficial effect on myocardial deformation of LV. The study of myocardial deformation (strain, strain rate) for performance evaluation RV seems useful in the early identification of regional systolic dysfunction in patients with PAH, before the onset of other echocardiographic signs[16]. Preliminary data in patients with PAH, compensated, without signs of right heart insufficiency, suggests that depression of systolic function of RV occurs early at the level of admission tract, of the smooth section of RV[17]. The conventional echocardiography showed a significant improvement in the global function of RV. In the patients included in this study, the speckle tracking imaging performed at enrollment and at 9 months from the treatment initiation certifies an improvement in myocardial deformation and rotation. Data obtained from our study are in full agreement with those reported in several previous studies[18,19].

Despite the relatively small number of patients enrolled in the study there were obtained some significant statistic data. The number of patients was limited by the high cost of treatment, so that we were able to analyze mostly the patients who are also part of the national program for treatment of PAH. The two-dimensional speckle tracking analysis is seldom used in practice due to the small number of existing advanced equipment in our country. In addition, the method is time-consuming and relatively low feasibility. The implementation of the tri-dimensional technique will allow in the not very distant future to solve these limitations at least partially.

CONCLUSION

Speckle tracking imaging performed at enrollment and subsequently after 9 months from treatment initiation certifies/ documents the improved myocardial deformation and rotation.

Improvement of global longitudinal strain of LV and of LV torsion was noticed. The LV twist, although it showed a clear trend of improvement, did not reach a statistically significant level. The torsion increase is due to the overwhelming emphasis from the treatment of the LV basal rotation, the apical rotation being not sufficiently influenced.

REFERENCES

1. Rubin J.L. Diagnostic and management of Pulmonary Arterial Hypertension: ACCP Evidence Based Clinical Practice Guideline. Chest 2004; 126:7-10S.

3. Galie N, Torbicki A, Barst R et al. Guidelines of diagnoses and treatment of pulmonary arterial hypertension. European Heart Journal 2004; 25:2243-2278.

3. Galie N. Pulmonar hypertension 2006: definitions and classification. Kardiol Pol 2006; 64; 5 (Suppl 1): 5-8.

4. Jansa P, Aschermann M, Riedel M, Pafko P, Susa Z. Recommendations for diagnostics and treatment of pulmonary arterial hypertension in the Czech Republic. Vnitr Lek. 2004; 50(9):698-708.

5. Badesch DB, McLaughlin VV, Delcroix M et al. Prostanoid therapy for pulmonary arterial hypertension. J Am Coll Cardiol 2004; 43:56S-61S.

6. Fortin TA, Tapson VF. Intravenous prostacyclin for pulmonary arterial hypertension. In Pulmonary circulation Diseases and their treatment. Edited by Peacock AJ, Ruin LJ 2nd Edition, Arnold , 2004, London, pg 255-267.

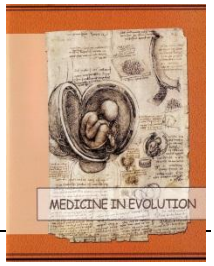
7. Galie N, Ghofrani AH, Torbicki A, et al. Sildenafil Citrate Therapy for pulmonary arterial hypertension. N Engl J Med 2005; 353 : 2148-57.

8. Humbert M, Barst RJ, Robbins IM et al. Combination of bosentan with epoprostenol in pulmonary arterial hypertension. Eur Respir J 2004; 24:353-359.

9. Hoeper MM, Faulenbach C, Golpon H et al. Combination therapy with bosentan and sildenafil in idiopathic pulmonary arterial hypertension. Eur Respir J 2004; 24:1007-1010.

10. Cicalini S, Chinello P, Grilli E, Petrosillo N. Treatment and outcome of pulmonary arterial hypertension in HIV-infected patients: a review of the literature. Curr HIV Res 2009; 7(6):589-96.
11. Toricki A, Van Beek EJR, Charbonnier B et al. Guidelines on diagnosis and management of acute pulmonary embolism. Eur Heart J 2000; 21:1201-336.
12. Saggar R, Saggar R, Aboulhosn J, Belperio JA, Zisman DA, Lynch JP 3rd. Diagnosis and hemodynamic assessment of pulmonary arterial hypertension. Semin Respir Crit Care Med. 2009;30(4):399-410.
13. Maiya S, Hislop AA, Flynn Y, Haworth SG. Response to bosentan in children with pulmonary hypertension. Heart. 2006; 92(5):664-70.
14. Braunwald's Heart Disease, 7th ed., Ed. Elsevier Saunders, 2004; 1807-1842.
15. Elliot C, Kiely DG. Pulmonary hypertension: diagnosis and treatment. Clin Med. 2004; 4(3):211-5.
16. Damrauskaite V, Herbots L, Claus P, et al. The differing regional response in right ventricular free wall function caused by increased afterload in pulmonary arterial hypertension: an ultrasonic strain and strain rate imaging study (abtract). Eur J Echocardiogr 2002;3 (suppl I): S55.
17. Lopez – Candales A., Dohi K., Iliescu A., et al. An abnormal right ventricular apical angle is indicative of global right ventricular impairment, Echocardiography: A Jrnl of CV Ultrasound & Allied Tech 2006; 23 (5): 361-368.
18. Cottrell C, Kirkpatrick JN. Echocardiographic strain imaging and its use in the clinical setting. Expert Rev Cardiovasc Ther 2010 ;8(1):93-102.
19. Pirat B, McCulloch ML, Zoghbi WA. Evaluation of global and regional right ventricular systolic function in patients with pulmonary hypertension using a novel speckle tracking method. Am J Cardiol 2006;98(5):699-704.

AN INTERDISCIPLINARY APPROACH IN THE DIAGNOSIS OF GRAVES OPHTHALMOPATHY GENERAL REVIEW



ALINA FEILER[1], MARIA MOGOȘEANU[1], IOANA ZOSIN[2]

[1]University of Medicine and Pharmacy Victor Babes, Timișoara, City University Emergency Hospital Timișoara, Radiology Department
[1]University of Medicine and Pharmacy Victor Babes, Timișoara, City University Emergency Hospital Timișoara, Endocrinology Department

ABSTRACT

The ophthalmopathy is the most common extrathyroid manifestation of Graves disease, being a multifactorial pathology which involves autoimmune reactions that affect the orbit. Although they usualy mannifest together, they can also appear at different times, the presence of antibodyes to TSH-R (Thyroid Stimulating Hormone Receptor) being characteristic for Graves disease. The clinical exam reveals proptosis, palpebral retraction, periorbital edema, conjunctival hyperemia, corneal ulcerations, all tipical for the disease. There are two phases in the evolution of Graves ophthalmopathy, an acute, inflammatory phase and a chronic, fibrotic phase, and by using MRI we can differentiate between the of them, by using T2w TIRM coronal sections . It also allows us to measure the response of the muscles to the immunomodulatory treatment according to the Clinical Activity Score (CAS), and it is an exact tool for measuring proptosis of the eyes in T1w axial sections, by drawing an horizontal line between the zigomatic borders and perpendicular lines on it from the apex of the corneas. CT does not provide such detailed images of the intraorbital changes, but it provides great images of the oseous changes made by the edematous phase in the muscles and the fat, thus being used to prepare the decompresion surgery of the orbit.

Key words: *Graves, MRI, CT, MRI- (Magnetic Resonance Imaging), CT (Computed Tomography)*

Correspondence to

Dr. Alina Adriana Feiler,
First County Emergency Hospital, Timisoara, Radiology Department, Romania,
Bd I. Bulbuca Nr. 10, 300736 Timişoara, UMF Victor Babes Timisoara,
email: alinafeiler@gmail.com

INTRODUCTION

Graves ophthalmopathy is the most common orbital pathology in adults, accounting for up to 28% of unilateral proptosis and 80% of bilateral proptosis. It can occur simultaneous with an episode of hyperthyroidism or it can precede thyroid hormonal changes. Euthyroidian or hypothyroidian patients can also be affected. [1,2]

This pathology has two phases, an active inflammatory phase and an inactive, fibrotic phase. The active phase is characterized by inflammation, congestion, hypertrophy of muscle and fat, which affects the orbit and eyelids and may last from several months to several years, while the inactive phase is dominated by fibrosis. [1,2]

Clinical manifestations

The acute inflammatory phase is characterized by lymphocytic infiltration and edema of the extraocular muscles, frecvently after about a year from the thyroid dysfunction episode, manifested by increased volume of the muscles, along with changes in the retroorbital fat, and it can cause proptosis, compression or elongation of the optic nerve. [1,2]

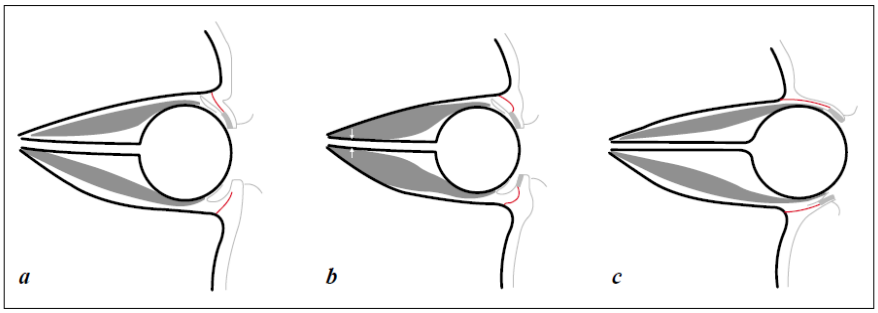


Fig. 1 Effects of intraorbital changes, also depending on the laxity of the anterior orbital septum. a) normal orbit, b) optic nerve compression due to increased volume of the intraorbital muscles accompanied by a slight proptosis, c) decompression by proptosis and optic nerve elongation [2]

Proptosiss occures in most cases bilateraly, but it may also be unilateral. Other relevant clinical changes that appeare due to alternations between inflammation and vascular congestion consist of upper and lower eyelid retraction, periorbital edema, conjunctival hyperemia, corneal ulceration. [1,2]

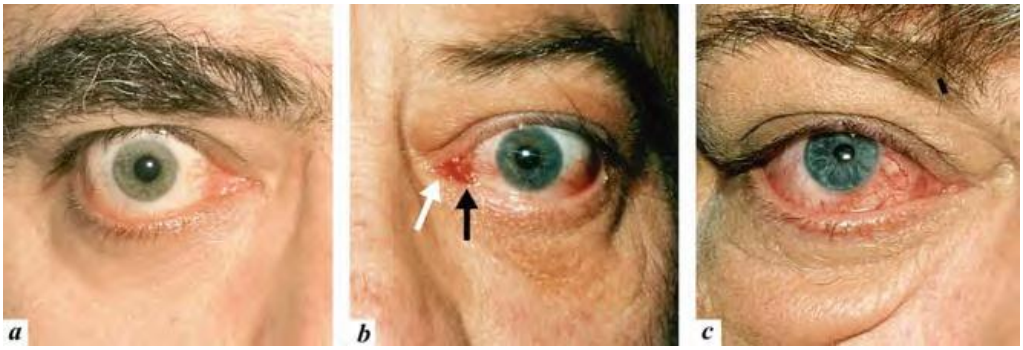


Fig.2 a) proptosis b) Inflammation of the caruncula (white arrow) and moderate hyperemia of the conjunctiva (black arrow), c) marked conjunctival hyperemia.[2]

In 1989 Mourits and his collaborators have introduced the clinical activity score (CAS) that is still used today, being an easy method of evaluation that allows a classification of patients in the active or inactive stage of the disease. Investigated patients are first evaluated for 7 points, 2 symptoms and 5 signs evident in the soft tissues.The EUGOGO atlas is used for a perfect correlation between the signs and the symptoms (www.eugogo.org). Each present aspect is currently granted a point. [4.5]

Another way to assess the severity of the disease is the modified NOSPECS classification, which divides patients into VI severity classes according to the clinical manifestations. The hyperthyroid state is highlighted, although eu or hypothyroid patients can manifest changes in the orbit or proptosis. [4,5] During the clinical examination the Hertel exophthalmeter is also used for measuring the proptosis.

Imaging diagnosis in Graves ophthalmopathy

MRI is the investigation of choice when it comes to Graves ophthalmopathy, because using it we can evaluate the volume changes inside the extraocular muscles, especialy using T2w images, which are prolonged in patients with this pathology, highlighting the edema in the muscles. These changes mean that the patient is in the acute, inflammatory stage of the disease, wich means that MRI can distingush and quantify the response to the immunomodulatory treatment. [6,12,20]

MRI findings consist in spindle like enlargements of the extraoculary muscles, larger than 5 mm but with sparing of the insertions, enlargement of intraconal and extraconal fat. These specific changes can produce the elongation of the orbital septum and proptosis, elongation of the optic nerve, compression of the optic nerve at the apex of the orbit. Other changes consist in impressions on lamina papiracea, hipertrophy of the lacrimal gland, edema of the upper and lower eye lids. Muscular hipertrophy with enhanced T2w images consist with the acute , inflammatory stage of the disease, while low intensity signal in T1w and T2w images is representative for the chronic, fibrotic stage of the disease. Hipodense intramusculary foci in T1w and T2w images are sugestive for chronic fat degeneration. [6,12,20].

Advantages in using MRI :

- the precision with wich you can measure the degree of proptosis by drawing in an T1w axial section an horizontal line between the zigomatic arches- the interzigomatic line, and anoter two lines from in to the apex of the corneas, measuring thus the degree of proptosis-the Hertel index, wich is considered patological if greater than 22 mm.

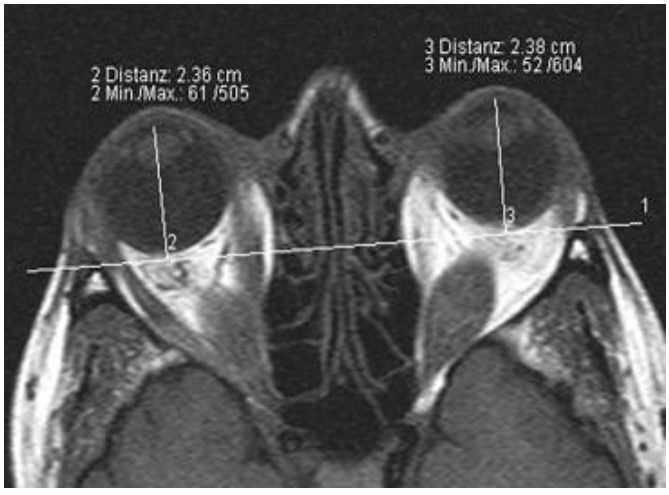


Fig. 3 Axial T1w section with the measurments for proptosis. An horizontal line was drawn between the zigomatic arches and two horizontal lines from it to the apex of the corneas, showing a distance of 24 mm bilateral, a measurement over 22 mm being considered pathological. [20]

- T1w images without FATSAT are usefull in observing the fibrotic changes in the extraocular muscles, and its characteristic consists in the lack of contrast media intake, like in T1w FATSAT. When evaluating the edema in the extraoculary muscles,
- T2w TIRM are the best sections to be used, because the intensity of the signal can be corelated with the Clinical Activity Score (CAS), gaining thus importance in establishing the treatment, respectively immunosumpressive treatment or surgery. The response to the immunomsuppressive treatment can be quantified during the course of treatment by measuring the intensity of the signal of the extraocular muscles in an coronal section, when the muscle with the most edematous changes, showing the most signal, can be compared with the adjacent temporal muscle, as a reference. [6,8,12]

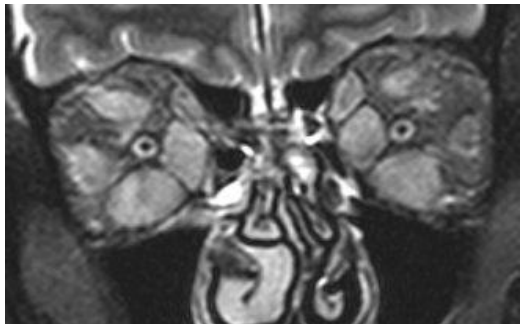
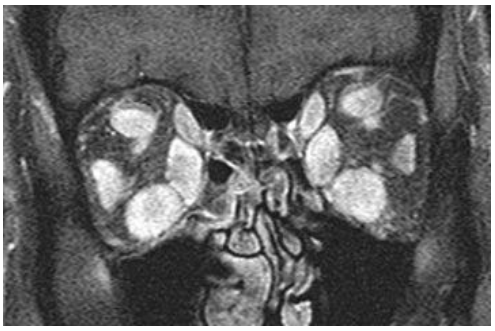
a)  b) 

Fig. 4 a) T2w TIRM section showing marked edematous enlargements of the muscles (arrows); b) T1w with contrast media showing marked enlargements of the bilateral inferior and medial rectus muscles (arrows).

The differential diagnosis in Graves ophthalmopathy is made mainly with myositis, the difference between them being that Graves ophthalmopathy is not painfull and it affects mainly the medial and inferior rectus muscles, it spares the insertions, the muscles edges are well defined and have a spindle like shape, are separated from the surrounding fat, and the periostum is not affected. Myositis is painfull, it can affect any of the muscles, the insertions are affected, the fat and the periostum are infiltrated. Other differential diagnostics include intraorbital tumors or pseudotumors, wich are predominant unilateral, they do not spare the insertions and they are painfull [6,8,12,20].

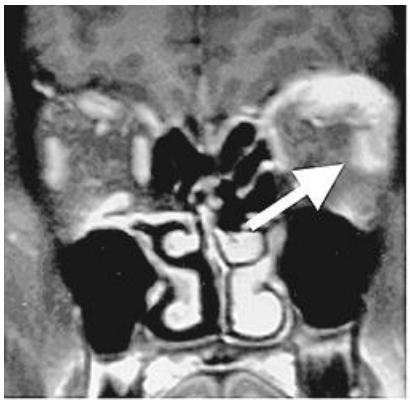
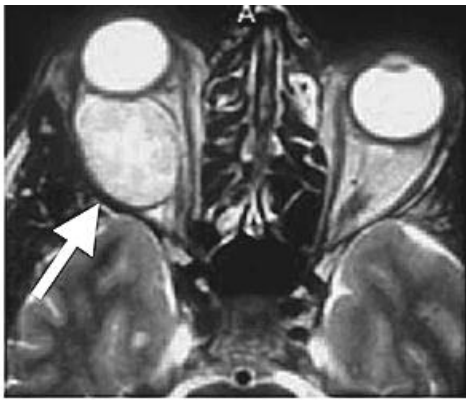
a)   b)

Fig. 5 a) Coronal T1 contrast enhanced with myositis (arrow), b) axial T2w with intraconal hemangioma (arrow). [21]

The disadvantages are: poor evaluation of the bones, difficulty in detecting calcifications, the impossibility of doing the investigation to patients with metal implants,it is difficult with patients that are claustrofobic and it is expensive

The use of Computer Tomography in the diagnostic of Graves ophthalmopathy

CT without contrast media is done to evaluate the bony structures of the orbit when orbit decompresion surgery is prepared, or to evaluate a patient that has already had the surgery for decompresion. When MRI can not be performed, contrast enhanced CT can be performed, with multiplanar reconstructions, but there is a risk to induce thyrotoxicosis due to the iodine in the contrast media. The oseous alterations consist in bulging of the orbital walls due to increased preasure inside the orbit. Also, axial 3 mm CT acquisitions are very usefull in evaluating the apex of the orbit, where the optic nerve suffers compression when there is fat hipertrophy. [18,19,21,22]

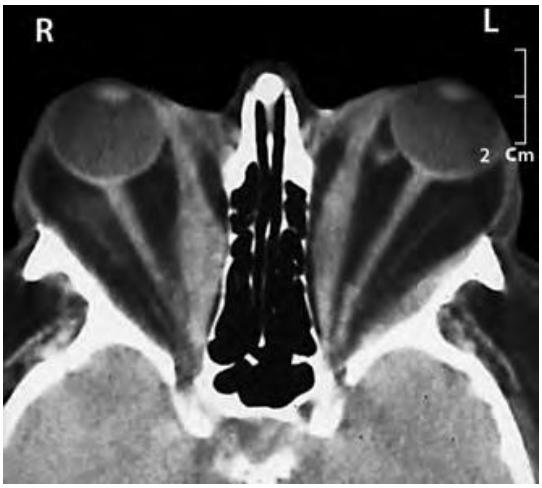


Fig. 6 Axial CT showing proptosis, enlarged intraconal fat, elongated optic nerve and bulging of the internal orbital wall of the orbit, due to bilateral medial rectus muscle hypertrophy. [23]

The advantages of using CT in Graves ophthalmopathy are: detailed imaging of the orbital bones, calcifications detection, good images of the apex of the orbit, short time investigation, the possibility to perform the exam to patients with metal implants, and it has a lower price, while the disadvantages remain the large irradiation dose and few informations about the inflammatory processes in the muscles. [18,19,21,22]

CONCLUSION

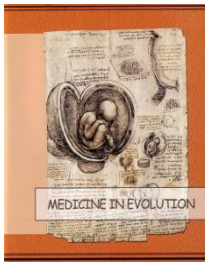
Graves ophthalmopathy is an affection that needs interdisciplinary colaboration between the endocrinology and the radiology/imaging departments, for a full diagnosis and a correct stadialisation of the inflammatory or fibrotic processes that happen inside the orbit. The clinical examination and hormonal dosages are sucessfuly completed with MRI and CT for a correct and complete diagnosis. The findings during the clinical exam consist in proptosis, upper and lower eyelid retraction, periorbital edema, conjunctival hyperemia, corneal ulcerations.

MRI differentiates between the two stages of the disease, highlighting the edema in the extraoculary muscles, during the acute inflammatory phase, with coronal T2wTIRM images, and it quantifyes the response to the immunomodulatory treatment, without irradiating the orbit, while CT, a shorter investigation than MRI, produces detailed images of the apex and the bony orbital walls, being usualy used to plan a orbital decompression surgery during hte fibrotic, inactive phase of the disease. These two investigations complete each other very well in the diagnosis and treatment of Graves ophthalmopathy.

REFERENCES

1. Wiersinga WM, Smit T, van der Gaag R, Mourits M, Koornneef L. Clinical presentation of Graves' ophthalmopathy. Ophthalmic Res. 1989;21:73–82.
2. Mourits MP. Diagnosis and Differential Diagnosis of Graves' Orbitopathy. In: Wiersinga WM, Kahaly GJ editors: Graves' Orbitopathy: A Multidisciplinary Approach. Basel, Karger, 2007, pp 66–77.
3. Bartalena L, Baldeschi L, Dickinson AJ, Eckstein A, Kendall- Taylor P, Marcocci C, et al. Consensus Statement of the European Group on Graves' Orbitopathy (EUGOGO) on Management of Graves' Orbitopathy. Thyroid. 2008;18:333–46.
4. European Group on Graves' Orbitopathy (EUGOGO), Wiersinga WM, Perros P, Kahaly GJ, Mourits MP, Baldeschi L, Boboridis K, et al. Clinical assessment of patients with Graves' orbitopathy: the European Group on Graves' Orbitopathy recommendations to generalists, specialists and clinical researchers. Eur J Endocrinol. 2006;155:387–9.
5. Werner SC. Modification of the classification of eye changes of Graves' disease. Am J Ophthalmol. 1977;83:725–7.
6. Kahaly GJ. Imaging in thyroid-associate orbitopathy. Eur J Endo. 2001;145:107–18.
7. Ott M, Breiter N, Albrecht CF, Pradier O, Hess CF, Schmidberger H. Can contrast enhanced MRI predict the response of Graves' ophthalmopathy to orbital radiotherapy? Br J Radiol. 2002;75:514–7.
8. Prummel MF, Gerding MN, Zonnevedl FW, et al. The usefulness of quantitative orbital magnetic resonance imaging in Graves' ophthalmopathy. Clin Endocrinol (Oxf). 2001;54:205–9.
9. Majos A, Pajak M, Grzelak P, et al. Magnetic resonance evaluation of disease activity in Graves' ophthalmopathy: T2-time and signal intensity of extraocular muscles. Med Sci Monit. 2007;13 Suppl 1:44–8.
10 . Lennerstrand G, Tian S, Isberg B, et al. Magnetic resonance imaging and ultrasound measurements of extraocular muscles in thyroid-associated ophthalmopathy at different stages of the disease. Acta Ophthalmol Scand. 2007;85:192–201.
11. Ohnishi T, Noguchi S, Murakami N, et al. Extraocular muscles in Graves ophthalmopathy: usefulness of T2 relaxation time measurements. Radiology. 1994;190:857–62.
12. Aydin K, Güven K, Sencer S, et al. A new MRI method for the quantitative evaluation of extraocular muscle size in thyroid ophthalmopathy. Neuroradiology. 2003;45:184–7.
13. Cakirer S, Cakirer D, Basak M, Durmaz S, Altuntas Y, Yigit U.Evaluation of extra-ocular muscles in the edematous phase of Graves' ophthalmopathy on contrast-enhanced fat-suppressed magnetic resonance imaging. Comput Assist Tomogr. 2004;28: 80–6.
14. Mourits MP. Diagnosis and Differential Diagnosis of Graves' Orbitopathy. In Wiersinga W.M., Kahaly GJ Graves' Orbitopathy: A Multidisciplinary Approach. Karger, Basel, 2007; pp: 66– 77.
15. Mayer EJ, Fox DL, Herdman G, Hsuan J, Kabala J, Goddard P,et al. Signal intensity, clinical activity and cross-sectional areas on MRI scans in thyroid eye disease. Eur J Radiol. 2005;56:20–4.
16. Yokoyama N, Nagataki S, Uetani M, Ashizawa K, Eguchi K. Role of magnetic resonance imaging in the assessment of disease activity in thyroid-associated ophthalmopathy. Thyroid. 2002;12:223–7.
17. Szucs-Farkas Z, Toth J, Balazs E, Galuska L, Burman KD, Karanyi Z, Leovey A, Nagy EV. Using morphologic parameters of extra-ocular muscles for diagnosis and follow-up of Graves' ophthalmopathy: diameters, areas, or volumes? Am J Roentgenol. 2002;179:1005–10.
18. Kahaly GJ. Recent developments in Graves' ophthalmopathy imaging. J Endocrinol Invest. 2004;27:254–8. Review.
19. Pauleit D, Schüller H, Textor J, Leutner C, Keller E, Sommer T, et al. MR relaxation time measurements with and without selective fat suppression (SPIR) in endocrine orbitopathy. Rofo.1997;167:557–64.
20. Eberhard Kirsch, Beat Hammer, Georg von Arx, Graves' orbitopathy: current imaging procedures, S W I S S M E D W K LY 2 0 0 9 ; 1 3 9 (4 3 – 4 4) : 6 1 8 – 6 2 3 · w w w . s m w . c h, review
21. Goldberg RA. The evolving paradigm of orbital decompression surgery. Arch Ophthalmol. 1998; 116:95–6.
22. Karina Freitas Soares Machado, Marcelo de Mattos Garcia, Thyroid ophthalmopathy revisited, Radiol Bras. 2009;42(4):261–266.
23. Imam Subekti, Asman Boedisantoso, Nila Djuwita F. Moeloek, Sarwono Waspadji, Muchtaruddin Mansyur, Association of TSH Receptor Antibody, Thyroid Stimulating Antibody, and Thyroid Blocking Antibody with Clinical Activity Score and Degree of Severity of Graves Ophthalmopathy, Acta Medica Indonesiana - The Indonesian Journal of Internal Medicine, Vol 44 • Number 2 • April 2012

BENEFITS OF SPECIFIC EARLY DIAGNOSIS AND TREATMENT IN INFLAMMATORY RHEUMATIC DISEASES



RADU PETROMAN[1], DAN NEMEŞ[1,2], MIHAI DRĂGOI[1,2]; DANIEL POPA[1,2]; DAN SURDUCAN[1]

[1]University of Medicine and Pharmacy "Victor Babeş", Timişoara, România
[2]City Emergency Hospital, Timişoara, România – Department of Rehabilitation, Physical Medicine, Balneology, Rheumatology

ABSTRACT

Aim and objectives: *Assessment of the effectiveness of new diagnostic criteria for the early therapeutic approach of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthropathy.*

Material and method: *The assessment included 167 patients with early rheumatoid syndrome, of whom 48 patients were early diagnosed with the previously mentioned diseases according to novel criteria and monitored by quantifiable biological (ESR and CRP) and functional (HAQ scale) parameters. The subjects entered an early, staged therapeutic protocol. Assessments were performed at the time of diagnosis, and every 3 months throughout one year after being included in the study.*

Results: *The new diagnostic criteria allowed reducing the period between the first visit and the positive diagnosis to about 3.98 months thus allowing an early and focused therapeutic approach.*

Conclusions: *Early therapy allows the avoidance/decrease of complications rate and thus of the degree they impair the rehabilitation capacity and prognosis. The used criteria diminish the number of cases requiring aggressive treatment (DMARD and biologic therapy) in order to achieve a lower disease activity, in contrast with patients approached during the stage of already active disease.*

Key words: *rheumatoid arthritis, spondyloarthropathy, early diagnosis, staged treatment*

Correspondence to

Radu Petroman, MD, PhD student.
Address: "Victor Babeş" University of Medicine and Pharmacy, Timişoara, România
Phone: 0720036805
E-mail: petromanradu@yahoo.com

INTRODUCTION

Rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthropathy (PsA) are rheumatic inflammatory diseases with major disabling potential, high frequency worldwide nowadays, generating diverse manifestations and crucially influencing the life of affected persons by morbidity increase and important decreases of life quality and life span in affected patients. Previous diagnostic and staging criteria, designed after the study of established disease cases, proved to be deficient in current medical practice, excluding a confirmatory positive diagnosis during early, pre-radiologic and oligosymptomatic stages, when patients would benefit most from a focused treatment, instituted „at the very beginning", preventing/delaying the rapid clinical-biological degradation and the onset of complications and co-morbidities occurring during the prolonged evolution of these diseases and influencing in their turn the progress and short, medium and long term prognosis of these patients, directly increasing, morbidity and mortality rates as well as the difficulty to gain an effective therapeutic control over the disease.

Thus, in the case of RA, the former criteria have around 90% specificity and sensibility only in cases of clearly established disease [1], with no applicability for the diagnosis of early forms; this phenomenon is also encountered in the case of AS, where a positive diagnosis may be sometimes delayed for more than 10 years from the onset of the first symptoms [2]. Moreover, in around 80% of cases, PsA becomes manifest after around 10 years since the onset of psoriasis [3], only 10-15% of patients also presenting concomitant skin and articular symptoms, phenomenon which may accelerate diagnosis [4], while the manifestation of psoriasis after the onset of arthritis may initially validate a non-differentiated SpA [4].

In conclusion, in order to eliminate the weak points of previous diagnostic criteria, in September 2010, the joint teams of ACR and EULAR (European League Against Rheumatism) imposed novel diagnostic criteria for early defined RA (figure 1 - [5]).

A. Joint involvement : 0-5 points	
1 large joint (shoulder, elbow, hip, knee, and ankle) 2-10 large joints	**0** **1**
1-3 small joints(metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, wrists) ,with or without involvement of large joints	**2**
4-10 small joints (with or without involvement of large joints) >10 joints (at least 1 small joint)	**3** **5**
B. Serology (at least 1 test result is needed for classification) : **0-3 points**	
Negative RF and negative ACPA Low-positive RF or low-positive ACPA	**0** **2**
High-positive RF or high-positive ACPA	**3**
C. Acute-phase reactants (at least 1 test result is needed for classification) : **0-1 point**	
Normal CRP and normal ESR Abnormal CRP or abnormal ESR	**0** **1**
D. Time from first appearance of symptoms (of synovitis) : **0-1 point**	
<6 weeks	**0**
≥6 weeks	**1**

Figure 1 : Novel RA diagnostic criteria defined according to ACR and EULAR [5], where the ***presence of synovitis*** *(visible as tumefaction upon clinical examination)* ***in at least one articulation, unexplainable by another diagnosis*** *(SLE, PsA, gouty arthropathy) and* ***an overall score of at least 6 out of 10 points in the 4 reference domains,*** *certifies the early diagnosis. ESR- erythrocyte sedimentation rate; CRP - C reactive protein; RF - rheumatoid factor; ACPA - anti citrullinated peptide antibodies*

More recent and effective diagnostic **criteria** for spondyloarthropathies (SpA), also useful in cases of early AS and PsA, are those released by **ASAS** (Assessment of SpondyloArthritis International Society) in 2009 [6,7], which are given in figure 2, with a sensibility/specificity ratio of 82.9% / 84.4% in the **early diagnosis of axial** and of 75% / 82% in the case of **peripheral SpA** cases, respectively (Rudwaleit et al. Ann Rheum Dis 2009 – [6]).

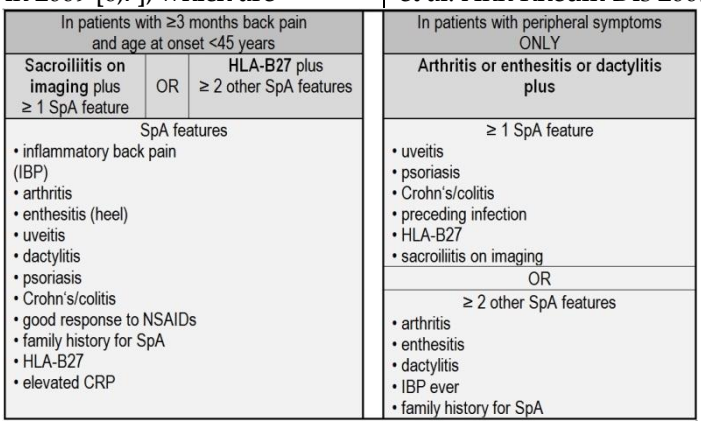


Figure 2: Early diagnosis of axial and peripheral SpA, respectively, according to ASAS criteria [6,7]

AIM AND OBJECTIVES

The study aims to evaluate the effectiveness of the new diagnostic and staging criteria, regarding the possibility to implement early treatment, before the onset of irreversible changes which characterize the established disease, offering the patient the chance for a focused treatment leading to remission or decreased disease activity during the most favourable stage, requiring less aggressive therapeutic means for the effective control of disease activity and maximizing the therapeutic effect while maintaining functionality and life quality.

MATERIAL AND METHOD

During the period between January 2010 – June 2011, 167 patients with early rheumatoid syndromes were clinically and biologically assessed, of whom, according to the new criteria, 22 RA (13.17% of the total), 17 AS (10.17%) and 9 PsA (5.38%) cases were early diagnosed. These patients were monitored and treated from the moment of diagnosis, being assessed every 3 months for a one year period, observing changes in the evolution of quantified parameters. As the analyzed diseases are different from one another and require specific assessment scales to evaluate disease activity, and also for the purpose of imposing a certain therapeutic protocol in order to obtain comparable results, quantifiable biological (ESR – erythrocyte sedimentation rate and CRP – C reactive protein, as well as parameters directly reflecting the disease activity level) and functional (HAQ – Health Assessment Questionnaire - scale, which, even though representing a general health indicator is considered an indirect disease activity indicator, by the capacity to perform daily activities) parameters were used. Throughout the entire period from diagnosis to the end of the 12 months needed for the assessment, all the subjects were early therapeutically approached, receiving diet and life hygiene regimens and orthopaedic hygiene measures, complex rehabilitation treatment for 10 days every 3 months during the assessment period, as well as individualized, staged drug therapy according to approved therapeutic protocols, consisting of symptomatic, DMARD and biological therapies.

RESULTS AND DISCUSSIONS

Upon the initial assessment (E1 – at the time of diagnosis) we obtained the following average values for the monitored parameters: ESR = 38 mm/h, CRP = 3.7mg/dl and HAQ = 2.3. All patients who were included in the study received symptomatic and individualized rehabilitation treatments. At the second assessment (E2 – 3 months after diagnosis) we obtained average values of 29 mm/h for the ESR, 2.9 mg/dl for CRP and a 2.1 HAQ score. After analyzing the above presented data, we decided to introduce a remissive DMARD into the treatment plan in about 40% of the patients, this percent representing the cases in whom the average values recorded on the second assessment showed an insufficiently favourable evolution. Upon the third assessment after the positive diagnosis (E3 – after 6 months) a slight improvement was found in the parameters of patients in whom the first remissive had been introduced (average ESR = 21 mm/h, average CRP = 1.9 mg/dl, average HAQ score = 2.1) and a slight deterioration in parameters of patients exclusively treated with symptomatics (average ESR = 27 mm/h, average CRP = 3.1 mg/dl, average HAQ score = 1.9), with further decision for only 30% of the total number of evaluated patients to continue to receive symptomatic treatment, in the remaining 70% an associated DMARD being decided. During the fourth assessment (E4 – at 9 months), in the group of patients receiving DMARD therapy, the average values of quantified paramaters remained close to the levels recorded at 6 months (average ESR = 23 mm/h, average CRP = 1.8 mg/dl, average HAQ score = 2.2) while a deterioration was found in those who only continued with symptomatic treatment (average ESR = 29 mm/h, average CRP = 3.3 mg/dl, average HAQ score = 2.2). For this reason, depending on the state of the patients, decision was made in cases refractory to previous therapies (30% of the total in E1) to associate a first line biological agent, while the remaining 70% to be divided as follows: 10% continue with symptomatic treatment and 60% receive DMARD as previously mentioned. During the last assessment (E5 – at 12 months after the early positive diagnosis and beginning of the specific therapeutic approach), the evolution of patients revealed an improvement of parameters in those in whom biological therapy had been initiated (average ESR = 10 mm/h, average CRP = 0.8 mg/dl, average HAQ score = 2.7), an approximately similar situation with the previous assessment in those who received DMARDs (average ESR = 20 mm/h, average CRP = 1.9 mg/dl, average HAQ score = 2.3) and a deterioration of parameters in those who continued only with symptomatic drugs (average ESR = 26 mm/h, average CRP = 2 mg/dl, average HAQ score = 1.7).

	E1	E2	E3		E4		E5		
		S	S	S+D	S	S+D	S	S+D	S+D+B
ESR	38	29	27	21	29	23	26	20	10
CRP	3.7	2.9	3.1	1.9	3.3	1.8	2	1.9	0.8
HAQ	2.3	2.1	1.9	2.1	1.8	2.2	1.7	2.3	2.7

Table 1: Evolution of parameters and decisions made accordingly, regarding the staged implementation of drug therapy. The following values are considered physiological: ESR ≤15mm/h (men), ≤ 20mm/h (women), respectively, CRP<0,3mg/dl, and the HAQ scale varies from 0 (activities impossible to perform) to 3 (activities performed without any difficulty). S = symptomatic treatment, D = DMARD therapy, B = biological agents therapy.

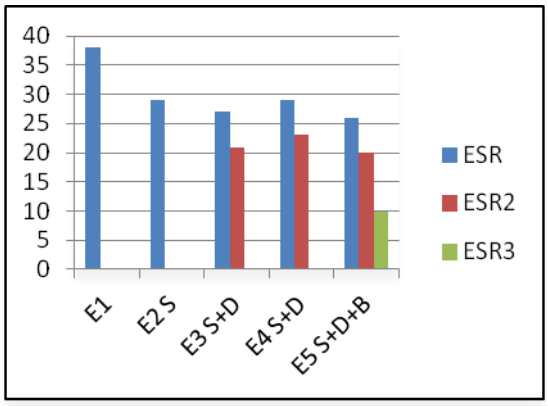


Figure 3: Evolution of the ESR in patients treated with symptomatic drugs (ESR), with DMARD's (ESR2) and with biological agents (ESR3), respectively

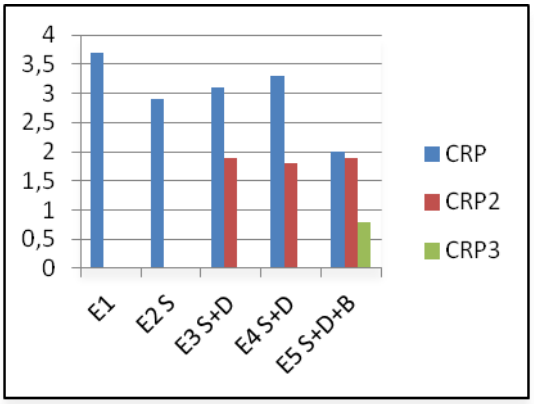


Figure 4: Evolution of CRP levels in patients treated with symptomatic drugs (CRP), with DMARD's (CRP2) and with biological agents (CRP3)

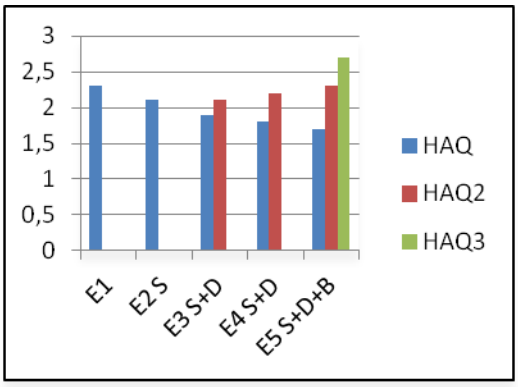


Figure 5: Evolution of the HAQ scale in patients treated with symptomatic drugs (HAQ), DMARD's (HAQ2) and biological agents (HAQ3)

CONCLUSION

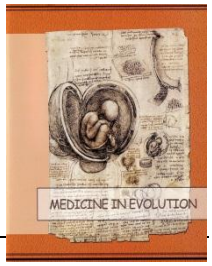
The new diagnostic criteria allow the reduction of the time interval between the onset of the first symptoms determining the visit to the physician and the moment of the positive diagnosis to around 3.98 months, as compared to the much longer period required in the case of the previously used criteria [1,2,3,4], allowing the early initiation of a

specific treatment. As a consequence, complications are avoided as much as possible or their occurence rate and their intensity decrease, as does the degree they affect the rehabilitation capacity and, implicitely, the prognosis of patients in question. The early and complex approach consisting of life hygiene and diet regimens, individualized rehabilitation treatment, as well as staged drug therapy, according to therapeutic protocols depending on the evolution, may lead to the improvement of symptoms and to a lower disease activity before irreversible changes occur, as opposed to patients during the stage of established disease. The effect is represented by a better preservation of functionality and, generally, by a better status of affected patients, also reflected in the considerable improvement of their life quality. Also, by decreasing the need for early implementation of an aggressive drug treatment, the unwanted side effects of medication may be significantly decreased.

REFERENCES

1. Arnett F., Edworty S., Bloch D. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24
2. Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27negative vs. positive patients with ankylosing spondylitis. Rheumatol Int. 2003;23:61–6.
3. Mease P, Menter A. Psoriatic Arthritis: Understanding Its Pathophysiology and Improving Its Diagnosis and Management Published: 07/28/2005 on MEDSCAPE
4. Pană C, Suta M. Diagnosticul precoce în artropatia psoriazică. Journal of Internal Medicine Society. Nr.5 din 2011. http://www.medicina-interna.ro/ articol.php?articol=693&lang=ro
5. Aletaha D, Neogi T, Silman SJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*.2010;62(9): 2569-2581.
6. Rudwaleit M, van der Heijde D, et al. The development of Assessment of SpondyloArthritis International Society(ASAS) classification criteria for axial spondyloarthritis(Part II): validation and final selection. Anals of Rheumatic Diseases 2009; 68:777 – 783.
7. Sieper J., Braun J. Ankylosing Spondylitis in clinical practice. Ed. Springer-Verlag London Limited . 2011. p18-96

THE ROLE OF PORPHYRIN PRECURSOR-BASED PHOTODYNAMIC THERAPY IN DERMATOLOGY



CLARA MATEI[1], MIRCEA TAMPA[2], SIMONA-ROXANA GEORGESCU[2], ISABELA SARBU[2], RODICA-MARIANA ION[3], CAROLINA CONSTANTIN[4], MONICA NEAGU[4]

1 University of Medicine and Pharmacy "Carol Davila", Elias Hospital, Dermatology Department, Bucharest
2 University of Medicine and Pharmacy "Carol Davila",Faculty of Dental Medicine, Elias Hospital, Dermatology Department, Bucharest
3 ICECHIM Institute for Chemistry Research, Bucharest
4 National Institute of Pathology "Victor Babes", Immunobiology Department, Bucharest

ABSTRACT

Photodynamic therapy (PDT) is a modern treatment method applied for destroying tumors in the field of urology, gynaecology, pneumology or gastroenterology. During the last years, PDT has been employed with increasing frequence in dermatology; its use is not restricted to the treatment of malignant cutaneous lesions, but also extends to the therapy of various inflammatory disorders and in the area of aged skin rejuvenation. The present article aims to present the main applications of PDT in dermatology.

Key words: *photodynamic therapy, aminolevulinic acid, methyl aminolevulinate, cutaneous tumors*

Correspondence to

Mircea TAMPA, MD, PhD student
Address: Dermatology Department, Faculty of Dental Medicine,
"Carol Davila" University of Medicine and Pharmacy,
Dionisie Lupu Street, no. 37, sector 1, 020022, Bucharest, Romania
Phone: +40785040752;
E-mail address: tampa_mircea@yahoo.com

INTRODUCTION

Photodynamic therapy (PDT) is a recently introduced approach in the treatment of cancer. Its main role consists in destroying tumor cells through a complex mechanism based on the photoactivation of a chemical compound selectively captured in the malignant cells. Photodynamic therapy requires the simultaneous presence in the target area of a photosensitiser with neoplastic cell tropism, of light with an adequate wavelength for activating the photosensitizer, as well as tissue oxygen (1).

The photosensitiser is a chemical compound with the ability to selectively accumulate in neoplastic cells and subsequently absorb luminous radiation; after capturing an appropriate energy quantum, the photosensitiser molecule switches from the fundamental ground *singlet* state to an excited *singlet* state. These energetic states are not stable, resulting either in the desexcitation of the molecule by energy release or in transition into a more stable *triplet* state; having a longer life-span, the latter allows the deployment of particular photochemical reactions characterized by electron transfer (photochemical reactions type I) and/or by energy release (photochemical reactions type II), resulting in the appearance in the intracellular medium of reactive oxygen species such as hydroxyl radical(OH•), singlet oxygen ($^1O_2$) or superoxide anion (O_2^-). These reactive species appear inside the tumoral cell where the photosensitizer is selectively accumulated and will alter nucleic acids, lipids and proteins, leading to the death of the neoplastic cells (fig.1). This effect is associated with induction of apoptosis in tumoral cells and lesions of the tumor vessels; the induction of programmed cell death and local ischemia, acting synergistically with the induction of oxygen reactive species, will complete the destructive effect of PDT on cancer cells (2).

The photosensitisers are various chemical compounds based on a tetrapyrrolic macro-heterocyclic structural model, sharing the aromatic character and the delocalization of the electrons from the conjugated bonds of the molecule, both of which allow a good absorption of the wavelength employed in PDT; the latter is chosen in such way so that it possesses the best tissue penetrance possible, in the circumstances of minimum shielding in case of absorption by other cromophore molecules present in the target tissue (1;2).

Therefore, the compounds most commonly used as photosensitizers in PDT are the porphyrins (2). The porphyrins can either be administered intravenously and subsequently be uptaken from the circulation selectively by the neoplastic cells, or they can be directly synthesized in the neoplastic tissue after topical application of porphyrin precursors. The porpyrin precursors most commonly used in PDT are 5-amino-levulinic acid (ALA) and its methyl esther, methyl aminolevulinate (MAL).

After topical administration, ALA will penetrate the skin where it will be preferentially captured by the neoplastic cells, inside which it will be transformed by the enzymatic system of heme synthesis into protoporphyrinogen and consequently into protoporphyrine IX, a compound with good fotosensitising proprieties, that can then be activated within the tissue by red light at a wavelength of λ=630, leading to the destruction of the tumor cells in which it was synthesized. The methyl esther of the aminolevulinic acid (MAL) permeates the membrane of the tumoral cells and is lysed in the cytosol, releasing ALA intracellularly, which will further on be transformed into protoporphyrine IX, the target molecule of porphyrin precursor-based PDT (3) (fig.1).

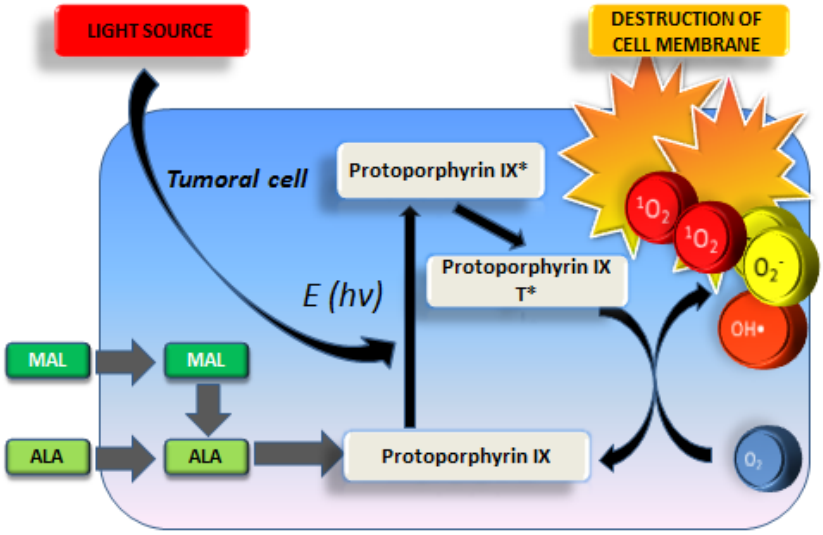


*Fig. 1- Mechanism of Photodynamic Therapy action on tumoral cells (detailed explanations in the text). MAL=methyl-esther of aminolevulinic acid; ALA=aminolevulinic acid; *=symbol for excited energetic state; T=symbol for triplet state*

Initially approved in the field of pneumology and gastroenterology, during the last years PDT has been used with increasing frequency in dermatology, not only for the treatment of oncologic cutaneous lesions, but also for a great variety of inflammatory disorders or even for cutaneous rejuvenation (4). The most commonly used dermatologic applications of PDT with porphyrin precursors are photodynamic therapy using ALA 20% concentration, topically applied (with the consecrated abbreviation ALA-PDT) and photodynamic therapy with topical 16% MAL (MAL-PDT), employed in conjuction with non-coherent light source or, more commonly, laser light source (fig.2).

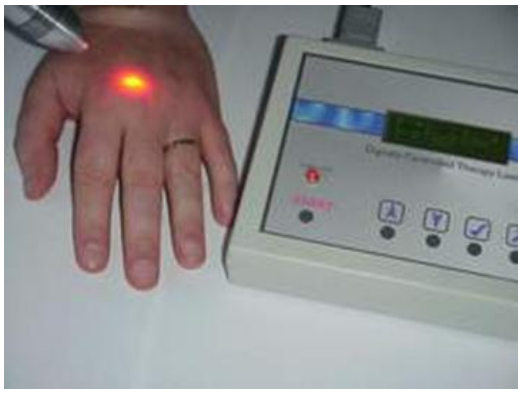


Fig. 2- HeNe laser source for skin irradiation employed in various applications of photodynamic therapy in dermatology

Porphyrine precursor-based PDT applications in dermatology

The main indications of PDT in dermatology are:

-basal cell epitheliomas. Basal cell epithelioma is the most frequently encountered cancer of the human species (5). A study published by Christensen et al. in 2012 evaluates the clinical and histological changes 10 years after topical ALA photodynamic therapy; complete remission rate was observed in 60% of the patients who were subjected to only one session of ALA-PDT and 87% in the ones who completed two

treatment sessions. One decade after the procedure, the aesthetic outcome was considered very good in over 90% of the treated patients (6).

A study published in 2011 aimed to assess MAL-PDT efficacy on a group of 135 patients presenting 194 basal cell epitheliomas at the beginning of the study; the authors reported a 62% complete remission rate post-treatment; the superficial type basal cell epitheliomas responded better than the nodular one (82% remssion for the former, compared to only 33% in case of the latter). The study also proved that the presence of ulceration in the malignant lesion and the localization of the epitheliomas on the extremities significantly reduce MAL-PDT efficiency, whilst the tumor dimensions do not alter the overall result of the therapy (7). Also, it appears that PDT is very efficient not only in the case of extensive epitheliomas with large dimensions that make the surgical approach difficult (8), but also for epitheliomas occurred within Gorlin syndrome, where the extremely high number of malignant lesions makes the repetitive surgical excision improper (9).

- actinic keratoses. Actinic keratoses are premalignant lesions, *in situ* cutaneous neoplastic lesions composed of aberrant proliferations of keratinocytes, occurred as a response to UV radiation exposure. A multicentric, double-blind study, performed in the United States and published in 2008, randomized patients between MAL-PDT (49 patients, with 363 actinic keratoses) and placebo-PDT – photodynamic therapy which only used the vehicle innocuous cream instead of MAL (47 patients with 360 actinic keratoses). The PDT session was repeated after one week. As for the lesions taken separately, complete remission rate was achieved in 86.2% in the first group vs. 52.2% in the second, and, as for the individual response of the patients, complete remission rate was achieved in 59.2% patients in the first group, as compared to only14.9% in the placebo-PDT treated group (10). Other data also support the efficiency of MAL-PDT in the treatment of actinic keratoses: a study published by Fai et al. in 2009 proved that, in 210 patients treated with one or two sessions of MAL-PDT separated by a period of 7 days, complete remission was achieved in 79% of the patients at 3 months after the procedure (11).

Response rates of actinic keratoses treated with MAL-PDT and cryotherapy are similar, but MAL-PDT is associated with less significant side effects, according to a randomized study performed by Szeimies et al. in 2002 (12).

In terms of patient satisfaction, a study from 2001 compared the tolerability of the MAL-PDT treatment and topical treatment with imiquimod 5% in actinic keratosis; 93% of the patients were satisfied with MAL-PDT, as compared to only 62% of the ones treated with imiquimod (p=0.004) (13).

Moreover, MAL photodynamic therapy can also be used in the treatment of actinic cheilitis- the correspondent of actinic keratoses on the lip mucosa- according to several recent studies (14;15).

***-in situ* squamous cell carcinoma**. *In situ* squamous cell carcinoma (Bowen's disease) is a premalignant condition that occurs more frequently in elderly patients, following exposure to ionizing radations, ultraviolet radiation or after chronic arsenic exposure; immunosuppression is a predisposing factor in the appearance of the disorder. A study performed on 239 patients presenting Bowen's disease plaques on the skin revealed complete remission rates in 222 lesions at one year follow-up , with a recurrence rate of 10.3% at 3 years post-therapy (16). Salim et al. showed that ALA-PDT is superior to topical applications of 5-fluorouracil (5-FU) in terms of efficiency (17). As for MAL-PDT in the treatment of Bowen's disease, its efficaicy is at least similar to that of topical application of 5-FU and cryotherapy, but MAL-PDT has the advantage of excellent cosmesis; the method is especially addressed to patients with multiple Bowen plaques or lesions with such an extension that make surgical approach very difficult (18).

PDT can also be used in dermatology for the treatment of non-tumor disorders:

- acne vulgaris. Riddle et al. showed in 2009 that PDT is efficient in reducing the number and severity of acne inflammatory lesions (19), and Fabbrocini et al. showed that ALA-PDT is also effective in the treatment of retentive lesions of comedonian acne (20). PDT is an important therapeutic alternative especially in patients oterwise unresponsive to other treatment modalities and/or in patients where administration of systemic retinoids is contraindicated (19).

-psoriasis vulgaris. Results regarding the use of PDT in the treatment of psoriasis are contradictory, there existing a lack of agreement when it comes to the efficacy of the method. Thereby,while Boehncke states that PDT is a safe and efficient treatment for this particular skin condition (21), Beattie et al. show that PDT is inferior to narrowband (311 nm) UVB therapy in terms of effectiveness and tolerability (22) and Radakovic-Fijan et al. observe, in a study that included 29 psoriatic patients subjected to PDT, that the results of the procedure are disappointing (23).
-lichen sclerosus. ALA-PDT also seems to be effective in the treatment of refractory forms of sclero-atrophic lichen; however, no large studies were performed for this matter, but only individual cases or series of cases (24).
-hidrosadenitis suppurativa and pylonidal cyst. ALA-PDT also seems to be efficient in the treatment of hidrosadenitis and pilonidal cyst; data regarding ALA-PDT treatment of these skin conditions is limited (25).
-cutaneous infections caused by HPV virus. Recent studies confirm that ALA-PDT can be successfully used in the treatment of condyloma accuminata and common warts caused by HPV virus (26;27) or in cutaneous lesions caused by infection with molluscum contagiosum virus (28).
-aged skin rejuvenation. During the last years, the use of photodynamic therapy for cosmetic purpose expanded. Recent studies support the usefulness of PDT in dermatocosmetology; ALA-PDT is able to reduce facial lines (29) either alone or in conjunction with intense pulsed light (IPL) treatments (30).

CONCLUSION

Photodynamic therapy can be successfully employed in the treatment of malignant (basal cell epithelioma) or premalignant (actinic keratosis, squamous cell carcinoma *in situ*) skin conditions, but also for inflammatory or infectious diseases such as acne vulgaris and viral cutaneous infections. The high efficiency of the procedure and its low adverse reaction rate recommend PDT as an extremely valuable dermatologic treatment method, especially when surgical excision of the tumors is difficult or contraindicated. As the indications of PDT continuously extend from tumor pathology to non-tumor pathology, the possibility of setting up standardized treatment protocols (in order to include the entire variety of skin conditions that respond to PDT and to optimize the use of the existing photosensitizers) may readily predicted. Minimal adverse reactions and high efficacy of PDT are sustainable arguments that support the increasing use of photodynamic therapy in the field of dermatology.

REFERENCES

(1) Josefsen LB, Boyle RW. Photodynamic therapy and the development of metal-based photosensitisers. Met Based Drugs 2008; 2008:276109.

(2) Ion, R.M., Porfirinele si terapia fotodinamica a cancerului, Editura Stiintifica FMR, 2003, ISBN: 973-8151-13-9

(3) Perotti C, Fukuda H, DiVenosa G, MacRobert AJ, Batlle A, Casas A. Porphyrin synthesis from ALA derivatives for photodynamic therapy. In vitro and in vivo studies. Br J Cancer 2004; 90(8):1660-1665.

(4) Moan J, Peng Q. An outline of the hundred-year history of PDT. Anticancer Res 2003; 23(5A):3591-3600.

(5) Smith V, Walton S. Treatment of facial Basal cell carcinoma: a review. J Skin Cancer 2011; 2011:380371.

(6) Christensen E, Mork C, Skogvoll E. High and sustained efficacy after two sessions of topical 5-aminolaevulinic acid photodynamic therapy for basal cell carcinoma: a prospective, clinical and histological 10-year follow-up study. Br J Dermatol 2012; 166(6):1342-1348.

(7) Fantini F, Greco A, Del Giovane C, Cesinaro AM, Venturini M, Zane C et al. Photodynamic therapy for basal cell carcinoma: clinical and pathological determinants of response. J Eur Acad Dermatol Venereol 2011; 25(8):896-901.

(8) Eibenschutz L, Marenda S, Buccini P, De Simone P, Ferrari A, Mariani G et al. Giant and large basal cell carcinoma treated with topical photodynamic therapy. Eur J Dermatol 2008; 18(6):663-666.

(9) Pauwels C, Mazereeuw-Hautier J, Basset-Seguin N, Livideanu C, Viraben R, Paul C et al. Topical methyl aminolevulinate photodynamic therapy for management of basal cell carcinomas in patients with basal cell nevus syndrome improves patient's satisfaction and reduces the need for surgical procedures. J Eur Acad Dermatol Venereol 2011; 25(7):861-864.

(10) Pariser D, Loss R, Jarratt M, Abramovits W, Spencer J, Geronemus R et al. Topical methyl-aminolevulinate photodynamic therapy using red light-emitting diode light for treatment of multiple actinic keratoses: A randomized, double-blind, placebo-controlled study. J Am Acad Dermatol 2008; 59(4):569-576.

(11) Fai D, Arpaia N, Romano I, Vestita M, Cassano N, Vena GA. Methyl-aminolevulinate photodynamic therapy for the treatment of actinic keratoses and non-melanoma skin cancers: a retrospective analysis of response in 462 patients. G Ital Dermatol Venereol 2009; 144(3):281-285.

(12) Szeimies RM, Karrer S, Radakovic-Fijan S, Tanew A, Calzavara-Pinton PG, Zane C et al. Photodynamic therapy using topical methyl 5-aminolevulinate compared with cryotherapy for actinic keratosis: A prospective, randomized study. J Am Acad Dermatol 2002; 47(2):258-262.

(13) Serra-Guillen C, Nagore E, Hueso L, Llombart B, Requena C, Sanmartin O et al. A randomized comparative study of tolerance and satisfaction in the treatment of actinic keratosis of the face and scalp between 5% imiquimod cream and photodynamic therapy with methyl aminolaevulinate. Br J Dermatol 2011; 164(2):429-433.

(14) Fai D, Romano I, Cassano N, Vena GA. Methyl-aminolevulinate photodynamic therapy for the treatment of actinic cheilitis: a retrospective evaluation of 29 patients. G Ital Dermatol Venereol 2012; 147(1):99-101.

(15) Castano E, Comunion A, Arias D, Minano R, Romero A, Borbujo J. [Photodynamic therapy for actinic cheilitis]. Actas Dermosifiliogr 2009; 100(10):895-898.

(16) Clark C, Bryden A, Dawe R, Moseley H, Ferguson J, Ibbotson SH. Topical 5-aminolaevulinic acid photodynamic therapy for cutaneous lesions: outcome and comparison of light sources. Photodermatol Photoimmunol Photomed 2003; 19(3):134-141.

(17) Salim A, Leman JA, McColl JH, Chapman R, Morton CA. Randomized comparison of photodynamic therapy with topical 5-fluorouracil in Bowen's disease. Br J Dermatol 2003; 148(3):539-543.

(18) Morton CA. Methyl aminolevulinate: actinic keratoses and Bowen's disease. Dermatol Clin 2007; 25(1):81-87.

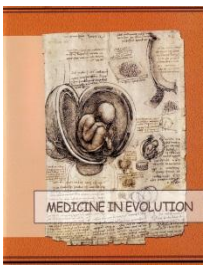
(19) Riddle CC, Terrell SN, Menser MB, Aires DJ, Schweiger ES. A review of photodynamic therapy (PDT) for the treatment of acne vulgaris. J Drugs Dermatol 2009; 8(11):1010-1019.

(20) Fabbrocini G, Cacciapuoti S, De V, V, Fardella N, Pastore F, Monfrecola G. The effect of aminolevulinic acid photodynamic therapy on microcomedones and macrocomedones. Dermatology 2009; 219(4):322-328.

(21) Boehncke WH, Elshorst-Schmidt T, Kaufmann R. Systemic photodynamic therapy is a safe and effective treatment

for psoriasis. Arch Dermatol 2000; 136(2):271-272.
(22) Beattie PE, Dawe RS, Ferguson J, Ibbotson SH. Lack of efficacy and tolerability of topical PDT for psoriasis in comparison with narrowband UVB phototherapy. Clin Exp Dermatol 2004; 29(5):560-562.
(23) Radakovic-Fijan S, Blecha-Thalhammer U, Schleyer V, Szeimies RM, Zwingers T, Honigsmann H et al. Topical aminolaevulinic acid-based photodynamic therapy as a treatment option for psoriasis? Results of a randomized, observer-blinded study. Br J Dermatol 2005; 152(2):279-283.
(24) SOTIRIOU E, APALLA Z, PATSATSI A, PANAGIOTIDOU D. Recalcitrant vulvar lichen sclerosis treated with aminolevulinic acid-photodynamic therapy: a report of five cases. J Eur Acad Dermatol Venereol 2008; 22(11):1398-1399.
(25) Saraceno R, Teoli M, Casciello C, Chimenti S. Methyl aminolaevulinate photodynamic therapy for the treatment of hidradenitis suppurativa and pilonidal cysts. Photodermatol Photoimmunol Photomed 2009; 25(3):164-165.
(26) Liang J, Lu XN, Tang H, Zhang Z, Fan J, Xu JH. Evaluation of photodynamic therapy using topical aminolevulinic acid hydrochloride in the treatment of condylomata acuminata: a comparative, randomized clinical trial. Photodermatol Photoimmunol Photomed 2009; 25(6):293-297.
(27) Nucci V, Torchia D, Cappugi P. Treatment of anogenital condylomata acuminata with topical photodynamic therapy: report of 14 cases and review. Int J Infect Dis 2010; 14 Suppl 3:e280-e282.
(28) Gold MH, Moiin A. Treatment of verrucae vulgaris and molluscum contagiosum with photodynamic therapy. Dermatol Clin 2007; 25(1):75-80.
(29) Ruiz-Rodriguez R, Lopez L, Candelas D, Zelickson B. Enhanced efficacy of photodynamic therapy after fractional resurfacing: fractional photodynamic rejuvenation. J Drugs Dermatol 2007; 6(8):818-820.
(30) Kosaka S, Yasumoto M, Akilov OE, Hasan T, Kawana S. Comparative split-face study of 5-aminolevulinic acid photodynamic therapy with intense pulsed light for photorejuvenation of Asian skin. J Dermatol 2010; 37(12):1005-1010.

5-AMINOLEVULINIC ACID PHOTODYNAMIC THERAPY IN THE TREATMENT OF CUTANEOUS SQUAMOUS CELL CARCINOMA IN SITU (BOWEN'S DISEASE)



MIRCEA TAMPA[1],CLARA MATEI[2], SIMONA-ROXANA GEORGESCU[1], VASILE BENEA[3], ISABELA SARBU[3], RODICA-MARIANA ION[4], CAROLINA CONSTANTIN[5], MONICA NEAGU[5], SANDA POPESCU[6]

[1] University of Medicine and Pharmacy "Carol Davila", Faculty of Dental Medicine, Dermatology Department, Bucharest
[2] University of Medicine and Pharmacy "Carol Davila", Dermatology Department, Elias Hospital, Bucharest
[3] „Victor Babes" Clinical Hospital, Dermatology Department, Bucharest
[4] ICECHIM Institute for Chemistry Research, Bucharest
[5] "Victor Babes" National Institute of Pathology, Department of Immunobiology Bucharest
[6] University of Medicine and Pharmacy "Carol Davila", Dermatology Department, Bucharest

ABSTRACT

Photodynamic therapy (PDT) is a modern antitumoral treatment that implies the use of a chemical compound with a photosensitising role and a light source with an adequate emission spectrum for its activation. During the last years, the method has been successfully applied for the treatment of tumors in various medical fields such as urology, gynaecology, pneumology and gastroenterology, as well as for the treatment of oral cavity tumor lesions.

Additionally, photodynamic therapy is extremely useful in dermatology, especially for the treatment of cutaneous malignant and premalignant lesions. Bowen's disease (squamous cell carcinoma in situ) is a premalignant cutaneous disorder possessing a great potential to transform into invasive squamous cell carcinoma (SCC). The present article attempts to introduce the principles of this innovative therapeutic method and to review the main studies underlying the use of photodynamic therapy for the treatment of Bowen's disease.

Keywords: *photodynamic therapy, 5-aminolevulinic acid, Bowen's disease, squamous cell carcinoma*

Correspondence to
Mircea TAMPA, MD, PhD student
Address: Dermatology Department, Faculty of Dental Medicine,
"Carol Davila" University of Medicine and Pharmacy, Dionisie Lupu Street, no. 37, sector 1, 020022, Bucharest, Romania
Phone: +40785040752
E-mail address: tampa_mircea@yahoo.com

INTRODUCTION

Photodynamic therapy is a modern antineoplastic treatment method that implies the use of a chemical compound with a photosensitising role and a light source that emits radiation of an adequate wavelength, suitable for activating the photosensitizer. The photosensiziter is a chemical compound that possesses the property to selectively accumulate in the tumor cell and capture the energy delivered by a light source, energy which it subsequently released in the surrounding tissue, leading to the destruction of neoplastic cells through complex mechanisms encompassing disruption of tumoral microvasculature, formation of reactive oxygen species and induction of apoptosis.

5-aminolevulinic acid (ALA) (5-amino4-oxo-pentanoic acid) is a porphyrin precursor devoided of any photosensitising activity *per se.* After topical application, ALA is able to penetrate to the interior of the tumoral cells, where it will be taken over by the enzymatic equipment of heme synthesis existing in the neoplastic cells, being transformed into protoporphyrin IX, a compound with important photosensitising proprieties that will be the actual target of PDT.

The conduct of the procedure implies topical administration of 20% (w/v) ALA on the cutaneous surface of the lesion to be treated, followed by the placement of an occlusive dressing for improving intralesional penetrance of the photosensitiser. Four hours after ALA application, the occlusive dressing is removed and the area is subsequently exposed to irradiation by a light source with an adequate wavelength for activating ALA, after chosing the convenient irradiation parameters such as fluence rate, radiance and duration.

The mechanism of photodynamic therapy (PDT)

The first stage consists in the absorption by the photosensitizer molecules accumulated in the cancer cells of energy quanta delivered from the light source. The latter must emit adequate wavelength radiation, in order to minimize the unwanted light absorbtion by other skin cromophores (melanin, water, reduced haemoglobin and oxihaemoglobin) and, in the same time, to overlap as much as possible with the maximum absorption spectrum of the photosensitiser. The illumination will determine the formation of *singlet* energetic excitation states of the photosensitizer molecules, with a short life span, which will rapidly dissipate the energy either by florescence type dezexcitation, either through the process of inter-system crossing, becoming *triplet* excitation states, with the kinetic moments of the two electrons from the peripheral molecular orbital oriented in the same direction. Having a longer life-span (of about 10^{-3}s-1s), the *triplet* excitation states will be able to participate in type I photodynamic reactions (oxidoreduction reactions) and type II reactions (energy transfer reactions), giving rise to reactive oxygen species such as superoxide anion (O_2^-), hydroxyl radical ($OH\bullet$) and singlet oxygen ($^1O_2$). Singlet oxygen is extremely aggressive and is considered to be the main promoter of the destructive effects of PDT at cellular level. The action of the reactive oxygen species determines –in addition to the induction of apoptosis and autophagy through incompletely elucidated mechanisms- the removal of the tumor cells (1).

The antitumoral effect of PDT is used in numerous medical applications in urology, gynaecology, ENT and ophthalmology; it can also be successfully used for the treatment of malignant or premalignant lesions of the oral cavity, as well as for the therapy of various dermato-oncologic disorders (2).

Cutaneous squamous cell carcinoma in situ

Bowen's disease (cutaneous squamous cell carcinoma *in situ*) is a cutaneous premalignant condition, more frequently encountered in elderly patients. Exposure to UV radiation, ionizing radiation and arsenic are incriminated in its appearance. Immunosuppression, as well as HPV viral infection, play a major role in the emergence of the disorder.

Bowen's disease appears clinically as an usually unique erithematous squamous plaque that varies in size from a few mm to a couple of cm, sharply marginated, with a polycyclic border (fig.1). In the uncommon

eventuality of coexistence of multiple lesions, extensive investigations are imposed in order to highlight the exposure to various carcinogens. The plaques in Bowen's disease may present a slow, centrifugal extension; several scarring areas or an apparent central involution field can be noticed at the surface of the lesions. The removal of the squamo-crust reveals a moist, exsudative, papillomatous area. The condition is asymptomatic, and only rarely may be accompanied by pruritus. It can appear both on photo exposed areas (upper limb, cephalic extremity) and on unexposed to radiation areas (inguinal and genital regions). The co-occurrence of indurate, nodular lesions, of erosions and ulcerations, of very thick scales on the surface of the plaques or the growth in dimensions could indicate transformation into invasive squamous cell carcinoma (SCC). The cumulative risk of transforming into invasive SCC is 3-5%; SCC lesions emerged on Bowen's disease plaques are very aggressive, 13% of cases evolving towards the development of metastasis and an unfavorable prognosis (3).

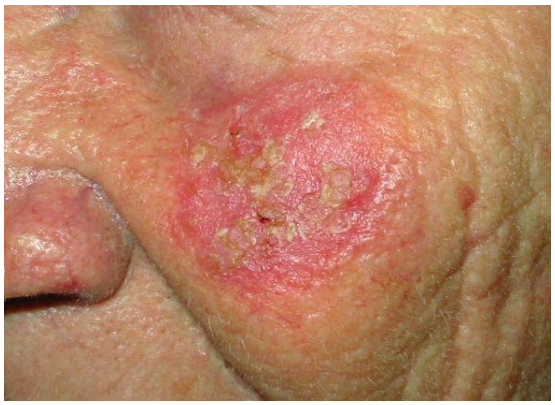


Fig. 1 –Clinical features of Bowen's disease: unique erythematous plaque, well-defined borders, polycyclic margins, partially covered by yellowish scales, on left malar region of a 73 years-old female patient

Histopathologically, Bowen's disease lesions present hyperkeratosis and diffuse paraketatosis extending in the squamous layer above the cutaneous appendages, acanthosis with elongated, thickened interpapillary ridges, sometimes to the point whereon dermal papillae are reduced to a filiform appearance; the squamous layer appears cluttered, with atypical and dyskeratotic cells, multinucleated keratinocytes and horn pearls, but the basal membrane remains intact (fig.2). In the upper dermis, a moderate inflammatory infiltrate consisting of lymphocytes, histiocytes and plasmocytes is usually identified (3).

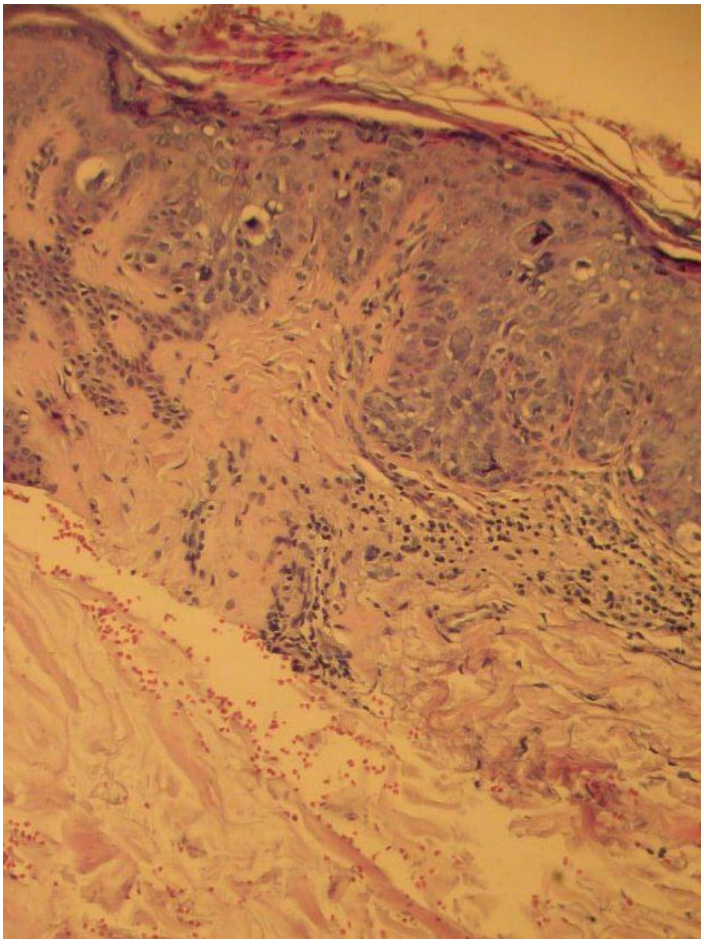


Fig. 2-Microscopic aspect in Bowen's disease (squamous cell carcinoma in situ)-hematoxylin-eozin stained skin specimen, 20X – hyperkeratosis, parakeratosis in stratum corneum, widened rete ridges, thinned dermal papillae; dezorganised squamous layer of epidermis, with numerous crowded atypical keratinocytes and dyskeratotic cells; intact basal membrane; moderate inflammatory infiltrate in upper dermis

The treatment must be individualized based on the type and location of the lesion; one can chose from a large variety of therapeutic approaches, such as surgical excision with a safety margin, Mohs micrographic surgery, electrodessication, curettage, cryotherapy, topical trichloro-acetic acid or 5-fluorouracil (twice a day for 4-6 weeks), imiquimod 5% daily for 6 weeks, laser ablation or radiotherapy (40-60 Gy daily divided over 15-20 sessions). During the last years, ALA photodynamic therapy (ALA-PDT) has been successfully used for the treatment of Bowen's disease; we shall discuss the benefits of the procedure as following.

ALA-PDT in the treatment of Bowen's disease

Most studies performed in the field of Bowen's disease treatment by ALA-PDT therapy employ 20% topically applied ALA. Generally, for activating ALA, red light (λ=630 nm) is used. Even so, some studies use sources which emit light with other wavelengths. A study published in 2000 randomized a group of patients presenting 61 Bowen's disease lesions between red light (λ=630+/-15 nm, n=32 patients) ALA-PDT and green light (λ=540 nm, n=29 patients) ALA-PDT, and achieved complete remission in 94%, respectively 72% of cases (4).

A study performed by Varna et al., involving 88 patients presenting a total of 239 various tumor lesions, including cases of Bowen's disease, superficial basal cell carcinoma and actinic keratosis, treated with

PDT using topically applied ALA 4 hours before irradiation (640 nm, fluence rates 105 J/cm^2) in 2 successive sessions proved complete remission rates stratified on each of the cutaneous pathologies of 88%, 95% and 99% respectively; twelve months after the procedure, complete remission was maintained in 69% of the cases of Bowen's disease included in the study (5).

Wennberg et al. obtained a 61% complete remission rate at 6 months after red light (620-670 nm) ALA-PDT at fluence rates of 75 and 100 J/cm^2, applied on a group of 5 patients presenting 18 Bowen's disease plaques (6). Cairnduff et al. also have obtained very good results in the treatment of Bowen's disease using ALA-PDT, reporting complete remissions maintained for at least 18 months in 89% of the 36 lesions subjected to treatment in their study (7).

Wong et al. proved that red light ALA-PDT (λ=630nm) is also effective in Bowen's disease of the finger, leaving no scarring or residual loss of finger function (8). Usmani et al. reported in 2005 a case of subungual Bowen's disease successfully treated with ALA-PDT administered as two treatment sessions 4 weeks apart, without recurrence of lesions over a period of post-therapeutic follow-up of 3 years and, moreover, with total preservation of the nail unit (9).

PDT using 20% ALA combined with 2% EDTA for iron chelation (procedure proved to enhance protoporphyrine IX accumulation in tumor lesions) and 2% DMSO (to improve ALA penetrance) was reported as effective for the treatment of penile Bowen's disease (10).

A study conducted by Salim et al. on a group of 40 patients randomized between ALA-PDT (λ=630 nm, fluence rate of 100 J/cm^2) and topical treatment using 5-fluorouracil (5-FU) applied locally for 4 weeks showed post-treatment complete remission rates of 88%, respectively 67%, proving that ALA-PDT is more efficient in the treatment of Bowen's disease than topical 5-FU treatment (11).

Morton et al. compared, in a randomized study, the efficiency of ALA-PDT (ALA applied under occlusive dressing 4 hours before illumination with xenon arc lamp at a fluence rate of 125 J/cm^2 and an irradiance of 70mW/cm^2) with liquid nitrogen cryotherapy (-196°C), on 40 patients with Bowen's disease, and concluded that ALA-PDT is superior to cryotherapy when it comes to both efficiency (complete remission rate in 75% of the cases treated by ALA-PDT, as compared to 50% for cryotherapy) and safety (ALA-PDT did not lead to the appearance of ulcerations or infections, adverse reactions which could be commonly observed in patients treated with cryotherapy) (12).

Photodynamic therapy followed by local radiotherapy (topical ALA 20%, 630 nm, 50 J/cm^2 repeated every 2-3 days up to 4 sessions followed by local radiotherapy of 3 Gy dose) has proved a higher efficiency than ALA-PDT alone, with a considerable decrease in the post-treatment reoccurrence rate (13).

The degree of satisfaction among patients who were administered ALA-PDT for the treatment of Bowen's disease is high, as more than 90% of the patients having been subjected to the procedure consider the treatment very effective and easy to tolerate, as asserted by a study which interrogated 95 patients exposed to ALA-PDT for Bowen's disease between 2000 and 2008; the adverse reactions of the therapy were graded by the patients as minor and predictable; of these, most commonly encountered were burning sensations during the therapy -acknowledged by 21% of the patients subjeceted to ALA-PDT-and the appearance of crusts, in 14% of them (14).

CONCLUSIONS

ALA-PDT is a therapeutic method that offers excellent healing rates in all applications in the treatment of Bowen's disease, including those in particular topographic areas such as the genital area or the digits, areas where conventional surgical procedures are difficult to perform, as local particularities require very economic tissue resections. The procedure is associated with low disease recurrence rates and very good aesthetic outcomes; adverse reactions are minimal, ALA-PDT usually being very well tolerated by patients. The method effectiveness is higher than that of cryotherapy or local treatment using cytotoxic drugs like 5-fluorouracil, a fact that assures ALA-PDT an important role in the management of Bowen's disease patients.

REFERENCES

(1) Ion, R.M., Porfirinele si terapia fotodinamica a cancerului, Editura Stiintifica FMR, 2003, ISBN: 973-8151-13-9

(2) Tsai JC, Chiang CP, Chen HM, Huang SB, Wang CW, Lee MI et al. Photodynamic Therapy of oral dysplasia with topical 5-aminolevulinic acid and light-emitting diode array. Lasers Surg Med 2004; 34(1):18-24.

(3) Duncan K, Geisse J, Leffell DJ-Epithelial Precancerous lesions, In: Wolff K, Goldsmith LA, Katz SI, et al., eds.: Fitzpatrick's Dermatology in General Medicine. 7th ed. New York, NY: McGraw-Hill , 2008, pp 1022-23.

(4) Morton CA, Whitehurst C, Moore JV, MacKie RM. Comparison of red and green light in the treatment of Bowen's disease by photodynamic therapy. Br J Dermatol 2000; 143(4):767-772.

(5) Varma S, Wilson H, Kurwa HA, Gambles B, Charman C, Pearse AD et al. Bowen's disease, solar keratoses and superficial basal cell carcinomas treated by photodynamic therapy using a large-field incoherent light source. Br J Dermatol 2001; 144(3):567-574.

(6) Wennberg AM, Lindholm LE, Alpsten M, Larko O. Treatment of superficial basal cell carcinomas using topically applied delta-aminolaevulinic acid and a filtered xenon lamp. Arch Dermatol Res 1996; 288(10):561-564.

(7) Cairnduff F, Stringer MR, Hudson EJ, Ash DV, Brown SB. Superficial photodynamic therapy with topical 5-aminolaevulinic acid for superficial primary and secondary skin cancer. Br J Cancer 1994; 69(3):605-608.

(8) Wong TW, Sheu HM, Lee JY, Fletcher RJ. Photodynamic therapy for Bowen's disease (squamous cell carcinoma in situ) of the digit. Dermatol Surg 2001; 27(5):452-456.

(9) Usmani N, Stables GI, Telfer NR, Stringer MR. Subungual Bowen's disease treated by topical aminolevulinic acid-photodynamic therapy. J Am Acad Dermatol 2005; 53(5 Suppl 1):S273-S276.

(10) Harth Y, Hirshowitz B, Kaplan B. Modified topical photodynamic therapy of superficial skin tumors, utilizing aminolevulinic acid, penetration enhancers, red light, and hyperthermia. Dermatol Surg 1998; 24(7):723-726.

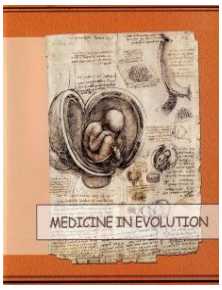
(11) Salim A, Leman JA, McColl JH, Chapman R, Morton CA. Randomized comparison of photodynamic therapy with topical 5-fluorouracil in Bowen's disease. Br J Dermatol 2003; 148(3):539-543.

(12) Morton CA, Whitehurst C, Moseley H, McColl JH, Moore JV, MacKie RM. Comparison of photodynamic therapy with cryotherapy in the treatment of Bowen's disease. Br J Dermatol 1996; 135(5):766-771.

(13) Nakano A, Watanabe D, Akita Y, Kawamura T, Tamada Y, Matsumoto Y. Treatment efficiency of combining photodynamic therapy and ionizing radiation for Bowen's disease. J Eur Acad Dermatol Venereol 2011; 25(4):475-478.

(14) Hu A, Moore C, Yu E, Mount G, Jordan K, Vujovic O et al. Evaluation of patient-perceived satisfaction with photodynamic therapy for Bowen disease. J Otolaryngol Head Neck Surg 2010; 39(6):688-696.

LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PAROXISMAL ATRIAL FIBRILLATION PATIENTS WITHOUT STRUCTURAL CARDIAC DIDEASE, WITH AND WITHOUT ARTERIAL HYPERTENSION



I. GYALAI[1,2], M. TOMESCU[1,2], O. ANCUȘA[1,2]

[1]University of Medicine and Pharmacy "Victor Babes" Timisoara
[2]City University Emergency Hospital, Cardiology Department, Timișoara

ABSTRACT

Introduction: *Paroxysmal atrial fibrillation (PAF) and arterial hypertension lead to diastolic dysfunction and atrial dilatation. In our study we measured the diameters and the area of the left atrium in patients with and without PAF, both in hypertensive and non-hypertensive patients.*

Material and method: *The echocardiography was performed in standard views; the Doppler study was recorded on tape or compact disc, at a speed of 50 and 100 mm/second. All the standard echocardiographic measurements, the interventricular septum thickness, the telediastolic diameter and the ejection fraction were perform in all patients. We studied the following echocardiographic parameters: left atrial (LA) dimensions – maximal, end-systolic, before mitral valve (MV) opening; LA length – parasternal long axis M mode (La d) ; LA transversal length – apical, 4 chamber 2D (La t); LA longitudinal – apical, 4 chamber 2D (La l); LA surface – apical, 4 chamber 2D (La s) ; Maximum E and A wave velocity in pulsed Doppler at MV apex; E/A ratio; E wave deceleration time (TDE). We studied 96 patients (pts) which we divided in two groups: the first group (47 pts) with normal value of the blood pressure and the second group (49 pts) with hypertension. Each of these groups we divided once more in pts with and without PAF. Group I (non- hypertensive) had 47 pts from whom 23 pts had PAF and group II (hypertensive) had 49 from whom 24 pts had PAF.*

Results*: The groups were homogeneous and they didn't have any significant differences regarding age, weight, height and blood pressure values. In group I (non-hypertensive) and without PAF the diameters are: LA d (mm)=36,88±4,41; LA l (mm)=47,36±5,55; La t (mm)=37,83±4,67; LAs (cm2)=15,84±3,36; in group I (non-hypertensive) and PAF the diameters are: LA d (mm)=40,57±3,28; LA l (mm)=51,40±2,48; LA t (mm)=41,02±4,21; LA s (cm2)=19.15±3,32. In group I the differences were statically significant: LA d (p=0,002), LA l(p=0,003), LA t(p=0,018), LA s(p=0.001). In group II (hypertensive) without PAF: LA d (mm)=38,75±3,68; LA l (mm)=52,47±6,64; LA t (mm)=39,15±5,09; LA s (cm2)=17,63±4,18 and in group II (hypertensive) with PAF: LA d (mm)=44,13±3,29; LA l (mm)=58,59±5,81; LA t (mm)=43,40±5,18; LA s (cm2)=23.51±4.88. In group II the differences were statistically significant: LA d (p=0,001), LA l(p=0,001), LA t(p=0,005), LA s (p=0.001). PAF pts presented significantly alterated diastolic dysfunction (DD) parameters in comparation with non-PAF pts. In non-PAF pts 20% had DD and in PAF pts 48% had grade 1 DD and 22% grade 2 DD. In hypertensive pts DD had a higher incidence if the pts had PAF. Hypertensive pts non-PAF had 48% DD grade 1 and 16 % grade 2; hypertensive pts with PAF had 18% DD grade 1 and 12,5% grade 2. There were not included pts with DD grade 3. TDE is statistically significant in hypertensive pts (p=0.05)and in non-hypertensive pts is almost significant (p=0.056).*

Conclusions: *Our study showed that PAF and hypertension lead to DD and atrial dilatation. In PAF pts the diameters and the area of the left atrium are bigger than in non-PAF pts. This trend is maintained in hypertensive pts too, where the same diameters and area of the left atrium is bigger in PAF pts than in non-PAF pts.*

Key words: *Paroxysmal atrial fibrillation, diastolic dysfunction, arterial hypertension*

Correspondence to

Dr. I. Gyalai,
Cardiology Department, City Hospital,
Bv. Revolutiei din 1989 Timișoara, Timiș,
e-mail: dgyalai@yahoo.com,
tel.: 0723251856.

INTRODUCTION

Acute and chronic atrial dilatation, atrial conduction and high filling pressure have an important role in atrial fibrillation (AF) physiopathology (1,2,3). Recent studies showed that hypertension is a major factor in pulmonary veins atrialization with a great impact in paroxysmal atrial fibrillation (PAF) etiology (4). Although atrial dilatation, diastolic and left atrial function were not studied enough, especially in comparison. There were only a few studies regarding PAF and diastolic pressure elevation in hypertensive patients (pts). The aim of the study is to compare, in groups of pts., left atrial remodeling and diastolic dysfunction in pts. with and without PAF, hypertensive or non-hypertensive.

MATERIALS AND METHOD

The patients were included in the study if they meet the following criteria:
-hypertensive pts. with PAF, symptomatic or asymptomatic
-non-hypertensive pts. with PAF

The PAF was documented, in both cases, by 12 lead ECG or by 24 hour ECG Holter.

The exclusion criteria were: evident structural heart disease, excluding left ventricular hypertrophy (LVH), moderate or severe mitral regurgitation, aortic regurgitation, coronary heart disease (CHD) and severe comorbidities. Patients with severe or secondary HTA were excluded from this study. The control group consisted of normal patients. We studied hypertensive patients without PAF as control group for the hypertensive patients with PAF to match these groups as closely as possible mainly by age and weight.

The exclusion criteria for the control group: documented PAF (included by programmed stimulation), structural heart disease, moderate or severe mitral regurgitation, CHD and severe co morbidities. We also excluded normotensive subjects with echocardiographic LVH signs., On first visit, we rule out structural heart disease by history, physical examination, 12 lead ecg, X-ray and transthoracic echocardiography. CHD was excluded by monitoring the risk factors, symptoms, exercise test or angiography if it was considered necessary.

Study protocol – echocardiographic measurements

We use two echo machines (HP Sonos 5500 and Sono ACE 9900 Hrety Tehnic). The echocardiography was performed in standard views; the Doppler study was recorded on tape or compact disc, at a speed of 50 and 100 mm/second. All the standard echocardiographic measurements, the interventricular septum thickness, the telediastolic diameter and the ejection fraction were perform in all patients (5).

We studied the following echocardiographic parameters: left atrial (LA) dimensions – maximal, end-systolic, before mitral valve (MV) opening;
-LA length – parasternal long axis M mode (La d)
-LA transversal length – apical, 4 chamber 2D (La t)
-LA longitudinal – apical, 4 chamber 2D (La l)
-LA surface – apical, 4 chamber 2D (La s}
-Maximum E and A wave velocity in pulsed Doppler at MV apex
-E/A ratio
-E wave deceleration time (TDE)

Diastolic dysfunction (DD) was quantify in different grades, in each patient, according to the general and validated criteria (11) (Table 1).

Table 1 - general and validated criteria

	Normal diastolic function	DIASTOLIC DYSFUNCTION		
		1	2	3
TDE (ms)	160-240	>240	160-200	<160
E/A	1-2	<1	1-1.5	>1.5
TRIV (ms)	70-90	>90	<90	<70

For the patients who did not meet the criteria for the diastolic dysfunction while using the specified parameters, additional criteria were used, such as the Valsalva maneuver at which the E/A ratio from the diastolic dysfunction (grade 2-pseudonormal) becomes sub unitary and the duration of wave A is smaller than the duration of wave A of pulmonary veins, being a favorable criteria for the grade 2 diastolic dysfunction; however these have not been used as parameters for all of the pts, which is why they will not be presented in the results.

Statistical analysis

The data was compared using "t-test" for the continual variables, all the results being expressed in average values ± standard deviation (SD) and the correlation between the measurements was made using the simple regression analysis. The statistical analysis was made using the Stat View 6.0 (SAS Institute USA) software.

RESULTS

General characteristics of patients

We studied 96 pts. whom were divided in two groups: the first group (47 pts) with normal value of the blood pressure and the second group (49 pts) with hypertension. In both groups there were differentiated patients with and without PAF.

-group I (non-hypertensive) with 47 pts from whom 23 pts exhibited PAF

-group II (hypertensive) with 49 pts from whom 24 pts exhibited PAF.

Clinical and basic echocardiography data are presented in table 2 and Table 3.

Table 2 - Clinical and basic echocardiography data for group I

Non–hypertensive pts (n=47)	**Non PAF pts (n=24)**	**PAF pts (n=23)**	**P**
age	42,33±9,77	49,30±14,19	0,055
weight (kg)	67,33±13,10	68,48±7,89	0,720
height (cm)	170,04±7,79	168,00±7,26	0,358
systolic (mmHg)	118±11	114±16	0.09
diastolic (mmHg)	71± 7	70±8	0,650
LV EF %	63±9	60±11	0,311

Table 3 - Clinical and basic echocardiography data for group II

Hypertensive pts (n=49)	**Non PAF pts (n=25)**	**PAF pts (n=24)**	**P**
age	47,72±15,72	53,33±8,60	0,130
weight (kg)	77,40±11,01	72,92±8,30	0,115
height (cm)	169,00±7,16	168,29±8,23	0,749
systolic (mmHg)	158±11	159±16	0,799
diastolic (mmHg)	98.5± 9	102±10	0,204
LV EF %	56±9	59±11	0,301

Table 2 and 3: clinical and echocardiography data: systolic= systolic blood pressure; Diastolic = diastolic blood pressure; LV EF= left ventricular ejection fraction

Echocardiography results: atrial dilatation

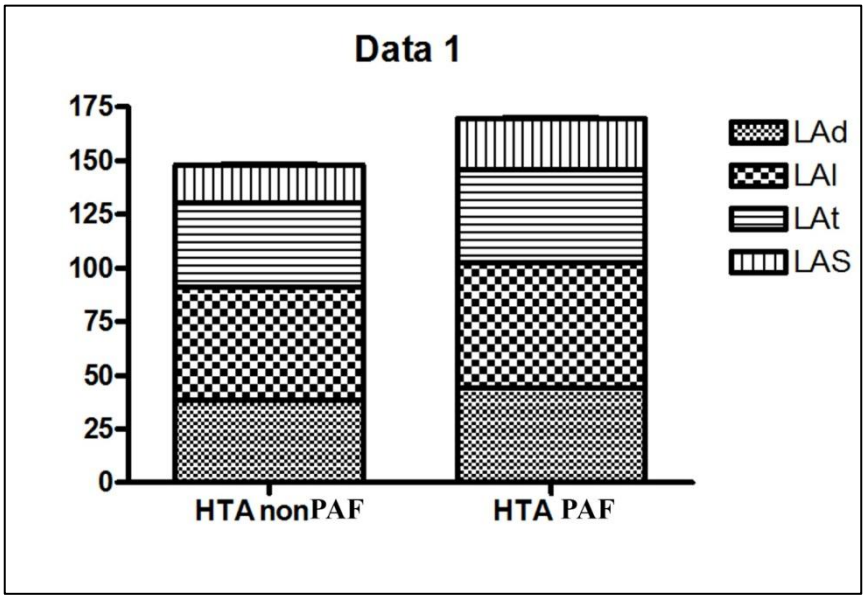
Table 4 - Echocardiography results: atrial dilatation – group I

Non -hypertensive pts (n=47)	**LA d (mm)**	**LA l (mm)**	**LA t (mm)**	**LA s (cm^2)**
non PAF (24 pts)	36,88±4,41	47,36±5,55	37,83±4,67	15,84±3,36
PAF (23 pts)	40,57±3,28	51,40±2,48	41,02±4,21	19.15±3,32
P	0,002	0,003	0,018	0.001

Table 5 - Echocardiography results: atrial dilatation – group II

Hypertensive pts (n=49)	**LA d***	**LA l****	**LA t**	**LA s***
non PAF (25 pts)	38,75±3,68	52,47±6,64	39,15±5,09	17,63±4,18
PAF (24 pts)	44,13±3,29	58,59±5,81	43,40±5,18	23.51±4.88
p	0.001	0.001	0.005	0.001

Figure 1 - Multivariable analysis: LA d vs LA s:p<0,05, LA l vs LA s: p<0,01 , LA t vs LA s:p<0,05



Echocardiography results: diastolic dysfunction

Patients with PAF had significant alterations of DD parameters, compared to patients without PAF: 20% of normal patients presented DD unlike 48% - grade 1 and 22% - grade 2 from the pts with PAF.

Also, in the hypertensive group, DD is significantly more remarkable if patients have PAF: 48% of the pts with HTA have DD grade 1 and 16% grade 2 unlike 18% grade 1 and 12,5% grade 2 at hypertensive pts with PAF. Patients with DD grade 3 were not included.

Table 6 - The data is presented in absolute values (number of pts) and percentage:

GRADE Diastolic dysfunction	**N**		**1**		**2**	
	Nr	*%*	**Nr**	*%*	**Nr**	*%*
N (24 pts)	**20**	*80*	**4**	*20*	**0**	*0*
AF (23 pts)	**7**	*30*	**11**	*48*	**5**	*22*
Hypertensive (25 pts)	**9**	*36*	**12**	*48*	**4**	*16*
Hypertensive PAF (24 pts)	**3**	*12,5*	**18**	*75*	**3**	*12,5*

Using TDE it can be observed that this parameter is statistically significant only at the group of pts. with hypertension, while mentioning that in non-hypertensive pts. it almost reaches the statistical value.

Table 7 – TDE findings

	Non-hypertensive pts (n=47)		**Hypertensive pts (n=49)**	
	non PAF (24 pts)	PAF (23 pts)	non PAF (25 pts)	PAF (24 pts)
TDE	211,54±25,48	228,04±31,86	225,72±28,38	241,63±26,87
p	**0,056**		**0,050**	

The detailed results, in groups, show that the absolute value of atrial dilatation and diastolic dysfunction in hypertensive pts. with PAF are more statistically significant than in other groups.

DISCUSION

The study demonstrates the appearance of diastolic dysfunction at studied pts. and it shows the presence of atrial remodeling at pts. with PAF and hypertension, thus proving the existence of structural modifications at these pts. The subgroup analysis shows that DD at pts. with PAF is significantly higher than at pts. in the control group without PAF. This trend is also maintained at group II, that of hypertensive pts. objectivity being kept through the measurements of the diameters and atrial area; diameters are statistically significant at both groups. The left atrium area was statistically significant at both groups. TDE is statistically significant only at group II. Comparing Las in non-hypertensive pts. with PAF and hypertensive pts. without PAF, we can note that it is not statistically significant (p=0,127). Recent data has showed that high intra-atrial pressure, at healthy patients, provides conditions for outbreaks of PAF (6). In that study the dysfunction of the left ventricle was associated with high values of the inferosuperior dimension of the left atrium in primary PAF, as it was also determined in our study.

The cause and effect relationship, between DD and atrial dilatation, is a subject in discussion at patients with PAF, while the atrial dilatation at hypertensive patients is consecutive to the diastolic dysfunction and the growth of filling pressure. The acute and chronic extensions alter the microarchitecture of the normal atrium, generating conditions for "trigger" like activity or for arrhythmogenic electrical dispersion (1). In medical literature it is showed that hypertension and hypertensive cardiopathy are associated with the growth of pulmonary veins diameter (8,10), so the left atrial dilatation was associated with the expansion of the pulmonary veins diameter. In hypertensive pts. especially with left ventricular hypertrophy, the pulmonary vein diameter was bigger than in pts. with PAF without hypertension. In hypertensive pts. the diameter of the pulmonary vein was bigger than in non-hypertensive pts. same with chronic atrial fibrillation and PAF pts. The masculine gender, hypertension and chronic atrial fibrillation have proven to be

independent factors in the growth of pulmonary veins diameter. In our study the pulmonary vein was not measured. Pulmonary vein dilatation as a possible arhytmogenic factor was also debated in other studies (9), Knackstedt & colab. demonstrated that Lad and Lav values were significantly higher than in baseline patients, associated with more severe diseases like persistent and chronic atrial fibrillation.

LIMITATION

The small number of patients was the main limitation of this study. Also patients with DD grade 3 were not included, however the studied groups were homogenized. The exclusion of persistent atrial fibrillation patients could be the explanation for the lack of patients with severe DD.

CONCLUSION

Our study showed that PAF and hypertension lead to diastolic dysfunction and atrial dilatation. In patients with PAF the diameters and area of the left atrium are bigger than in patients without PAF. This tendency is also maintained in hypertensive patients where the area and diameters of the left atrium are bigger in those with PAF than in those without PAF.

REFERENCES

1.Allessie MA, Boyden PA, Camm J, Kleber A, Lab M, Legato M et al Pathophysiology and prevention of atrial fibrillation Circulation 2001;103:769-777

2. Kannel WB, Wolf PA, Benjamin EJ, et al. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol. 1998;82:2N–9N.

3. Schotten U, Neuberger HR, Allessie MA. The role of atrial dilatation in the domestication of atrial fibrillation. Prog Biophys Mol Biol. 2003 May;82(1-3):151-62.

4. Benght Herweg, Hypertension and hzpertensive heart disease…, J Cardiovasc Electrophysiol, vol 16,pp2-5,ian 2005

5. American Society of Echocardiography Committee onStandards. Recommendations for quantitation of the left ventricleby two-dimensional echocardiography. J Am Soc Echocardiogr1989;2:358-87.

6. Kalifa J, Jalife J, Zaitsev AV, Bagwe S, Warren M, Moreno J et al Intra-atrial pressure increases rate and organization of waves emanating from the superior pulmonary veins during atrial fibrillation. Circulation. 2003 Aug 12;108(6):668-71. Epub 2003 Aug 04

7. Jais P, Peng JT, Shah DC, Garrigue S, Hocini M, Yamane T, Haissaguerre M, Barold SS, Roudaut R, Clementy J. Left ventricular diastolic dysfunction in patients with so-called lone atrial fibrillation. J Cardiovasc Electrophysiol. 2000 Jun;11(6):623-5.

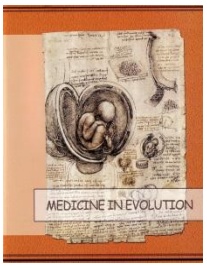
8. Yamane T, Shah DC, Jais P, Hocini M, Peng JT, Deisenhofer I, Clementy J, Haissaguerre M. Dilatation as a marker of pulmonary veins initiating atrial fibrillation.
J Interv Card Electrophysiol. 2002 Jul; 6(3):245-9.

9. Knackstedt C, Visser L, Plisiene J, Zarse M, Waldmann M, Mischke K, Koch KC, Hoffmann R, Franke A, Hanrath P, Schauerte P. Dilatation of the pulmonary veins in atrial fibrillation: a transesophageal echocardiographic evaluation. Pacing Clin Electrophysiol. 2003 Jun; 26(6):1371-8.

10.Bengt Herweg, M.D., Tina Sichrovskz, M.D., Leo Polosajian, M.D., Anna Rozenshtein, M.D., and Jonathan S. Steinberg, M.D. Hypertension and Hypertensive Heart Disease Are Associated with Increased Ostial Pulmonary Vein Diameter. Cardiovasc Electrophysiol, Voi. 16, pp. 2-5, January 2005.

11. Derek G Gibson, Darrel P Francis, Clinical Assessment Of Left Ventricular Diastolic Function Heart 2003;89:231–238.

COMMON AND PROFFESIONAL LANGUAGE IN ORAL HEALTH EDUCATION



LOREDANA DUMITRAȘCU[1], MIHAELA ADINA DUMITRACHE[1], CRISTIAN COMES[2], IRINA DONCIU[3] RUXANDRA MORARU [4]

[1] University of Medicine and Pharmacy "Carol Davila ", Department of Oral Health and Behavioral Sciences, Faculty of Dentistry, Bucharest
[2] University of Medicine and Pharmacy "Carol Davila ", Faculty of Dentistry, Department of Oro-dental Diagnosis, Ergonomy and Scientific Research Metodology, Bucharest
[3] University of Medicine and Pharmacy "Carol Davila ", Faculty of Dentistry ,Department of Prosthetic Technology and Dental Matherials, Bucharest
[4] Barts & The London School of Medicine and Dentistry, Adult Oral Health Department, Queen Mary University of London, UK

ABSTRACT

The mass-media use for dental education is justified by their impact in building or changing attitudes and behaviors and by the important number of the receptors. In order the communication process to be successful, the source's language must be designed in a way that receptor (the public, the patient) to understand it. The present study consider the eficiency of a radio feature about dental medicine in transmiting information to the listeners. The study demonstrate that professional language without any explanation is followed by confusions and imposibility of receive or accept the health information.

Key words: *health, radio, show, education, mass-media*

Correspondence to

Dr. Loredana Dumitrascu,
Department of Oral Health and Behavioral Sciences,
Faculty of Dentistry, "Carol Davila " University of Medicine and Pharmacy, Bucharest
Str. Eforie nr. 4-6, Bucuresti, sector 5 UMF "Carol Davila " Bucuresti

Tel: 0755032986

email: lore.dumitrascu@gmail.com

INTRODUCTION

Mass media have become a constant presence in various sectors of social life, trasmitting information and making connections between people, places, ideas and events to which otherwise we would not have access. Therefore, since the '40s, has been questioned of "social responsibility of the press". Press Freedom Commission Report (Commision on Freedom of Press) since 1947 highlighted four functions of mass media in democracy system: information dissemination, resulting incresing the level of knowledge among the population; interpretation of facts, leading to crystallization own opinion, expression events and critical opinions or reporting them, which leads to increased adaptability of the public[1].

This classification actually enriches Harold Lasswell's approach, who said that the press has three major functions: surveillance by covering world events, the interpretation of these events and to facilitate the social integration of the individual[2]. Subsequently, other researchers (Walter Lippmann, Paul Lazarsfeld, Denis McQuail) added other roles already defined, but critics have brought debate on the issues and methods of organizing reality. We emphasize the statement of Walter Lippman, who believes that education is the primary means by which man can acquire the skills to investigate the sources of information and to find possible errors[3]. In this paper we will focus on the importance of using mass media to meet in a democratic society, the public's right to information and to constantly correct interpretation of this information.

Oro-dental health education made through mass media has the advantage that it addresses a large number of recipients. Addressing a large audience, the message must meet educational needs, to meet curiosity. Furthermore, studies conducted on the public radio show that mass communication effects are cumulative and are visible on a long-term basis[4], so any health education program for oro-denatal health through the media should be planned with continuity over time.

The communication includes a transmitter, a message, a channel, a receiver, a transmitter and receiver relationship, an effect and sometimes even a purpose of communication[5]. The proper behavior coding assumes that the message is translated by the physician in a language (or code) that can be understood (decoded, re-translated) by the receptor - the patient. Feedback is essential to adjust communication processes. Because the message is unidirectional media, without the possibility of instant feedback, a particular attention must be granted to the used code. Quality of an act of communication mostly depends on the pertinent code used to be adapted to the nature of the information provided, the purpose of communication and the characteristics of the target audience[6]. Optimal code is one that allows the understanding of the message and it must be tailored for the receiver. "Scientific language, unlike ordinary language, expresses the need of accuracy in communication"[7]. However, any scientist must define their terms or language closer to current conventions.

To analyze how the proper message reaches the audience, we analyzed Stuart Hall's model[8], put in connection with television, but possibly extended to other environments. The message is represented on the choice of transmitter (in our case, the physician) and is organized in signs and symbols specific to the culture to which it belongs. The message is so constructed that serves to guide the public to certain ideas, beliefs, points of view (in our case, about oro-dental health). On the other hand, the audience (listeners, patients) often resist this approach and interpret information in terms of their own experience and culture of belonging. So Stuart Hall's theory says that the meaning of a message sent does not always correspond with what the receivers understand, despite the common language systems.

The educational approach through the media can appear different communication barriers that prevent achieving the goal. In the communication process, a barrier is anything that reduces the fidelity and efficiency of message transfer[9]. In the present study we approached the barriers of language, that are to be avoided when spreading the message to achieve and proper behavior. This category includes situations where the same words have different meanings for transmitter and receiver (eg, the term "board" means "microbial plaque" for physician-emitter and "hip replacement mobile" receiver). Language barriers may result from differences in training and practical experience, but also the emotional state of the participants in the communication. Confusing words and phrases must be avoided in speech. Also preconceived

ideas about a topic (see conceptions of fluoride toxicity induced by the Romanian press a few years ago) may represent obstacles in the acceptance message.

MATERIALS AND METHODS

Between 2001 and 2005 we conducted a weekly radio broadcast feature in the dental field, "Periuta de dinti" (The toothbrush), at "Voice of Hope" in Bucharest (94.2 FM). The editor was a dentist and a graduate of a Journalism Postgraduate Course. Themes were planned and then written, recorded and processed.

Each feature had a duration of three to five minutes and addressed a single subject, using common language or explaining scientific terms used. For threads that have allowed this were also used sound effects (eg, the sound of water flowing, the electric toothbrush or rotary instruments in the cabinet).

At the end of the study, we designed a self-administered questionnaire and we mailed it to a number of 80 subjects, whose contacts were in a database that we made from weekly contests winners at the end of feature. The mailed envelope contained a questionnaire, a letter requesting cooperation in the study, stating the scientific purpose and the anonymity of participation in the research, and how to fill in the questionnaire and a self-addressed stamped envelope for reply. In the next two days after sending the letters, I talked on the phone with each of the 80 listeners in the database, presenting myself and asking their help for this study.

Subjects were asked to answer a questionnaire consisting of 26 items representing 13 topics, each made in two ways: using common language and using specialty terms. Statements included the following themes: prevention of dental caries, periodontal disease prevention, prevention of dento-maxillary and anxiety towards dental treatment.

The study aimed to check the way the message, encoded by the physician in the programs was received and decoded by the receiver (listener), testing the knowledge acquired and the level of understanding of oral health concepts transmitted by the media (radio), to identify the level of understanding of the message stated in scientific language and in common language, identifying and removing barriers in communication through radio and the control over the response to the health behavior message.

Of the 80 subjects interviewed, 49 responded. Mail response rate is very high (61%) and is due on the one hand, to the stamped envelope attachment response and, on the other hand, to the individual telephone approach to all subjects after sending letters and request support for research protocols. To this response rate helped the fact that radio "Vocea Sperantei" (Voice of Hope) is a niche radio, specifically religious, non-commercial, benefiting from a stable audience, turned loyal over time.

Each set of two statements which addressed the same subject was given a code, the data being statistically analyzed using SPSS. The codes 1 to 4 for each question were observed, in the same sequence (1 = "disagree", 2 = "partially agree", 3 = "agree", 4 = "strongly agree"). We conducted descriptive statistics, aiming for each set of items, the distribution of scores 3 and 4 ("agree" and "strongly agree"), these certifying that listeners have acquired knowledge about topics.

We also observed the number of pairs of responses 1-4 in sets of statements ("disagree" and "strongly agree"), which indicate confusion between the concepts presented in technical terms and common language. However, statistical analysis was done to correlate the studied sets of statements expressed by Spearman's correlation coefficient. We did not used analysis using Pearson coefficient, because the variables do not have a distribution depending on the normal curve.

RESULTS AND DISCUSSION

Respondents were aged between 21 and 80 years, With a higher proportion of females (86%). Study participants were at a rate of 46%, employed persons and 54% retired. More than half of survey participants had secondary education and only 9% were primary school graduates (Figure 1.). Statements which addressed the same topic, one in scientific language and the other in the common language, were grouped and analyzed in parallel.

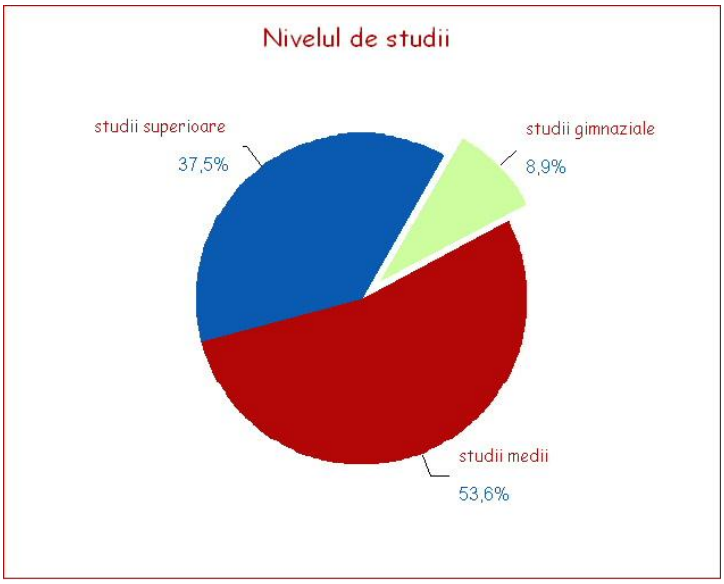


Fig. 1. Distribution of subjects according to education (N = 49)

The first set of allegations (1 and 25) refers to bleeding gums when brushed. Statement 1 uses common language, "gum disease vessels" and statement 25 specialized language and "gum capillary fragility." We noticed, in both forms of questions about gum disease, the large number of responses type 3 (41% and 35%) and 4 (47% and 33%), meaning that respondents know the subject. We identified only 4 pairs of answers 1 to 4, indicating confusion as to the manner of expression. Spearman coefficient is not statistically significant.

Allegations 2 and 16 approach dental anxiety topic in specialized language and common language. We observed a lack of correlation between responses and a small percentage of responses 3 and 4, the most common, but to the statement that uses specialized language.

Allegations 3 and 26 relate to pathology of oral mucosa. We observed a high rate of ignorance of terms: 37% type 1 responses to each of the two statements. There were three groups of answers 1-4, indicating some confusion regarding the terms used. Spearman coefficient (0.452) indicates a better correlation between responses.

We used set of statements 4-11 to find out whether respondents know that a radiograph before tooth extraction is necessary. We noticed that subjects know well the subject: 61% and 67% of responses 4 - "strongly agree" - and no answer "disagree" to the statement made in GCL. We obtained a statistically significant degree of correlation between responses, with a Spearman coefficient of 0.646.

Spearman's rho	Allegation 4	Correlation Coefficient	1,000	,646(**)
		Sig. (2-tailed)	.	,000
		N	49	49
	Allegation 11	Correlation Coefficient	,646(**)	1,000
		Sig. (2-tailed)	,000	.
		N	49	49

Spearman coefficient for the pair of allegations 4 and 11, on dental radiographs

Allegations 21 and 5 refers to bone deformations present in rickets. We observed a high rate of responses of "strongly agree" (57% and 65%) and have not recorded any 1-4 response pair, which would have indicated some confusion. Spearman correlation coefficient is statistically significant (0,637).

Statements 18 and 6 tests knowledge of calculus deposition. The subject is very well known: 53% and 61% responses "strongly agree. Spearman correlation coefficient is statistically significant (0,512).

Mouthwash use is the topic addressed in allegations 7 and 19. We observed a high rate of responses 3 and 4, which show a good knowledge of the subject. Spearman correlation coefficient tends to a significant value (0,526).

The set of statements 8-14 approach brushing theme. We obtained a larger number of type 3 responses (49 and 40%) and 4 (20% and 40%), which marks a misunderstanding of the content of the sentence. We also obtained four pairs of responses 1-4, indicating confusion on the subject proposed. The two statements do not correlate statistically, the Spearman coefficient being 0.231.

The pair of allegations 9-22 refers to vicious habits. The most numerous answers are "strongly agree" (57% and 65%) but a lower percentage of survey participants answered correctly to the question using scientific terms. I met only two answers that show confusion on the subject. Spearman correlation coefficient is not statistically significant.

In formulating statement 10, we used the term "colony of germs" that defines plaque. In technical terms (statement 24), we used the term "ecosystem responsible for producing caries". We obtained a very high rate of responses "strongly agree" (55, or 53 percent), perhaps because the subject is well known by the audience. Spearman's coefficient value of 0.740.

Spearman's rho	Allegation 24	Correlation Coefficient	1,000	,740(**)
		Sig. (2-tailed)	.	,000
		N	49	49
	Allegation 10	Correlation Coefficient	,740(**)	1,000
		Sig. (2-tailed)	,000	.
		N	49	49

Allegations 8 and 12 verify if the subjects understood the role of fluoride in the oral cavity. We noticed an increased rate of type 1 responses (31 and 49%), which indicates an ignorance of the topic. The correlation coefficient has a value of 0.532.

Questions 17 and 13 focused on tooth anatomy. Enamel is a "layer covering the tooth" (question 13) and a "protective tissue" (question 17). We got a great rate responses "strongly agree" (67% and 81%), and a large number of pairs 1 to 4, indicating a lack of knowledge on the concepts. The results are statistically significant, the Spearman coefficient of 0.548.

The last set of statements relate to the role of fluoride and how to use it. We noticed that the respondents do not know the subject, the responses were almost equally distributed between ranks. There are 10 pairs of responses 1-4, indicating notions ignorance and confusion about the terms used. Spearman coefficient is not statistically significant.

CONCLUSIONS

Using mass media in oro-dental health education is an opportunity that we always have to consider. The large number of subjects receiving the health behavior message, but also the authority enjoyed by the media are strengths in educational approach. However, we must not lose sight of how encoding takes place and then decoding the message.

Using scientific language without being reviously explained in common language leads to confusion among the public, to the inability to acquire or accept information transmitted. In this way, practically, the goal of educational communication is not achieved. Therefore, when creating a radio show or giving an interview for a newspaper or when speaking with the patient in the dental office, the dentist must use a common language or, if professional concepts are necessary, they must be explained in simple words to the patient.

The message should be tailored to the demographics and lifestyle of the target audience, on the one hand, and to the editorial policy of media institution participating in health education campaign, on the other hand. Topics that do not directly affect the public interest will not be retained. In addition, any oro-dental health education program should be designed on a long-term basis, in order to cumulate effects of exposure to information.

REFERENCES

[1] Van Cuilenburg, J.J., Scholten, O. şi Noomen, G.W. [1991](2004). *Ştiința comunicării*. Bucureşti: Editura Humanitas, 255.

[2] Dobrescu, P. şi Bârgăoanu, A. [2003]. *Mass-media și societatea*. Bucureşti: Editura Comunicare.ro, 128.

[3] Lippmann, W. [1922](1991). *Public opinion*. New Brunswick: Transaction Publichser, *apud.* Dobrescu, P. şi Bârgăoanu, A., *idem*, 49.

[4] Herzog, H. *Motivations and Gratifications of Daily Serial Listeners*. în W. Schramm. The Process ans Effects of Mass Communication, apud. Dobrescu, P. şi Bârgăoanu, A. [2003]. *Mass-media și societatea.* Bucureşti: Editura Comunicare.ro, 199.

[5] McQuail, D. şi Windahl, S. [1982](2004). *Modele ale comunicării pentru studiul comunicării de masă*. Bucureşti: Editura Comunicare.ro, 12.

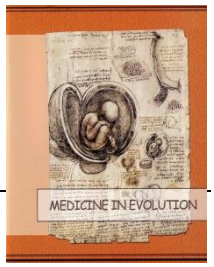
[6] Abric, J.C. [1999](2002). *Psihologia comunicarii. Teorii și modele*. Iaşi: Editura Polirom, 25.

[7] Van Cuilenburg, J.J., Scholten, O. şi Noomen, G.W., *Idem*, 159.

[8] Hall, S. (1980). Encoding and Decoding în Television Discourse. în Hall, S., Hobson, D. şi Lowe, P. (eds), *Culture, Media, Language*. London: Hutchinson, *apud.* McQuail, Denis şi Windahl, Sven., idem, 121.

[9] Tran, V. şi Stănciugelu, I. (2003). *Teoria Comunicării.* Bucureşti: Editura Comunicare.ro, 20-21.

COMPREHENSIVE APPROACH OF THE PERIARTICULAR SOFT TISSUE INJURIES OF THE KNEE



PAULA BICOV[1], DAN NEMES[1,2], LILIANA CATAN[1], ELENA AMĂRICĂI[1], DANIEL POPA[1,2]

[1] University of Medicine and Pharmacy "Victor Babes", Timisoara
[2] City University Emergency Hospital, Rehabilitation and Rheumatology Department, Timisoara

ABSTRACT

Introduction and Objectives: *Assessment of the rheumatic lesions impact (degenerative and inflammatory) preexisting to injury on the soft tissues of the knee, revealed by the complex evaluations: clinical, functional and ultrasound and highlighting the specific role of the rehabilitation therapy, combined with complex drug therapy, applied early and sustained in recovering these patients functionality and quality of life.*

Material and Methods: *Throughout one year, we have studied 80 patients with traumatic soft tissue injuries of the knee, divided into 2 groups according to the knee appearance before the injury (group A-39 patients, previously undamaged knee; group B-41 patients, previously pathological knee). Each patient has been submitted to 3 examinations (complex clinical examination, assessing the functionality and quality of life - Koos questionnaire: Knee Injury and Osteoarthritis Outcome Score and musculoskeletal ultrasound). All the patients have received the same type of therapy: drug and rehabilitation.*

Outcomes*: Increasing both the functionality and the quality of life of the patients to whom the injury has occured on an undamaged knee.*

Conclusions: *The key to the successful treatment of the posttraumatic lesions of the soft tissues of the knee is the early establishment of the comprehensive rehabilitation therapy after a comprehensive assessment: clinical, functional, ultrasound. The knee joint integrity, previous to an injury in the periarticular soft parts, is of major importance in the recovery of its functionality.*

Keywords: *traumatic knee, soft tissue, examination / assessment.*

Correspondence to

Dr. Liliana Catan;
Victor Babes University of Medicine and Pharmacy, Timisoara, România.
Telephone number: 0721790980;
Email: lilicatan@gmail.com

INTRODUCTION

The knee, through its position, through its role in static and dynamic biomechanics of the lower limb, and by its poor soft tissue coverage, is very injury prone and vulnerable to both direct and indirect injuries. (1,2,3)

The posttraumatic injuries of the soft tissues of the knee, less studied, at the expense of the joint injuries at this level, are potentially disabling disease, having a variable impact on the functionality and quality of life of these patients, with important socio-economic impacts; therefore early diagnosis, proper assessment and adoption of the appropriate medical management are of extreme importance to the progession of these diseases. (4,5,6,7)

Underlying diseases of the knee, from the degenerative or inflammatory rheumatic category, are felt by some patients while performing every day activities and involved in causing the injury not only by the presence of the pain and the limitation of the joint mobility, but also by a sense of instability, of knee falling,. (8,9,10)

An adequate knowledge of both the condition and the treatment, together with an active participation in decision making for therapeutic management, may cause patients with disabilities make decisions that will allow them to improve their quality of life in terms of needs, goals and circumstances. (11,12)

In the absence of a proper medical management applied early and sustained, after a correct diagnosis and a thorough assessment, which includes functional assessments and high fidelity imaging (MRI, soft parts or articular musculoskeletal ultrasound, EMG, Doppler echography, specific Rx-graphics, etc.), in addition to rigorous, complex and clinical examination, the progession of these diseases is unfavorable, causing varying degrees of disability. (4,5,6)

OBJECTIVES

1. Assessing the impact of rheumatic lesions (degenerative and inflammatory) preexisting the injury on the soft tissues of the knee, revealed by complex examinations: clinical, functional and ultrasound examinations;
2. Clinical and functional assessment of how early implementation of the complex treatment influences the quality of life, functionality and compliance to the treatment of patients with traumatic injuries of the soft tissues of the knee;
3. Highlighting the role of specific rehabilitation therapy, combined with complex drug therapy, applied early and sustained, in recovering the functionality and the quality of life of patients with periarticular soft tissue injuries of the knee;
4. Developing an individual rehabilitation program, allowing a significant change in the management of traumatic injuries of the knee and soft tissues leading to improved quality of life through family, social integration and even professional integration of the patients, with decreased social and economic costs.

MATERIAL AND METHODS

Throughout one year, we have studied 80 patients with traumatic soft tissue injuries to the knee, 23 women (28.75%) and 57 men (71.25%), aged between 15 and 88, with a diagnosis of posttraumatic lesions of the soft tissues of the knee , single or associated (soft tissue edema, quadriceps tendon: tendinitis, partial or total rupture, avulsion; prepatellar and infrapatellar bursitis; pes anserinus; bursitis, patellar retinaculum; elongation, partial or total rupture; medial collateral ligament: elongated, partial rupture or complete; iliotibial tract: friction syndrome or friction syndrome + bursitis), who have been divided into 2 groups according to the knee joint integrity before the injury:

-group A - 39 patients with posttraumatic lesions of periarticular soft tissue in the knee, occured on a previous undamaged knee ;
-group B - 41 patients with posttraumatic injuries of periarticular soft tissue in the knee, occurring on a previous pathologic knee.

Each patient has been submitted to 3 examinations (initial, after 6 months and final, after 12 months), consisting of: complex clinical examination, functional / daily activities - Koos questionnaire (Knee Injury and Osteoarthritis Outcome Score), that assesses: stiffness, pain, daily activities (functionality, the ability to move and self-care), performing sports and recreational activities and quality of life (13,14,15) and musculoskeletal ultrasound of the injured knee, obtaining an own ultrasound final score, for lesion quantification. (Table 1).

In the first month after the injury, each patient in the three groups, received mobile knee brace to enhance stability and to prevent vicious attitudes.

Each patient in both groups has received comprehensive treatment: analgesics (Gabapentin 1 pill 300mg/day, Ketorolac tromethamine 1 tablet 10mg/day), NSAIDs (Celecoxib 1 tablet 200mg/day, Diclofenac 1tablet 150mg/day, Meloxicamum 1 tablet 15mg/day), trophic (Regenovex 1 tablet/day, ALAnerv 1 tablet/day, Lenifast gel 2x1usage/day) and an intensive, sustained, early applied rehabilitation program for one year (30 sessions daily - initially, and then for 10 sessions 3x/week every three months until the end), with the following goals: pain relief, prevention / correction of postural changes, functional improvement (increase muscle strength, increase joint mobility, increased stability, coordination, control, balance to prevent falls, gait training , performing daily activities).

Table 1. Ultrasound examination protocol of the traumatic knee periarticular soft tissue (own protocol)

KNEE			RIGHT	LEFT
Soft tissue edema - subcutaneous tissue		1		
		2		
KNEE			RIGHT	LEFT
Quadriceps tendon	Tendinitis	1		
	Partial rupture, Teaca Integra	2		
	Total rupture, ruptured sheath, avulsion	3		
KNEE			RIGHT	LEFT
Prepatellar Bursa	Liquid < 15 Mm	1		
	Liquid > 15 Mm	2		
KNEE			RIGHT	LEFT
Patellar Retinaculum	Elongation	1		
	Partial Rupture	2		
	Total Rupture	3		
KNEE			RIGHT	LEFT
Infraprepatellar Bursitis		1		
KNEE			RIGHT	LEFT
Medial collateral ligament	Elongated	1		
	Partial fibrillar rupture	2		
	Complete rupture	3		
KNEE			RIGHT	LEFT
Pes anserinus	Bursitis	1		
KNEE			RIGHT	LEFT
Iliotibial tract	Friction Syndrome	1		
	Friction Syndrome + Bursitis	2		
KNEE			RIGHT	LEFT
TOTAL SCORE				

Score: *- between 1 and 3 minor changes - between 4 and 7 moderate changes - between 8 and 12 severe changes.*

RESULTS

The group has the total initial, intermediate and final ultrasound score significantly lower than group B, p <0.001, effect size is medium. (Table 2 and Chart 1)

As to Koos total score, group A, as well as for ultrasound score at initial, intermediate and final assessments, is significantly lower than in group B, p <0.001, effect size is increased. (Table 3 and Chart 2)

These aspects emphasize the importance of the absence of pre-existing knee joint injury prior to the occurrence of injury damaging the periarticular soft tissues and with an important role in the clinical, paraclinical and functional recovery and thus significantly increasing the quality of life of these patients, regardless of the age or the injury mechanism.

Table 2 - Comparative results of the mean values, total ultrasound score: group A and group B

	Group	N	Mean	Std. Deviation	Std. Error Mean
Total Ultrasound Score Initial	A	39	6,92	1,403	,225
	B	41	8,51	1,287	,201
Total Ultrasound Score Intermediate	A	39	5,08	1,222	,196
	B	41	7,12	1,187	,185
Total Ultrasound Score Final	A	39	3,10	1,142	,183
	B	41	4,54	1,142	,178

Chart 1 - Comparative results of the mean values, total ultrasound score: group A and group B

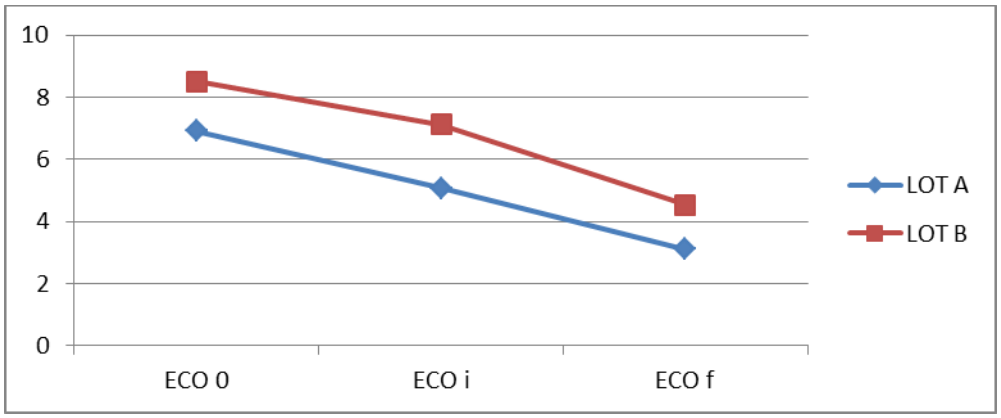
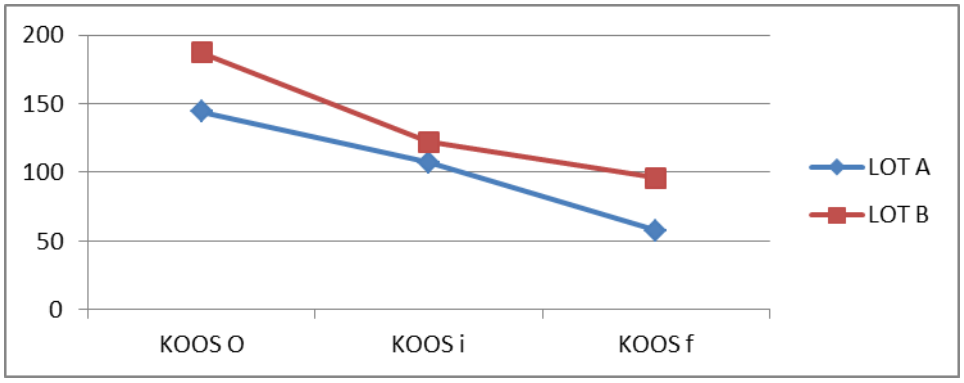


Table 3 - Comparative results of the mean values KOOS total score: group A and group B

	Lot	N	Mean	Std. Deviation	Std. Error Mean
Total KOOS Initial	A	39	144,33	8,358	1,338
	B	41	187,17	10,899	1,702
Total KOOS Intermediate		39	107,26	7,843	1,256
		41	122,39	12,101	1,890
Total KOOS Final	A	39	57,44	5,702	,913
	B	41	95,80	9,988	1,560

Chart 2 - Comparative results of the mean values KOOS total score: group A and group B



The rehabilitation program, applied early and sustained, associated with a complex therapy, has proved effective for the 80 patients in groups A and B, their quality of life being significantly improved, the most favorable progressions have been achieved in patients with previously undamaged knee (Table 2,3 and Chart 1,2).

CONCLUSION

An important role in adopting an appropriate medical management and in assessing its therapeutic effectiveness is played by the diagnosis and the complex, correct assessment of the posttraumatic soft tissue injuries of the knee, using specific and global systems, that consist of complex clinical examination, functional assessment (KOOS questionnaire) and musculoskeletal ultrasound and, finally, the correlation of these results, with contributions in the management of these diseases.

The ultrasound examination protocol of the soft tissue injuries of the knee (Table 1) used in this study can be used to address complex injuries of this type associated with complex clinical examination and functional assessment using the KOOS questionnaire, its approval can bring major benefits in the management of these injuries, gaining valuable time in terms of adopting a proper medical management, and there are also socio-economic benefits.

Recovery of the posttraumatic soft tissue injuries of the knee should be progressive, gradual, customized for each case, depending on the type of lesion, its degree, as well as the pre-existing knee pathology or the associated general pathology.

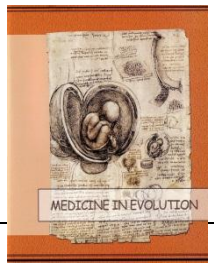
The best outcomes, objectified through complex assessment methods have been recorded by the patients with posttraumatic lesions of the soft parts of the knee that have occurred on an undamaged knee before the injury and who have received comprehensive medical treatment and specific rehabilitation, applied early and on the long run, allowing us to claim that this is the key to successful treatment, obviously, after a comprehensive assessment: clinical, functional, ultrasound and the correlation of the results, before adopting the appropriate medical management, physical therapy is urgently needed as soon as local inflammatory processes have been resolved, especially since the „time" factor is a key factor in the resumption of daily activities and especially walking.

The patient's age, the associated pathology, his/her previous level of training and his / her psycho-intellectual capacity have to be taken into account in the recovery treatment.

REFERENCES

1. American College of Rheumatology (ACR) sub-committee on Osteoarthritis Guidelines. recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on osteoarthritis Guidelines. Arthritis Rheum. 2000;43:1905–1915.
2. American College of Rheumatology Subcommittee on rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. Arthritis Rheum. 2002;46:328–346.
3. OARSI recommandations for management of hip and knee osteoarthritis. Parti and II based expert consensus guidelis,. Oateoarthritis and Cartilage, 2008, 16, 137- 162.
4. Sarraf P, Reginato A M. Periarticular Rheumatic Diseases, in Bartlett J Susan et all (editors), Clinical Care in the Rheumatic Diseases, Association of Rheumatology Health Professionals, a Division of the American College of Rheumatology, Atlanta, Georgia, 2006: 145-151.
5. Pellicci P, McCormack R R. Bursitis and Tendinitis, in Paget S A et all (editors), Hospital for Special Surgery manual of rheumatology and outpatient orthopedic disorders: diagnosis and treatment 5th Ed, Lippincott Williams & Wilkins, 2006:203-206.
6. Dieppe PA. Recommended methodology for assessing the progression of osteoarthritis of the hip and knee joints. Osteoarthritis Cartilage 1995; 3: 73–7.
7. Webb J, Corry I. Injuries of the sporting knee, epidemiology of knee injuries: diagnosis and triage. Br. J Sports Mes, 2000; 34:227-228.
8. Fitzgerald GK, Piva SR, Irgang JJ. Reports of joint instability in knee osteoarthritis: its prevalence and relation ship to physical function. Arthritis Reum, 2004; 51 (6): 941-946.
9. Felson DT, Niu J, MC Clennan C, et al Knee Buckling: Prevalence, Risk Factors, and Associated Limitation in Function. Ann Intern Med, 2007; 147: 534-540.
10. Wada M, Imura S, Baba H, et al. Knee laxity in patients with osteoarthritis and rheumatoid arthritis. Brit J Rheumatol, 1996; 35: 560-563.11.
11. DeLisa J.A.- Physical medicine and rehabilitation: principles and practice, 4th edition. Lippincott Williams-Wilkins Publisher 2005, p.721-786, 855-872, 1193-1204
12. Guyatt G.H., Eagle D.J.- Measuring quality of life in the frail elderly. J Clin Epidemiol 1993;46, p.1433-1444
13. Stewart A.L., Ware J.E.- Measuring functioning and well-being: the medical outcomes study approach. Durham: Duke University Press 1992, p.345-371
14. Aaronson N.K.- Quantitative issues in health-related quality of life assessment. Health Policy 1988;10, p.217-230
15. Cella D., Nowinski C.J.- Measuring quality of life in chronic illness: the functional assessment of chronic illness therapy measurement system. Arch Phys Med Rehab 2002;83, p.10-17

FOLFOX4 – A THERAPEUTIC OPTION IN COLORECTAL LIVER METASTASES



ANDREEA DAN[1], ȘERBAN NEGRU[1], IZABELLA ȘARGAN[2], RADU DAN[3]

[1] Timișoara Oncohelp Clinic
[2] University of Medicine and Pharmacy "Victor Babeș", Department of Anatomy and Embryology, Timisoara
[3] PhD student of University of Medicine and Pharmacy "Victor Babeș", Department of General Surgery, City University Emergency Hospital, Timisoara

ABSTRACT

Introduction: *In colorectal cancer, the liver is the most common site of distant metastatic spread. The role of chemotherapy in the complex and multimodal approach of colorectal liver metastases is to control tumor growth.*

Material and method: *This study is a retrospective study on 11 patients treated with FOLFOX4 chemotherapy regimens between January 2007 and January 2012 in Timișoara Oncohelp Clinic. Chemotherapy regimens were associated with Cetuximab in 2 patients. Patients were evaluated by CT scans three months after the initiation of treatment with FOLFOX4 and the response was assessed using RECIST 1.1 criteria.*

Results: *The study group included 11 patients, 6 males (54.55%) and 5 women (45.45%), aged 24-83 (mean 54.09) years. Three month after the initiation of FOLFOX4 treatment, 8 patients (72.73%) had a partial remission, one (9.09%) stationary disease and 2 (18.18%) progressive disease. One year survival after the diagnostic of liver metastases was 90.90% in our study group. Mean overall survival in our group was 25.62 months. Patients treated with Cetuximab survived 21 and 53 months respectively.*

Conclusions: *FOLFOX 4 is useful in the management of colorectal liver metastases. Addition of monoclonal antibodies seems to bring benefits in terms of survival.*

Key worlds: *FOLFOX4, colorectal liver metastases, response, survival*

Correspondence to

Radu Dan, PhD student of "Victor Babeș" University of Medicine and Pharmacy
Address: Eftimie Murgu Squ, no.2, Timisoara, Romania
Tel: +40744561930
E-mail: radudan12@yahoo.com

INTRODUCTION

Colorectal cancer is the third most common cancer worldwide [1], the liver being the most common site of distant metastatic spread. Treatment of metastatic colorectal cancer requires a multidisciplinary approach involving the surgeon, oncologist, radiation oncologist, radiologist and pathologist.

The role of chemotherapy in the management of metastatic colorectal cancer is to control tumor growth, as an attempt to prolong survival, improve quality of life and, in fortunate situations, to convert to resecability initially unresectable tumors. The most widely used chemotherapeutic agents in colorectal cancers are 5-fluorouracil (5-FU), capecitabine (an oral precursor of 5-FU), oxaliplatin and irinotecan. These drugs can be administered as monotherapy or in various combinations. The use of monoclonal antibodies such as Bevacizumab, Cetuximab or Panitumumab, alone or associated with classical chemotherapy, increased overall survival [2].

The regimen should be chosen according to patient`s age, performance status, comorbidities, its adverse effects and type of chemotherapy used (neoadjuvant, conversion therapy, adjuvant or palliative).

OBJECTIVES

The aim of this study is to evaluate the response to FOLFOX4 therapy, 3 months after its initiation, survival at one year after diagnosis of liver metastases and after initiation of FOLFOX4 treatment, and the mean survival for this group.

MATERIAL AND METHOD

This study is a retrospective study on 11 patients treated with FOLFOX4 chemotherapy regimens between January 2007 and January 2012 in Timișoara Oncohelp Clinic. We selected both, patients in first-line chemotherapy (in synchronous liver metastases) as well as patients previously treated with other regimens (for metachronous liver metastases or in cases of metastatic progression with other chemotherapy regimens).

The chemotherapy regimen was chosen after the oncologist discussed with the patient how every chemotherapy regimen is administered, its results, advantages and side effects. Before each cycle of chemotherapy, clinical and biological parameters (performance index, blood counts, liver and kidney tests) were evaluated to assess the opportunity of chemotherapy regimen administration and received antiemetic premedication to prevent side effects of chemotherapy.

The FOLFOX4 regimen consisted of Leucovorin 200 mg/m^2 given as a 2-hour infusion on day 1 and 2, Oxaliplatin 85 mg/m^2 given as a 2-hour infusion on day 1 concurrent with Leucovorin, then 5-FU 400 mg/m^2 i.v. bolus and 600 mg/m^2 22-hours infusion on day 1 and 2. The regimen was repeated every 2 weeks. Based on the response rate, performance index and degree of toxicity, patients received between 3 and 28 cycles of chemotherapy. Cetuximab was combined with FOLFOX4 in 2 patients. Cetuximab was administered in patients with EGFR overexpression (epidermoid growth factor receptor) that could be included in various studies.

Patients were evaluated by CT scans three months after the initiation of treatment with FOLFOX4 and the response was assessed using RECIST (Response Evaluation Criteria in Solid tumors) 1.1 criteria[3]. Complete remission involved the disappearance of lesions detected on previous investigation, partial remission requires at least 30%

reduction of the amount of tumor diameters, while progressive disease is defined as an increase of at least 20% of the sum of tumor diameters (with an absolute increase of at least 5 mm) or the appearance of new lesions. Stable disease is defined as the interval between progressive disease and partial response.

At the end of the study, all patients concluded FOLFOX4 treatment and they were followed for at least 12 months. Survival was calculated from the time of diagnosis of liver metastases and from the time of FOLFOX4 treatment initiation respectively, until death or loss of evidence.

RESULTS

The study group included 11 patients, 6 men (54.55%) and 5 women (45.45%), aged between 24 and 83 years (mean 54.09 years). Two of the patients (18.18%) were rural dwellers and 9 patients (81.82%) were urbanites.

Regarding the type and number of liver metastases, they were synchronous in 8 patients (72.73%) and metachronous in 3 (27.27%), multiple in 9 patients (81.82%) and 2 patients (18.18%) had a single lesion. At the time of diagnosis, one patient (9.09%) had several metastatic sites and for the others 10 (90.91%) dissemination was confined to the liver. In patients with metachronous liver metastases, time from primary tumor diagnosis to onset of liver metastases ranged between 11 and 28 months, with a median of 17.3 months.

Eight patients (72.73%) underwent resection for primary tumor while the other 3 (27.27%) did not benefit from this type of treatment. It worth mentioning that 5 (62.5%) of 8 patients with synchronous liver metastases had primary tumor removed, while the other 3 (37.5%) underwent a palliative surgery (colostomy). Hepatic resection was performed in one patient (9.09%) with metachronous metastases confined to the liver.

Regarding the evaluation of patients, 3 months after initiation of FOLFOX4 chemotherapy, response to treatment was partial in 8 cases (72.73%), stable disease in one case (9.09%) and progressive disease in 2 cases (18.18%). No complete remission was observed.

One year after the diagnosis of liver metastases, 10 of 11 patients were alive (1 year survival rate 90.91%). One year survival rate after the initiation of FOLFOX4 therapy was 81.82%. Mean overall survival in our group was 25.62 months and 3 patients were still alive one year after completion of the study. In patients treated with Cetuximab, survival was 21 and 53 months, respectively.

DISCUSSION

Due to the small number of patients included in the analysis and the heterogeneity of the group, the aim of this study is not to confirm or to refute the data from the literature regarding FOLFOX4 efficiency, but to report the results of Timișoara Oncohelp Clinic with this chemotherapy regimen in patients with colorectal liver metastases.

It should be noticed that 11 (18.33%) of the 60 patients with colorectal liver metastases treated during the study period received FOLFOX4. This relatively low percentage can be explained on one hand, by the large numbers of regimens available for the treatment of colorectal liver metastases, with some oral Capecitabine based regimens that are better tolerated and easily accepted by the patients, avoiding continuous infusions of FOLFOX4. On the other hand, in some cases of metachronous liver metastases, administration of FOLFOX4 was no longer indicated, these patients developing recurrent disease during FOLFOX4 treatment as first line chemotherapy.

Analyzing the results, there is an overwhelming rate of patients coming from urban areas (81.82%), which can be explained by the socio-economic conditions of the

environment (diet, stress, sedentary lifestyle) and by a better addressability to healthcare services and compliance to chemotherapy regimens observed in urbanites.

Although the rate of synchronous colorectal liver metastases in the literature is described somewhere around one third of the cases [(1)], in our group, 72.73% of the patients developed synchronous liver metastases, percentage available for all 60 patients treated for this condition in Oncohelp Clinic. A possible explanation for this high percentage could include lack of national screening programs in colorectal cancer leading to the lack of early detection, many patients with this condition being diagnosed only in a metastatic stage, knowing the fact that up to 70% of patients with colorectal cancer could develop liver metastasis during the course of their disease [(4)]. Late presentation of patients with colorectal cancer is supported by the observation that, in our study, only in 5 of 8 patients with synchronous liver metastases, a curative intervention for the primary tumor could be performed.

Given the small number of patients in the study group and its heterogeneity, the results regarding survival are difficult to compare with those in the literature. However, the mean survival rate of 25.62 months seen in our group is consistent with the interval published in the literature [(5-7)]. Moreover, knowing the fact that 10 of 11 patients received palliative chemotherapy, none of the 10 patients undergoing a hepatic resection, the results seen in our group are encouraging. Addition of Cetuximab to FOLFOX4 regimen seems to improve survival in selected patients, reflected by 53 months survival seen in one of the patients that received Cetuximab.

The fact that there are still living patients from our group compels us to further observation in order to complete the study and communicate final results regarding distant survival.

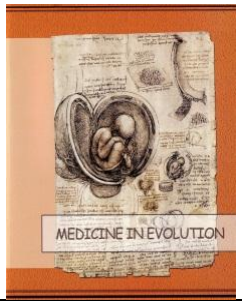
CONCLUSIONS

FOLFOX4 regimen chemotherapy is useful for the management of metastatic colorectal cancer, providing good results, although there is a tendency to replace it with Capecitabine based regimen (XELOX) which is better tolerated and accepted by the patients. Addition of monoclonal antibodies, such as Cetuximab, seems to bring benefits in terms of survival.

REFFERENCES

1. Ismaili N. Treatment of colorectal liver metastases. World J Surg Oncol. 2011; 9:154.
2. El Zouhairi M, Charabaty A, Pishvaian MJ. Molecularly Targeted Therapy for Metastatic Colon Cancer: Proven Treatments and Promising New Agents. Gastrointest Cancer Res. 2011; 4(1): 15–21.
3. Eisenhauera EA, Therasseb P, Bogaertsc J. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). Eur J Cancer. 2009; 45:228–247.
4. Ward J. New MR techniques for the detectionof liver metastases. Cancer Imaging. 2006; 6: 33-42.
5. Alberts SR, Horvath WL, Sternfeld WC et al. Oxaliplatin, fluorouracil, and leucovorin for patients with unresectable liver-only metastases from colorectal cancer: a North Central Cancer Treatment Group phase II study. J Clin Oncol. 2005; 23(36):9243-9.
6. Xu J, Zhu D, Ren L et al. Survival investigation in patients with colorectal liver metastasis: A single-institution analysis. J Clin Oncol 30, 2012 (suppl 4; abstr 617).
7. Lami L, Areces F, Lence JJ et al. FOLFOX-4 Regimen as a First-line Therapy for Cuban Patients with Metastatic Colorectal Cancer. MEDICC Rev. 2009; 11(3):34-8.

PATHOLOGICAL COMPLETE REMISSION IN RECTO SIGMOID CANCER PATIENT WITH LIVER METASTASES AFTER XELOX/BEV ACIZUMAB TREATMENT: -A CASE REPORT



RADU DAN[1], ANDREEA DAN[2], OCTAVIAN CREȚU[3], LAURENȚIU SIMA[3], ȘERBAN NEGRU[2]

[1] PhD student of University of Medicine and Pharmacy "Victor Babeș" , Department of General Surgery, City University Emergency Hospital, Timișoara
[2] Timișoara Oncohelp Clinic
[3] City University Emergency Hospital, Department of General Surgery, Timișoara

ABSTRACT

***Introduction**: Although hepatic resection is the single potentially curative treatment option in colorectal cancer metastatic to the liver, chemotherapy plays an important role in the management of such patients.*

***Case report:** We herein report the case of a 42 years old patient with recto sigmoid cancer and multiple liver metastases with maximum diameter of 1.7cm in which a Hartmann procedure was performed and that achieved both, clinical and pathological complete remission in liver resected specimen following one cycle of XELOX and 7 cycles of XELOX and bevacizumab.*

***Conclusion:** Use of combination XELOX and bevacizumab can achieve complete pathological remission in patients with liver metastases from colorectal cancer and can prolong survival.*

***Key words:** XELOX, bevacizumab, metastatic colorectal cancer, pathological complete remission*

Correspondence to

***Șerban Negru**, MD, PhD, Discipline of Oncology,*
"Victor Babeș" University of Medicine and Pharmacy, Timișoara Oncohelp Clinic
***Address:** Eftimie Murgu Squ, no.2, Timisoara, Romania*
Tel: +40744644381
***E-mail:** snegru@yahoo.com*

INTRODUCTION

Hepatic resection is the only potentially curative treatment option in colorectal liver metastases, with best survival, but unfortunately less than one third of the patients can benefit from this type of treatment [(1)], due to the presence of unresectable extra hepatic disease or the number and location of liver metastases. In unresectable patients, palliative chemotherapy represents the standard strategy [(1)] and the use of systemic chemotherapy can convert to resecability 13% of initially unresectable tumors [(2)]. In addition, the use of chemotherapy can improve the rate of R0 resections and promotes limited resections, sparing functionally liver parenchyma [(3)]. The appearance of bevacizumab, a monoclonal antibody, and its association with chemotherapy, led to an increased effectiveness in tumoral cells by improving their oxygenation and decreasing interstitial pressure [(4)].

CASE PRESENTATION

Patient, 42 years of age, was admitted in November 7th 2010 in a gastroenterology service for diffuse abdominal pain, mostly in the lower left quadrant, flatulence and the absence of bowel movements, associated with nausea and vomiting. Following colonoscopic examination, the patient is diagnosed with a vegetant, stenosing tumor at the level of recto sigmoid junction, starting about 17cm away from the anus, which does not allow further examination. Abdominal ultrasound and contrast enhanced ultrasound (CEUS) were performed, discovering two hepatic masses pleading for hemangiomas. The patient is transferred in a surgical service were a Hartmann procedure is performed, leaving a 9cm long rectal stump. Pathological examination revealed a moderately differentiated G_2 tubular adenocarcinoma, intestinal type, $pT_4N_0M_x$, with safe resection limits, without lymph nodes involvement in the 26 specimens examined. In December 6th, 2010, the patient was admitted in Oncohelp Clinic from Timişoara and he began adjuvant oncologic treatment using intravenous oxaliplatin (130mg/m^2) and oral capecitabine (1000mg/m^2 twice a day) – XELOX. Later, after discharge, the patient performed a CT exam of the abdomen which showed, in addition to the two hepatic hemangiomas, four hipodense lesions in the liver, located in the segments 6 and 8, that does not uptake the contrast agent, with maximum size of 1.7cm. The MRI exam performed three weeks later revealed two lesions, less than 1cm, located in segment 6, hypointense in T1 signal and slightly hiperintense in T2 signal. The CT thoracic scan did not reveal any lesion in the lungs. Starting with cycle 2 of chemotherapy, from December 28th, 2010, bevacizumab (7,5mg/kg) is associated, the patient receiving 7 cycles of XELOX + bevacizumab, the last one in May 9th, 2011. In March 1st, 2011, the patient performs a new CT scan that shows the persistence of same number of liver lesions, with the same behavior regarding the contrast agent, but with decreased sizes, maximum of 9mm, compared with previous examination. In May 31st, 2011, the PET-CT scan showed that the liver was free of any lesion, beside the two hemangiomas, without fluorodeoxyglucose (FDG) uptake. In June 28th, 2011, a right hepatectomy was performed and the resected specimen sent for pathological examination. Since no viable tumor cells were observed in any of the whole sections of the resected specimen, the effect of XELOX in combination with bevacizumab was interpreted as the pathological complete remission (PCR). In October 23rd, 2011, a new CT scan showed a liver free of tumors and later on, the colostomy was closed, restoring continuity of the digestive tract. At this moment, 19 months since liver resection and more than 2 years after diagnosis of liver metastases and initiation of oncologic treatment, the examinations showed no evidence of disease.

DISCUSSION

Pathological complete remission, defined as the absence of cancerous cells on the examined specimen, is a rare possibility, with an overall incidence of 4% - 9% of all resected patients for liver metastases [3,5,6]. There is a good correlation between pathological response and survival of the patients [6]. Adam et al [7], reported that of 767 patients with colorectal liver metastases receiving neoadjuvant chemotherapy, survival rates at 3 and 5 years were 91% and 76% respectively in patients with pathological complete response, compared with 61% and 45% in patients without PCR. Similarly, in a study performed on 305 patients treated with neoadjuvant oxaliplatin or irinotecan based chemotherapy, Blazer et al [6] reported a 5 years survival of 75% in patients with pathological complete response and only 33% in those with minor response. These results are compelling advocates for the use of neoadjuvant chemotherapy, even in initially resectable cases, distant results being superior to surgery alone in the case of a pathological complete response. In this case, a complete remission constituted a positive prognosis factor so far, with no sign of recurrence in more than 2 years from diagnosis of liver metastases.

There are few reports of PCR occurring after treatment with XELOX or XELOX associated with bevacizumab [8], most of the cases being reported after FOLFOX or FOLFIRI treatment. In this patient, PCR followed neoadjuvant chemotherapy with 8 cycles of XELOX, associated with bevacizumab from the second cycle.

Clinical remission is not always concordant with pathological response, the persistence of tumoral cells and early recurrence being a possibility. In his study, Adam et al[7] reported that all the patients with PCR didn't have a complete clinical response and the two patients with complete clinical response had tumoral cells in resected specimens. Regarding this patient, the absence of hepatic lesion and FDG uptake in PET- CT, entitle us to affirm the existence of a clinical complete remission and that there is a concordance, for this case, between clinical and pathological remission.

The usefulness of hepatic resection for this patient with negative PET-CT scan for malignant lesions could come into question. However, taking into account the fact that the pathological examination is the only one that could state pathological complete response and that there could be a disparity between the presence of PCR and imaging of the liver lesions, we believe that hepatic resection should be performed even in cases of complete clinical response.

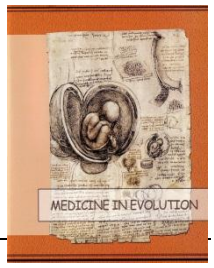
CONCLUSION

Treatment with XELOX in combination to bevacizumab can determine pathological complete remission in patients with colorectal liver metastases, leading to an improved survival and, why not, to cure the patient.

REFERENCES

1. Konopke R, Roth J, Volk A et al. Colorectal liver metastases: an update on palliative treatment options. J Gastrointestin Liver Dis. 2012; 21(1):83-91.
2. Adam R, Avisar E, Ariche A et al. Five-Year Survival Following Hepatic Resection after Neoadjuvant Therapy for Unresectable Colorectal Liver Metastases. Ann Surg Oncol. 2001; 8(4):347-53.
3. Malavasi N, Ponti G, Depenni R et al. Complete pathological response in a patient with multiple liver metastases from colon cancer treated with Folfox-6 chemotherapy plus bevacizumab: a case report. J Hematol Oncol. 2009; 2: 35.
4. Tanaka T, Tamura K. Recent advances in molecular targeted therapy for advanced colorectal cancer and non–small cell lung cancer. J Phys Chem Biophys. 2012; 2:108.
5. Skuja E, Āboliņš A, Priedīte I et al. Pathological Complete Remission in Young Colon Cancer Patient with a Large Liver Metastasis after FOLFOX-4/Bevacizumab Treatment – A Case Report. Int J Clin Med. 2012; 3(4):307-10.
6. Blazer DG 3rd, Kishi Y, Maru DM et al. Pathologic response to preoperative chemotherapy: a new outcome end point after resection of hepatic colorectal metastases. J Clin Oncol. 2008; 26(33):5344-51.
7. Adam R, Wicherts DA, de Haas RJ et al. Complete pathologic response after preoperative chemotherapy for colorectal liver metastases: myth or reality? J Clin Oncol. 2008; 26(10):1635-41.
8. Hisatsune Y, Nakano H, Mihara I et al. A patient who showed a pathologically complete response after undergoing treatment with XELOX plus bevacizumab for synchronous liver metastasis of grade H2 from sigmoid colon cancer. J Gastrointest Oncol. 2012; Nov 14. DOI: 10.3978/ j.issn.2078-6891.2012.060.

DRY-EYE SYNDROME IN PATIENTS WITH TYPE 2 DIABETIC MELLITUS



VALERIA MOCANU[1], ROMULUS TIMAR[2], MIHNEA MUNTEANU[1], BOGDAN TIMAR[2], RALUCA HORHAT[3], ADINA BUCUR[4], VIOREL SERBAN [2]

[1] University of Medicine and Pharmacy "Victor Babes", Department of Ophthalmology, Timisoara
[2] University of Medicine and Pharmacy "Victor Babes", Diabetes Clinic, Timisoara
[3] University of Medicine and Pharmacy "Victor Babes", Department of Biophysics and Medical Informatics, Timisoara
[4] University of Medicine and Pharmacy "Victor Babes", Department of Management and Public Health, Timisoara

ABSTRACT

Introduction: Diabetes mellitus (DM) is one of the most common leading causes of blindness in the world and it is associated with cataract, neovascular glaucoma and retinopathy as ocular complications. Tear film abnormalities are common in diabetic patients and can lead to important vision deficit, perforation of the cornea and secondary to bacterial infection.

Material and method: Totally 30 patients with type 2 diabetes mellitus , aged between 40-70 and 30 age- and sex-matched control subjects were studied. The OSDI dry-eye questionnaire (Ocular Surface Disease Index) was used in order to establish the presence and severity of the symptoms. Tear film function was evaluated by tear breaking up time (BUT), corneal fluorescein staining and Schirmer test. All the subjects underwent direct ophthalmoscopy. Diabetic retinopathy (DR) was graded according to early Treatment Diabetic Retinopathy *(ETDRS) criteria.*

Results: The dry-eye syndrome was more frequent in the diabetes mellitus group than in the control group (70% vs. 40%). The dry-eye symptoms were significantly related to an abnormal BUT and Schirmer test. Severe dry-eye symptoms were found in patients with advanced stages of diabetic retinopathy. Dry eye score had a good correlation with diabetic retinopathy*, but was poorly correlated with age, gender and duration of diabetes mellitus.*

Conclusions: Patients with type 2 diabetes tend to develop tear film dysfunction. The disorders of tear film quantity and quality seem relevant to the stage of diabetic retinopathy. The examination for dry eye should be an integral part of the assessment of diabetic eye disease.

Keywords: *type 2 diabetic mellitus, dry-eye syndrome, diabetic retinopathy.*

Correspondence to

Dr. Valeria Mocanu, MD, PhD student, RO – 300592 Timisoara,
Severin 6B Street, Timisoara, Romania.
Tel. +40721790966
Email: valeria_mocanu@yahoo.com

INTRODUCTION

Diabetes mellitus (DM) is one of the most common leading causes of blindness in 20–74-year old persons (1). Cataract, neovascular glaucoma and retinopathy are well-known as ocular complications of diabetes. Tear film abnormalities are common in diabetic patients, who also experience an increased incidence of dry eye. Several studies cite poor metabolic control (2), neuropathy (3), advanced retinopathy (4) or an abnormal lachrymal secretion (5) as risk factors for dry eye syndrome.

Symptoms of dry eye syndrome may include: a stinging, burning or scratchy sensation in the eyes, increased eye irritation from smoke, wind or after exposure to air conditioning, eye fatigue after short periods of reading or using computer, sensitivity to light, periods of excessive tearing, blurred vision, often worsening at the end of the day or after focusing for a prolonged period.

Dry eye can lead to vision deficit, scarring and perforation of the cornea and secondary to bacterial infection. This syndrome must be diagnosed at first stage and treated to avoid complications.

In a randomized study carried out on 199 type 2 diabetes patients, Manaviat (5) published a dry eye prevalence of 54.3%, utilizing the diagnostic criterion that one of the tests, Schirmer or tear break-up time (TBUT), is pathological.

The purpose of this study is to analyze the association of the dry-eye in patients with type 2 diabetes, by investigating the tear function and the corneal surface damage.

MATERIAL AND METHOD

A total of 60 subjects were enrolled in this study, divided in two groups: group I comprises 30 patients with type 2 DM, aged between 40-70 and group II comprises 30 age and sex-matched control subjects.

Inclusion criteria for group I are represented by patients with type 2 DM previously diagnosed and under treatment.

Exclusion criteria for group I are represented by: type 1 diabetes, autoimmune diseases (such as Gougerot-Sjogren's syndrome, rheumatoid arthritis, lupus), ocular inflammations (blepharitis, conjunctivitis, keratitis, dacryoadenitis, uveitis), contact lens, ocular surgery (cataract, glaucoma, refractive, eyelid or lacrimal surgery), eyelid disorders (ectropion, eyelid coloboma, lagophthalmia), allergies, Parkinson disease, some medications such as antihistamines, tricyclic antidepressants, oral contraceptives, and drugs used to treat high blood pressure and diuretics. Moreover vitamin A deficiency, children and pregnancy were excluded.

Subjects from group II- control group were selected from non-diabetes patients without diseases or medication that can affect tear production.

Clinical data were collected from all patients using direct patient interview. It was recorded data like sex, age, symptoms, history of diabetes for group I and/or history of other diseases for both groups.

Each of the study participants completed an OSDI dry-eye questionnaire (Ocular Surface Disease Index) in order to establish the presence and severity of the symptoms. The scores were classified in 4 severity classes: normal, mild, moderate and severe (6).

Tear film function was evaluated by tear break up time (TBUT) (normal value above 15s), fluorescein stain degrees, following the Oxford (7) scheme, that classifies the stain degrees in 6 ranges, Schirmer test (normal value 15 mm or above in 5 min), according to American Academy of Ophthalmology (8). Structures of the eye were assessed with slit lamp biomicroscopy examination. All the subjects underwent direct ophthalmoscopy after dilation by Tropicamid drop. Diabetic retinopathy was graded according to early Treatment Diabetic Retinopathy (ETDRS) criteria (9).

The dry eye syndrome diagnosis was considered positive if one of the TBUT or Schirmer test was pathological.

RESULTS

The median age in the group I-subjects with type 2 DM was 58.36±8.6 years. Of the 30 patients, 13 were male (43.33%) and 17 female (56.64%). The average time duration from the diagnosis of the diabetes has been 12.63 years.

In the control group, from the 30 patients 15 were male (50%) and 15 were female (50%). The median age was 56.2 years.

According to the ETDRS criteria 12 patients (40%) were diagnosed with nonproliferative diabetic retinopathy (NPDR), 6 (20%) with proliferative diabetic retinopathy (PDR) and 2 (6.66%) with clinically significant macular edema. In 10 patients diagnosed with diabetes mellitus (33.33%) lesions of DR were absent. From the 12 patients with NPDR, 8 presented mild lesions (26.66%) and 4 moderate lesions (13.33%). From the 6 patients with PDR, 2 (6.66%) presented early PDR and 4 (13.33%) high risk PDR.

From the 30 patients with diabetes, the dry eye syndrome has been present in 21 (70%), whereas in the control group, it was present in 12 of the 30 subjects (40%). The dry eye syndrome has been significantly more frequent in the patients with DM than in the healthy subjects (p=0.02, 1.06<RR<2.88).

The severity of the symptoms according the OSDI dry-eye questionnaire was the following: normal in 6 patients (20%), mild in 9 patients (30%), moderate in 7 patients (23.33%) and severe in 8 patients (26.66%). It can be noticed that severe dry-eye symptoms can be found in patients with advanced stages of diabetic retinopathy.

In the control group, the severity of the symptoms according the OSDI questionnaire was the following: normal in 16 patients (15.33%), mild in 5 patients (16.66%), moderate in 5 patients (16.66%) and severe in 4 patients (13.33%).

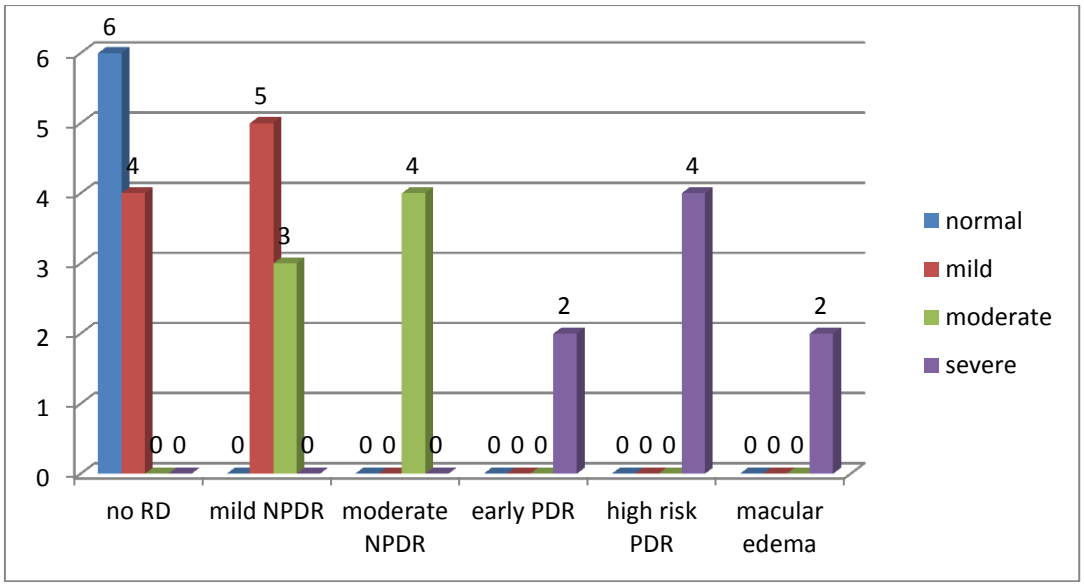


Figure 1 – Results of the OSDI dry-eye questionnaire in the patients with diabetes mellitus graded according the ETDRS criteria

The mean value of the TBUT has been 11.46±6.55s in the group of subjects with DM, while in the control group it was 13.33±5.15s. In 20 patients with diabetes (66.66%) the values were below 15s and in 10 patients (33.34%) the TBUT was 15s or more. In the control group the TBUT was below 15s in 14 patients (46.66%) and 15s or more in 16 patients (53.33%). Lower TBUT values were encountered in advanced stages of DM.

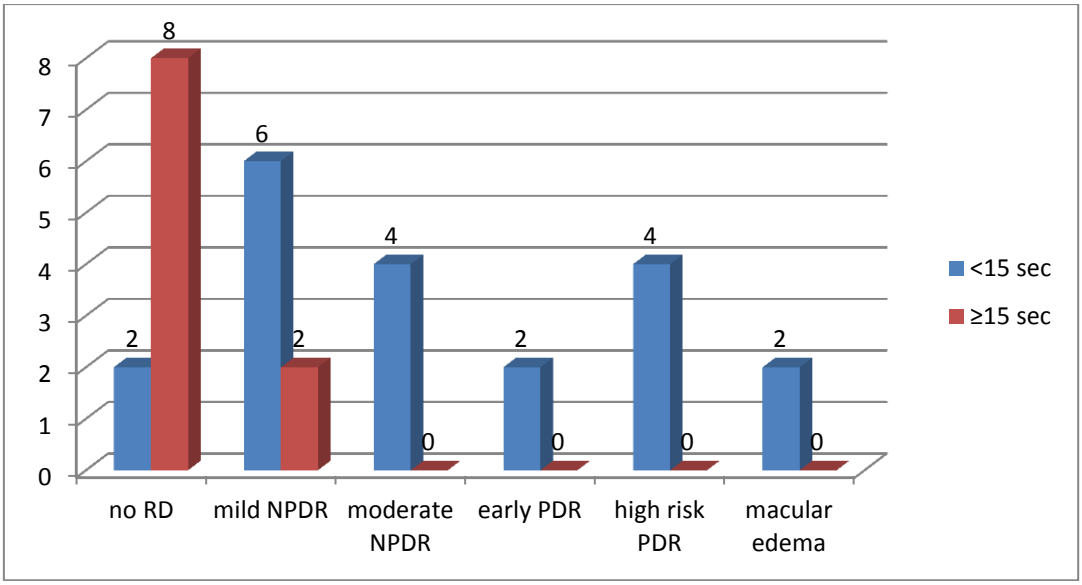


Figure 2 - Results of the TBUT in the patients with diabetes mellitus graded according the ETDRS criteria

Analyzing the relationship between the OSDI score and the TBUT we found that there is a strong correlation between them for the entire studied population. This was indicated by Pearson's correlation factor r = -0.89.

The mean value of the Schirmer test was 11±6.11 mm in the group of patients with DM and 13.06±5.27 mm in the control group. The values of the test were <15 mm at 5 min in 21 patients with diabetes (70%) and in 13 patients from the control group (43.33%).

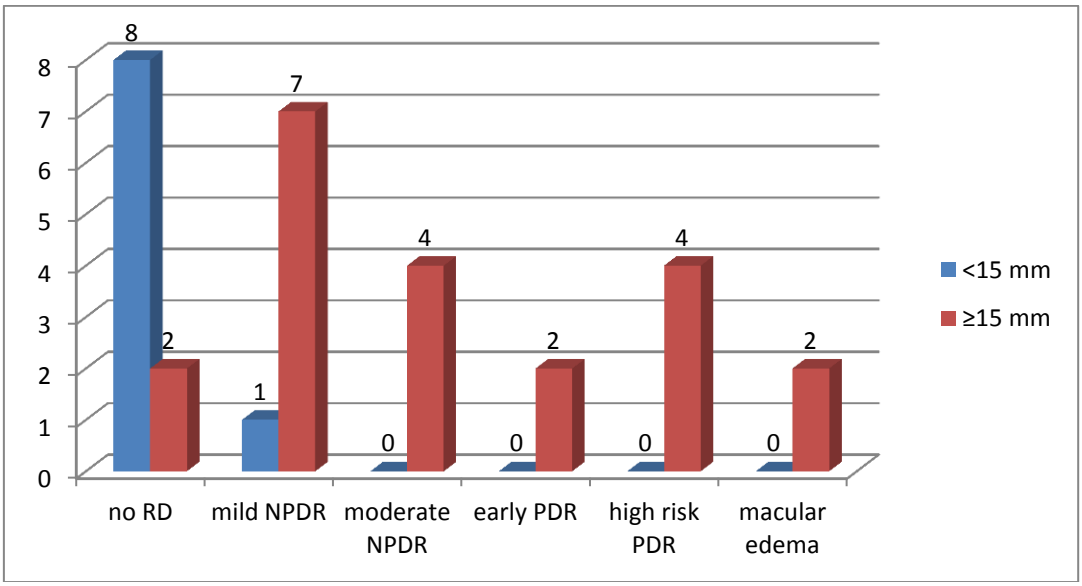


Figure 3 - Results of the Schirmer test in the patients with diabetes mellitus graded according the ETDRS criteria

Analyzing the relationship between the OSDI score and Schirmer test we found that there is a strong correlation between them for the entire studied population. This was indicated by Pearson's correlation factor r = -0.92.

Applying the Oxford test (7) to the DM group we obtained the following results: 23 patients (76.66%) with grade 0, 3 patients (10%) with grade I and 4 patients (13.33%) with grade II. In the control group the results were: 25 subjects (83.33%) with grade 0, 4 patients (13.33%) with grade I and 1 patient (3.33%) with grade II.

Photocoagulation was performed in 8 patients (26.66%): in 2 patients with early PDR, in 4 patients with high risk PDR and in 2 patients with macular edema.

DISCUSSION

Numerous studies have demonstrated that diabetic patients have lachrymal instability.

The Schirmer test is a useful screening method for diagnosing lachrymal hyposecretion. In diabetes patients, the Schirmer test exhibits lower than normal values (10, 11). In our study on 30 patients with type 2 DM and 30 control subjects, Schirmer tests were <15 mm at 5 min in 21 patients with DM (70%) and in 13 patients from the control group (43.33%) showing a strong relation with the stage of the diabetic retinopathy.

In a series by Dogru (12) 22.7% of the eyes impregnated the strip under 5.5 mm and in the Ozdemir (13) series, 34% did the same. Yu (14) described lower values for this test in eyes with proliferative diabetic retinopathy compared with those with nonproliferative diabetic retinopathy.

In an Iranian randomized study (5), carried out in 2007 on 199 type 2 DM patients, the dry eye prevalence was 54.3%, (108 patients) utilizing the diagnostic criterion that one of the tests, Schirmer or BUT, is pathological. Prevalence of dry eye syndrome was significantly higher in longer duration of diabetes, but sex and age did not seem to affect dry eye syndrome.

In the Ortiz study, in 2010, on a total of 129 diabetic eyes, 51.5% had a normal Schirmer test against 48.85% that gave a pathological result (15).

In Goebels study, Schirmer test and tearing reflex was significantly lower in DM patients compared with control group (16).

The tear breakup time (BUT) test is shortened in some diabetic patients. (3, 14). In our study TBUT was under the value of 15 sec in 66.66% of the diabetic patients, compared with the 46.44% from the control subject group. Lower TBUT values were encountered in advanced stages of DM. The results of this test are lower in the patients who suffer from proliferative diabetic retinopathy compared with nonproliferative diabetic retinopathy patients. Ortiz identifies only 19% of patients with pathological Schirmer and BUT tests (15). In Jin study, 100 patients with type 2DM were compared with 80 normal healthy controls. In this study TBUT was significantly lower in type 2 DM patients (17).

Using the Ocular Surface Disease Index (OSDI) questionnaire we identified that severe dry-eye symptoms can be found in patients with advanced stages of diabetic retinopathy (26.66%). Seifart et al compared 92 patients with types 1 and 2 DM, aged from 7 to 69 years with a group of normal healthy controls comparable in number, age and sex. The results show that 52.8% of all diabetic subjects had dry eye symptoms, compared with 9.3% of the controls. They revealed that close monitoring of diabetic patients and good blood sugar regulation is important for the prevention of dry eye syndrome and retinopathy (18).

In other study the tests were carried out on a 100 individuals (50 healthy subjects in control group and 50 subjects with diabetes), age 50–70 years. In the DM group (N = 50) they found that 37 patients (74%) had lower values of tear secretion and a number of 23 (46%) had lower values of TBUT. In the control group (N = 50) they found 28 patients (56%) with lower values of tear secretion and 17 (34%) with lower values of TBUT (19).

CONCLUSION

Our results support the idea that diabetic patients have an elevated prevalence of dry eye syndrome. Diabetic retinopathy and dry eye seem to have a common association. Further studies need to be undertaken to establish an etiologic relationship. However, examination for dry eyes should be an integral part in evaluating diabetic patients.

"Research carried out with financial support (in part) of the European Social Fund, through the HRD (POSDRU) 107/1.5/S/78702".

REFERENCES

1. Harrison TR: Diabetes Mellitus. In Harrison Principle of Internal Medicine 15th edition. Edited by: Branwald E, Fauci S, Kasper D, Hauser LS, L Longo D, Jameson JL. USA, Mc Grow-Hill; 2001:2121.

2. Sánchez Thorin J. The cornea in diabetes mellitus. Int Ophthalmol Clin. 1998;38:19-36.

3. Dogru M, Katakami C, Inoue M. Tear function and ocular surface changes in noninsulin-dependent diabetes mellitus. Ophthalmology. 2001;108:586-92.

4. Inoue K, Kato S, Ohara C, Numaga J, Amano S, Oshita T. Ocular and systemic factors relevant to diabetic keratoepitheliopathy. Cornea. 2001;20:798-801.

5. Manaviat MR, Rashidi M, Afkhami-Ardekani M, Shoja MR.Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. BMC Ophthalmology.2008;8:10.

6. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000;118:615-621

7. Bron AJ. The Doyne Lecture: reflections on the tears. Eye.1997;11:583-602.

8. American Academy of Ophthalmology: Basic and Clinical Science Course Section 7 2002–2003: Orbit, Eyelids, and Lacrimal System (Basic & Clinical Science Course). American Academy of Ophthalmology 1st edition. 2002:244-245.

9. Early Treatment Diabetic Retinopathy Study research group. Photocoagulation for diabetic macular edema: Early Treatment Diabetic Retinopathy Study report number 1. Arch Ophthalmol. 1985;103:1796–1806.

10. Lemp MA, Hamill JR. Factors affecting tear film breakup in normal eyes. Arch Ophthalmol. 1973;89:103-5.

11. Nelson JD, Havener VR, Cameron JD. Cellulose acetate impressions of the ocular surface. Dry eye states. Arch Ophthalmol. 1983;101:1869-72.

12. Dogru M, Katakami C, Inoue M. Tear function and ocular surface changes in noninsulin-dependent diabetes mellitus. Ophthalmology. 2001;108:586-92.

13. Ozdemir M, Buyukbese MA, Cetinkaya A, Ozdemir G. Risk factors for ocular surface disorders in patients with diabetes mellitus. Diab Res Cl Pract. 2003;59:195-9.

14. Yu L, Chen X, Qin G, Xie H, Lv P. Tear film function in type 2 diabetic patients with retinopathy. Ophthalmologica. 2008;222:284-91.

15. Figueroa-Ortiz L.C, Jiménez Rodríguez E, García-Ben A, García-Campos J. Study of tear function and the conjunctival surface in diabetic patients. Arch. Soc. Esp. Oftalmol. 2011;86(4):107–112.

16. Goebbels M: Tear secretion and tear film function in insulin dependent diabetics. Br J Ophthalmol 2000, 84(1):19-21.

17. Jin J, Chen LH, Liu XL, Jin GS, Lou SX, Fang FN: Tear film function in non insulin dependent diabetics. Zhonghua Yan Ke Za Zhi 2003, 39(1):10-3.

18. Seifart U, Strempel I: The dry eye syndrome and diabetes mellitus. Ophthalmologe 1994, 91(2):235-239.

19. Janjetovi Ž, Vukovi-Arar Š, Bešli R, Vajzovi - Dalipi V, Marini M, Samardži K: The dry eye syndrome and diabetes. Institute: Opa bolnica "Dr. Josip Ben.evi", Slavonski Brod.

20. Moss SE, Klein R, Klein BEK: Prevalence of and Risk Factors for Dry Eye Syndrome. Arch Ophthalmol 2000, 118:1264-1268.

21. Early Diabetic Retinopathy Study Research Group, Grading diabetic retinopathy from stereoscopic color fundus photograph- an extension of the modified Airlie House classification: ETDRS Report number 10. Ophthalmology. 1991;98:786–806.

22. American Academy of Ophthalmology: Basic and Clinical Science Course Section 7 2002–2003: Orbit, Eyelids, and Lacrimal System (Basic & Clinical Science Course). American Academy of Ophthalmology 1st edition. 2002:244-245.

23. Cousen P, Cackett P, Bennett H, Swa K, Dhillon B. Tear production and corneal sensitivity in diabetes. J Diabetes Complicat. 2007;21:371-3.

24. Nepp J, Abela C, Polzer I, Derbolav A, Wedrich A. Is there a correlation between the severity of diabetic retinopathy and keratoconjunctivitis sicca?. Cornea. 2000;19:487-91.

25. Yoon K, Im S, Seo M. Changes of tear film and ocular surface in diabetes mellitus. Korean J Ophthalmol. 2004;18:168-74.

26. Moss SE, Klein R, Klein BEK: Incidence of Dry Eye in an Older Population. Arch Ophthalmol 2004, 122:369-373.

27. Sendecka M, Baryluk A, Polz-Dacewicz M: Prevalence of and risk factors for dry eye syndrome. Przegl Epidemiol 2004, 58:227-33.

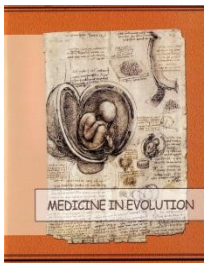
Centrele de Cercetare blend-a-med și Oral-B

Este nevoie de efort - zi de zi - pentru a îmbunătăți cu adevărat sănătatea orală a pacienților. De aceea, P&G Oral Health, cu Centrele sale de Cercetare blend-a-med și Oral-B îi susține pe medicii dentiști atât în cabinet, cât și prin extinderea influenței lor dincolo de unitul dentar. Când pacienții părăsesc cabinetul de medicină dentară, produsele și serviciile noastre sunt un sprijin pentru ei.

blend-a-med RESEARCH CENTERS Oral-B

P&G Oral Health

CAMOUFLAGE THERAPY IN CLASS II ANGLE ANOMALIES -APLICABILITY AND LIMITATIONS



MELINDA ONEŢ[1], ANGELA CODRUŢA PODARIU [2], RAMONA AMINA POPOVICI [2], RODICA JIANU[1], RUXANDRA SAVA-ROŞIANU[,2], ROXANA OANCEA[2]

1. **West University "Vasile Goldiş", Faculty of Dentistry, Arad**
2. **University of Medicine and Pharmacy "Victor Babeş", Timişoara**

ABSTRACT

Therapy based on the extraction of two upper premolars 14 şi 24, also called „Camouflage therapy" is well renonwed in the treatment of class II Angle anomalies. Nevertheless, it has to be mentioned that it can not be used in every situation, but only when the cephalometric analisys indicates and sustaines this approach. A ferm diagnostic has to be set at the beginning and throughout the treatment because some problems that need immediate fixing, may occur.

***Keywords**: Class II Angle anomalies, underdivision 1 and 2, camouflage therapy*

Correspondence to:

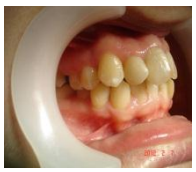
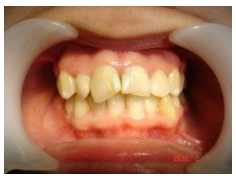
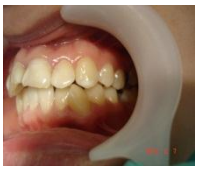
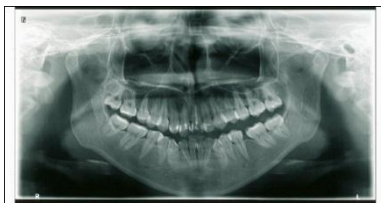
Dr. Melinda Onet. University of Medicine „Vasile Goldis" Arad
Str. Calarasilor nr. 3,
tel. 0744625572,
e-mail: melindaonet@gmail.com

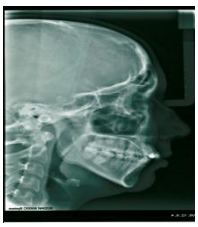
INTRODUCTION

A treatment plan choosen by an orthodontist does not always comply with the patient's expectation. The therapist has to find the way to obtain the desired results but also keep the patient's wishes, regarding treatment time and aesthetics, in mind. Aestethics plays a major part in these cases but, optimizing the functionality of the dento-maxillary system is also very important. In class II Angle anomalies, both the alveolar as well as the skeletal component should always be kept in mind. These patients show an incorrect position of the upper incisors and a mandibular retrognatia or maxillary prognatia.
If the therapist can't influence the bone dimension during growth, there are two treatment alternatives:
1. camouflage therapy; after the extraction of the two upper premolars, the distalized occulsion is maintained in the lateral arches, the retraction of the upper canine and a neutral occlusion is obtained.
2.when extraction therapy is not indicated, mesialization of the mandibula is needed using a complex device like "Easy Fit Jumper".
Any of these two alternatives modify the patient's aspect, leading sometimes to disapproval from the patient.

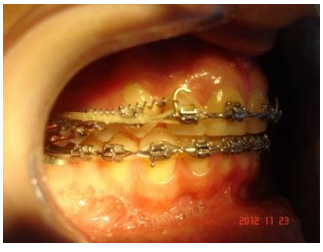
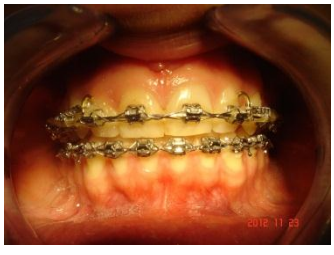
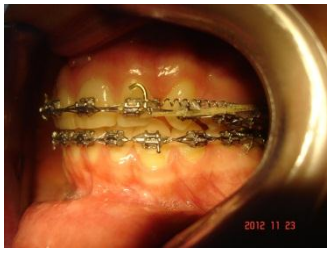
MATERIAL AND METHOD

Case 1
21 years old patient, comes to the clinic because of the inaesthetic aspect of the incisors seen when the patient smiles. Beside the problems signaled by the patient, the diagnostic is much more complex, in the lateral arches as well. The diagnostic is dento-alveolar disarmony with crowdings, class II Angle anomaly, multiple rotations, lack of 36 and 45.



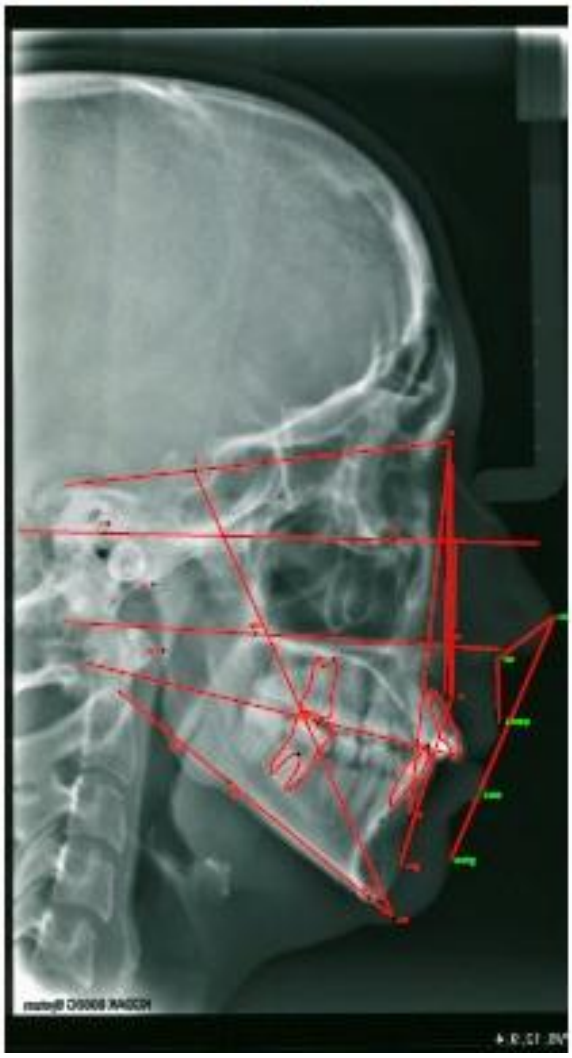
A multiband self ligatured device was used togheter with the Nance-Eva device, upper premolar extraction have been performed, NITI de 0,014"; 0,016"; 0,022"/0,025" wires were applied, then a retraction SS 0.020" wire to put the upper canines in place. The Nance – Eva device was removed, and a 0,019"/0,025" SS retraction wire for the whole frontal group as well as a brased posted SS wire was applied, obtaining an intermediate result as shown in the pictures. Neutral occlusion has been obtained for the canines, class II relation for the molars.

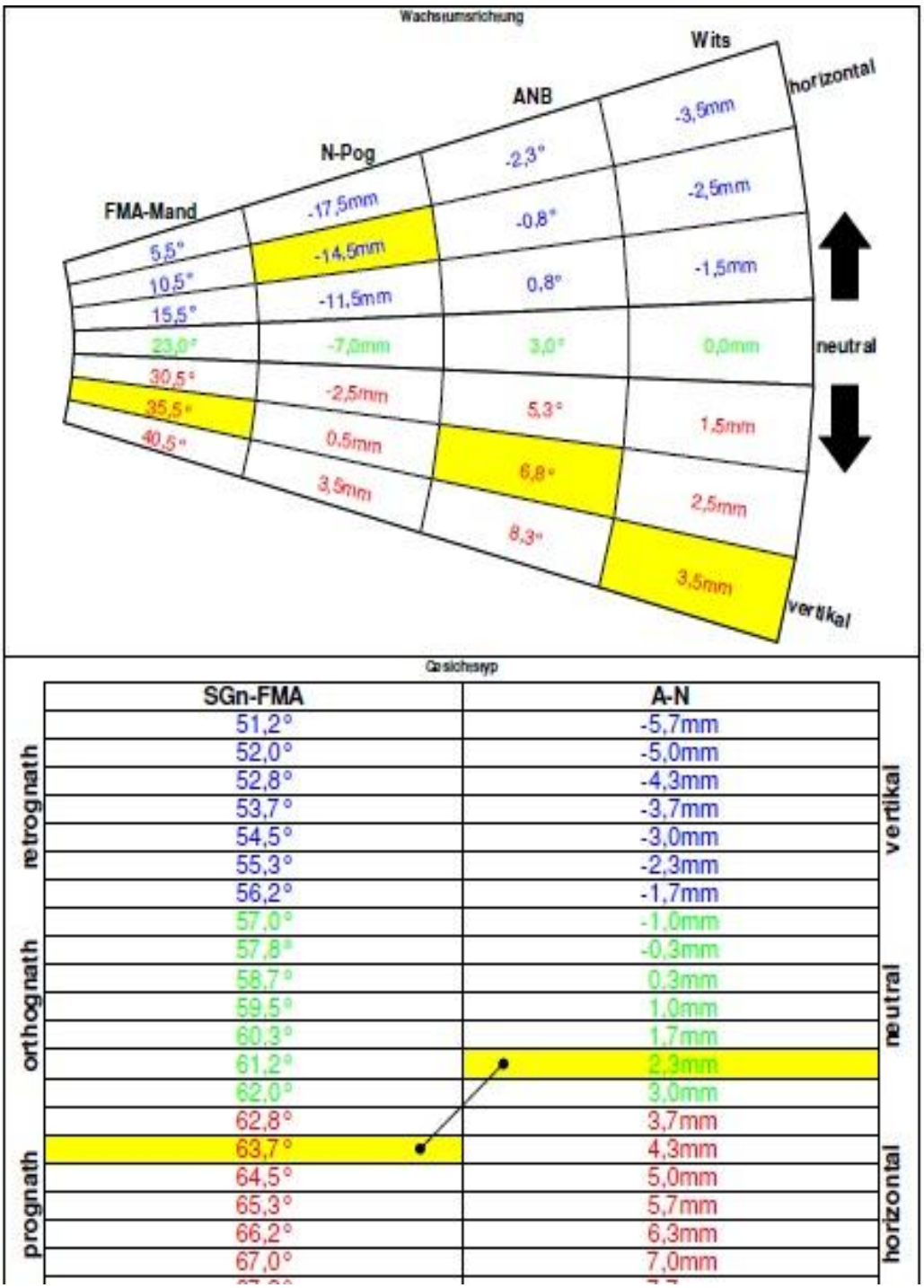




Analyse : «MacGan» - MacGan-Analyse

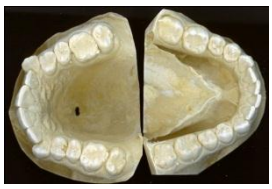
Parameter	Norm	Messwert	Kommentar / Befund
Pal-Mand	28,5 ± 4,5	34,9 °	offen
FMA-Mand	23,0 ± 5,0	37,0 °	offen
SGn-FMA	59,5 ± 2,5	63,8 °	vertikal
A-N	1,0 ± 2,0	2,6 mm	
SNA	79,5 ± 3,5	84,2 °	prognath
N-Pog	-7,0 ± 3,0	-15,1 mm	retrogen
SNB	79,0 ± 4,0	77,3 °	
ANB	3,0 ± 1,5	6,9 °	Skel. Klasse II
Wits	0,0 ± 1,0	5,3 mm	Klasse II
1OK-1UK	127,5 ± 2,5	125,6 °	bestes Finish
1UK-ME	93,5 ± 4,5	84,2 °	retroklin.
1UK-NB	3,5 ± 2,5	3,8 mm	
1UK-APog	2,0 ± 2,0	-3,2 mm	retrudiert
1OK-SN	102,5 ± 3,5	104,8 °	
1OK-APog	4,5 ± 2,5	8,3 mm	protrudiert
1OK-A-FMA	4,0 ± 2,0	-2,3 mm	retrudiert
SnW	100,0 ±10,0	124,1 °	
LbSup-ELinie	1,5 ± 2,5	-3,4 mm	hinter
LbInf-ELinie	1,5 ± 2,5	0,0 mm	

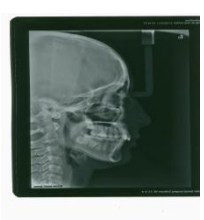
Femrönogen, sonlich -> Der Ausdruck ist nicht für die primäre Befundung und Archivierung bestimmt

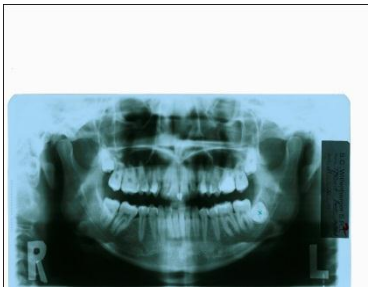




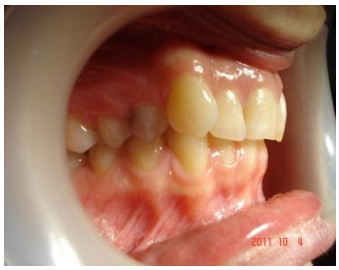
Case 2
26 years old patient, class II Angle anomaly, deep bite, upper canine ectopy, multiple rotations.

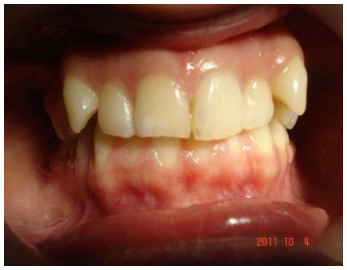


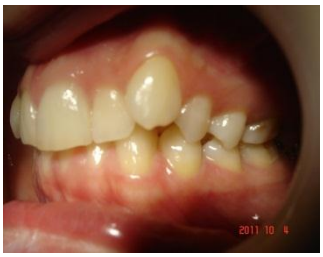


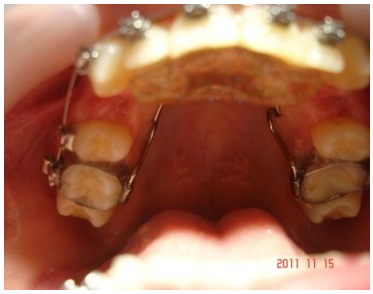


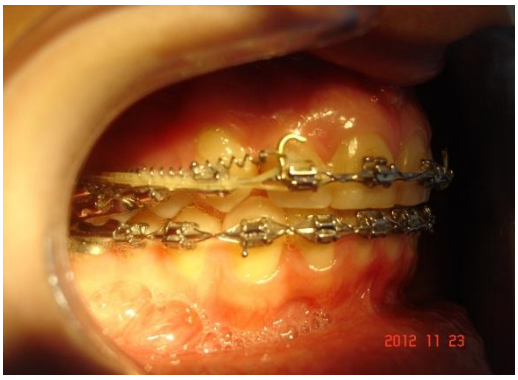
A multiband self ligatured device was used togheter with the Nance-Eva device, upper premolar (14, 24) extraction have been performed. After the round and rectangular NiTi wires, the canine retraction 0,020" SS wire has been placed. When the canines reached the dsired position, the Nance-Eva device has been removed, and the retraction of the whole frontal groub has been obtained using a 0,019"/ 0,025" brased
posted SS wire, with NITI closed coils and elastic forces.
At this time point, there still are 1 mm spaces to be closed both on the left and the right handside. The evolution is good.

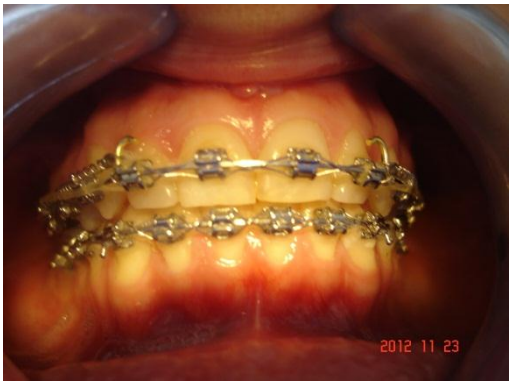


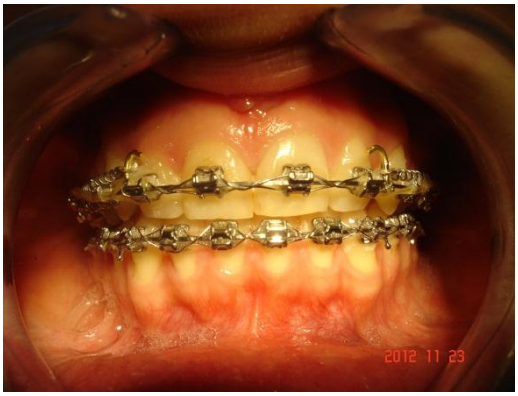


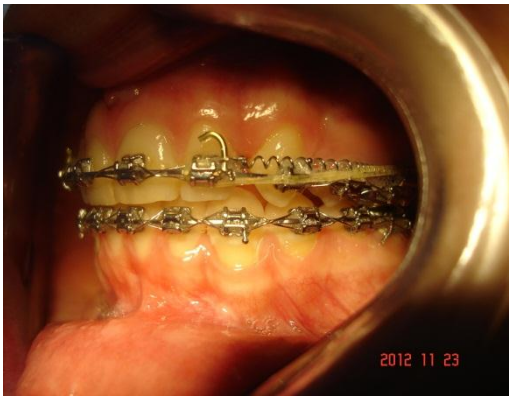












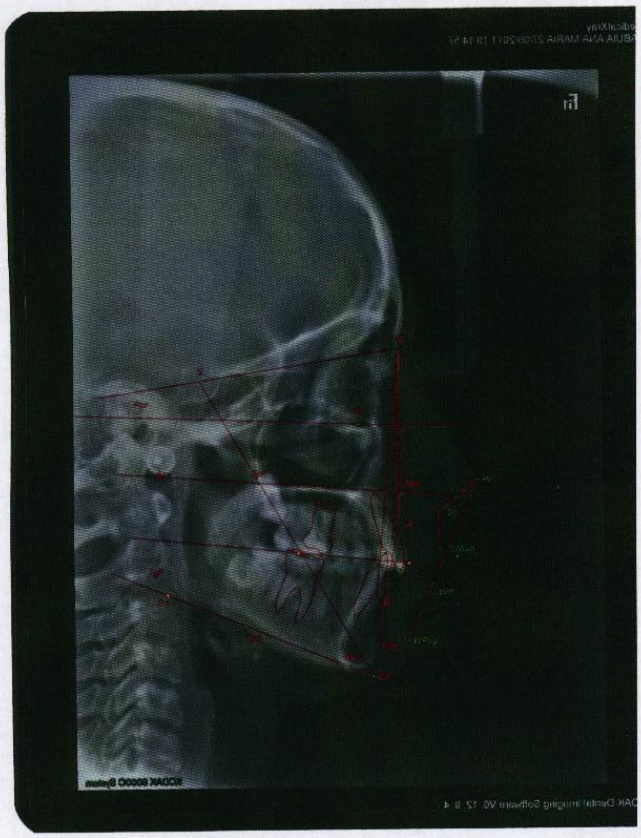
PatNr. : 323
Name : TABUIA, ANA MARIA
Geschlecht : w, kaukasisch
Geboren am : 21.03.1986 (25 J + 6 M)
Datum : 12.10.2011
Behandler : DR ONET
Gedruckt am : Di, 06.11.2012, 13:05:46

Analyse: «MacGan» - MacGan-Analyse

Parameter	Norm	Messwert	Kommentar / Befund
Pal-Mand	28,5 ± 4,5	17,7 °	geschlossen
FMA-Mand	23,0 ± 5,0	19,9 °	
SGn-FMA	59,5 ± 2,5	57,6 °	
A-N	1,0 ± 2,0	1,6 mm	
SNA	79,5 ± 3,5	80,7 °	
N-Pog	-7,0 ± 3,0	-4,3 mm	
SNB	79,0 ± 4,0	75,5 °	
ANB	3,0 ± 1,5	5,2 °	Skel. Kasse II
Wits	0,0 ± 1,0	4,8 mm	Klasse II
1OK-1UK	127,5 ± 2,5	134,7 °	
1UK-ME	93,5 ± 4,5	94,3 °	
1UK-NB	3,5 ± 2,5	1,7 mm	
1UK-APog	2,0 ± 2,0	-2,3 mm	retrudiert
1OK-SN	102,5 ± 3,5	100,1 °	
1OK-APog	4,5 ± 2,5	3,1 mm	
1OK-A-FMA	4,0 ± 2,0	-0,9 mm	retrudiert
SnW	100,0 ±10,0	127,2 °	
LbSup-ELinie	1,5 ± 2,5	-2,3 mm	hinter
LbInf-ELinie	1,5 ± 2,5	-0,9 mm	

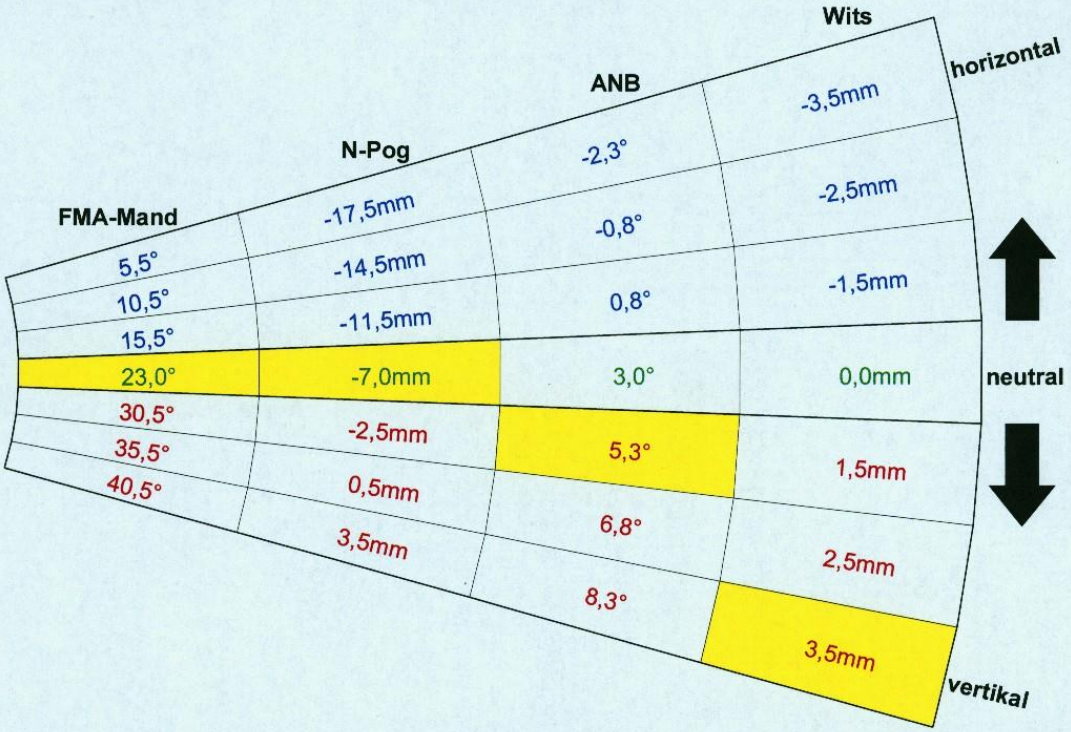
Lineare Werte berechnet für Fokus-Filmdist.: Inf. cm / V = 1,000

Fernröntgen, seitlich **-> Der Ausdruck ist nicht für die primäre Befundung und Archivierung bestimmt!**



PatNr. : 323
Name : TABUIA, ANA MARIA
Geschlecht : w, kaukasisch
Geboren am : 21.03.1986 (25 J + 6 M)
Datum : 12.10.2011
Behandler : DR ONET
Gedruckt am : Di, 06.11.2012, 13:05:47

Wachstumsrichtung



Gesichtstyp

	SGn-FMA	A-N	
retrognath	51,2°	-5,7mm	vertikal
	52,0°	-5,0mm	
	52,8°	-4,3mm	
	53,7°	-3,7mm	
	54,5°	-3,0mm	
	55,3°	-2,3mm	
	56,2°	-1,7mm	
orthognath	57,0°	-1,0mm	neutral
	57,8°	-0,3mm	
	58,7°	0,3mm	
	59,5°	1,0mm	
	60,3°	1,7mm	
	61,2°	2,3mm	
	62,0°	3,0mm	
prognath	62,8°	3,7mm	horizontal
	63,7°	4,3mm	
	64,5°	5,0mm	
	65,3°	5,7mm	
	66,2°	6,3mm	
	67,0°	7,0mm	
	67,8°	7,7mm	

DISCUTIONS

The age of the patient influences the type of device as well as the anomaly. If, for young ages, functional devices were used (Activator, Bionator, double mandibular propultion plate) and the desired results havn't been obtained – especially for genetic determined cases – the treatment has to be focused on a multiband technique. Taking into consideration the patient's profile, the therapist can use:

-Camouflaj treatment – bilateral extraction of the upper premolars and fixed therapy.

-Fixed therapy togheter with other accessories like Easy Fit Jumper, Herbst, Jasper-Jumper etc.

For patients who are not caught during the growth period, the modifications are predominantly dento-alveolar.

"HARZER" says that without the lack of space, a determinant role in deciding the diagnostic have: the appical base, the profile, the naso-labial angle, the growth direction, the leaning of the upper incisors and the implantation and inclusion of the other teeth.

For more anchorage, miniimplants can be used vestibular or palatal.

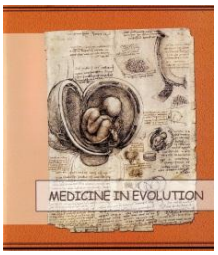
CONCLUSION

Camouflage therapy is an alternative for the treatment of class II anomalies. It has to be used only after carefull evaluation and diagnosis. Diagnosis has to be set before starting the therapy and has to be sustained, because problems can occur and have to be solved immedialtly.

REFERENCES

1. Bauer N, Heckmann K, Sand A, Lisson JA – Craniofacial growth patterns in patients with congenitally missing permanent teeth. J Orofac Orthop 2009;70:139-151;
2. Katsaros C, Ripplinger B, Hogel A, Berg R – The influence of extraction versus non-extraction orthodontic treatment on the soft tissue profile. J Orofac Orthop 1996;57:354-365;
3. Kinzinger G, Frye L, Dietrich P – Class II treatment in adults: comparing camouflage orthodontics, dentofacial orthopedics and orthognathic surgery – a cephalometric study to evaluate various therapeutic effects. J Orofac Orthop 2009;70:63-91;
4. Wedler S, Trankmann J, Lisson JA – Treatment outcome in Angle class II, division 1 patiens in pre-puberty and puberty after jumping the bite appliance. J Orofac Orthop 2006;67:105-115;
5. Weyrich C, Lisson JA – The effect of premolar extraction or incisor position and soft tissue profile in patiens with class II, division 1 malocclusion. J Orofac Orthop 2009;70:128-138;
6. Zetu I – Ortodonție. Tehnica arcului drept, editura Tehnopress, Iași 2010.

RELATIONSHIP BETWEEN AESTHETIC MOTIVATION AND PREFERENCES FOR ORTHODONTIC TREATMENT



ALI FAHS[1], ANCA TEMELCEA[1], DANIELA MĂNUC[1]

[1] University of Medicine and Pharmacy „Carol Davila" Bucharest

ABSTRACT

The aim of this study was to evaluate the relationship between aesthetic motivation and preferences for orthodontic treatment.

The cluster sample consisted of twenty consecutive patients.

The impact of aesthetic on patients' life was confirmed in this study.

In conclusion, facial appereance should be evaluated and taken into consideration in treatment planning.

Keywords: *orthodontic treatment, facial appearance, aesthetic.*

Correspondence to

Dr. Ali Fahs,
University of Medicine and Pharmacy „Carol Davila"
Dionisie Lupu 37,
Bucharest, Romania,
e-mail address: dr.ali.fahs@gmail.com

INTRODUCTION

The objective of orthodontic treatment is to accomplish improved functional occlusion and aesthetic appearance [1].

Although appropiate functional changes in the dento-maxillary system is highly valued
in orthodontic treatment, satisfaction is usually high if the patient's expectations concerning facial appearance are also fulfilled [2].

Thereby, the aesthetic motivation of the patient for seeking orthodontic therapy and his expectations of the results must be considered in treatment planning.

Reports on how patients experience orthodontic treatment are lacking in Romania, although in the last decades this treatment approach has increased.

The aim of this study was to determine the motivation for orthodontic patients seeking orthodontic treatment.

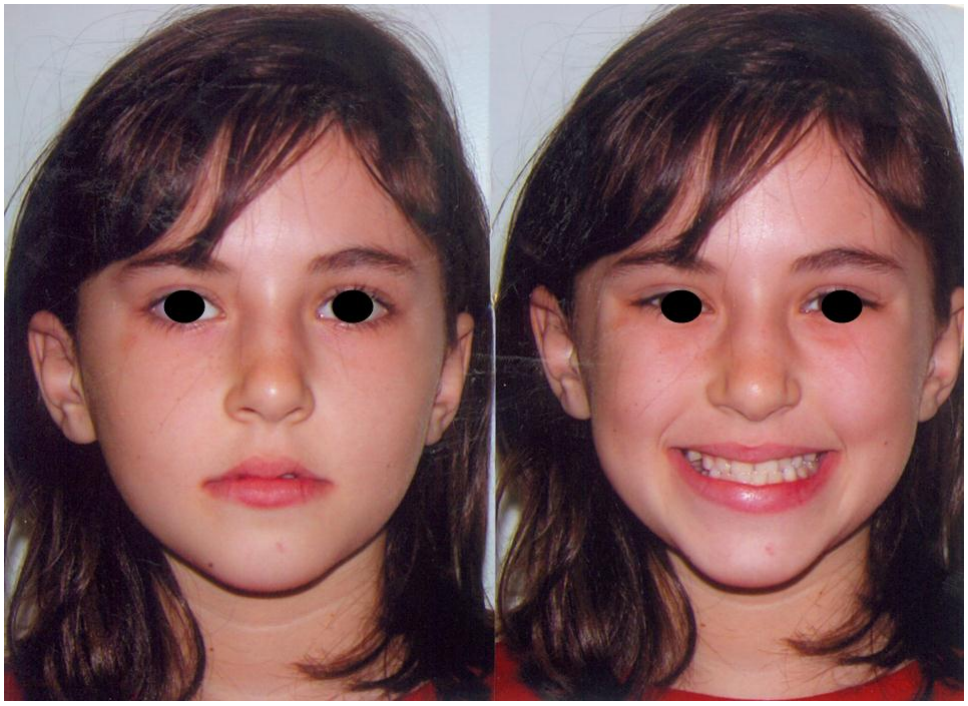
MATERIAL AND METHODS

We have preformed a retrospective analysis on 20 consecutive patients treated during the period 2009–2012 by the main author who carried out the study.

All patients had a follow-up period of 24 months .

Motivations for starting treatment and patients'satisfaction with treatment results were evaluated on the basis of replies to a questionnaire collected on the examination day.

The orthodontic evaluation included medical history, a dental and orthodontic history, clinical examination, photographs of the patient's face (Figure 1) and teeth (Figure 2), plaster study models of the teeth (Figure 3), a panoramic x-ray and a full lateral skull x-ray of the patient's profile (Figure 4).



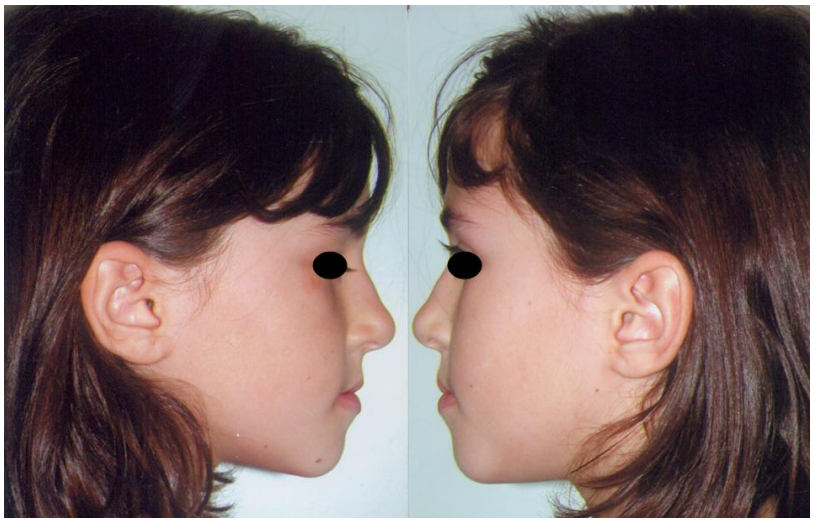


Fig.1 *Facial photographs before orthodontic treatment*

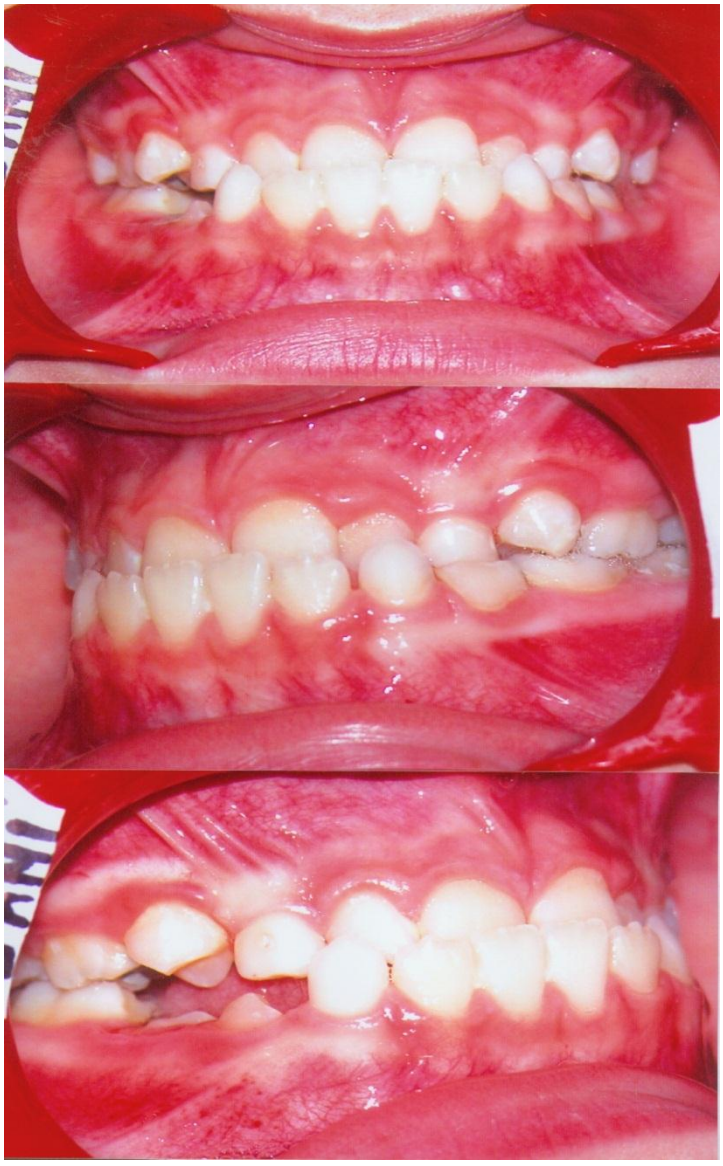


Fig.2 *Intraoral photographs before orthodontic treatment*

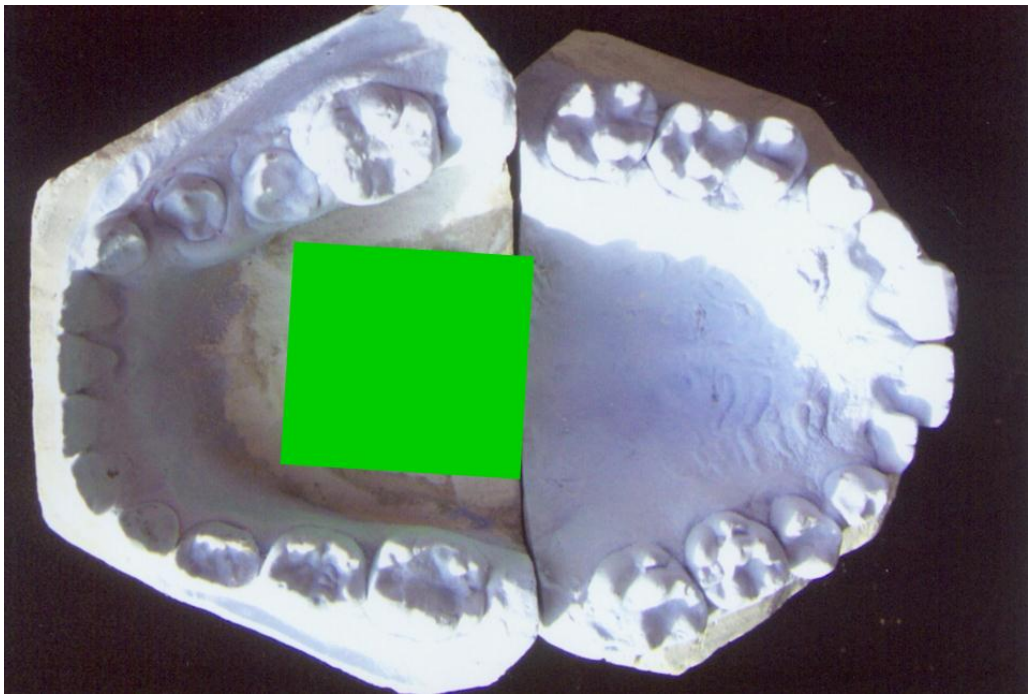


Fig. 3 *Preliminary setup of a plaster study model*

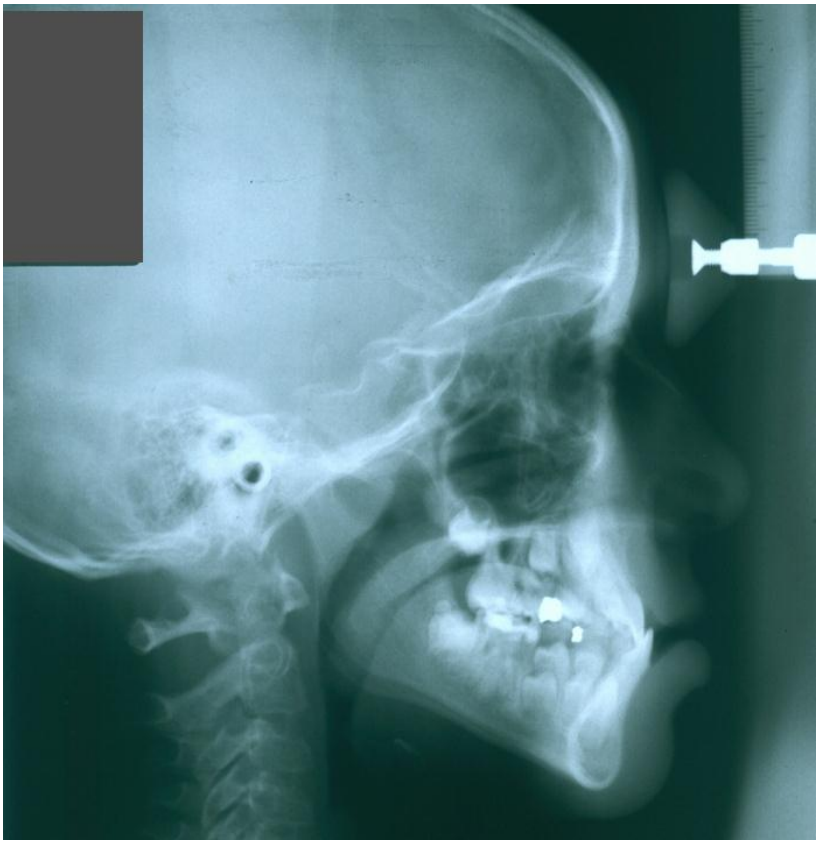


Fig. 4 *Cephalometric radiography*

The records from the follow-up examination were compared with the respective pre-treatment records to evaluate the treatment outcome objectively (Figure 5).

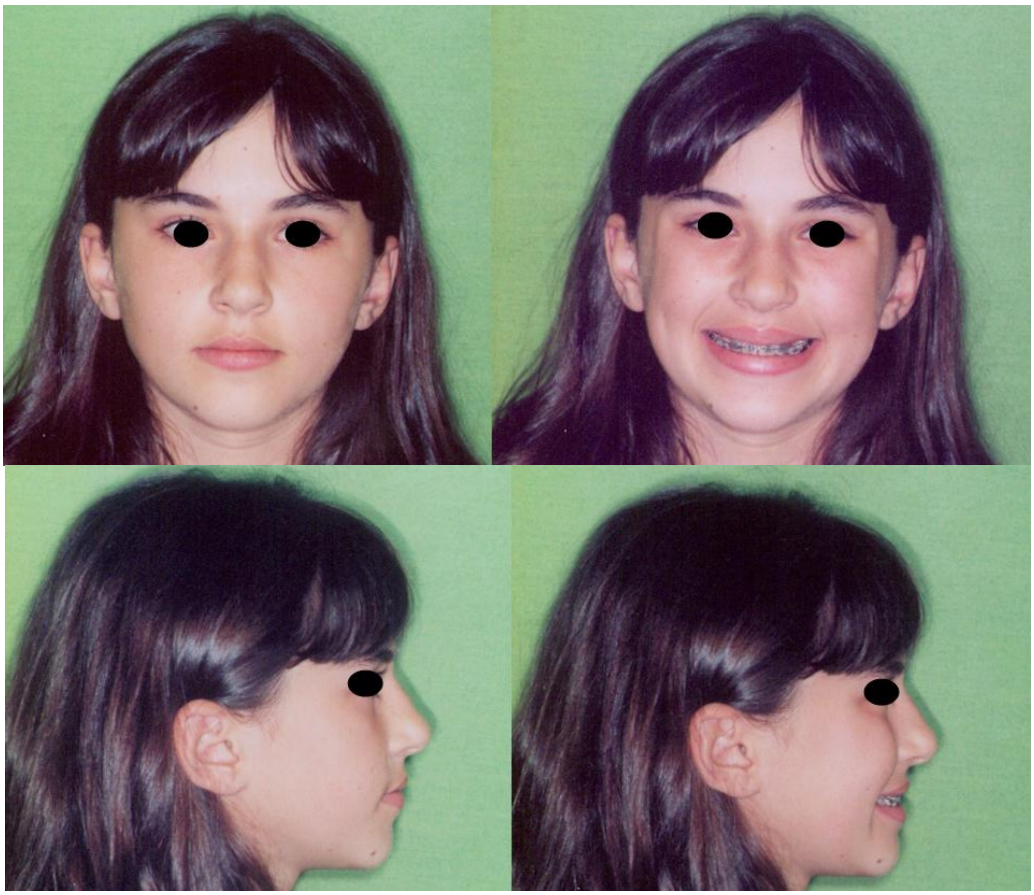


Fig. 5 *Facial photographs after orthodontic treatment*

The improvement in the occlusion was assessed by comparing the plaster models, photographs and panoramic x-ray (Figure 6).

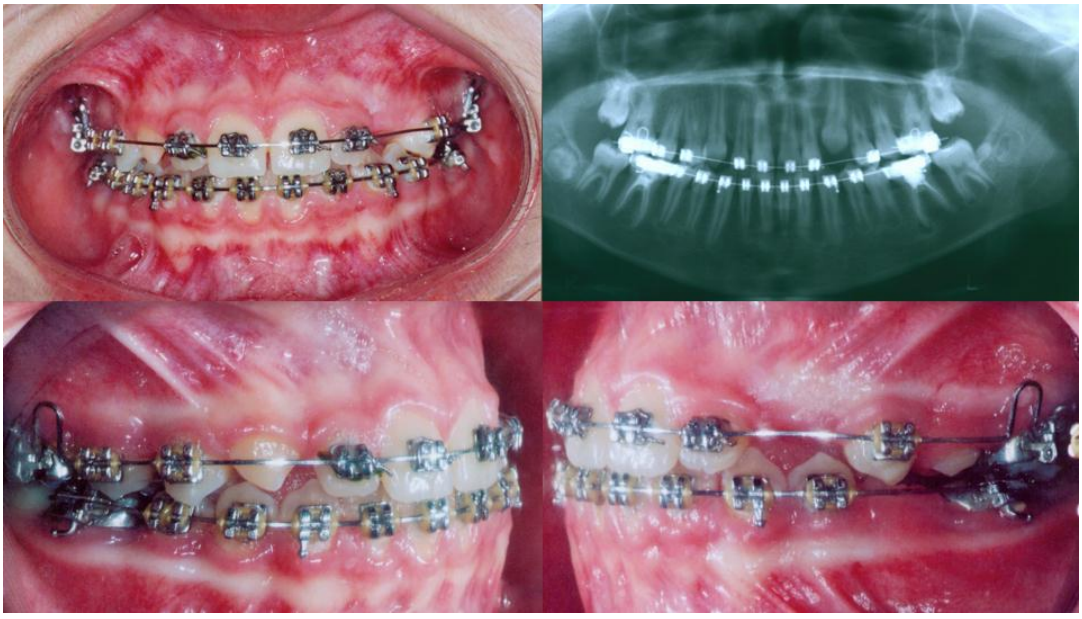


Fig. 6 Clinical and radiological outcome following orthodontic treatment, with dramatic improvement in the occlusal relationship

The lateral cephalometric radiographs were analysed using the classic cephalometric analysis (Figure 7).

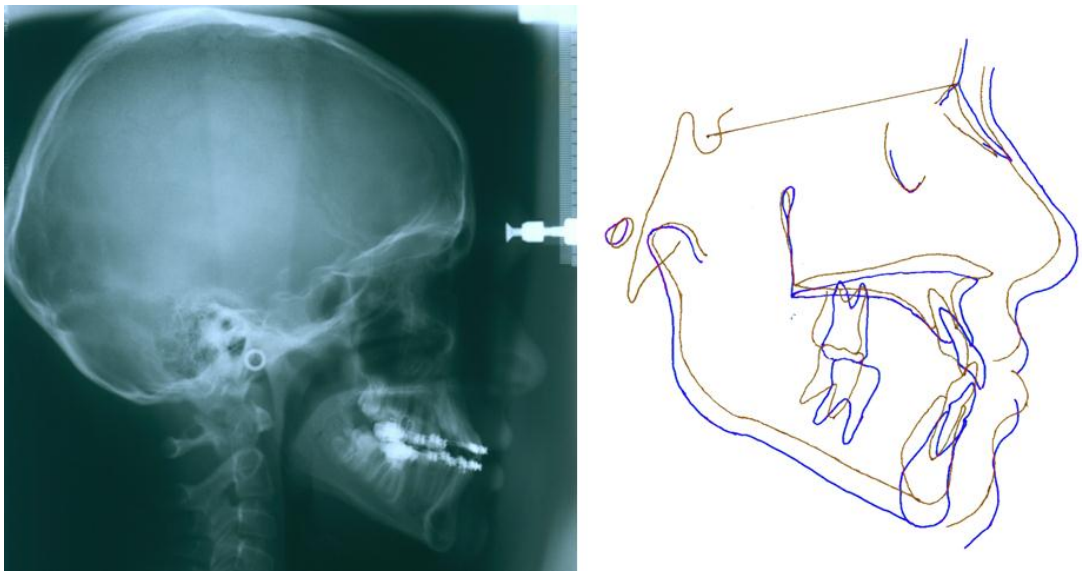


***Fig. 7** Conventional linear and angular cephalometric measurements*

RESULTS

In our sample the most common reasons for seeking orthodontic treatment was dissatisfaction with facial appearance (%) and eating problems (%). Another reason of complain was temporomandibular joint pain (%) (Table 1).

	Number of patients	**%**
Dissatisfaction with facial appearance	13	65
Chewing difficulties	4	20
TMJ pain	3	15

Table 1

The satisfaction of the patients at the end of treatment is depicted in the Table 2.

	Very satisfied	**Fairly well satisfied**	**Somewhat dissatisfied**	**Very dissatisfied**
Facial appearance	9	2	2	0
Chewing	0	4	0	0
TMJ painless	0	0	2	1

Table 2 The patient satisfaction with the treatment outcome

Eleven patients considered that their facial appearance had improved after orthodontic treatment. Two other patients felt that her facial appearance had worsened.

The most satisfied patients were those whose main motivation for seeking orthodontic treatment eating problems (Table 2).

The anatomical occlusion had improved in all the patients.

The cephalometric analysis revealed that the number of patients, whose cephalometric dimensions were two standard deviations outside the mean values, had decreased.

DISCUSSION

The wish for improved facial aesthetics is the major reason for seeking orthodontic treatment.

The majority of our patients noticed an considerably improvement in their facial appearance post-treatment. This result is in agreement with earlier studies[3,4].

As the result is based on subjective assessment by the patients, it is impossible to say whether a real improvement in chewing ability had occurred.

In this study, two patient were dissatisfied with her facial appearance, most possible due their false expectations.

The most satisfied patients were those who had undergone orthodontic treatment because of facial appereance and eating disorders.

CONCLUSION

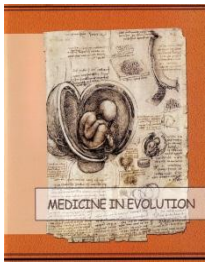
Quality of orthodontic treatment has profound implications for the practicing orthodontist and the patient.

Orthodontists usually evaluate the outcome of treatment by evaluation of malocclusion and cephalometric changes. The patients are usually more concerned with facial appereance implications. This may result in a lack of concordance between the orthodontist and the patient when evaluating success of the outcome of the treatment.

REFERENCES

1. Pogrel MA. What are normal esthetic values? *J Oral Maxillofac Surg* 1991; 49(9):963-969.
2. Philip C, Bennet ME, Brader HL. Dentofacial disharmony, psychological status of patients seeking treatment consultation. *Angle Orthod* 1998;68:547-56
3. Shue-Te Yeh M, Koochek AR, Vlaskalic V, Boyd R, Richmond S. The relationship of 2 professional occlusal indexes with patients' perceptions of aesthetics, function, speech, and orthodontic treatment need. *Am J Orthod Dentofacial Orthop* 2000; 118(4):421-428.
4. Flores-Mir C, Silva E, Barriga MI, Lagrave MO, Major PW. Lay person's perception of smile aesthetics in dental and facial views. *J Orthodont* 2004; 31(3):204-209

THE EFFECT OF INTERDISCIPLINARY TREATMENT ON MAXILLARY COMPRESSION CAUSED BY ORAL BREATHING



MATEESCU TEODORA[1], ALINA ANGLITOIU[2], PODARIU ANGELA[3] , RAMONA AMINA POPOVICI [3], MOJSE MARCEL[4], ROXANA OANCEA[3], RUXANDRA SAVA ROSIANU[3], DANIELA JUMANCA[3]

[1] City University Emergency Hospital "T. Andrei", ENT Department, Lugoj
[2] City University Emergency Hospital Timisoara, ENT Department
[3] University of Medicine and Pharmacy "Victor Babes" Timisoara, Department I
[4] Dental Private Practice, Timisoara

ABSTRACT

Lack of growth affects the whole face and is associated with flat cheeks, unattractive lips, large noses, tired eyes, double chin, receding chins and sloping forehead, features that will be readily recognized when there is a pronounced crowding of teeth.(1) Given the extent of information available, it is surprising that few dentists seem to be aware of the craniofacial effects from mouth breathing.

The journal General Dentist noted that "the vast majority of health care professionals are unaware of the negative impact of upper airway obstruction (mouth breathing) on normal facial growth and physiologic health. Children whose mouth breathing is untreated may develop long, narrow faces, narrow mouths, high palatal vaults, dental malocclusion (crooked teeth), gummy smiles and many other unattractive facial features. These children do not sleep well at night due to obstructed airways; this lack of sleep can adversely affect their growth and academic performance. Many of these children are misdiagnosed with attention deficit disorder (ADD) and hyperactivity. (1)

key words: *mouth breathing, nasal breathing, maxillary compression, dental malocclusion.*

Correspondence to

Dr. Mojse Marcel.
Adress: Bul. Revolutiei No.22 ap.1 Profident, Timisoara.
E-mail address: drzuba79@yahoo.com

INTRODUCTION

Mouth breathing is a situation that has been related to hypoxia (1). The term mouth breathing is not always an appropriate term. In most conditions, there is a combination of oral and nasal breathing (2). In fact, combination of oral and nasal breathing and only 4.3% are truly mouth breathers (3). Mouth breathing could be an outcome of nasal obstruction; therefore, any sign of such situation must be considered in order to detect its underlying cause. Mouth breathing patients could have a relatively high chance of being hypoxemic and attempts to improve nasal breathing could be beneficial (3,4).

CASE 1

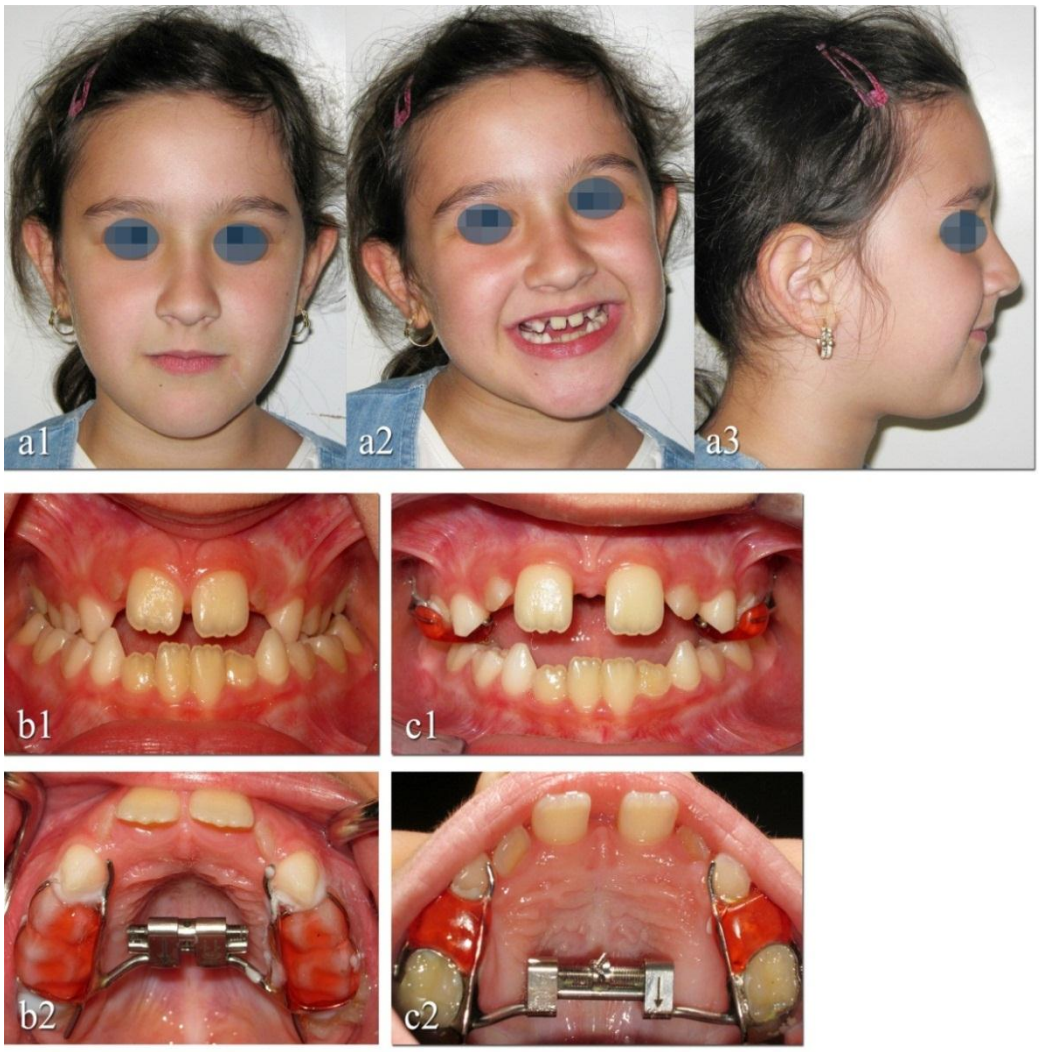


fig.1 clinical facial and oral aspect at the beginning of the orthodontic treatment
a1, a2, a3 – initial facial aspect; the proportion of the face is not respected; facial symmetry is not affected, labial competence.
b1, b2 – oral frontal and occlusal clinical aspect having the disjunctor; dento-alveolar incongruency, lack of space in the upper jaw, bilateral crossbite, tendency for class III malocclusion, open front bite.
c1, c2 – clinical oral aspect after rapid expansion, open expansor, diasthema, improvement of the transversal intermaxillary relationship.

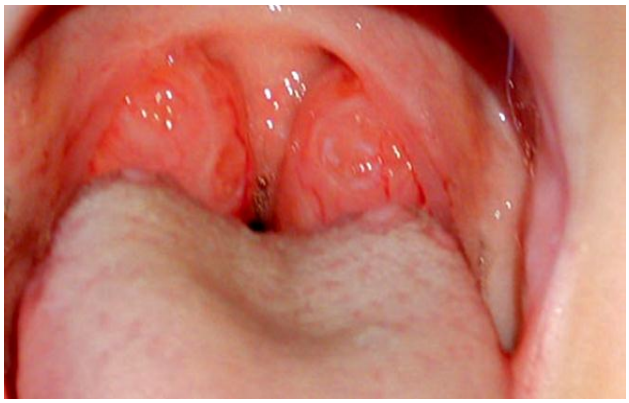


fig.2 Tonsils hipertrophya

fig.3 clinical facial and oral aspect during orthodontic treatment
a1, a2, a3 – facial aspect 5 months after treatment start clinic
b1, b2 – clinical oral aspect after rapid expansion

CASE 2

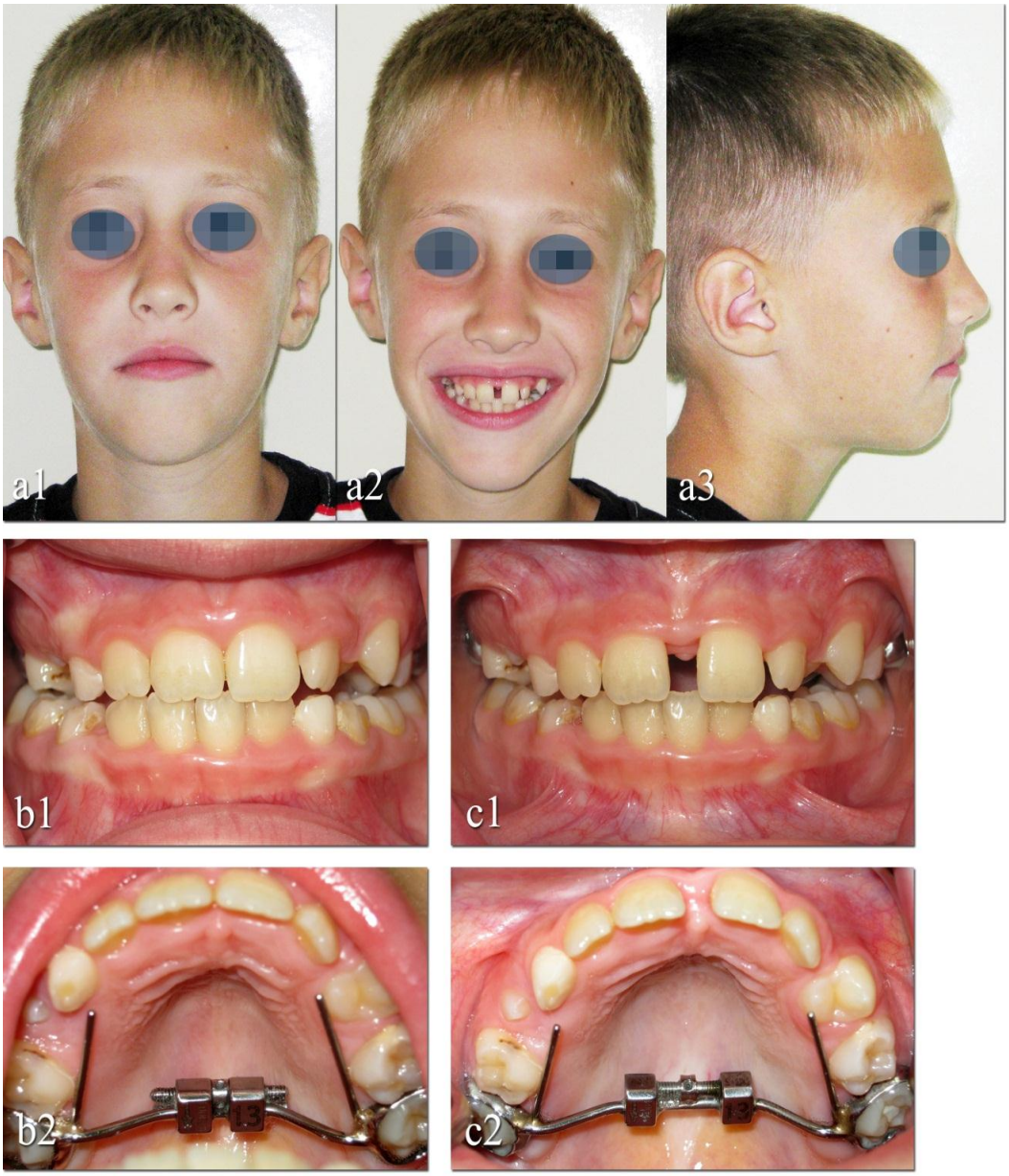


fig.4 facial and oral aspect at the beginning of orthodontic treatment.
a1, a2, a3 –initial facial aspect clinic
b1, b2 – oral frontal and occlusal aspect clinic; severe dento-alveolary incongruency, loss of temporary canine. 6.3 and mesialization of 2.4;
c1, c2 – clinical oral aspect after finalizing the expansion

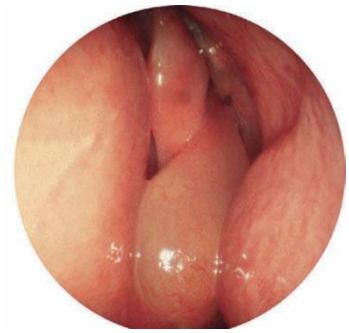


fig.5 Cause of oral breathing.

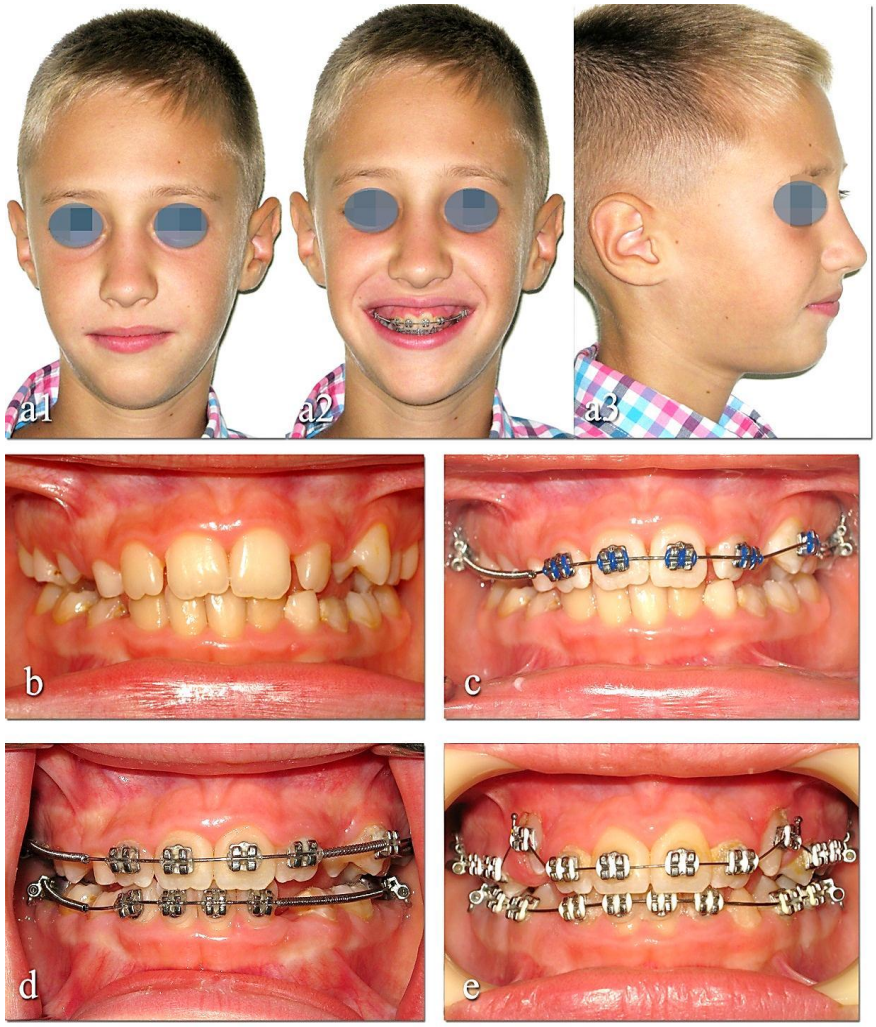


fig.6 Clinical facial and oral aspect during orthodontic treatment

a1, a2, a3 – clinical aspect 15 months after beginning of the orthodontic treatment
b – oral aspect aspect 4 months after rapid maxillary expansion
c, d, e – orthodontic fixed appliance at different time points.

CONCLUSION

All children who are chronic mouth-breathers will develop a malocclusion.
It is possible to help many children establish nasal breathing. For many children mouth breathing is a habit that can be broken.

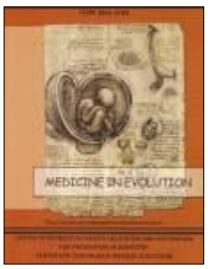
Often before establishing nasal breathing we need to expand the upper arch to make room for the tongue to rest and function there. After expansion, unless the tongue learns to rest and function in the palate the arch form will relapse.

To establish nasal breathing in growing children requires very few technical skills on the part of the practitioner. The dentists and orthodontists who are most successful at helping children change any pattern are those practitioners who relate well and communicate well with children.

REFERENCES

1. Bresolin, Shapiro E.T. al. Mouth Breathing in Allergic Children: It's Relationship to Dentofacial Development. American Journal of Orthodontics 1983.
2. Aragon SB. Surgical management for snoring and sleep apnea. Dent Clin North Am 2001; 45(4):867-79.
3. Diamond O. Tonsils and adenoids: why the dilemma? Am J Orthod 1980; 78(5):495-503.
4. Ung N, Koenig J, Shapiro PA, Shapiro G, Trask G. A quantitative assessment of respiratory patterns and their effects on dentofacial development. Am J Orthod Dentofacial Orthop 1990; 98(6):523-32.
5. Timms DJ. The reduction of nasal airway resistance by rapid maxillary expansion and its effect on respiratory disease. J Laryngol Otol 1984; 98(4):357-62.

CLINICAL TRIAL EVALUATING THE EFFECTIVENESS OF RAPID MAXILLARY EXPANSION TECHNIQUE (RME) TO RESOLVE UPPER MAXILLARY COMPRESSION ASSOCIATED WITH ORAL BREATHING



RAMONA AMINA POPOVICI[1], ANGELA CODRUTA PODARIU[1], MOJSE MARCEL[2], ROXANA OANCEA[1], RUXANDRA SAVA ROSIANU[1], GALUSCAN ATENA[1], MELINDA ONET[3], ALEXANDRA SABINA PODARIU[1]

1. **University of Medicine and Pharmacy "Victor Babes", Timisoara**
2. **Private practice, Timisoara**
3. **University of Medicine and Pharmacy ,Arad**

ABSTRACT

Rapid maxillary expansion allows for a short time to obtain a significant widening of the upper arch, palate, nasal passages and even the face. Moving the two palatal bones we make some similar position changes in muscle inserts. It is characterized by mid-palatal suture dissolution and the increasing of the distance between the two hemimaxilla, resulting in increased transversal cross of the upper jaw.

***Key words**: rappid maxillary expansion, oral breathing, maxillary bone, nasal passage.*

Correspondence to

Mojse Marcel
Adress: Bul. Revolutiei No.22 ap.1 Profident, Timisoara
E-mail address: drzuba79@yahoo.com

INTRODUCTION

Rapid maxillary expansion (RME) is a common treatment modality used in orthodontic practice today. It is an effective and reliable method for increasing transverse dimension in patients with constricted maxillary arches.

Maxillary constriction is one of the features that characterize the so-called skeletal developmental syndrome, represented by bilateral dental maxillary crossbite, high palatal vault, nasal obstruction derived from elevation of the nasal floor, turbinate hypertrophy, and mouth breathing.[1]

Immediately following RME there is an increase in the width of the nasal cavity, particularly at the floor of the nose adjacent to the mid-palatal suture. As the two halves of the maxilla separate, the anterior walls of the nasal cavity move laterally, so the total effect was an increase in the intra nasal space. [2, 3, 4, 5]

AIM

- To emphasize the negative effects on the development of the upper jaw in the presence of associated pathology ORL (oral breathing);
- To highlight the role and impor-tance of rapid maxillary expansion: jaw conformation occlusion, inter-maxillary relationship, nasal volu-me, improve oral breathing, scar-city of space in the upper jaw.

MATERIAL AND METHOD

The study included 20 children who had upper jaw compression, breathing problems (oral breathing, mixed). Patients were selected from dental clinics: Profident and GM Clinic. Every pat0ient developed clinical history dental extraoral photographs (front, profile, and smile), intraoral (former side - left, right), model study, radiological examinations. Patient age ranged from 6 to 11 years. This fact is a very important for rapid expansion technique of the upper jaw. Because, once patients exceeded the pubertal growth peak, which occurs at age 12-13 years for girls and 14-15 years for boys [6], rapid maxillary expansion protocol cannot be applied.

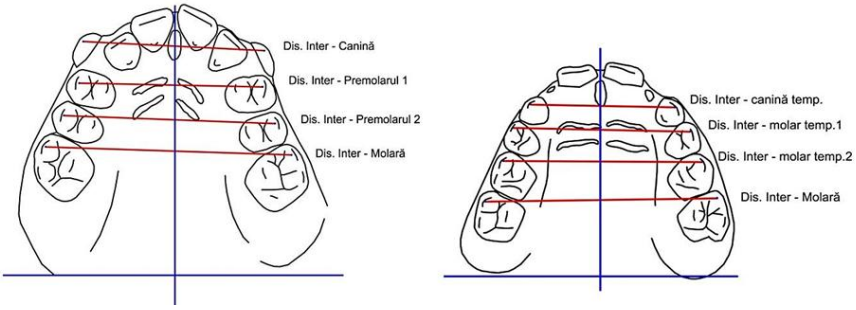


Fig.1. *Upper jaw oclusogram in permanent (a) and mixed dentition (b). The identification of the paramenters used for evaluation: DI, DP1, DP2, DMT1, DMT2, DM6.*

RESULTS

Interim study models were made after finalizing rapid maxillary expansion (after 17 days after the applying of the expansors). To achieve this, the expansor were removed, the jaws were marked immediately and the expansors were recimentated. The post period of rapid maxillary expansion retainers was to maintain the expansor for a period of three months, this was followed by the mecanical and functional orthodontic treatment with braces or fixed or mobile ambulant type trainer.

Table 1 Descriptive statistics for variable crossbite

	CROSSBITE					Total
1.6, 2.6	anterior	bilateral	nu	unilateral dr.	unilateral stg.	
1	0	4	9	2	4	20
5.0%	0.0%	20.0%	45.0%	10.0%	20.0%	100.0%

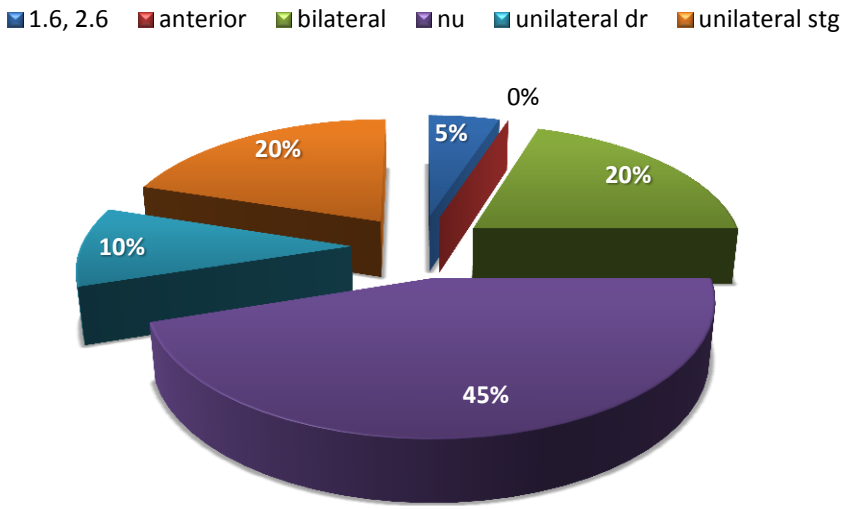


***Fig.2** Graphical representation according crossbite*

Tabel 2 ***Descriptive statistics for the variable breathing***

mixed	Normal Breathing	Oral Breathing	Total
15	0	5	20
75.0%	0.0%	25.0%	100.0%

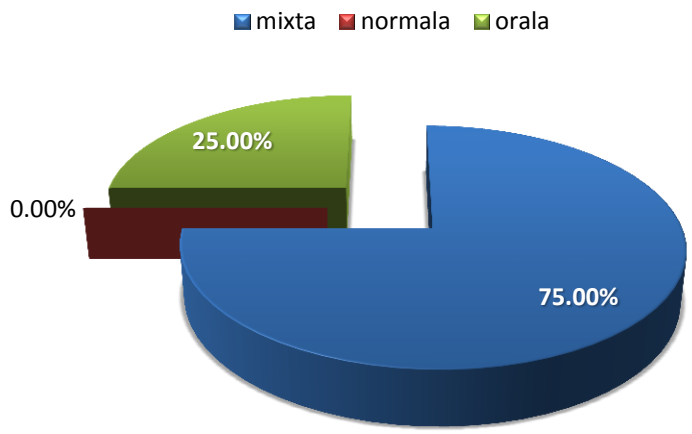


Fig.2 *Graphical representation according breathing.*

Mean values, standard deviations with minimum and maximum values for the 4 types of distances, for those 20 patients, both before and after rapid maxillary expansion are calculated in the following table:

Tabel 3 ***Measurement values before and after finalizing rapid maxillary expansion:***

Distance		N	Mean	Standard deviation	Minimum	Maximum
Before application	DI	20	29.80	2.876	26	35
	DIP1	20	36.20	3.054	30	42
	DIP2	20	40.35	3.066	35	47
	DIM6	20	47.30	3.294	42	53
After application	DI	20	36.65	1.785	34	39
	DIP1	20	44.75	2.221	41	48
	DIP2	20	48.25	1.970	44	51
	DIM6	20	54.05	1.317	51	56

To determine the therapeutic effect of the expansor these values were compared using SPSS v.16 applying nonparametric test "Wilcoxon Signed Ranks" [7, 8, 9]. The results of applying the test are:

Tabel 4 ***Results of nonparametric test:***

Comparisons	**DI**	**DIP1**	**DIP2**	**DIM6**
Z value	-3.928	-3.940	-3.928	-3.925
P value	<0.001	<0.001	<0.001	<0.001

Interpretation is that after applying the expansor all 4 types of distances increased significantly ($p < 0.001$, with a significance limit $\alpha = 0.001$) than the original distances. In conclusion the quick maxillary expansor had the expected effect. A significant increase was observed in DIP1 values, DI.

CONCLUSIONS

1. Indications for rapid maxillary expansion are clear and based not only on differential diagnosis of malocclusion itself but also the skeletal maturity of the patient.

2. Compression of the jaw is almost in all cases accompanied by oral breathing. All patients in the study reported an improvement in nasal breathing after the first week of expansor activation "deep nose cleaning".

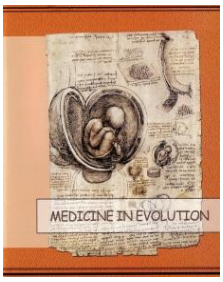
3. The increase of the transverse diameter of the jaw automatically created more space for the tongue. This is particularly important because the oral breathing, due to compression of the jaw among others, poor posture of the tongue. In these patients, the tongue has a lower and out position, permitting the patient to breathe through the mouth.

4. Wilcoxon Signed Ranks test result interpretation is that after applying the expansor, all 4 types of distances increased significantly ($p < 0.001$, with a significance limit $\alpha = 0.001$) than the original distances. In conclusion, the quick jaw expander had the expected effect. A significant increase was observed in DIP1 values, DI.

REFERENCES

1. Laptook T. Conductive hearing loss and rapid maxillary expansion. Am J Orthod. 1981; 80(3): 325-331.
2. Angell EC. Treatment of irregularities of the permanent or adult teeth. Dent Cosmos 1860; 1: 540-4.
3. Mesnard L. Immediate separation of the maxillae as a treatment for nasal impermeability. Dent Rec 1929; 49:371-372.
4. Isaacson RJ and Murphy TD. Some effects of rapid maxillary - Expansion in cleft lip and palate patients. Angle Orthod 1964; 143-154.
5. Graber T and Swain BF. Dentofacial orthopedics. In current orthodontic concepts and techniques. Vol. 1 Philadelphia: WBSaunders Company, 1975. Springer Verlag, Berlin Heidelberg, 2007; 5-6.
6. Marshall WA, Tanner JM. Puberty. In: Falkner F, Tanner JM, editors. Human growth; a comprehensive treatise. 2nd ed. New York: Plenum Publishing; 1986. p. 171–209.
7. Mihalaş G I, Lungeanu Diana - Curs de informatică medicală. Ed. Victor Babeş, Timişoara, 2009
8. Carol K. Redmond, Theodore Colton - Biostatistics in clinical trials, Wiley Reference Series in Biostatistics, 2001, ISBN 0-471-82211-6.
9. Dawson B. and Trapp R.G.: Basic & Clinical Biostatistics, 4 th edition, McGraw-Hill Companies, Inc., 2004, ISSN: 1045-5523 3.

EVALUATION OF SURGICAL-ORTHODONTIC TREATMENT ON PALATALLY IMPACTED CANINES



EZATOLLAH AGHAJANI[1], ANCA TEMELCEA[1]

[1]University of Medicine and Pharmacy „Carol Davila" Bucharest

ABSTRACT

This study evaluates the outcome of orthodontic eruption of palatally impacted canines. All teeth were successfully erupted.
The complications noticed were the failure of intraoperative bond, at the time of surgery and debonding at the time of suture removal.
There was no infection, eruption turmoils or gingival conditions associated with any of the exposed canines.

Keywords: *impacted canines, surgical exposure, surgery complications.*

Correspondence to

Dr. *Ezatollah Aghajani*
Adress: Department of Oral and Maxillo-facial Surgery,
University of Medicine and Pharmacy „Carol Davila"
Calea Plevnei 19 010221 Bucharesti, Romania
E-mail address: ezatstoma@gmail.com

INTRODUCTION

The purpose of our work was to evaluate the success of exposing impacted maxillary canines.

Permanent canines may be impacted for a variety of reasons, such lack of space, persistence of deciduous canines, ectopic path of eruption, reduced root length and agenesis of maxillary lateral incisors.[1]

The maxillary permanent canine ranks second to the mandibular third molar, with a prevalence of approximately 1% in the general population.

The location of the impacted canine determines the type of surgical approach. Impacted canines are positioned palatally in the large majority of cases.

The panoramic xray, in conjunction with the retroalveolar radiograph, is the preferred method to localize maxillary impacted canines.[2]

Various treatment modalities have been proposed to avoid the complications associated with maxillary impacted canines [3,4]. The main complication it is the resorption of the roots of lateral incisors [5].

A number of surgical techniques have been described to expose impacted teeth.[6] As bonding techniques developed in orthodontics, surgical procedures were modified, since less of the impacted crown now needed to be exposed. [7]

MATERIALS AND METHODS

This study included 40 consecutive patients (26 female, 14 male), between 2007 and 2010, who were followed for 12 months after the surgical exposure of unilateral palatally impacted canines. The patients were 14 to 16 years old.

At the time of surgical exposure, all the teeth had at least two-thirds of root formation completed. All the crowns of the impacted teeth were covered by bone.

Prior to surgery, the position of the impacted tooth was determined clinically and radiographically (panoramic and retroalveolar xray) (Figure 1).

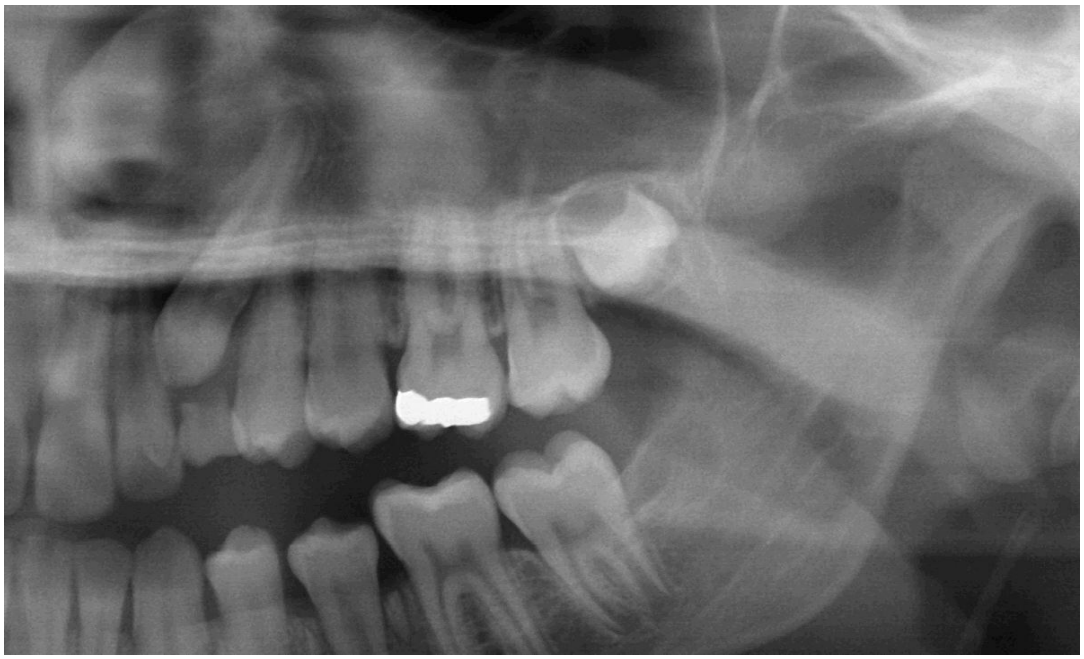


Fig.1 Preoperative panoramic radiograph showing impacted 23

A full thickness mucoperiosteal flap was raised from the mesiopalatal aspect of the upper second premolars.

Sufficient bone was removed from around the crown in order to place a bonded orthodontic appliance.

The enamel surface was etched for 60 seconds using 37% phosphoric acid and a conventional light cured resin cement was used for bonding (light cured for 30 seconds). The appliance used was a bonded orthodontic traction hook with a ligation chain (Figure 2).

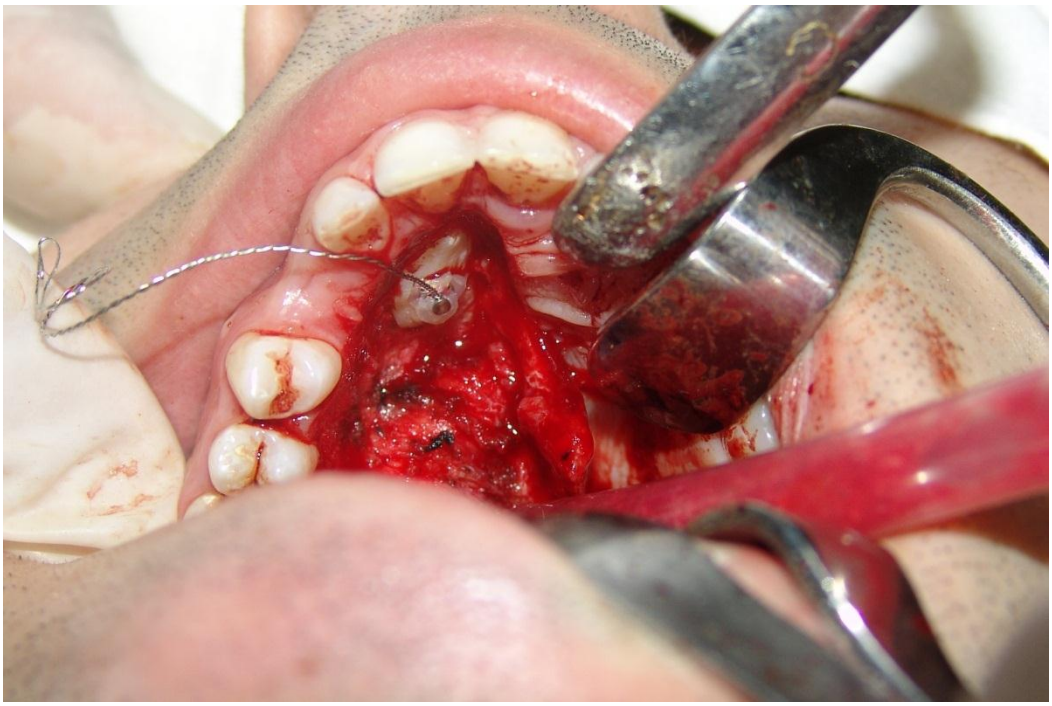


Fig.2 Intraoperative aspect of bonded orthodontic traction
(Reprinted with permission from Bucur A.: Compendiu de Chirurgie Oro-Maxilo-Facială, p. 165. © 2009 by Q Med Publishing, Bucureşti)

Palatal flaps were held in place by means of resorbable sutures.

Patients were then evaluated 7-10 days after surgery, when sutures were removed and 12 months after surgery. Clinical evaluation included assessment of bracket attachment, eruption failure, gingival inflamation or recession and infection [8].

Radiographic examination was performed 6 monts after surgery to assess the presence of root resorption.

The periods when complications occurred were classified as surgical and post-operative.

RESULTS

The only complication in the surgery phase consisted of failure of the initial bond at the time of operation in one case (2.5 %).

Bond failure results due to the difficulty of obtaining a dry field.

The palatal impacted canine was immediately rebonded.

Post-surgery, another palatal canine (2.5 %) required rebonding when the suture was removed.

Clinically, there were no cases of eruption failure, gingival inflammation / recession or infection.

Radiographically there was no evidence of root resorption.

Orthodontic treatment continued uneventfully until debonding in all cases.

CONCLUSION

Complication in treating impacted canines include bond failure, eruption turmoils and gingival defects.

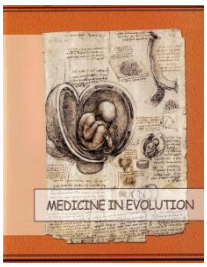
In our study, all of the forty palatally impacted canines treated, erupted. This success rate may be partly due to early diagnosis and to the age of the patients.

The frequency of bond failure it is an complication uncommon observed in this work.

REFFERENCES

1. Jacoby H. The etiology of maxillary canine impactions. Am J Orthod 1983; 84:125-32
2. Rădulescu M, Popescu V: Radiologie stomatologică. Editura Medicală, Bucureşti, 1985
3. Ericson S, Kurol J. Early treatment of palatally erupting maxillary canines by extraction of the primary canines. Eur J Orthod 1988; 10:283-95.
4. Suri S, Utreja A, Rattan V. Orthodontic treatment of bilaterally impacted maxillary canines in an adult. Am J Orthod Dentofacial Orthop. 2002;122(4):429-37.

MANDIBULAR BODY FRACTURE IN PATHOLOGICAL BONE TREATED BY RECONSTRUCTION WITH NONVASCULARIZED BONE GRAFT HARVESTED FROM ILIAC CREST- CASE REPORT



ŞERBAN ROŞU[1]

[1] University of Medicine and Pharmacy "Victor Babeş", Department of Oral and Maxillo - Facial Surgery, Timişoara

ABSTRACT

Reconstruction of mandibular defects is a challenge to the head and neck surgeon because of associated functional problems [6].

Our experience with the use of nonvascularized iliac crest bone graft is hereby reported.

The reported case consists of the mandibular reconstruction with iliac crest bone of a large mandibular defect caused by an asymptomatic residual cyst complicated with pathological bone fracture.

***Keywords**: mandibular defect, fracture, cyst pathological bone*

Correspondence to:

Dr. Şerban Roşu, Timişoara,
Str. Cozia 10, 300209 Romania,
E mail: serbanrosu@yahoo.com

INTRODUCTION

Nonvascularized bone provides a useful alternative for reconstruction of mandibular defects resulting from destructive lesions and trauma.[4] It is recommended for use in resource-limited situations where alternative modalities are not being practiced due to limited expertise or high cost[1]. Donor sites such as the ilium, fibula, clavicle or scapula have been described.[2] Most surgeons prefer the iliac crest bone for mandibular reconstruction. It provides adequate osseous tissue.[5] A study of the biomechanic properties of the iliac crest showed that the stress distribution on iliac crest graft is akin to that of the mandible[3].

AIM

The aim of this study is to report the experience of use of iliac crest bone graft for the reconstruction of a mandibular fracture produced in a pathological bone caused by a large rezidual cyst

MATERIAL AND METHOD

Patient, aged 51, treated, 7 years ago in our clinic for a fracture of the right mandibular body in pathological bone due to an asymptomatic residual cyst in the same region. The medical history of the patient reveals no symptomatic disease in the affected region. The patient accuses acute pain in the right mandibular body, and anesthesia of the right lower lip. Objectively, modified dental occlusion can be observed together with the pathological motility of the right ramus, modified bazilar contour and subgingival hematoma. The X-ray exam of the lower jaw reveals the presence of a mandibular defect caused by the asymptomatic evolution of a residual cyst crossed by a one line of fracture.

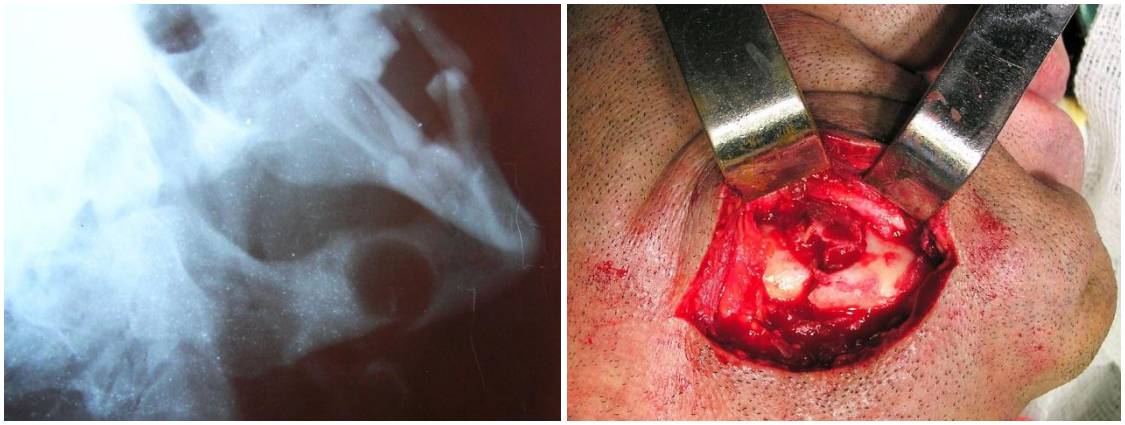


Fig 1 a) Preoperatory X-ray; b) Intraoperatory cyst membrane

The treatment plan consisted of surgical repositioning of the fractured bone and immobilization by means of ostheosynthesis with titanium plate and screws. The mandibular defect was reconstructed with crushed bone harvested from the iliac crest.

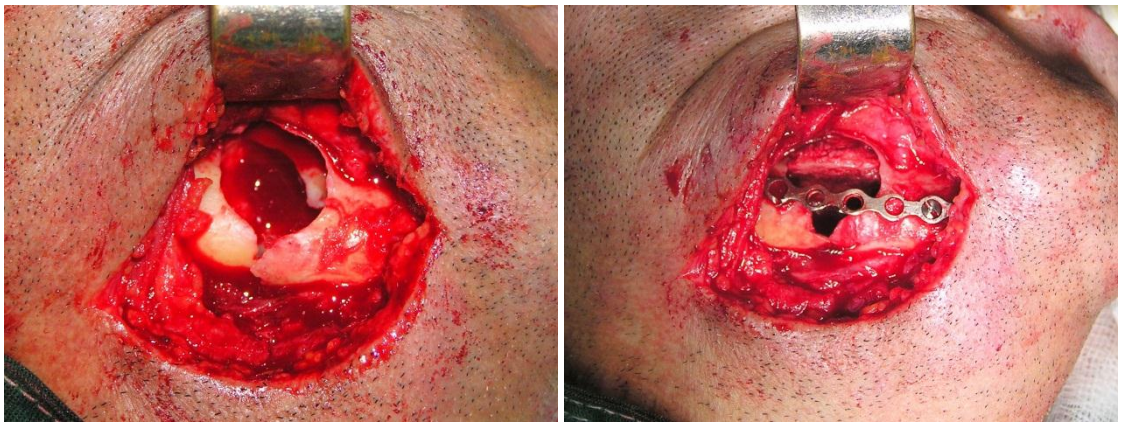


Fig 2 a) Intraoperatory aspect - fracture without cystic membrane; b) Intraoperatory aspect - ostheosynthesis

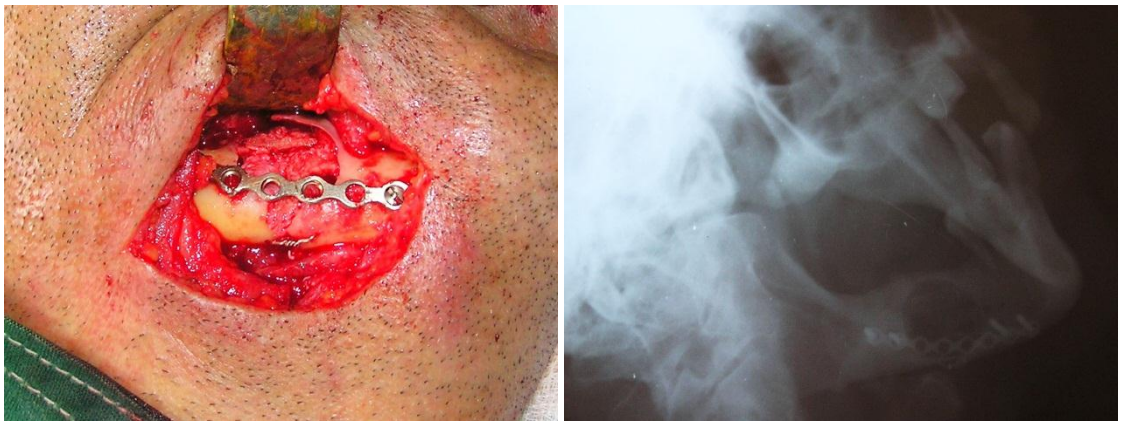


Fig 3 a) Intraoperatory aspect - ostheosynthesis and iliac graft; b) Postoperatory X ray

RESULTS AND DISCUSSIONS

Postoperatory X-ray showed satisfactory results. The continuity of the basilar margin of the mandibula has been restored together with the dental occlusion and all mandibular functions.

Positive results were recorded also in the long term follow up by lack of postoperative complications and good integration of the nonvascularized iliac bone graft visible on follow up X ray exam.

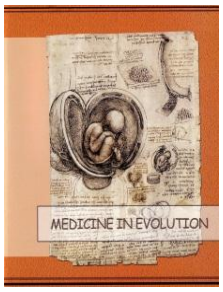
CONCLUSION

It can be concluded that nonvascularized bone provides an affordable and less technical choice for mandibular reconstruction with little complications. We therefore recommend its use for reconstruction of mandibular defects resulting from odontogenic cysts and trauma.

REFERENCES

1. Adamo AR, Szal RL. Timing, results and complications of mandibular reconstructive surgery: report of 32 cases. J Oral Surg 1979;37:755-63.
2. August M, Tompach P, Chang Y, Kaban L. Factors influencing the long-term outcome of mandibular reconstruction. J Oral Maxillofac Surg 2000;58:731-7; discussion 738.
3. Kim MR, Donoff RB. Critical analysis of mandibular reconstruction using AO reconstruction plates. J Oral Maxillofac Surg 1997;50:1152-7.
4. Kurz LT, Garfin SR, Booth RE Jr. Harvesting autogenous iliac bone grafts: A review of complications and techniques. Spine 1989;14:1324.
5. O'Brien CJ, Archer DJ, Breach NM, Shaw HJ. Reconstruction of the mandible with autogenous bone following treatment for squamous cell carcinoma.Aust N Z J Surg 1986;56:707-15.
6. Toshiyuki S, Kohsuke O, Mitsuiro M, Kazuyuki S, Ken-ichi M. An anatomical study of vascularised iliac bone graft for dental implantation. Journal of Cranio Maxillofacial Surgery is indexed as J Cr Maxillofac Surg 2002;30:184-8.

THE MARGINAL AND INTERNAL FIT OF ALL-CERAMIC INLAY-RETAINED FIXED PARTIAL DENTURES MADE WITH THE LAVA SYSTEM



CÂNDEA ADRIAN[1], TOPALĂ FLORIN[1], ROMÎNU MIHAI[2]

[1]University of Medicine and Pharmacy"Victor Babes", Faculty of Dentistry, Department of Prosthodontics, Timisoara
[2] University of Medicine and Pharmacy"Victor Babes", Faculty of Dentistry, Department of Dental Materials and Prostheses Technology, Timisoara

ABSTRACT

Purpose. *The aim of this study is to assess the marginal and internal adaptation of inlay-retained fixed partial dentures (IRFPDs) milled from semi-sintered zirconia blocks, made with the Lava system (3M ESPE). Evaluation was achieved using the cement replica technique with a light body silicone stabilized with a heavy body silicone.*

Materials and methods. *Standardized occluso-proximal inlay preparations for the retainers were performed on the abutment teeth of the Frasaco model. Eight impressions were taken with polyvinylsiloxane using the sandwich technique. Eight stone models were manufactured. The models were scanned using Lava Scan ST. Digital models were thus created. For each model, an IRFPD was designed using Lava CAD software. Lava Plus "green stage" zirconia blocks were milled and then the IRFPDs were sintered in the Lava Therm oven. Individualization was achieved with shades and pigments. Finally, eight three-unit zirconia IRFPDs were made.*

Assessment of marginal and internal adaptation was achieved using the cement replica technique with a light body silicone stabilized with a heavy body silicone. Mesio-distal sections of the silicone replicas were obtained with the aid of a razor-blade. The width of the light body silicone layer of the replica was considered to represent the fit of the restoration. Furthermore, photos of the widths of the gap between the IRFPDs and the abutments were taken with the aid of an optical microscope linked to a camera. An image processing software was used for the measurements.

Results. *The average marginal cervical gap was of 76.25±14.32µm for the mesial retainer, respectively 79.62±14.27µm for the distal retainer, and the average marginal occlusal gap was of 56.5±14.44µm for the mesial retainer, respectively 69.25±12.06µm for the distal retainer. The values of the average marginal gap were inferior to the acceptable gap size of 120µm. The average internal gap was of 142±63.84µm for the mesial retainer and 157.05±66.46µm for the distal retainer.*

Conclusion. *Within this study's limitations, Lava Zirconia IRFPDs showed an average marginal and internal fit within acceptable limits, thus being suitable for clinical use.*

Keywords: *All-ceramic, marginal and internal fit, IRFPD, minimally invasive, semi-sintered zirconia*

Correspondence to

Dr. Cândea,Adrian, Department of Prosthodontics,
Faculty of Dentistry, "Victor Babes" University of Medicine and Pharmacy Timisoara,
Address: 9 Revolutiei Blvd., 300070, Timisoara, Romania
Phone: +40 723 673790
E-mail address: adrian_candea@yahoo.com

INTRODUCTION

Single missing tooth situations may be restored in various ways [1]. Traditionally, the treatment requires circumferential preparation – for full crown retainers – of the abutment teeth adjacent to the gap. This invasive preparation requires massive sound tooth removal in order to make space for the restorative material (metal-ceramic, metal-polymer, all-ceramic, fibre-reinforced composite) [1, 2].

Metal-free restorations are gaining ground due to their enhanced aesthetics and biocompatibility. Minimally invasive restorative techniques are available nowadays, due to the continuous development and perfecting of dental materials, manufacturing processes and adhesive techniques. Of course, the least invasive treatment regarding two sound teeth adjacent to the gap is the insertion of an implant. But when implant therapy is neither possible nor indicated, fixed prostheses with minimally invasive retainers (partial crowns, inlays, wings) may be indicated and in some particular cases even removable prostheses [1, 2].

At the same time, the patients' demand for aesthetically pleasing, tooth-like, biocompatible, conservative and metal-free restorations is increasing. Several authors state that all-ceramic zirconia-based restorations provide a promising alternative to restorations with metal framework, showing excellent clinical performance on medium-term observation [3].

Partial-retainer zirconia fixed prostheses can be efficiently bonded to abutment teeth, displaying acceptable short-term results [2, 4]. Bonding strength values as high as 52MPa have been reported after selective infiltration-etching of the inner surface of zirconia FPDs [4].

It is well known that adaptation discrepancies have a negative impact on the clinical success of a fixed prosthetic restoration. A large marginal gap increases plaque retention and may cause secondary caries, pulpitis, gingivitis, periodontitis [5-7]. On the other hand, deficient internal adaptation may lead to reduced fracture resistance [8].

The study investigates the marginal and internal adaptation of all-ceramic IRFPDs, made with the Lava CAD/CAM system (3M ESPE, USA), in order to evaluate their suitability for clinical use.

MATERIALS AND METHODS

Preparation

A typodont model with a missing right second premolar was used (Frasaco, Germany).

Standardized occluso-proximal inlay preparations for the retainers were performed on the abutment teeth of the model (Fig. 1a). The margin of the preparations was clearly defined and all internal angles and edges were rounded. Preparations were freehand performed, simulating the clinical situation. No surveyor was used to complete the preparations.

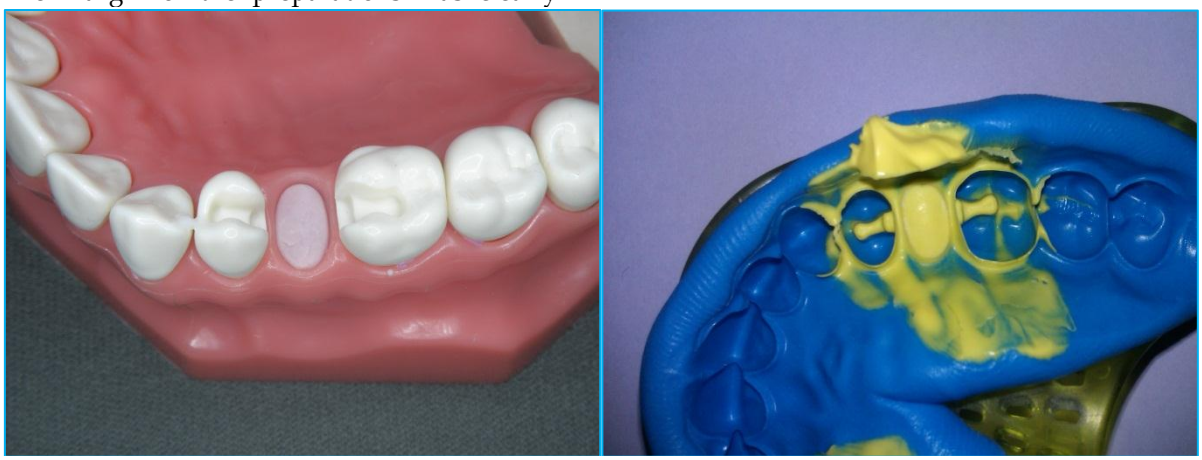


Fig. 1 *a. Occlusal view of the preparations; b. Impression; c. Working die; d. Final full contour Lava Zirconia restoration seating on the working die.*

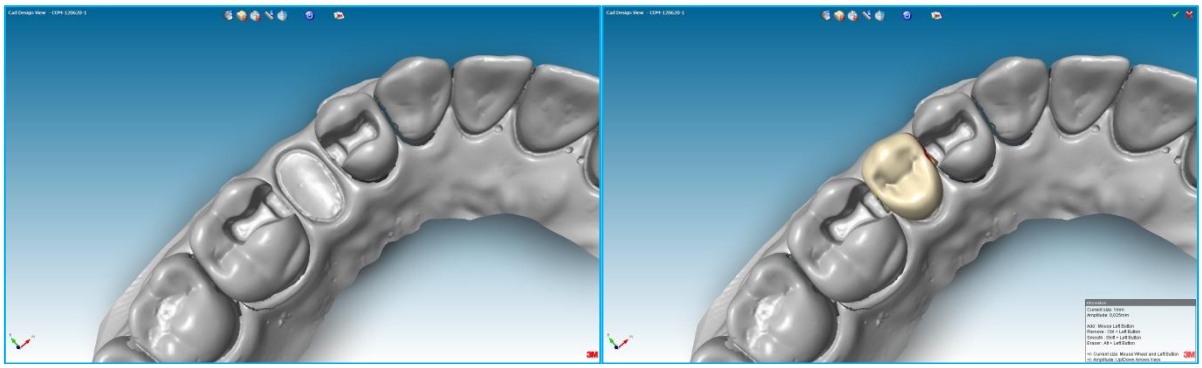
Impression taking

Eight impressions were taken with polyvinylsiloxane (Access Gold and Access Putty, Centrix, USA), using the one-step technique. Standard disposable plastic impression trays were used (Dental Tray System, DTS International, Italy) (Fig. 1b).

Manufacturing process

Impressions were poured in a class IV die stone (Thixo-Rock, Bredent, Germany). Eight stone models were prepared (Fig. 1c). Impressions were made by the same dentist and models were made by the same technician. The models were scanned using Lava Scan ST (3M ESPE, USA) (active triangulation), thus resulting in digital models. For each of the eight digital models, a zirconia IRFPD was designed using Lava Design CAD 7.2 software (3M ESPE, USA) (Fig. 2). A standardized protocol was used (Full contour modelling, virtual cement layer of 25µm and connector size of 9-12mm^2).

Lava Plus semi-sintered zirconia blocks were milled in an enlarged size. Then, the restorations were immersed into Lava Frame Shade (3M ESPE, USA) for 2 minutes and afterwards left to dry at room temperature. The process of sintering to full density of the IRFPDs was completed in the Lava Therm oven for 10.5 hours at 1450 °C. Adjustments were performed by the same dental technician under 6X magnification (Mantis, Vision Engineering, USA) using Presto Aqua II (NSK, Japan) handpiece and code red rotary instruments (NTI, Germany). Individualization was achieved using Lava Plus shades and pigments (3M ESPE, USA). Finally, eight three-unit zirconia IRFPDs were made (Fig. 1d).



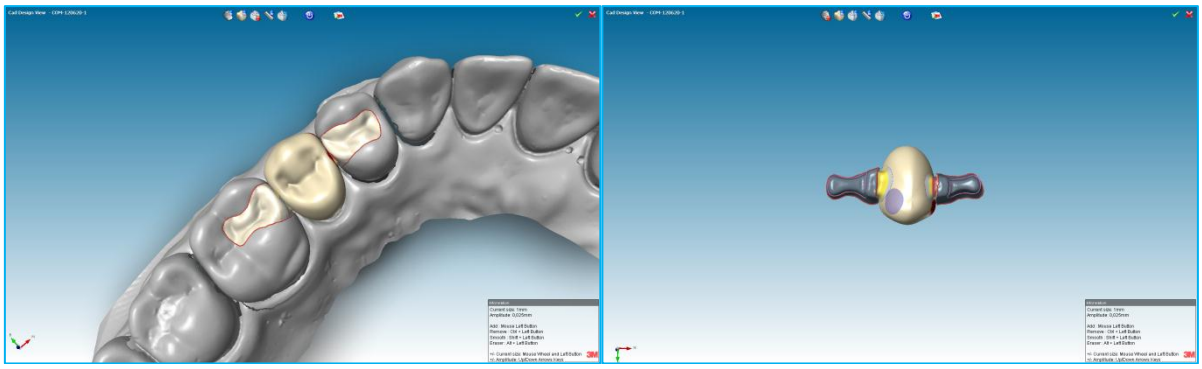


Fig. 2 *Digital die and design of the IRFPDs.*

Making of the replicas and microscope examination

Silicone replicas were obtained using the *Boening et al*. and *Molin & Karlsson* technique [9].

Light body silicone (Fit Checker, GC, Japan) was injected on the preparations of the typodont model, and then each of the eight IRFPDs was seated on the abutments under finger pressure [8], reproducing the clinical situation (Fig. 3a). After the setting of the light body silicone, stabilization was achieved using heavy body silicone (Genie, Sultan, USA) (Fig. 3b).

Standardized mesio-distal sections of the silicone replicas were obtained with the aid of a razor-blade [9] (Fig. 3c, d).

The width of the silicone replica was considered to represent the fit of the restoration [7-9].

Further on, the measurement points were defined. Two marginal points (marginal cervical and marginal occlusal) and 98 internal points/abutment/section were considered. Thus, for each of the eight zirconia IRFPDs, the gaps between the restoration and the abutments were measured.

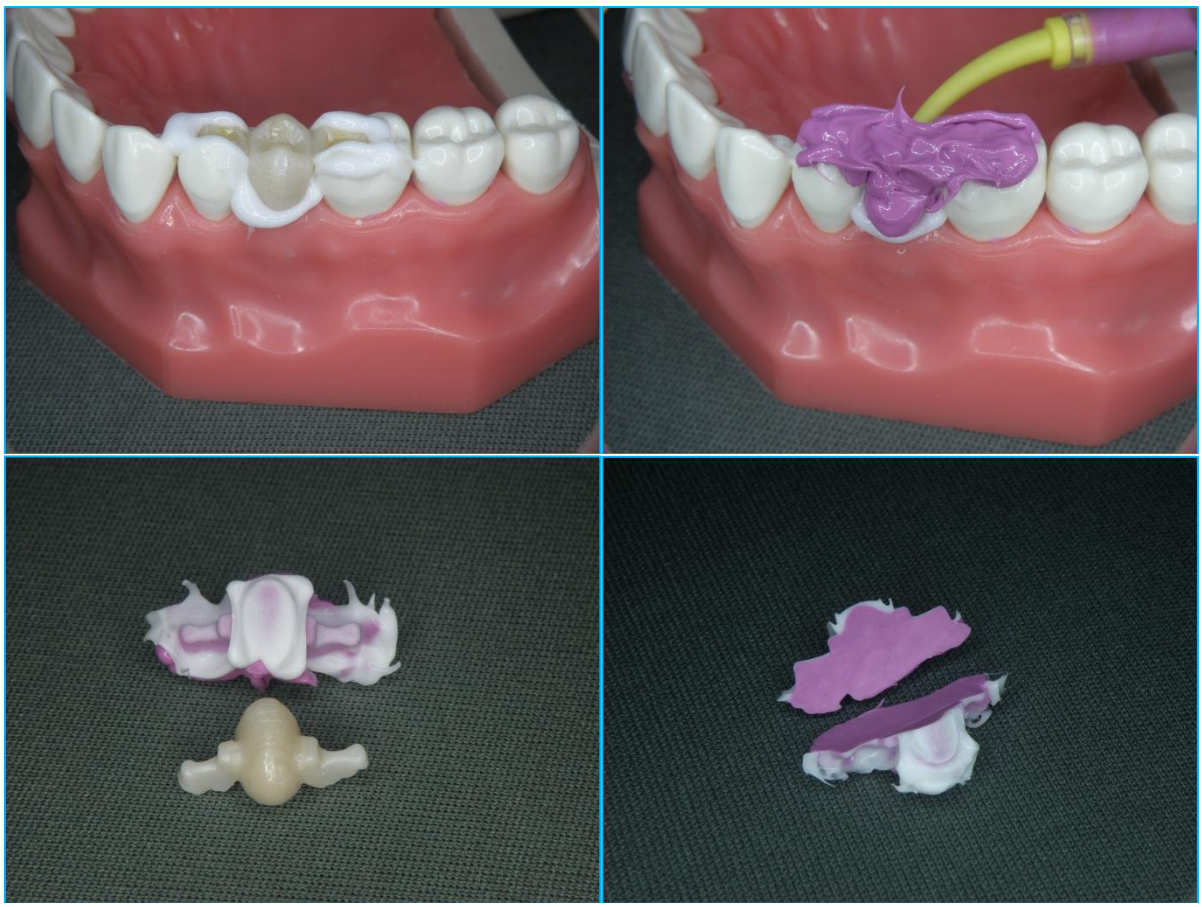


Fig. 3 *Aspects of the making of the silicone replicas: a. Seating of the restoration with soft body silicone; b. Stabilization by injection of heavy body silicone; c. Internal aspect of the silicone replica; d. Sectioned silicone replica.*

Furthermore, the photos of the silicone replicas were obtained with the aid of an operation microscope (Zeiss OPMI Pico, Carl Zeiss Meditec, Germany) linked to a photo camera (Sony NEX 5, Japan) (Fig. 4).

Imaging computer software was used for the measurements. First, the area corresponding to the cement layer was selected, cut and calibrated using Adobe Fireworks CS6 (Adobe, USA). Then, it was imported in custom image software (Dental Map – Image Processing) (Fig. 5). The results of the image processing were automatically exported in Office Excel (Microsoft, USA) to be analysed.

Statistics

The statistical analysis was performed using MedCalc for Windows, version 11.3 (MedCalc Software, Belgium). The minima, maxima, medians, averages and standard deviations were calculated for every location (marginal cervical, internal, marginal occlusal) and every abutment (premolar, respectively molar). The Mann-Whitney test was chosen to examine the differences of fit between the retainers. The level of significance was set at 0.05.

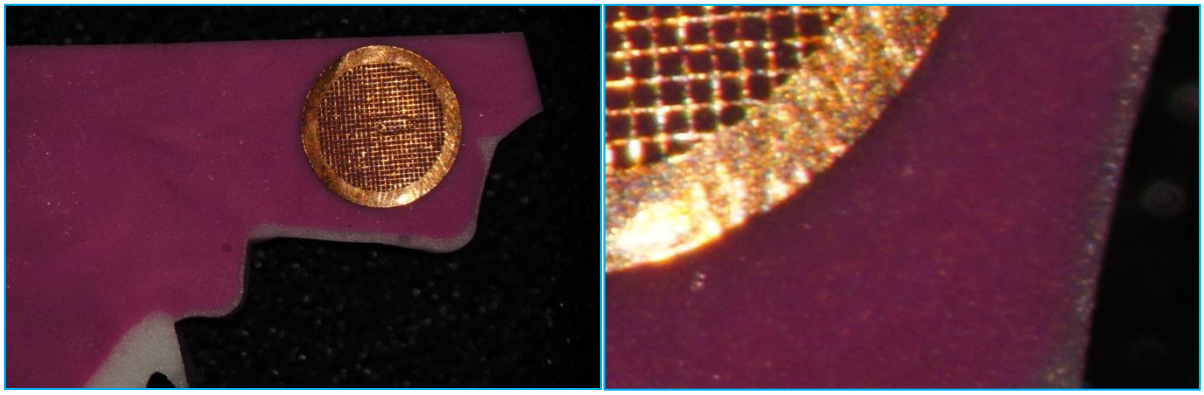


Fig. 4 *Optical microscope photos of the silicone replica.*

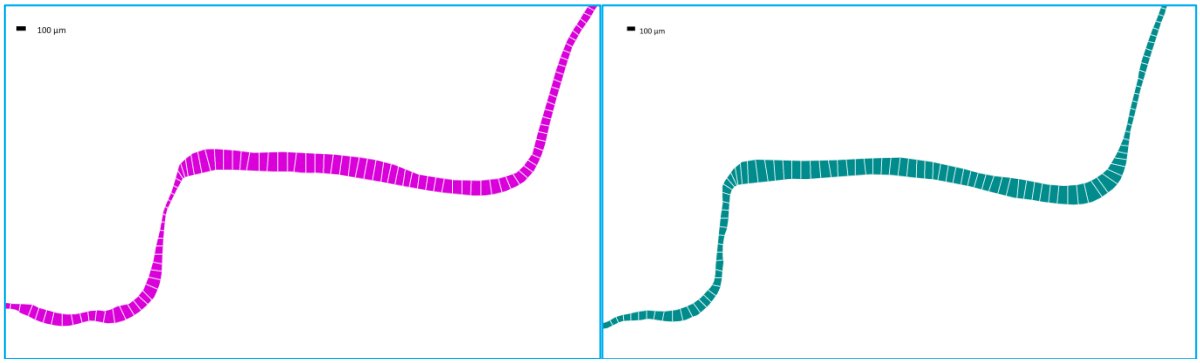


Fig. 5 *Calibrated processed images (left – premolar, right – molar). The white segments represent the 100 measurement points per section.*

RESULTS

The results of the study are presented in table I, table II and figure 6. Means and standard deviations were recorded as follows: the average marginal cervical gap was of 76.25±14.32µm for the mesial retainer, respectively 79.62±14.27µm for the distal retainer, and the average marginal occlusal gap was of 56.5±14.44µm for the mesial retainer, respectively 69.25±12.06µm for the distal retainer. The average internal gap was of 142±63.84µm for the mesial retainer, respectively 157.05±66.46µm for the distal retainer.

The Mann-Whitney test indicated no significant difference between the mesial and distal retainers regarding marginal cervical (P=0.71) and marginal occlusal (P=0.14) locations. The Mann-Whitney test showed statistically significant differences between the retainers regarding the internal adaptation (P=0.0011). The same test revealed that the marginal cervical gap was significantly higher than the marginal occlusal gap for the mesial retainer (P=0.0379) and insignificantly higher for the distal retainer (P=0.1563).

Table I. *Average marginal and internal gap widths, standard deviations, minima, maxima and medians for each location*

Abutment tooth	Location	Minimum	Average	Median	Maximum	STDEV
Premolar	marginal cervical	55	76.25	78	94	14.32
	marginal occlusal	36	56.5	61	78	14.44
	Internal	29	142	135	290	63.84
Molar	marginal cervical	60	79.62	79.5	102	14.27
	marginal occlusal	52	69.25	65	88	12.06
	Internal	34	157.05	174,75	289	66.46

Table II. *Average overall (cervical and occlusal) marginal gap widths, minima, maxima and standard deviations*

Abutment tooth	Location	Minimum	Average	Maximum	STDEV
Premolar	marginal (c+o)	46	66.37	77	17.23
Molar	marginal (c+o)	60	74.43	92.5	13.84

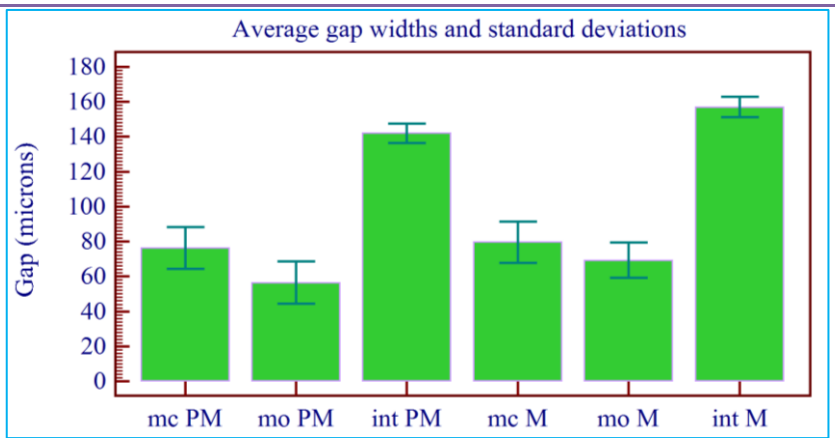


Fig. 6 *Means and standard deviations at different locations (marginal cervical, marginal occlusal and internal) for both mesial and distal retainers.*

DISCUSSION

The study revealed no significant difference between the two retainers regarding the marginal fit (cervical and occlusal measurement locations), but showed a significant difference between the two retainers regarding the internal fit. Both marginal and internal average width gaps were smaller in the case of the mesial retainer than in that of the distal retainer (Fig. 6). The values of the average marginal gap were inferior to the acceptable gap size of 120µm, reported by most of the authors [3, 5-8]. However, literature is not abundant in data when it comes to investigating the internal fit of fixed prostheses in general and that of inlays in particular. Addi et al. reported values of the internal fit of 208±85µm (25-610) for IPS Empress inlays, 260±84µm (0-700) for Opc inlays and 230±68µm (0-470) for Denzir inlays [10]. In another study, Audenino et al. reported values of the overall fit of 85±32µm for Colorlogic, 53±21µm for IPS Empress, 129±11µm for Celay Direct and 140±6µm for Celay Indirect [11]. Both previous studies used 7 points/section for the measurement of the internal fit. The present study used 98 points/section for the measurement of the internal fit. Values of the internal fit were 142±63.84µm (29-290) for the mesial retainer, respectively 157.05±66.46µm (34-289) for the distal retainer. Gap widths were generally smaller at the margins and at the axial walls and larger at the shoulder of the proximal box and at the floor of the preparations.

This study was limited by the fact that only one mesio-distal section was taken into account for each zirconia IRFPD, which might reflect neither the marginal, nor the internal fit of the restoration as a whole. The seating of the IRFPDs under finger pressure during the making of the replicas, instead of the use of standardized pressure, represented another limitation. Nevertheless, the authors opted for this particular seating in order to reflect as well as possible the seating of a restoration in daily clinical use.

CONCLUSION

Within this study's limitations, Lava Zirconia IRFPDs demonstrated an average marginal and internal fit within acceptable limits, thus being suitable for clinical use. The statistical analysis revealed significant differences between the retainers regarding the internal fit of the Lava Zirconia IRFPDs ($P=0.0011$). Values of the marginal gap were insignificantly lower for the mesial retainer than for the distal retainer ($P>0.05$). Values of the marginal cervical gap were significantly higher than those of the marginal occlusal gap for the mesial retainer ($P=0.0379$) and insignificantly higher for the distal retainer ($P=0.1563$).

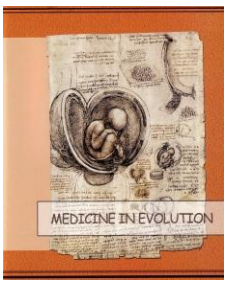
ACKNOWLEDGEMENTS

The authors would like to thank dental technicians Paul Papană and Marius Nisipeanu and computer engineer Andrei Oros for their support. This study was supported by the project "BddcAEC" from the POSDRU/88/1.5/S/63117.

REFERENCES

1. Monaco C, Cardelli P, Özcan M – Inlay-retained zirconia fixed dental prostheses: modified designs for a completely adhesive approach, J Can Dent Assoc 2011; 77: b86.
2. Monaco C, Krejci I, Bortolotto T, Perakis N, Ferrari M, Scotti R – Marginal adaptation of 1 fiber-reinforced composite and 2 all-ceramic inlay fixed partial denture systems, Int J Prosthodont. 2006 Jul-Aug; 19(4):373-82.
3. Komine F, Blatz MB, Matsumura H – Current status of zirconia-based fixed restorations, J Oral Sci. 2010 Dec; 52(4):531-9.
4. Aboushelib MN, Feilzer AJ, Kleverlaan CJ, Salameh Z – Partial-retainer design considerations for zirconia restorations, Quintessence Int. 2010 Jan; 41(1):41-8.
5. Mohsen C – Vertical marginal gap & retention of ceramic full coverage & inlay retained ceramic fixed partial dentures, Open Journal of Stomatology, 1, 140-149. doi: 10.4236/ojst.2011.14021.
6. Beuer F, Aggstaller H, Richter J, Edelhoff D, Gernet W – Influence of preparation angle on marginal and internal fit of CAD/CAM-fabricated zirconia crown copings, Quintessence Int. 2009 Mar;40(3):243-50.
7. Tsitrou EA, Northeast SE, van Noort R – Evaluation of the marginal fit of three margin designs of resin composite crowns using CAD/CAM, J Dent. 2007 Jan; 35(1):68-73. Epub 2006 Jun 15.
8. Komine F, Iwai T, Kobayashi K, Matsumura H – Marginal and internal adaptation of zirconium dioxide ceramic copings and crowns with different finish line designs, Dent Mater J. 2007 Sep; 26(5):659-64.
9. Reich S, Wichmann M, Nkenke E, Proeschel P – Clinical fit of all-ceramic three-unit fixed partial dentures, generated with three different CAD/CAM systems, Eur J Oral Sci. 2005 Apr; 113(2):174-9.
10. Addi S, Hedayati-Khams A, Poya A, Sjögren G – Interface gap size of manually and CAD/CAM-manufactured ceramic inlays/onlays in vitro, J Dent. 2002 Jan; 30(1):53-8.
11. Audenino G, Bresciano ME , Bassi F, Carossa S – In vitro evaluation of fit of adhesively luted ceramic inlays, Int J Prosthodont. 1999 Jul-Aug; 12(4):342-7.

CASE REPORT: RIDGE AUGMENTATION USING RETROMOLAR REGION



CRISTIAN IRIMIA[1], CRISTINA PĂDURARIU [2]

[1] PhD Student, University of Medicine and Pharmacy „Carol Davila", Faculty of Dentistry, Bucharest
[2] Assistant professor, University of Medicine and Pharmacy „Carol Davila", Faculty of Dentistry, Bucharest

ABSTRACT

The case reports that retromolar region provides a local and convenient source of autogenous bone for preprosthetic augmentation grafting.

Keywords: *bone graft, bovine bone, periapical lesion*

Correspondence to

Dr. *Cristian Irimia*
Adress: Clinica de Chirurgie Oro-Maxilo-Facială a UMF „Carol Davila"
Calea Plevnei 19 010221 Bucureşti, Romania
E-mail address: dr.cristianirimia@gmail.com

INTRODUCTION

A number of different methods have been reported to enhance the morphology of the bone defect and augment the alveolar bone: autogenous bone grafts, alloplast graft materials, xenografts [1].

It is widely considered that autogenous bone grafting techniques are the most predictable and can be thought of as the gold standard against which the other methods [2].

Autogenous bone has a number of advantages: biocompatible, non-immunogenic and osseoinduction capacity [3].

Intra-orally sites used for harvesting bone include the chin, maxillary tuberosity , mandibular ramus and retro-molar region [4].

This case report describes the use of maxillary tuberosity as a source of bone for grafting.

Case report

A 32-year-old female was referred to the Clinic of Oral and Maxillofacial Surgery for extraction of 46, due the fact that the patient had experienced recurrent panic attacks. She was found to have no other relevant medical history (Figure 1).

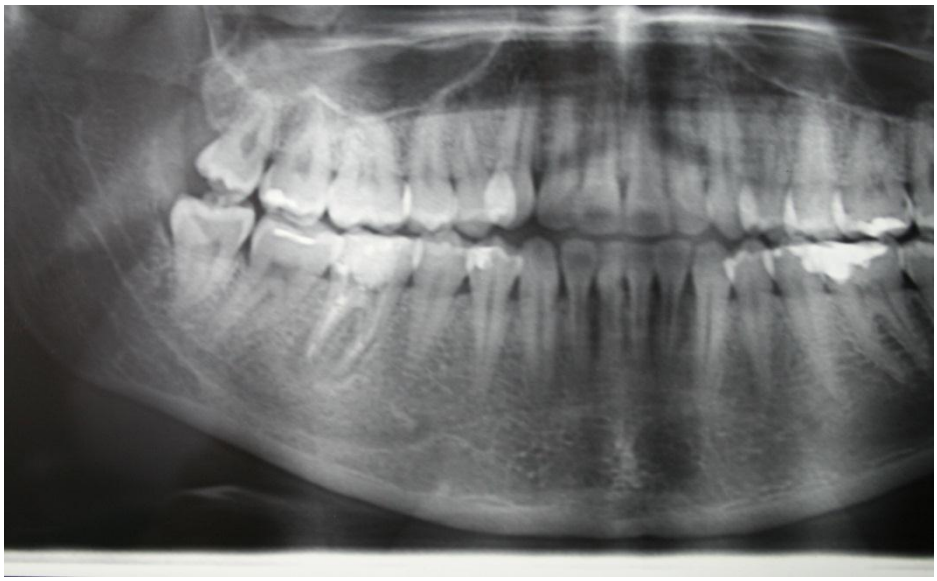


Fig.1 Irrecuperable 46 (preoperative xray)
(Photo courtesy of Prof. Dr. Alexandru Bucur)

The tooth was removed and various treatment options were considered.

The patient's preferred choice of treatment was fixed prosthodontic rather than endosseous implants.

Dentist noticed deficiency in the width of alveolar bone in the edentulous area and it was felt that to obtain a satisfactory result, alveolar ridge augmentation would be necessary (Fig. 2).

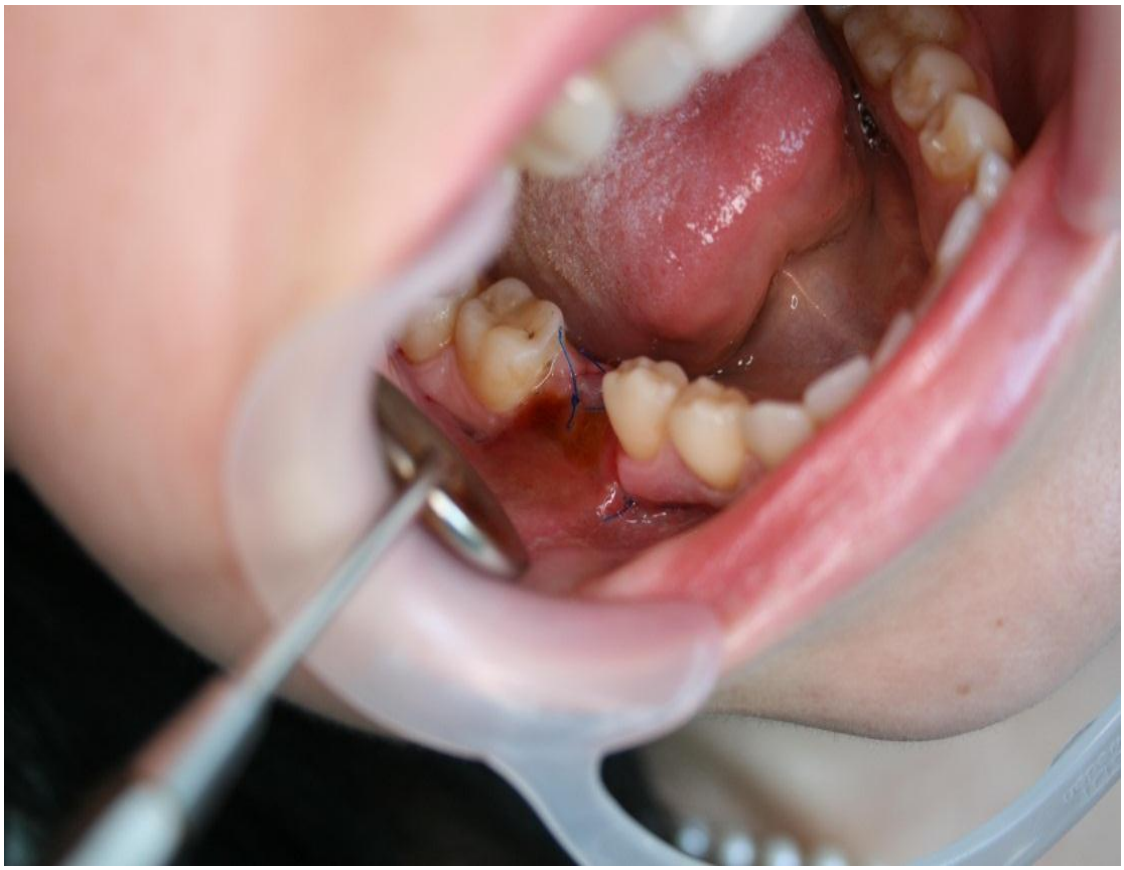


Fig. 2 Clinical postoperative aspect
(Photo courtesy of Prof. Dr. Alexandru Bucur)

The opposite retromolar region was identified as the site from which to harvest autologuos bone.

Treatment

The patient was admitted to hospital for the procedure to be carried out under local anaesthesia with intravenous sedation.

An mucoperiosteal flap was raised to reveal the edentulous area and to expose the opposite retromolar region.

The bone was harvested with a dedicated bur followed by sectioning with an osteotome.

The donor place was smoothed and irrigated with sterile saline.

The harvested bone was trimming of its shape in order to fit the dimensions of the recipient site.

Primary closure of the soft tissues was carried out at both donor and recipient sites.

No postoperative complications appeared.

Three months later, healing was seen to be progressing (Fig.3).

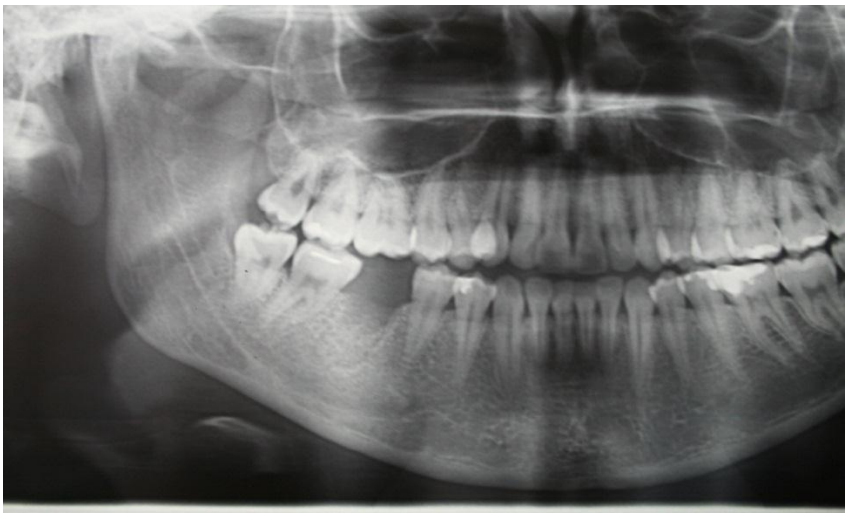


Fig.3 Three months postoperative xray
(Photo courtesy of Prof. Dr. Alexandru Bucur)

The edentulous space was restored with a bridge 12 months after surgery.

At this time no significant resorption of the augmented area was apparent.

DISCUSSION

Retromolar region it an convenient site for harvesting as the surgery results in no anatomical or aesthetic deficit [5].

The long-term stability of the bone grafts is uncertain, since autologous bone grafts, although the 'gold standard', tend to undergo resorption [6].

Bone grafts that are not loaded for long time may experience resorption due the lack of functional stimulation [7].

However, in this case, no significant resorption of the grafted bone has been seen to have taken place in the first year following surgery.

CONCLUSION

Retromolar region provide a local and convenient source of bone for ridge augmentation procedures.

REFFERENCES

1. Buser D, Dula K, Hirt HP, Schenk RK. Lateral ridge augmentation using autografts and barrier membranes: A clinical study with 40 partially edentulous patients. J Oral MaxiIlofac Surg 1996;54:420-32

2. Fukuda M, Takahashi T, Yamaguchi T. Bone grafting technique to increase interdental alveolar bone height for placement of an implant. Br J Oral Maxillofac Surg 2000;38:16-8.

3. Buser D, Dulak K, Hen D, Hirt H P, Belser U C. Localised ridge augmentation with autografts and barrier membranes. Periodontol 2000 1999; 19: 151–163.

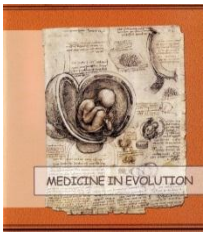
4. Boronat A, Carrillo C, Penarrocha M, Pennarocha M.Dental implants placed simultaneously with bone grafts in horizontal defects: a clinical retrospective study with 37 patients.Int J Oral Maxillofac Implants. 2010 Jan-Feb;25(1):189-96.

5. Fakhry A. The mandibular retromolar area as a donor site in maxillofacial bone grafting: surgical notes.Int J Periodontics Restorative Dent. 2011 Jun;31(3):275-83.

6. Simion M, Jovanovic SA, Trisi P, Scarano A, Benfati SP. Long-Term evaluation of osseointegrated implants inserted at the time or after vertical ridge augmenta-tion. A retrospective study on 123 implants with 1-5 years of follow-up. Clin Oral Implants Res 2001;12:35-45

7. Crespi R, Capparè P, Gherlone E, Romanos GE. Immediate occlusal loading of implants placed in fresh sockets after tooth extraction. Int J Oral Maxillofac Implants 2007;22:955-962

INFECTIOUS COMPLICATIONS FOLLOWING SURGICAL REMOVAL OF LOWER WISDOM TEETH



BILAL TAKOUZLI[1], CRISTIAN IRIMIA[1], TIBERIU NIŢĂ[1]

[1]University of Medicine and Pharmacy „Carol Davila" Bucharest

ABSTRACT

The aim of our study was to evaluate two methods that could be used to reduce the incidence of infectious complications following odontectomies. In addition, other variables including age and sex of patient were studied. Standard surgical technique was used. Antibiotcs cones were effective in reducing the incidence of infectious complications.

Keywords: impacted wisdom teeth, infectious complications, surgery.

Correspondence to

Dr. *Bilal Takouzli.*
Adress: Department of Oral and Maxillo-facial Surgery,
University of Medicine and Pharmacy „Carol Davila"
Calea Plevnei 19 010221 Bucharesti, Romania.
E-mail address: dr.bilaltakouzli@gmail.com

INTRODUCTION

The reported incidence of infectious complications for wisdom teeth surgical removal ranges from various sources between 10% to 25% [1].

Many causes of infectious complications have been studied: surgical trauma to the bone during removal, bacteria, inadequate postoperative care [2].

Many suggested methods are mentioned for prevention of infectious complications including topical and systemic antibiotics [3].

MATERIAL AND METHOD

A controlled prospective study was completed with 200 surgical extraction sites

Patients with no health problems were selected on the basis of having bilaterally impacted lower wisdom teeth of similar surgical difficulty (Figure 1).

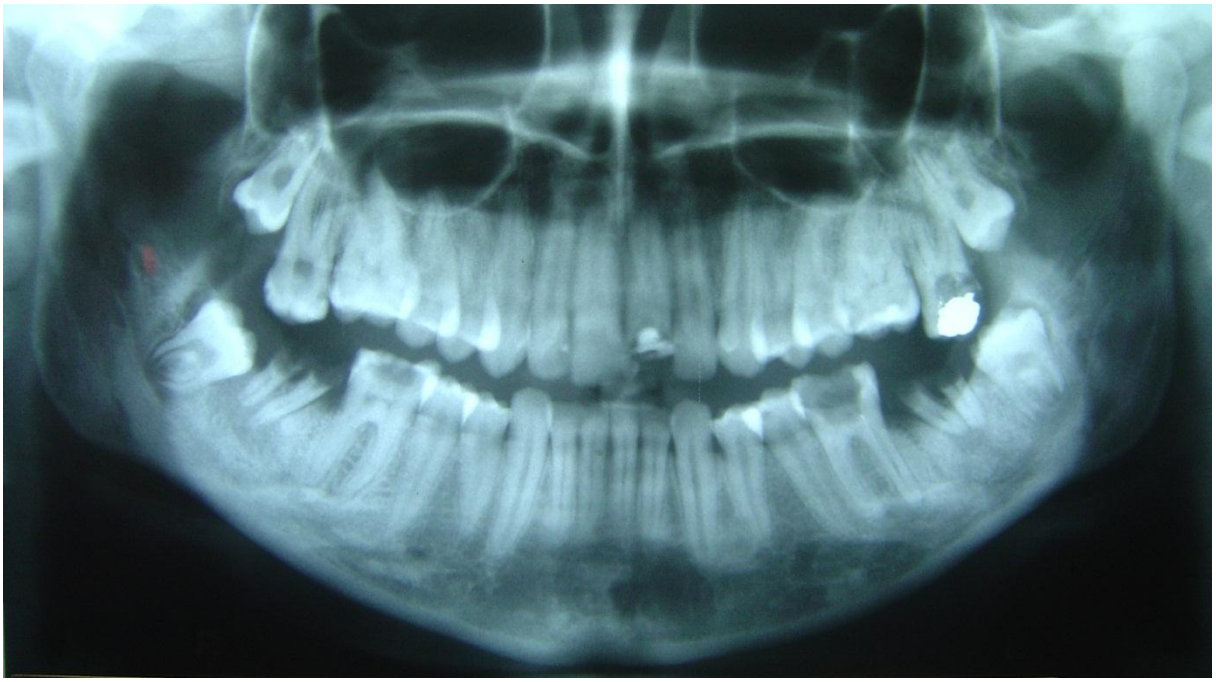


Fig. 1 Bilaterally impacted lower wisdom teeth

Partial bone impaction necessitated the raising of an mucoperiosteal flap and removal of bone, whereas the full impactions required a flap, bone removal, and sectioning of the impacted tooth (Figure 2).

Section was obtained with an electrical handpiece and a *Lindemann* bur with saline physiological saline solution irrigation.

The flaps were reapproximated with 4-0 gut suture.

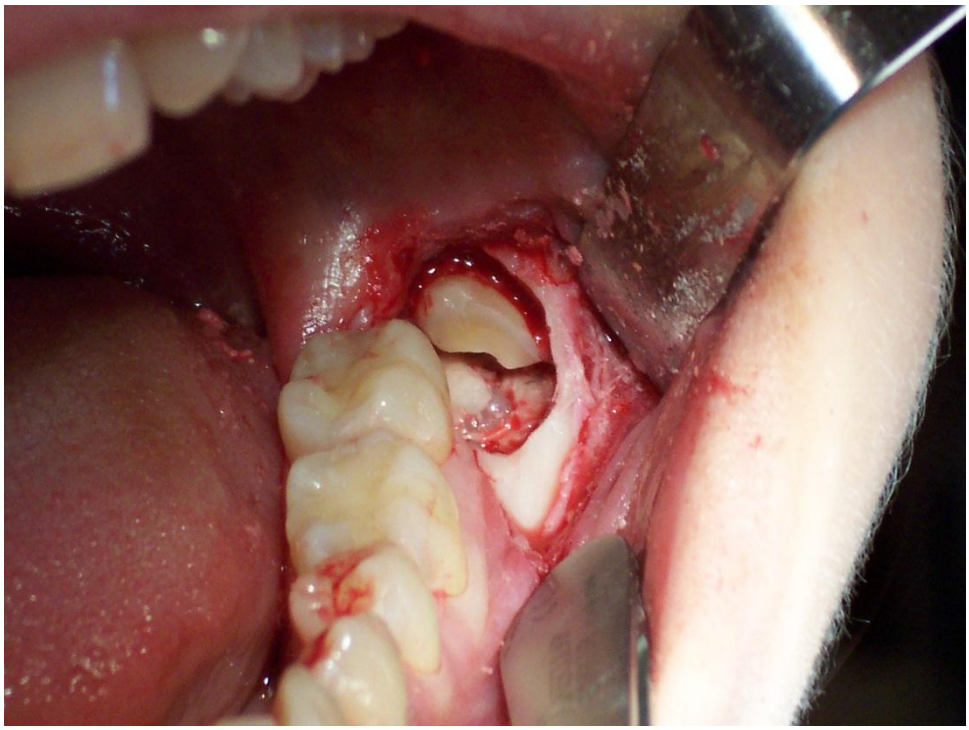


Fig.2 Sectioning of the impacted wisdom tooth

In all cases, local anesthetic with vasoconstrictor was administered with inferior alveolar nerve blocks and buccal infiltration. rve blocks and buccal infiltration.

Alveolar dressings were placed as follows:

1. 100 sockets with no dressings placed.
2. 100 sockets with antibiotics cones on one side-no treatment on the other.

The dressing was placed in the socket preselected at random, and the soft tissues were closed as described.

Gauze pressure packs were placed intraorally at the end of the surgery, to be kept in place for two hours.

A liquid diet was recommended for the first 48 hours postoperatively with instructions to advance to a normal diet as tolerated. Normal hygiene and warm bicarbonate rinses were initiated 24 hours postoperatively. Instructions were also given to avoid smoking.

Etoricoxib 120 milligrams daily as needed for postoperative discomfort was prescribed.

All patients were seen at one and seven days after surgery; any patients who developed complications were seen as necessary in addition to the scheduled visits. At the postoperative visits, the surgical sites were evaluated for infectious complications.

The patient were questioned regarding postoperative fever, pain or bleeding from the surgical sites.

Patients who developed infectious complications were treated in the Oro-Maxillo-Facial Surgery Clinic.

Incidence rates of infectious complications were determined for each treatment group studied; no adjustments were made for variables such as age or sex. A significance level of $P = 0.05$ was selected.

RESULTS

The overall incidence rates of infectious complications were as follows: no treatment antibiotics cones 19% and antibiotic cones 12% (Table 1).

Method	Age group	Incidence of infectious complications
no treatment	< 18 years	12%
no treatment	19-24 years	22%
no treatment	> 25 years	26%
antibiotics cones	< 18 years	8%
antibiotics cones	19-24 years	13%
antibiotics cones	> 25 years	17%

Table 1 *Incidence rates of infectious complications*

Antibiotic cones compared with no treat-ment was close to a statistically significant reduction in infectious complications, when analyzed between groups.

The control group showed that side was not important in relation to the incidence of infectious complications.

The incidence of infectious complications by age group is summarized in Table 1. No significant differences due to age were noted.

Genre effect was not significant ($P > 0.5$). Males had a higher incidence rate of infectious complications as compared with females, but the difference was not statistically significant.

DISCUSSION

Studies and publications concerning incidence of infectious complications are numerous [4,5].

Comparison of rates of infectious complications between studies has little meaning because of different diagnostic criteria.

The incidence of infectious complications in this study is uniformly higher than incidence rates often reported in the literature [6].

Antibiotics cones was more effective in reducing the incidence of infectious complications as compared with no treatment when reviewing clinical cases; that difference was not statistically significant.

Older patients had higher incidence rates of infectious complications than younger patients; this finding is supported by the literature [7].

Treatment comparisons taking age into account indicated that overall treatment effect was significant ($P < 0.05$) in reducing the incidence of infectious complications, but comparisons between treatment groups were not statistically significant with respect to age.

A slightly higher incidence rate of infectious complications for males was observed.

CONCLUSSION

Antibiotics cones alone are not effective in reducingthe incidence of infectious complications. Age was found in this study to be significant factor related to incidence of infectious complications.

REFERENCES

1. Chuang SK, Perrott DH, Susarla SM, Dodson TB: Risk factors for inflammatory complications following third molar surgery in adults.J Oral Maxillofac Surg 2008; 66:2213–2218

2. Capuzzi P, Montebugnoli L, Vaccaro MA: Extraction of impacted third molars: a longi-tudinal prospective study on factors that affect postoperative recovery. Oral Surg Oral Med Oral Pathol 1994;77:341–343

3. Mehrabi M, Allen JM, Roser SM: Therapeutic agents in perioperative third molar surgical procedures. Oral Maxillofac Surg Clin North Am 2007;19:69–84

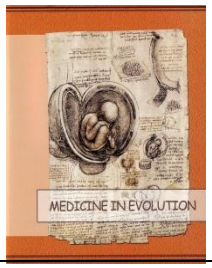
4. Chiapasco M, De Cicco L, Marrone G: Side effects and complications associated with third molar surgery. Oral Surg Oral Med Oral Pathol 1993;76:412–420

5. Piecuch J, Arazadon J, Lieblish S: Prophylactic antibiotics for third molar surgery: a supportive opinion. J Oral Maxillofac Surg 1995; 53:53–60

6. Shepherd JP, Brickley M: Surgical removal of third molars. BMJ 1994; 309: 620–621.

7. Bruce RA, Frederickson GC, Small GS: Age of patients and morbidity associated with mandibular third molar surgery. J Am Dent Assoc 1980; 101:240–245.

PREVALENCE OF ORAL PREMALIGNANT LESIONS



BELAL NIJIM[1], CRISTIAN IRIMIA[1], OCTAVIAN DINCĂ[1]

[1]University of Medicine and Pharmacy „Carol Davila" Bucharest

ABSTRACT

The prognosis for patients with oral squamous cell carcinoma remains poor in spite of advances in therapy of many other malignancies. Despite low prevalence, oral premalignant lesions show histopathological alterations. Early diagnosis remains the key to improved patient survival.

Keywords: *malignant tumors, premalignant lesions, biopsy*

Correspondence to

Dr. Belal Nijim
Adress: Clinica de Chirurgie Oro-Maxilo-Facială
UMF „Carol Davila"
Calea Plevnei 19 010221
Bucureşti, Romania
E-mail address: dr.nijimbelal@gmail.com

INTRODUCTION

Oral squamous cell carcinoma is a major health problem in Romania, with rising prevalence and mortality rates.

A couple of oral lesions such as leukoplakia, erythroplakia and oral lichen planus carry an increased risk for malignant transformation in the oral cavity [1].

Oral erythroplasia is rare, but its malignant transformation rate is the highest among all of the precancerous lesions in the mouth [2]. Although the potential for malignant transformation is higher in erythroplakia, leukoplakia and oral lichen planus should not be neglected, since the lesions have a similar histology to erythroplakia [3].

This study analyzes the prevalence of potentially malignant and malignant oral lesions in the Oro-Maxillo-Facial Surgery Clinic of Bucharest.

MATERIALS AND METHODS

We performed an retrospective study of conescutive 200 oral mucossa lesions from 2006 to 2009. Data was collected year wise in the context of age, genre, site involved and and histopathological findings.

RESULTS

From the total of two hundred biopsies in the study period, a number of 58 patients were reported as benign, 88 potentially malignant and 74 were malignant (Table 1).

Cases nr.	Benign lesions	Premalignant lesions	Malignant tumors
Males	38	61	63
Females	20	27	11
Total	58	88	74

Table 1 Distribution of cases by genre

In the benign group, 38 were males and 20 were females; of the potentially malignant cases, 61 were males and 27 were females.

According to the age distribution, majority of the benign and premalignant biopsies were reported in the age group of 30-40, while malignant lesions were observed mainly in the 50-60 years age group.

	Benign lesions	Premalignant lesions	Malignant tumors
20-30 years	7	0	0
30-40 years	23	38	0
40-50 years	14	27	8
50-60 years	5	13	37
60-70 years	13	8	11
70-80 years	6	2	18
Total	58	88	74

*Table 2 D*istribution of cases *into* age *groups*

On the basis of the site of involvement, biopsies from the oral mucossa revealed that in the benign and premalignant group, the buccal mucosa (Figure 1), was most frequently involved - 38 patients, followed by the tongue (Figure 2) - 27 patients.

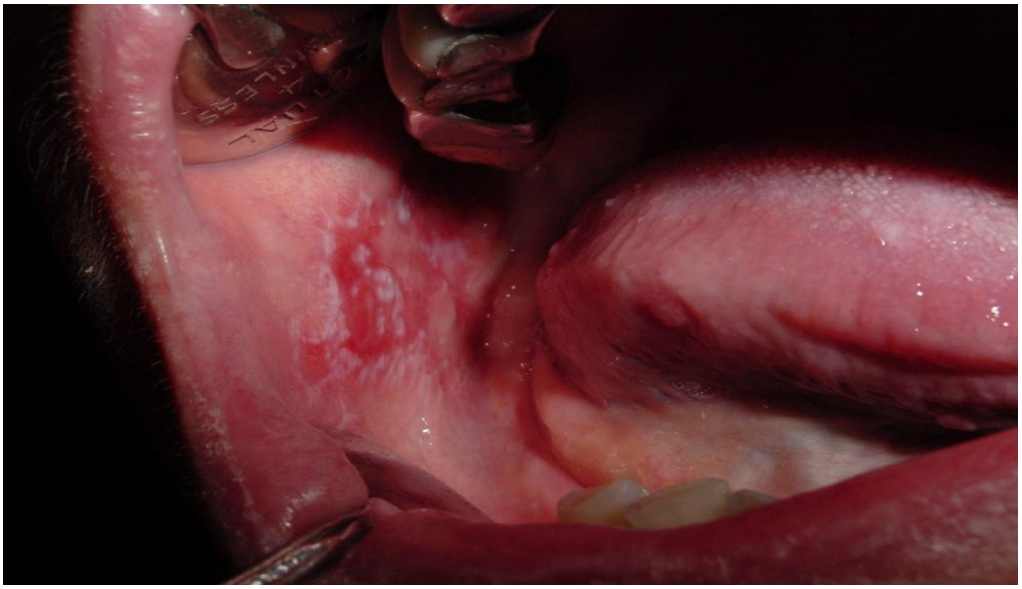


Fig.1 Erythroleukoplakia – clinical aspect
(Photo courtesy of Prof. Dr. Alexandru Bucur)

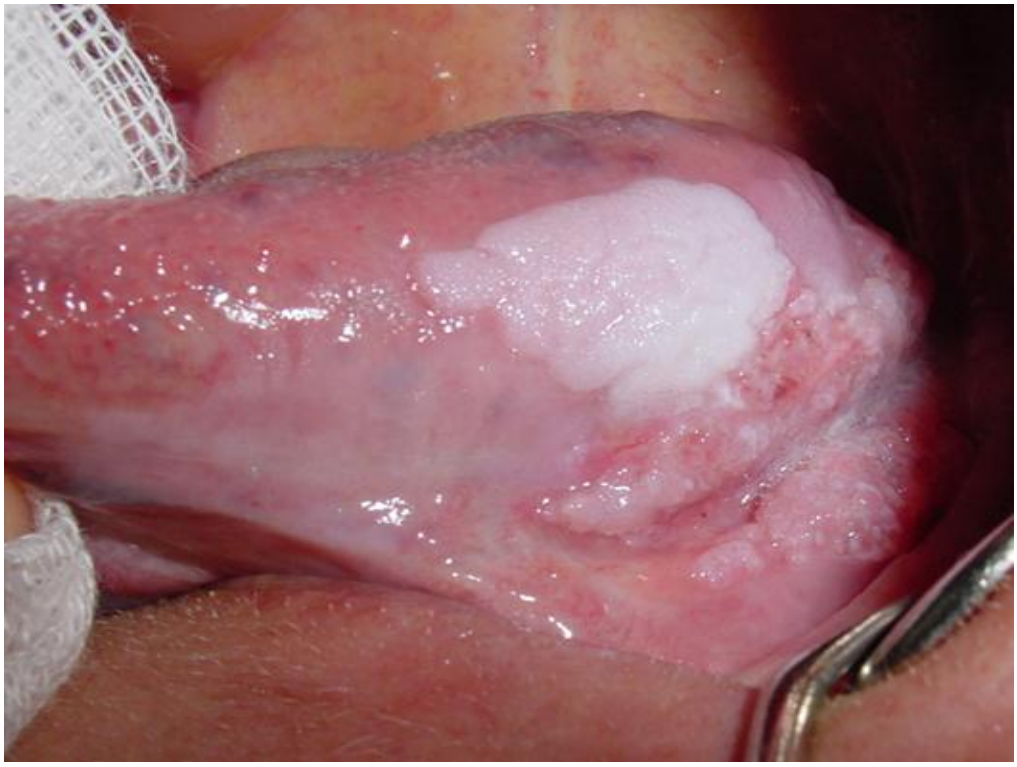


Fig.2 Oral leukoplakia – clinical aspect
(Reprinted with permission from Bucur A.: Compendiu de Chirurgie Oro-Maxilo-Facială, p. 552. © 2009 by Q Med Publishing, Bucureşti)

In malignant lesions, the tongue patients was the most common site (52 cases) (Figure 3).

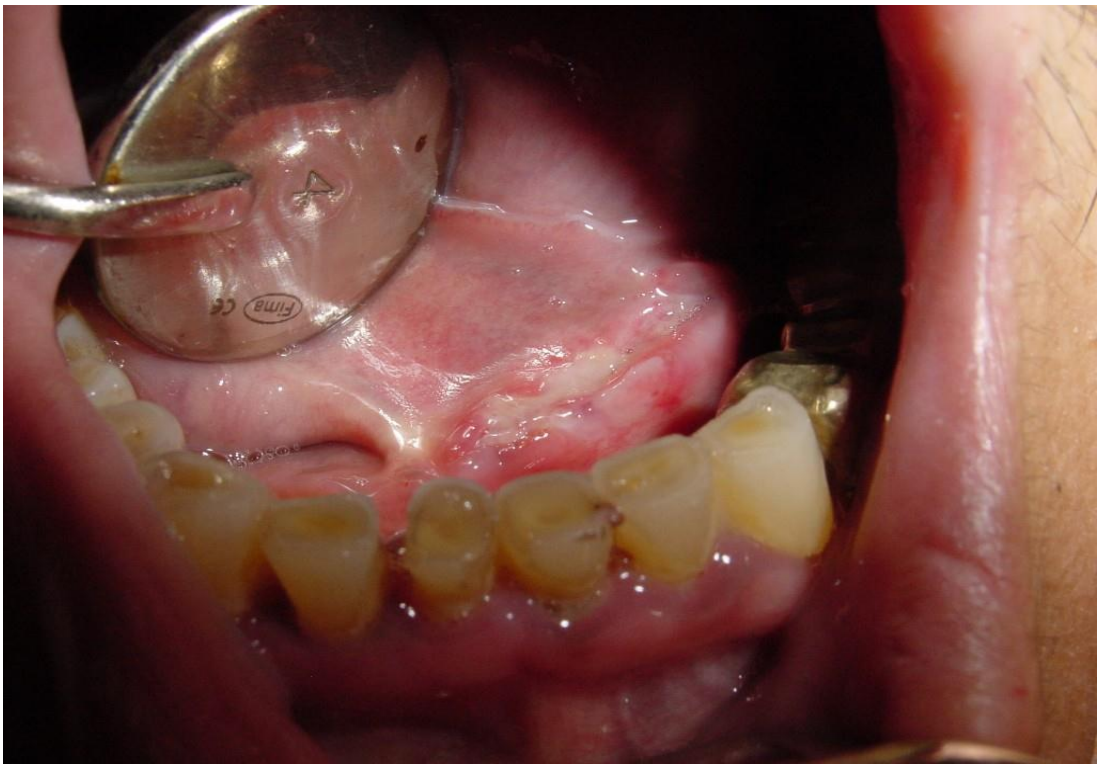


Fig. 3 Oral squamous carcinoma – clinical aspect
(Photo courtesy of Prof. Dr. Alexandru Bucur)

DISCUSSION

The male to female ratio reported in this study was was similar to the ratio generally reported in literature [4]. Similar findings with our observations related to the age group are available [5].

On the bases of site of involvement, in benign and premalignant group, the buccal mucosa was found to be most frequently involved site followed by tongue. In malignancy, the tongue was the most frequent site. This was similar to literature [6].

Since, the oral mucosa is accessible to clinical examination, it could be used in early detection of premalignant lesions, but to date the disease is still detected in later stages [7].

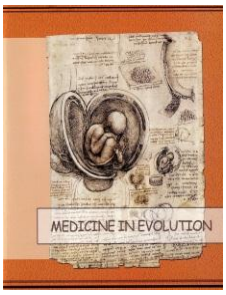
CONCLUSSION

The clinical and pathological features of the lesions analyzed in this study support the data in other published studies. Although their prevalence is low, premalignant lesions present histopathological features ranging from epithelial dysplasia to invasive carcinoma. This justifies periodic monitoring of these patients and cessation of risk factors in such cases.

REFERENCES

1. World Health Organizations. Collaborative Reference Centre for Oral Precancerous Lesions. Application of the international classification of diseases to Dentistry and stomatology. Geneva: WHO; 1978
2. Reichart PA, Philipsen HP. Oral erythroplakia: a review. Oral Oncol. 2005;41(6):551-61
3. Lapthanasupkul P, Poomsawat S, Punyasingh J. A clinicopathologic study of oral leukoplakia and erythroplakia in a Thai population. Quint Int. 2007;38(8):E448-55
4. Reibel J. Prognosis of oral pre-malignant lesions: significance of clinical, histopathological, and molecular biological characteristics. Crit Rev Oral Biol Med. 2003;14(1):47-62
5. Pindborg JJ, Daftary DK, Mehta FS. Studies in oral leukoplakia: a preliminary report on the period prevalence of malignant transformation in leukoplakia based on a follow-up study of 248 patients. Am Dent Assoc. 1968;76(4):767-71
6. Scully C, Sudbo J, Speight PM. Progress in determining the malignant potential of oral lesions. J Oral Pathol Med. 2003;32(5):251-6
7. Bsoul SA, Huber MA, Terezhalmy GT. Squamous cell carcinoma of the oral tissues: a comprehensive review for oral healthcare providers. J Contemp Dent Pract. 2005;6(4):1-16

COMPARATIVE STUDY BETWEEN KERR FILE NEEDLES USE FROM STAINLESS STEEL OR NICKEL-TITANIUM ALLOY AND PROTAPER CUTTERS USED IN MANUAL WIDENING OF ROOT CANALS WITH DIFFERENT DEGREES OF CURVATURE



CHRISTINA MIHAI[1], LAURENŢIU GONTARIU[2], DIANA GOLEA[3], ALEXANDRU-ANDREI ILIESCU[4], ANDREI ILIESCU[5]

[1] CMDTA Bucharest
[2] Private Practice, Bucharest
[3] National Institute of Biological Research, Bucharest
[4] University of Medicine and Pharmacy, Craiova
[5] University of Medicine and Pharmacy "Carol Davila", Bucharest

ABSTRACT

Chemomechanical endodontic treatment is the key of clinical success postoperative immediate an in time. This study aims to determine and interpret the changes generated during the treatment for three-dimensional enlargement of root canal walls with various degrees of curvature, processed with conventional Kerr file needles or with drills from nickel-titanium ProTaper, operated solely by hand.

Materials and methods. The study has as a starting point the simulation of 12 cases of root canals with curvatures 30^o, 45^o, 60^o, 90^o and radius 3, 4, 5 mm, based on the evaluation of 46 real cases treated with manual instruments, using needles Kerr file from stainless steel and ProTaper. Images of radiological aspects were obtained using 3D design software Solid Works 2012.

Results. In canals with moderate curvatures deviation from their natural trajectory were recorded downward from those Kerr file from steel, followed by nickel-titanium and ProTaper drills. In all 12 cases were obtained modifications, the highest values being obtained in the context of a rigid instrumentation with extreme anatomy.

Conclusions. Mathematically has been demonstrated the superiority of the use of nickel-titanium instruments and especially of him with special design ProTaper to achieve a expansion of curved root canals equidistant with their natural trajectory.

Key words: *mechanical treatment, curved canals, Kerr file, ProTaper.*

Correspondence to

Dr. Cristina Mihai, U.M.F. Carol Davila, Faculty of Dentistry,
Str. Eforie nr. 4-6, sector 5, Bucuresti,
Nr. tel. 0740090060
e-mail: mihaichris3@yahoo.com

INTRODUCTION

Anatomy of endodontic system is an unpredictable variable, potentially generating therapeutic incidents and accidents sometimes irreversible. Complexity of the morphology and spatial arrangement of root canals raises many biomechanical problems that technology of manufacturing endodontic instruments was called upon to resolve [5].
Are well known in practice the iatrogenic effects of stainless steel Kerr needle with conicity ISO 0.02 [2]. The main objectives to circumvent these drawbacks were the modification of the active part of the design tools for enlarged channels (creating a non-cutting pilot tip with decreasing angle of attack) and obtain elastic metal alloy with high resistance to bending and torsion forces exerted during specific clinical maneuvers [4, 7].

Use of endodontic instruments nickel-titanium alloy, thanks to super elasticity and low elasticity module allows regaining their original shape once released from compression and tension forces exerted by the walls curved channels (memory elasticity) [1, 6, 9].
Besides elasticity of 2-3 times higher, a especially advantage of nickel-titanium alloys to stainless steel also consists in maintaining the flexibility of endodontic instrument in terms of increasing the taper tip of active part by 2-6 times compared to the standard ISO 0.02 [3].
This study aimed to track changes of curved root canals size due to enlargement with needle Kerr file steel or nickel-titanium and with ProTaper, but only manually operated.

MATERIALS AND METHODS

Evaluating a trial lot of 50 molars endodontic treated for different pathologies we have chosen 46 images for an exact calculation due to similar incidents at a retroalveolar endocanicular pre- and post treatment radiography. Evaluating specifically the mesio-vestibular root at 30 lower molars and 16 upper molars we set up the size of a pattern to which, in order to facilitate the calculation method, we took the point of maximum curving at half the cervical-apical distance. In this pattern canal have been considered two variables: the angulation and the curving radius.
The chosen angles were 30°, 45°, 60°, and 90°, being well known from clinical practice how difficult it is to correctly apply a mechanical treatment for curves over 20°-25°. The curving radius varied from 3, 4 and respectively 5 mm, because for a radius of 2 mm have been no interpretable modifications.
The images have been obtained by using the 3D design software Solid Works 2012. They have been exported as image files used afterwards in the Adobe Photoshop work program where the area of extreme curving has been marked, naming it the area of maximum interest during the mechanical processing.

The processing was simulated for $F \rightarrow 0$ manual instrument characteristic, and the modelated ones were Kerr (Φ_o 25 mm) and ProTaper file (Φ_o 25 mm). The Kerr-file needle has been chose as a try gauge, being the one most frequently used in endodontion. The standard configuration of very tapered rectangular rod, with tight step and brushy/thick cutting edges represents the model for decresed flexibility and high resistence to torsion. For opposite, we have chosen F_2 Pro Taper, an instrument of the latest generation with which the cross section surface is an equilateral triangle with convex sides – that means an increased internal resisitance. Step and active part conicity varies, decreasing towards the handle for an increased flexibility and limited interference with the canicular walls
The images of the needles have been obtained by also using the 3D design sotware Solid Works 2012. Two variables have been taken into consideration: the form of the active part and the characteristics of the alloy: steel or nickel titanium. The interaction and the modifications resulted have been obtained by AutoCad 2012. The data have been put in a system of coordinates, worked on in Office Word files to get them organized, and then used in calculations of an Office Excel type.

The value of the endocanicular space print area has been registered before and after working on it and by correlating the deformation of the needle to the area, the modification of the internal or external wall in the maximum curved area could be defined.

RESULTS

Having the same standard configuration but a different behaviour given by the characteristics of the alloy (Table I) the Kerr needles will make big differencies for small angularities and large curving radii (angles 30^0, curving radius 5 mm). Due to the rigidity of steel there can be obtained a further stretching of the canalary hard tissues (Table II) resulting immediately in a modification of iys initial anatomy, (*Figure 1*).

Table I. Enlargement area for canals with Kerr file needle (ISO 25) at the point of maximum curvature

Instrument	**r = 3 mm**				**r = 4 mm**				**r = 5 mm**			
Angle of 30 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
NiTi	*32.86*	*34.95*	*2.09*	*5.97997*	*33.78*	*35.71*	*1.93*	*5.40464*	*34.35*	*36.44*	*2.09*	*5.7354*
Steel	*32.86*	*34.99*	*2.13*	*6.08745*	*33.78*	*35.72*	*1.94*	*5.43113*	*34.35*	*36.63*	*2.28*	*6.2244*
Angle of 45 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
NiTi	*32.46*	*34.29*	*1.83*	*5.33683*	*28.44*	*30.19*	*1.75*	*5.79662*	*30.64*	*32.01*	*1.37*	*4.2799*
Steel	*32.46*	*34.29*	*1.94*	*5.63953*	*28.44*	*30.3*	*1.86*	*6.13861*	*30.64*	*32.03*	*1.39*	*4.3396*
Angle of 60 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
NiTi	*33.28*	*34.99*	*1.71*	*4.88711*	*32.25*	*34.2*	*1.95*	*5.70175*	*33.28*	*34.41*	*1.43*	*4.1198*
Steel	*33.28*	*35.01*	*1.73*	*4.94144*	*32.25*	*34.32*	*2.07*	*6.03146*	*33.28*	*34.89*	*1.61*	*4.6145*
Angle of 90 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
NiTi	*35.14*	*36.44*	*1.3*	*3.56750*	*35.84*	*37.04*	*1.2*	*3.23974*	*36.24*	*37.78*	*1.54*	*4.0762*
Steel	*35.01*	*36.55*	*1.41*	*3.85772*	*35.84*	*37.13*	*1.29*	*3.47428*	*36.24*	*37.88*	*1.64*	*4.3294*

Table II. The difference in final diameter for the widening with Kerr steel needle (ISO 25) and NiTi

Angle	r = 3 mm	r = 4 mm	r = 5 mm
30º	*0.04*	*0.01*	*0.19*
45º	*0.11*	*0.11*	*0.02*
60º	*0.02*	*0.12*	*0.18*
90º	*0.10*	*0.09*	*0.10*

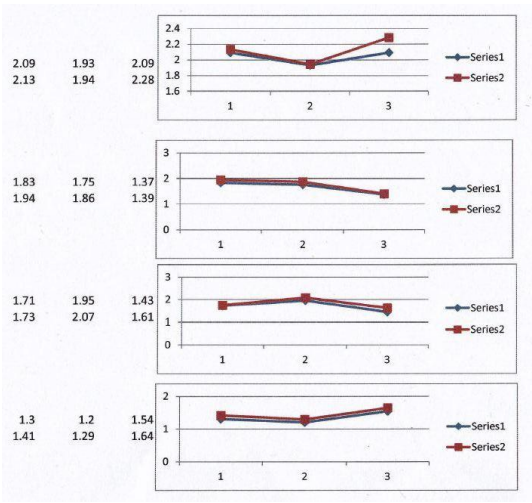


Figure 1. Chart for comparative widening of canals with needles steel Kerr file and NiTi alloy

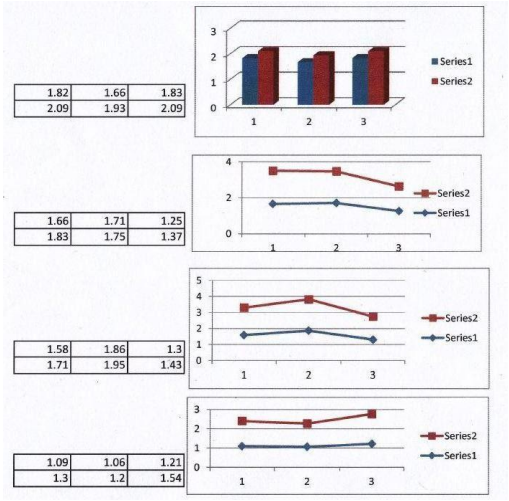


Figure 2. Chart for comparative widening of canals with needles Kerr file from NiTi and ProTaper F2

The aria of the endodontic space print increases a lot more in the case of the NiTi Kerr file, the highest value being registered for the 90^0 angle and 5 mm radius (Table III). Yet, the differencies obtained are smaller than in the case when the efficiency of the needle is associated to an increased rigidity, as in the previous case (Table IV). The files ProTaper F_2 activated manually will lead to maintaining the initial trajectory of the root canal, but there will be a risk of modificating it by apical translation of the curved zone (Figure 2).

Table III. Manual widening area at the t maximum curvature point - ProTaper F_2 file vs Kerr NiTi needle (ISO25)

Instrument	r = 3 mm				r = 4 mm				r = 5 mm			
Angle of 30 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
ProTaper	*32.86*	*34.68*	*1.82*	*5.24798*	*33.78*	*35.44*	*1.66*	*4.68397*	*34.35*	*36.18*	*1.83*	*5.0580*
Kerr needle	*32.86*	*34.95*	*2.09*	*5.97997*	*33.78*	*35.71*	*1.93*	*5.40464*	*34.35*	*36.44*	*2.09*	*5.7354*
Angle of 45 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %

ProTaper	*32.46*	*34.12*	*1.66*	*4.86518*	*28.44*	*30.15*	*1.71*	*5.67164*	*30.64*	*31.89*	*1.25*	*3.9197*
Kerr needle	*32.46*	*34.29*	*1.83*	*5.33683*	*28.44*	*30.19*	*1.75*	*5.79662*	*30.64*	*32.01*	*1.37*	*4.2799*
Angle of 60 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
ProTaper	*33.28*	*34.86*	*1.58*	*4.53241*	*32.25*	*34.11*	*1.86*	*5.45294*	*33.28*	*34.58*	*1.3*	*3.7593*
Kerr needle	*33.28*	*34.99*	*1.71*	*4.88711*	*32.25*	*34.2*	*1.95*	*5.70175*	*33.28*	*34.71*	*1.43*	*4.1198*
Angle of 90 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
ProTaper	*35.14*	*36.23*	*1.09*	*3.00855*	*35.84*	*36.9*	*1.06*	*2.87262*	*36.24*	*37.45*	*1.21*	*3.2309*
Kerr needle	*35.14*	*36.44*	*1.3*	*3.56750*	*35.84*	*37.04*	*1.2*	*3.23974*	*36.24*	*37.78*	*1.54*	*4.0762*

Table IV. The difference in final diameter for the widening with Kerr NiTi needle (ISO 25) and ProTaper F_2 file

Angle	r = 3 mm	r = 4 mm	r = 5 mm
30°	*0.27*	*0.27*	*0.26*
45°	*0.17*	*0.04*	*0.12*
60°	*0.13*	*0.09*	*0.13*
90°	*0.21*	*0.14*	*0.33*

The differencies between configuration, and especially between alloy (steel vs nickel-titanium) have led to important modifications (Table V), the most important being when the angle is smaller and the curved radius larger (Table VI). In this case, there can be supposed a dramatic modification in the curved zone tending to straighten and translate apically, dar also the possibility of creating thresholds, radicular perforations (Figure 3).

Table V. Manual widening area at the t maximum curvature point –Kerr steel needle (ISO25) vs ProTaper F_2 file

Instrument	r = 3 mm				r = 4 mm				r = 5 mm			
Angle of 30 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
ProTaper	*32.86*	*34.68*	*1.82*	*5.24798*	*33.78*	*35.44*	*1.66*	*4.68397*	*34.35*	*36.18*	*1.83*	*5.0580*
Kerr needle	*32.86*	*34.99*	*2.13*	*6.08745*	*33.78*	*35.72*	*1.94*	*5.43113*	*34.35*	*36.63*	*2.28*	*6.2244*
Angle of 45 degrees												
	Initial (mm^2	Final (mm^2)	Δ	Δ %	Initial (mm^2	Final (mm^2)	Δ	Δ %	Initial (mm^2	Final (mm^2)	Δ	Δ %

	)				)				)			
ProTaper	*32.46*	*34.12*	*1.66*	*4.86518*	*28.44*	*30.15*	*1.71*	*5.67164*	*30.64*	*31.89*	*1.25*	*3.9197*
Kerr needle	*32.46*	*34.4*	*1.94*	*5.63953*	*28.44*	*30.3*	*1.86*	*6.13861*	*30.64*	*32.03*	*1.39*	*4.3396*
Angle of 60 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
ProTaper	*33.28*	*34.86*	*1.58*	*4.53241*	*32.25*	*34.11*	*1.86*	*5.452946*	*33.28*	*34.58*	*1.3*	*3.7593*
Kerr needle	*33.28*	*35.01*	*1.73*	*4.94144*	*32.25*	*34.32*	*2.07*	*6.031469*	*33.28*	*34.89*	*1.61*	*4.6145*
Angle of 90 degrees												
	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %	Initial (mm^2)	Final (mm^2)	Δ	Δ %
ProTaper	*35.14*	*36.23*	*1.09*	*3.00855*	*35.84*	*36.9*	*1.06*	*2.87262*	*36.24*	*37.45*	*1.21*	*3.2309*
Kerr needle	*35.14*	*36.55*	*1.41*	*3.85772*	*35.84*	*37.13*	*1.29*	*3.47428*	*36.24*	*37.88*	*1.64*	*4.3294*

Table VI. The difference in final diameter for the widening with Kerr steel needlede (ISO 25) and ProTaper F_2 file

Angle	r = 3 mm	r = 4 mm	r = 5 mm
30°	*0.31*	*0.28*	*0.45*
45°	*0.28*	*0.15*	*0.14*
60°	*0.15*	*0.21*	*0.31*
90°	*0.32*	*0.23*	*0.43*

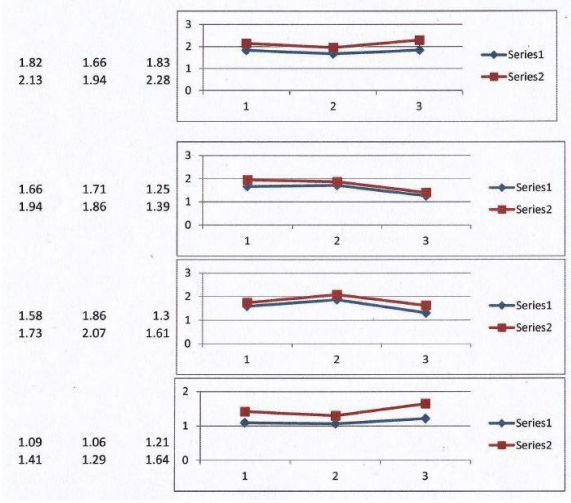


Figure 3 – Chart for comparative widening of canals with needles steel Kerr file and ProTaper F_2 file

DISCUSSION

This study approaches the problem of the curved root canals from a mathematical point of view aiming to determining a postoperative variation of the endodontic space configuration. As in current practice the dentist makes use of retroalveolar radiography taken pre- and post-operatively, the system taken into consideration has always been bidimensional, accepting the limits of a correct evaluation of a tridimensional anatomy summarized this way.
Registering the values before and after the biomechanical treatment led to obtaining modifications for all the 12 cases involved, in spite of the bidimensional interpretation. The biggest differencies appeared, as expected, when the comparison was made within the same type of endodontic instrument (Kerr file needle) for which we varied the characteristics for a different alloy, stainless steel or nickel-titanium.
The rigidity of the steel for Kerr file needle ISO 25 led to obtaining the biggest modifications in the case of the angulariry of 30^0 and the 5 mm radius; the logical consequences were either of modification in the canalary anatomy, or of breaking the overworked needle.
In the cases of modifications registered at the biomechanical treatment with endodontic instruments with a different configuration of the needle, a better image has been obtained for ProTaper, the mazximum obtained being for the 90^0 angularity and a radius of 5 mm, thus evincing the capacity of action centered of nickel-titanium F_2 file.
The latest research have come to support the clinical practice, and passing from „a rigid alloy to one with a memory of elasticity" [9], or from one simple design to a complicated one [2], ensuring a different zonal action, answered several frequent questions of the practice.
Yet, there are still situations difficult to approach, even by using the latest geneeration technology, because any advantage has a context of disadvanatages attached.
The current research focus is on optimizing the alloys microstructure of nickel-titanium [7, 8], obtaining a rotary instruments (GT Series X and Vortex ProFile) with a cyclic fatigue resistance significant higher compared with stretch conventional alloys of nickel-titanium.
Nevertheless, the research path is far from any arrival line and in this context we can mention the attempt to make the endodontic instruments from alloy with elasticity memory *M-Wire.* It meets a wear resistance and fracture superior to similar file from conventional nickel-titanium alloy stretch thanks to its metallurgical characteristics in which are found all 3 crystalline phase (martensite, R-phase and austenite) embedded in a unique nanocrystalline microstructure [8].

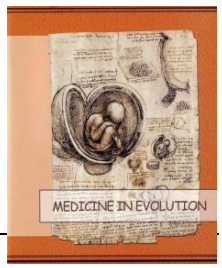
CONCLUSION

The needles Kerr file from steel produce during the widening strongest deviation from the curved channels path compared to nickel-titanium, but at small radius of curvature (3 mm) the differences are minimal if not exceed an angle of 60 °.
Although still made of nickel titanium alloy stretch, at canals with small curvature angle (30 °), the Kerr file needles constant cause, during widening, the most significant deviations from canals path compared with ProTaper F_2 milling, no matter the radius of curvature.
Regardless of the angle and curvatures radius analyzed, the most important differences between deviations from the curves canals path appear between Kerr file needles from steel and ProTaper F_2 milling from nickel-titanium.

REFERENCES

1. Arbab-Chirani R, Chevalier V, Arbab-Chirani S, Calloch S., Comparative analysis of torsional and bending behavior through finite-element models of 5 Ni-Ti endodontic instruments, Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011;111:115-121
2. Hülsmann M, Peters OA, Dummer PMH. Mechanical preparation of root canals: shaping goals, techniques and means, Endodontic Topics. 2005; 10:30-76
3. Saunders EM. Hand instrumentation in root canal preparation. Endodontic Topics. 2005; 10:163-167
4. Schäfer E, Lau R. Comparison of cutting efficiency and instrumentation of curved canals with nickel-titanium and stainless-steel instruments. J Endod. 1999; 25:427-430
5. Vaudt J, Bitter K, Neumann K, Kielbassa AM. Ex vivo study on root canal instrumentation of two rotary nickel-titanium systems in comparison to stainless steel hand instruments. Int Endod J. 2009; 42:22-33
6. Walia HM, Brantley WA, Gerstein H. An initial investigation of the bending and torsional properties of Nitinol root canal files. J Endod. 1988; 14:346-351
7. Ye J, Mishra RK, Pelton AR, Minor AM. Direct observation of the NiTi martensitic phase transformation in nanoscale volumes. Acta Mater. 2010; 58:490-498
8. Ye J, Gao Y. Metallurgical characterization of M-Wire nickel-titanium shape memory alloy used for endodontic rotary instruments during low-cycle fatigue. J Endod. 2012; 38:105-107
9. Zinelis S, Eliades T, Eliades G. A metallurgical characterization of ten endodontic Ni-Ti instruments: assessing the clinical relevance of shape memory and superelastic properties of Ni-Ti endodontic instruments. Int Endod J. 2010; 43:125-134

THE PERIODONTAL RISK FACTOR IN THE MANAGEMENT OF PERIODONTAL DISEASE



KRALEV CAROLINE[1], OANA VELEA[1], DERBAN PAULA[1], ONISEI DAN[2], ONISEI DOINA[2]

[1] PhDS University of Medicine and Pharmacy „Victor Babes", Timişoara
[2] University of Medicine and Pharmacy „Victor Babes", Faculty of Dental Medicine, Department of Periodontology, Timişoara

ABSTRACT

Prevention and treatment of the periodontal disease is based on the understanding of its etiology and pathogenesis. Prevention, the main goal of the medical profession, can be appropriately performed only after identifying and eliminating the causes of the disease.

Onset, clinical form and prognosis are influenced by individual patient characteristics, social and behavioral factors as well as systemic and genetic factors. Thus, these become risk factors for periodontal disease and serve in determining the individual periodontal risk profile.

Key words : periodontal disease, risk factors, periodontal prognosis, risk diagram

Corespondence to

Prof.Dr.Doina Onisei
Department of Periodontology,
Faculty of Dental Medicine
UMFVB Timişoara
Email : donisei@umft.ro
Tel.0722942607

INTRODUCTION

Controlling the risk factors is an important part of the periodontal treatment plan. Assessment of the periodontal risk of a certain patient regarding only one factor, offers an incomplete and thereby misleading overview [1]. Therefore, the simultaneous evaluation of all risk factors becomes necessary and this is achieved by imagining and applying a multi factorial risk diagram.

To obtain the diagram, we must undergo three critical steps:

-Identifying the risk factors

-Conceiving the treatment plan

-Interpreting the periodontal risk diagram

MATERIALS AND METHODS

6 periodontal risk factors were identified, in association with the onset, clinical form and evolution of the periodontal disease, and recorded in the patient's periodontal chart:

-Bleeding on probing ;

-Periodontal pockets ≥ 5 mm;

-Number of missing teeth;

-Bone loss/ age ratio;

-Systemic disease;

-Environmental factors.

1.Bleeding on probing

Bleeding on probing is considered an objective parameter of inflammation and must be included in a periodontal health evaluation system. It reflects periodontal pocket activity and the efficacy of the patient's home-care and of the performed periodontal treatment [2]. Statistically and for the assessment of bleeding as a risk factor, it is considered that a percentage higher than 50 indicates a maximum periodontal risk.

2.Periodontal pocket depth ≥ 5

Periodontal pockets ≥ 5 are areas were a long term plaque control is achieved with difficulty. Periodontal stability is reflected in the absence of periodontal pockets. Statistically, the presence of 10 or more such sites confers a maximum periodontal risk [3].

3.Number of missing teeth

This parameter reflects the patient's history of oral disease, home care status, presumable occlusal trauma and dental-periodontal functionality. Statistically, the loss of 10 or more teeth induces a severe dental-periodontal malfunction and confers a maximum periodontal risk [4].

4.Bone loss / age ratio

Bone loss points out the destructive character of periodontal disease. The extend and degree of lost bone are to be evaluated by clinical and imagistic investigations: bite-wing, retro alveolar radiographs and panoramic radiographs, as well as subtraction radiographs and CT scans. Bone loss is estimated at the site most affected by the disease and is expressed in mm; age is expressed in years.

5.Systemic disease and genetic factors

The most important systemic risk factor for periodontal disease is diabetes.

Medication used in treating systemic disease can become a risk factor for periodontal disease as it promotes gingival hyperplasia and plaque accumulation [5]. E.g.: nifedipin, used in the treatment of cardiac disease, fenitoin and hidantoin in epilepsy, and cyclosprines in the treatment of autoimmune diseases.

The classification of periodontal disease confirms the influence of hormonal factors on the periodontium. Progesterone has the most important influence in the occurrence of local imbalances, while estrogen plays a far lesser part in this respect. Thus , during pregnancy , due to progesterone, the level of CD3, CD4 and B- type lymphocytes in the gingiva drops, causing the cell-mediated immunity and the host response to bacterial antigens to decrease. The synthesis of glycosaminoglycans, key components of the collagen matrix is also impaired.

The genetic factor, if present, modulates the hosts response to the disease [6] .

As a result of the host- plaque interaction, the level of inflammatory mediators, such as cytokines, especially interleukin 1(IL-1), prostaglandin E2, tumor necrosis factor α, increases. The IL – 1 positive patients display a higher susceptibility to more severe forms of periodontal disease [7].

6.Environmental factors

Smoking and stress are the most important environmental risk factors for periodontal disease.

Smoking interferes with the hosts response and defense mechanisms. Smokers exhibit lower levels of salivary and serum antibodies (Ig A, Ig G), reduced numbers of T-lymphocytes, malfunctioning chemotaxis and phagocytosis mechanisms with consecutive accumulation of enzymes and redox components (collagenase, elastase) [8].

Excessive smoking stimulates the activation of inflammatory cells and leads to an increased discharge of destructive cytokines (IL- 1, α TNF). The whole array of products obtained in the process of tobacco burning (nicotine, acrolein, cyanides, carcinogenic substances: polycyclic aromatic hydrocarbons and nitrosamines, heavy metals, radioactive substances, carbon monoxide, nitrogen oxides, etc) is stored by the fibroblasts and leads to functional and morphological disorders: a decrease in the attachment capability of the fibroblasts to the root surface, as well as disorders in the proliferation and synthesis of collagen.

Stress is the psychosomatic response of the human body to an external challenge. Under these conditions the hypothalamic- pituitary-adrenal axis is stimulated, leading to an increased discharge of neurohormones, adrenalin, neuropeptides – substance P, which enables the body to respond to the situation and maintain its homeostasis. Long –term physical an psychological stress increases the cortisone and epinephrine levels and disturbs the body's homeostasis.

Stress exerts both a direct and indirect influence on the body, and can determine its burnout, that leads to anxiety and depression and indirectly to a neglect in oral hygiene and care, and also to a potential tobacco and alcohol abuse, as well as malnutrition and teeth clenching [9].

Environmental factors are the sixth and last factor of the risk diagram, and in direct correlation with time, frequency and intensity of exposure [10].

DISCUSION

Data for construction of the diagram is obtained with mathematical algorithms that convert information from the patient`s periodontal chart to graphic representations, using Microsoft Excel Programm.

Periodontal coordinates are:

-Bleeding index :

≤ 50% , represented as a number

>50%, represented as 100% (maximum risk)

-Periodontal pockets > 5mm:

≤10 represented as a number

>10, represented as 100%, (maximum risk)

Number of missing teeh:

- for 1 missing tooth the represented value will be 10%
- >10 missing teeth, represented as 100% (maximum risk)

Bone loss/age ratio (n) :

n≤1, represented as a percentage value (100 x n)

n>1, represented as 100%

-Systemic disease/ genetic factors:

medication is considered 10%

IL – 1 - 20%

osteoporosis, hormonal imbalances – 30%

controlled diabetes – 50%

genetic syndromes – 70%

uncontrolled (poorly controlled) diabetes – 90%

any association of these factors – 100% (maximum risk)

-Environmental factors

stress, poverty – 20%

former smoker (less than 5 years of abstinence) – 30%

active smoker : 1 -> 9 cigarettes/day – 50 %
10 -> 14 cigarettes/day – 60%
15 -> 19 cigarettes/day – 80%
< 20 cigarettes/ day – 100%

We will use a hexagonal radar – type risk diagram , with 6 periodontal risk vectors and percentage values, with a minimum of 0 % (no risk) and a maximum of 100%. (fig. 1)

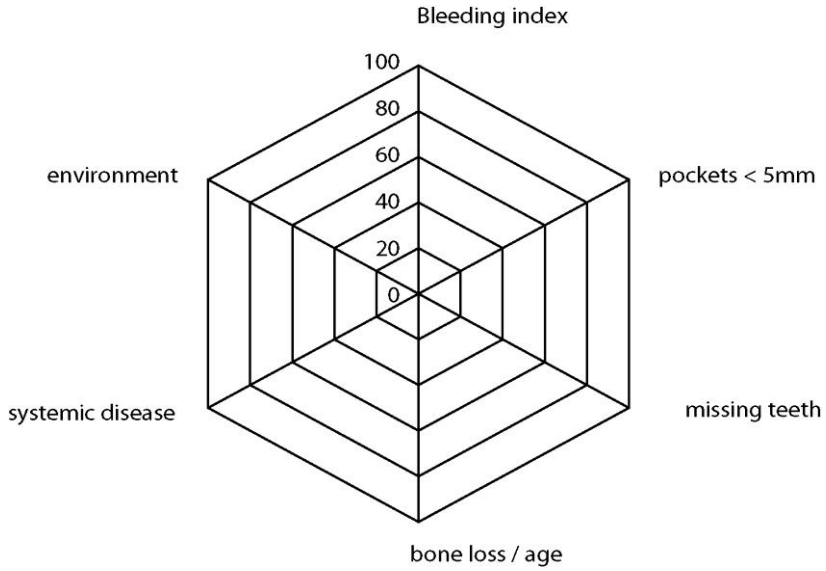


Fig.1 – Radar – type multifactorial risc diagram

Periodontal prognosis is correlated to the risk diagram and the necessary treatment. It is dependent on the severity of disease, risk factors, patient age and especially on the patient`s ability to maintain a rigorous daily hygiene [11].

There are several important prognostic types :

-*Excellent prognosis*: no bone loss, excellent gingival conditions, very good doctor – patient cooperation, no systemic or environmental risk factors ;

-*Good prognosis*: adequate bone conditions, good control possibilities of the etiological factors, absence of systemic or environmental risk factors ;

-*Satisfactory prognosis*: inadequate bone support, tooth mobility, class I furcation defect, adequate patient cooperation, limited systemic or environmental factors ;

-*Unfavorable prognosis*: moderate to important bone loss, tooth mobility, class I or II furcation defect, poor patient cooperation and inadequate oral hygiene, systemic and environmental risk factors ;

-*Questionable prognosis*: important bone loss, class I or II furcation defect, tooth mobility, inaccessible areas , systemic and environmental risk factors ;

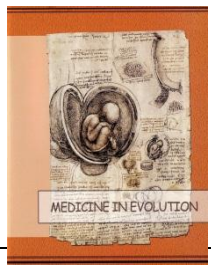
-*Severe prognosis*: advanced bone loss, areas inaccessible to means of oral hygiene, indication of multiple extractions, uncontrolled systemic and environmental factors [3] .

Several cases will require a temporary prognosis until the assessment of the initial treatment outcome.

REFERENCES

1. Garcia RI, Nunn ME, Dietrich T: Risk calculation and periodontal outcomes, *Periodontology 2000 June 2009 Volume 50, Issue 1: 65-77*
2. Feier I, Onisei D, Onisei Doina: The plurivalence of the interpretation of correlation between plaque score and bleeding score, *Medicina Stomatologică, 2009, nr. 1, Vol. 13:45-48*
3. Onisei D, Onisei D. Parodontologie clinică, Ed. Mirton 2011
4. Heitz-Mayfield LJA: Disease progression: identification of high-risk groups and individuals for periodontitis, *Journal of Clinical Periodontology, October 2005 Volume 32: 196–209*
5. Lang NP, Tonetti MS: Periodontal Risk Assessment (PRA) for Patients in Supportive. Periodontal Therapy (SPT), *Oral Health & Preventive Dentisty 1/2003, S. 7-16*
6. Loos BG, John RP, Laine ML: Identification of genetic risk factors for periodontitis and possible mechanisms of action, *Journal of Clinical Periodontology October 2005 Volume 32: 159–179*
7. Stabholz A, Soskolne W, Shapira L: Genetic and environmental risk factors for chronic periodontitis and aggressive periodontitis, *Periodontology 2000 June 2010 Volume 53, Issue 1: 138–153*
8. Heasman L., Stacey F., Preshaw P. M., McCracken G. I., Hepburn S., Heasman P. A.: The effect of smoking on periodontal treatment response: a review of clinical evidence, *Journal of Clinical Periodontology April 2006 Volume 33, Issue 4: 241–253*
9. Kinane DF, Peterson M, Stathopoulou PG: Environmental and other modifying factors of the periodontal diseases, *Periodontology 2000 February 2006 Volume 40, Issue 1: 107–119*
10. Leininger M, Tenenbaum H, Davideau JL: Modified periodontal risk assessment score: long-term predictive value of treatment outcomes. A retrospective study, *Journal of Clinical Periodontology May 2010 Volume 37, Issue 5: 427–435*
11. Onisei D., Oprescu I., Onisei D : The assessment of periodontal patient's risk factors, *Medicina Stomatologică, 2006, nr. 1, vol. 10:61-65*

SURFACE CONDITION INFLUENCE ON GALVANIC CORROSION



LUCIEN RECLARU[1], LAVINIA ARDELEAN[2], LAURA CRISTINA RUSU[2]

[1] Private Practice, La Chaux-de-Fonds, Switzerland
[2] University of Medicine and Pharmacy „Victor Babes", Timisoara, Romania

ABSTRACT

Surface condition influence on galvanic corrosion was investigated in this paper. We used five samples consisting of 2 plates of different noble dental alloys joined by a solder point. The samples underwent different surface treatments: no treatment (1), cleaning by a slight polishing with a polishing paste (2 and 3), chemical etching in a hot etching salt (4) and abrasion with ceramic abrasive disks followed by polishing and chemical etching (5).

After immersion in an artificial saliva solution at 37°C for 30 days samples 1, 2 and 3 show a significant corrosion products deposit. Sample 4 reacted very little. Sample 5 showed no sign of corrosion or any other change. For noble dental alloys combinations, a surface treatment that removes the oxide layers properly is essential to prevent the consequences, sometimes catastrophic, of the galvanic corrosion incidence.

Key words: *galvanic corrosion, surface condition, artificial saliva, noble dental alloy*

Corespondence to

Prof. Dr. Lavinia Ardelean, PhD
Head of Dept.of Technology of Materials and Devices in Dental Medicine
"Victor Babes" University of Medicine and Pharmacy Timisoara
25. C. Brediceanu str.
300012 Timisoara, Romania
+40722-625235
e-mail: lavinia_ardelean@umft.ro

INTRODUCTION

Bimetallic devices may present signs of corrosion after variable time [1]. Such degradations are quite frequent in the oral cavity, fortunately at a smaller scale in case of noble dental alloys [2] but may occur in various other situations (Fig. 1). Such degradations correspond to the galvanic corrosion type.

Fig. 1. Bimetallic wrist bracelet made of bimetallic rings gold/steel after corrosion in saline solution

To produce a degradation due to the galvanism, three conditions must be met:
- Two metallic materials must be present;
- Materials must be in electrical contact for a current to flow;
- The two materials must be immersed in an electrolyte.

Numerous factors influence the galvanic corrosion, especially:

- Parameters related to the material (composition, structure, impurities, surface condition etc.) [3,4]
- Parameters related to the nature of the electrolyte (composition, concentration, temperature, oxygen content, pH, heterogeneity etc.)
- Parameters related to the topography (surface ratio of the two materials, geometric distribution etc.)

MATERIAL AND METHOD

In order to illustrate the importance of the surface condition, we performed tests of galvanic corrosion in sections consisting of 2 plates of different noble dental alloys, joined by a solder point(Fig.2).

Fig. 2. The corrosion test samples are 2 plates of noble alloy connected by soldering

The two chosen alloys (Table 1) are an alloy for the metal-ceramic technique (Qualiceram 3) and an alloy for the conventional technique (Qualigold 4).

The two alloys are characterized by very different electronic properties. The secondary soldering was done with a noble gold soldering alloy (Table 1).

Table 1: Composition % weight of the couples tested at corrosion

Type	Alloy	Au	Pt	Pd	Ag	Cu	Zn	In
Metal-ceramic alloy	Qualiceram 3	84,4	7,9	4,6	0	0,4	0	2,6
Conventional alloy	Qualigold 4	68,5	2,3	4,2	12,5	10,3	2,2	0
Soldering alloy	Qualisold S2	75	0	0,3	4,8	11,4	3	5,5

Five samples were prepared by soldering in the oven at 860°C. The sections then underwent different surface treatments (Table 2): no treatment (1), cleaning by a slight polishing with a polishing paste (2 and 3), chemical etching in a hot etching salt (4) and abrasion with ceramic abrasive disks followed by polishing and chemical etching (5).

Table 2: Defining the surface treatments after soldering, before the corrosion testing

Sample	Couple	Surface treatment after soldering
1	Qualiceram 3/Qualigold 4	No treatament
2	Qualiceram 3/Qualigold 4	Cleaning by brush and polishing paste
3	Qualiceram 3/Qualigold 4	Cleaning with rubber, then with polishing paste
4	Qualiceram 3/Qualigold 4	Chemical etching in a hot etching salt
5	Qualiceram 3/Qualigold 4	Abrasion with ceramic abrasive disks followed by polishing and chemical etching

Human artificial saliva may vary to a considerable degree and is dependent on the age and sex of the patient, the time of day, eating habits, medication and oral hygiene [5]. The corrosion test consisted in immersion of the samples in Fusayama's artificial saliva (detailed composition in Table 3) at 37°C for 30 days. We selected Fusayama's artificial saliva because it was shown to produce results that were consistent with the clinical experience of dental alloys. The pH of such solution is about 5.6 [6].

Table 3: Artificial saliva Fusayama type

NaCl	0,40 g/l
KCl	0,40 g/l
$CaCl_2 \cdot 2H_2O$	0,79 g/l
$NaH_2PO_4 \cdot H_2O$	0,69 g/l
Urea	1,00 g/l
$Na_2S \cdot 9\ H_2O$	0,005 g/l
NH_2CONH_2	1.00 g/l
distilled water	up to 1000 ml

RESULTS AND DISCUSSION

The test results are illustrated in Fig. 3.
Samples 1, 2 and 3. The samples subjected to only a slight polishing or no treatment have significant corrosion products deposit.
The blue stains show the formation of copper-based compounds, deriving from the alloys for the conventional technique.

Sample 4. The sample subjected to chemical etching reacted very little. It is visible only a slight gloss change.
Sample 5. The sample subjected to surface abrasion, then to a polishing followed by chemical etching showed no sign of corrosion or any other change.
We also observed that areas protected by a fusing agent during soldering were not corroded.

Fig. 3. Illustration of galvanic corrosion observed in the 5 samples (1-5).

The corrosion observed on the surface states artificially created shows that the passivity and non-passivity phenomena of the surfaces strongly influence the formation and functioning of a cell.

Soldering, which is linked to a thermic treatment, produces a more or less thick layer on the surface, layer consisting in various oxides. In case of alloys for the conventional technique, this layer is typically a few tenths of microns thick and

contains highly corrosive oxides in saliva (as copper oxide, zinc etc). Thus, the behavior of the samples 1, 2 and 3, conditioned by non-removal of the oxide layer is under "anodic" control and leads to a significant corrosion despite the nobility of the two alloys.

Sample 4, for which this layer has been practically eliminated, reacted very little. Sample 5, for which the layer was completely removed, did not react at all and did not show any effect of corrosion.

CONCLUSIONS

For the noble dental alloys combinations, a surface treatment that removes the oxide layers properly is essential to prevent the consequences, sometimes catastrophic, of the galvanic corrosion incidence [7].

REFERENCES

[1] L. Reclaru, R.E. Unger, C.J. Kirkpatrick, C. Susz, P.Y. Eschler, M. H. Zuercher, I. Antoniac, H. Luthy, Ni-Cr based dental alloys; Ni release, corrosion and biological evaluation, Mater Sci and Eng., 2012, 32, 6, 1452.

[2] R. Galo, R. C. Rodriguez, L. A. Rocha, M. G. C de Matos, Effects of chemical composition on the corrosion of dental alloys, Braz Dent J., 2012, 23, 2, 141.

[3] L. Ardelean, L. Reclaru, C. Susz, L. C. Rusu, Scanning electron microscopy and energy-dispersive x-ray spectroscopy in determining the metallic-shine-loss causes of a low gold content conventional alloy Rev Chim., 2012, 63, 2, 232.

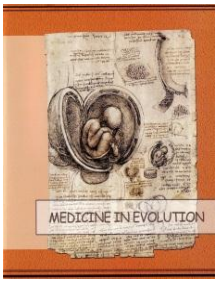
[4] C. Molina, L. Nogues, J. Martinez-Gomis, M. Peraire, J. Salrench, P. Sevilla et al, Dental casting alloys circuit during power toothbrushing with toothpastes of various abrasivities: Part II: corrosion and ion release, J Mater Sci Mater Med., 2008, 19, 3015.

[5] D. Mareci, G. Nemtoi, N. Aelenei, C. Bocanu, The electrochemical behaviour of various non-precious Ni and Co based alloys in artificial saliva, Eur Cell Mater., 2005, 10, 1.

[6] D. Mareci, R. Chelariu, S. Iacoban, C. Munteanu, G. Bolat, D. Sutiman,The estimation of localized corrosion behaviour of Ni-based dental alloys using electrochemical techniques, J Mater Eng Perform., 2012, 21, 7, 1431.

[7] L. Reclaru, H. Luthy, P. Y. Eschler, A. Blatter, C. Susz, Corrosion behaviour of various non-precious Ni and Co based alloys in artificial saliva, Biomaterials, 2005, 26, 4538.

A CRITICAL REVIEW UPON SOME PROPERTIES OF THE RESINS USED IN COMPLETE DENTURES TECHNOLOGY



OTILIA CORNELIA BOLOS[1], CRISTINA MARIA BORTUN[1]*, ANCA SILVIA VÂLCEANU[1]

[1] University of Medicine and Pharmacy "Victor Babes" , Faculty of Dentistry, Timisoara

ABSTRACT

The achieving of complete dentures implies different technologies and different dental polymers, like: heat-curing resins, self-curing resins, thermoplastic materials, light-curing resins and microwave curing materials.

Choosing the right material for achieving of complete dentures is very important, because it has direct effect on its quality and lifetime. Due to brittle fracture behavior, mobile prosthetic restorations made of resins have a limited lifespan in the mouth, the more so as, following laboratory technological steps may remain small defects (holes in the polymer structure). To this is added the stress exercised by the force of mastication and the oral environment.

The deterioration of complete dentures in oral environment can be induced not only by manufacturing technology, but also by defects in polymer´s structure, polymer´s distortion in hot and humid environment, material fatigue. Other factors like acids or alkalis (from food and drinks), alcohol, tobacco, thermal variations, and also the contact with water and salivary enzymes, fermented or not food residues, biological products excretion, oral swab system changes, contact with living tissues, bacteria, viruses should not be neglected.

Therefore, it is important to have knowledge about dental polymers´ physicochemical and mechanical properties, and also about their biocompatibility and biodegradation.

Key words: *complete dentures, dental polymers, mechanical properties, biodegradation*

Correspondence to

Prof. Dr. Bortun Cristina Maria,
"Victor Babes" University of Medicine and Pharmacy Timisoara,
Faculty of Dentistry, Department of Dental Technology,
Address: Blv: Revolutiei 1989, no.9,
e-mail: cristinabortun@yahoo.com

INTRODUCTION

In the early 21st century we can say that biomaterials are widespread and used not only in medicine but also in dentistry. With only 50 years ago but, biomaterials did not exist the way we perceive them today and academic courses about the biomaterials or biocompatibility didn't join the discussion.

The market introduction of the resin based dental materials has revolutionized the dentistry at 20 mid-century [1]. These resins are polymeric biomaterials, widely used in dental prosthetics (for complete or partial acrylic dentures, temporary single crowns or temporary fixed dentures). The most common polymeric materials for denture bases are bicomponent, obtained by mixing the powder polymer (polymethylmethacrylate-PMMA or polietilmethacrilat-PEMA) and liquid monomer (methyl methacrylate-MMA). Activation of polymerization, thermal or chemical, initiates formation of free radicals from benzoyl peroxide (BPO), thus taking place an exothermic reaction with addition of free radicals. However, polymerization shrinkage is the greatest disadvantage of this materials. Dimensional alteration is a critical factor for the retention and stability of complete dentures, although some factors may compensate this effect, including water absorption by the acrylic resin, resilience of the gingival mucosa and the action of saliva [2,3].

Polymer materials for denture base, with thermal or light polymerization are relatively fragile. Choosing the right material for obtaining of complete dentures is very important because it has direct effect on its quality and lifetime [4,5]. Due to brittle fracture behavior, mobile prosthetic restorations made of resins have a limited lifespan in the mouth, the more so as, following laboratory technological steps may remain small defects (holes in the polymer structure). To this is added the stress exercised by the force of mastication (continuous repeated movement of low amplitude) and the oral environment [6].

MATERIALS AND METHODS

Among the technologies used for achieving complete dentures, we distinguish: heat-curing, self-curing, injection, light-curing, casting and microwave-curing [7,8]. Therefore, the resins are classified in **5 types** (DIN EN ISO – 1567), after the factor that initiates the polymerization reaction:

Type 1 include the **heat-curing resins** (require a temperature higher than 65°C for polymerization), which can be subdivided in: bicomponent (powder and liquid) and monocomponent. Examples of bicomponent heat-curing resins are: Meliodent (Heraeus Kulzer, Senden, Germany), Royaldent Plus (Royaldent, Palatinál Foggyártó KFT, Gyöngyös Batthyány, Ungaria), Superacryl (SpofaDental, Markova, Czech Republic), Triplex (Ivoclar Vivadent) and so on. The monocomponent heat-curing resins use pressing as technology for obtaining the dentures bases, plasticized acrylic resin being injected under pressure (S. R. Ivocap–Ivoclar system): Luxene (Astron Dental Corporation)-copolymer of vinyl chloride and vinyl acetate, containing traces of methyl methacrylate; Sinomer (Alldent) doesn't contain PMMA.

The conventional heat-curing technology includes investment of the future denture wax-pattern, which is further embedded in a compliance. Following wax plastification and removal, a pattern is obtained. In this pattern the acrylic resin is inserted (manually or by injection), then is pressed manually and follows a well established thermal cycle. This technology is cumbersome, lengthy and with loss of materials along the intermediate steps, that do not appear in the finished denture. Classical technology hasn't undergone major changes, but what has changed over time was the quality of heat-curing polymers.

The manually insertion of the acrylic resin has many disadvantages: possibility of wrong dosage, including of impurities by manual insertion, polymerization is sometimes incomplete, with a large amount of residual monomers, high polymerization shrinkage, need for laborious processing. By contrast, injection systems offer a number of advantages, such as: optimal marginal sealing,

minimal polymerization shrinkage, minimum content of residual monomers (in case of the heat-curing acrylics), higher wear resistance, compact structure without porosity, minimal processing after deflasking, they eliminate occlusal reports distortions [7,8].

Type 2 include **self-curing resins/** resins with chemical polymerization (require a temperature lower than 65°C for polymerization). The degree of polymerization is lower than that achieved in heat-curing resins. These resins have a greater irritant effect than the heat-curing one, due to higher amount of residual monomer and its toxic effect. This resins type has also 2 groups. Group 1 comprises bicomponent systems (powder and liquid): Paladur (Heraeus Kulzer), Selectaplus (Dentsply DeTrey), PalaXpress (Heraeus Kulzer), ProBase cold (Ivoclar), Duracryl (Spofa). Group 2 includes bicomponent systems (powder and liquid) for casting: Perform Inkovac (Hedent), Castapress (Vertex), Dreve (Dentamid GmbH), Opti-Cast (Bredent). The casting systems offer following advantages: low polymerization time, wide color range, minimum adjustments. Their disadvantages would be expensive technology (requires purchase of thet system), and the fact that require a high enough skill [8,9].

Type 3 include **thermoplastic materials**, such as polyamide (nylon), acetal resins, epoxy resins, polystyrene, polycarbonate resins, etc. They are presented as granulated monocomponent cartridges of different sizes; they plaster under thermal action and inject into patterns using special equipment. - R-3C injector of IND company (Budapest, Hungary). This class of materials include BioDentaplast (Acetal resin based on Polyoxymethylenes), Flexiplast (polyamide resin), Flexite Plus (polyamide resin). Some important features are: do not contain monomer, and are therefore non-toxic, non-allergenic, are biocompatible, have high aesthetic and chemical resistance. Among the disadvantages are: they cannot be polished very well, required injection systems, have poor adaptation / produce lesion, in time plaque accumulation and pigmenting [8].

Type 4 include **light-curing materials.** Light-curing technology has emerged around the 70s. The modern technology of light-curing the dentures bases resort to a quick realization of prosthetic bases from aliphatic urethanedimetacrilates - urethane oligomers and acrylic copolymers, a submicron silica anorganic filler, a photopolymerization initiation system and additives, eliminating intermediate stages of work as investment and classical heat-curing. Eclipse Resin System (Dentsply International Inc. – DeguDent GmbH, Hanau, Germany) contains 3 types of polymers Base plate, Set Up and Contour Resin, from which only the first two are in contact with the oral tissues. (Set Up- is used only for assembling the artificial teeth). The system includes also the light-curing device Eclipse Processing Unit II. Although the time required to obtain a prosthesis base is about 30 minutes, the big disadvantage is that the UDMA resins denture have low durability up to 5 years [5]. The major advantage of these resins is the elimination of the intermediate phases of work, time and material consuming.

Type 5 include **the microwave curing materials –** at dry heat. Microbase (Dentsply DeTrey) is a monocomponent system, pasty, delivered in special cartridges. The main component is a diurethanedimetacrilate in combination with trace elements, inorganic fillers, organic fiber reinforcement, initiators, and pigments. Acron MC (GC) is a bicomponent system [8]. Such materials have a number of advantages, such as rapid polymerization (several minutes), complete and consistent, which ensures superior physical properties and excellent dimensional stability. But technology is quite expensive, as it requires acquisition of the system.

DISCUSSION

Fairly high rate of failure in terms of long term sustainability of complete dentures in the oral cavity caused a series of studies on biomechanical behavior of resins. But before the evaluation of the polymers' biomechanical behaviour, it is very important to know their properties.

-Water sorption

Water absorption of a material refers both to water adsorbed on its surface and the water absorbed during its preparation and use. Polymers absorb water in wet environment [4,10]. The water molecules can penetrate into the spaces between the polymer chains and push them farther apart. Consequently the secondary chemical bonding forces (van der

Waals forces) between the polymer chains decline and results in weight and volume increase to cause an expansion. The greater absorption of water by the material, the greater will be the associated dimensional change. With time water molecules can act as plasticizers, altering the mechanical properties of the polymer [11].

As water molecules penetrate, the un-reacted monomer molecules and other small constituents get out until equilibrium is reached and the polymer is weight relatively constant. Volume of water absorbed by the polymer depends on its structure, content in various polar and hydrophilic groups, temperature, concentration of additives but not least the presence of voids within the matrix [10]. The cross-linking agents reduce water absorption of self-curing acrylic resins. Regarding polymers for prosthetic bases, water uptake varies over time and water saturation is usually achieved after 2-3 months, depending on the size and size [10].

-Electrical and thermal conductivity of polymeric materials is reduced.

-Mechanical strength

Mechanical strength of polymeric materials is quite modest. The values are higher for heat-curing resins than for self-curing ones, because of the polymerization quality [12]. Mechanical strength can be improved by adding glass fibers, metal plates and following proportion powder/liquid and polymerization protocol [13]. Mechanical strength decreases with time, because of the material aging [14].

Bortun et al. [4] studied the mechanical properties of several types of resins and reached the following conclusions: elasticity modulus and tensile strength of the resins vary by application to which they are subjected (tensile or bending). They also showed that saliva plays an important role in dentures biodegradation, that there are differences between the mechanical properties of resins in wet / dry and also between different types of resins. Thus, mechanical strength values are lower in wet environment, their decline being evident in light-curing resins compared to the heat-curing. In terms of elasticity, heat-curing resins have a lower modulus compared with UDMA resins, its decrease in wet environment being more pronounced for the first category.

-Fracture toughness

The fracture toughness of a material reflects its resistance to fracture and is the energy required for a crack to propagate through a material to its complete fracture. The fracture toughness of polymers depends on the type of polymer and the reinforcement materials. An increase in fracture toughness can be achieved by adding reinforcement fibres to a polymer to prevent or slow down the crack growth or by adding rubber-like substances [12,15].

-Linear coefficient of thermal expansion

Intraoral temperature changes may be induced by routine eating and drinking. Thermal fluctuations encountered *in vivo* can induce surface stresses due to the high thermal gradients near the surface [16]. Variation of the coefficient of thermal expansion between different materials is important because a mismatch can lead to tension, stress and adverse effects. By adding fibers to a polymer, the linear coefficient of thermal expansion decreases.

Foods and drinks can also affect dental materials by the direct effect of their additives, like ethanol, and their capacity of changing the intraoral pH values.

-Fatigue- Fracture Mechanics

Fatigue is material's weakening caused by repeated loading at a stress below the tensile strength. Evaluation of fatigue behavior of polymers can be made at different types of loads, and is difficult and time consuming. According to ASTM E647 standard [17], the fracture fatigue phenomenon is analyzed on samples type CT– „compact tension". Cernescu *et al* [18] have made fatigue tests on various types of resins using a servo-hydraulic testing machines for variable amplitude cyclic loading. Among the findings of this study are: that crack propagation or stopping depends on the material, existing defects and fatigue of the tested object; the fracture length plays an important role in crack growth.

-Hardness

Acrylic resin hardness is much lower than that of dentin and thus do not suffer comparison with the enamel. The conventional resins based on polymethylmethacrylate without flexible agents in its composition such as plasticizers have higher values of microhardness. UV and temperature are factors that increase the microhardness values [19].

-Compressive strength of these materials is good. **Abrasion resistance** is very low and is a major disadvantage of these resins.

DENTAL POLYMERS BIOCOMPATIBILITY

Biocompatibility can be defined as the acceptance (or rejection) of artificial material by the surrounding tissues and by the body as a whole. Biological and toxicological aspects of dental materials are important in relation to their clinical usage. The biocompatibility of a dental resin is determined by several factors. In this determination, one cannot consider only the cytotoxic effect of the amount and type of individually compounds that are eluted from the set material, but also the complex interaction with the medium.

According to Bettencourt [6], biodegradation of a biomaterial can occur either by alteration of biosafety-release of material components with adverse toxic effects or by alteration of biofunctionality.

Biodegradation is considered the degradation due to biological environment and should be tested, to predict the changes on the physical and mechanical properties of the materials as well as the biologic implications due to release of compounds from the polymer matrix. The clinical success of dental resins depends not only on the physical and chemical properties of the materials but also on their biological safety.

Polymer degradation is often an undesired secondary reaction that appears in chemical transformations, processing or use of polymers. Polymer degradation may arise under the influence of chemical agents (water, acids, alcohol, O2, etc.) or under the influence of physical agents (heat, light, radiation, mechanical) [14]. Polymer degradation does not occur as a result of isolated processes, multiple factors as saliva, chewing, thermal and chemical dietary changes may be responsible for the biodegradation processes. All these reactions cause the **aging process** (changing of physical-chemical and physical-mechanical properties of the polymer during operation).

Both conventional and flexible resins suffer color alteration following aging due to intrinsic and extrinsic factors [20]. The intrinsic factors include discoloration of the material, with alteration of the matrix. In general, this intrinsic discoloration occurs with aging as a result of physical-chemical conditions such as thermal and humidity changes. Extrinsic factors such as absorption and adsorption of substances in conventional resins may also lead to discoloration. Absorption and adsorption may lead to staining of the resins by pigments in the oral environment, and are more responsible for chromatic alterations than inherent color instability of the material.

Some studies that compared the chromatic alterations of autopolymerizing and heat-polymerized acrylic resins observed greater chromatic instability for the autopolymerizing resins since these present a great amount of additional reagents such as benzoyl peroxide [19]. The anti-organic, anti-fungal and antioxidant substances are considered color stabilizers.

THE RESIDUAL MONOMER

Biological characteristics and mechanical properties of polymeric materials are strongly influenced by monomer-polymer conversion (only in case of self-curing and heat-curing resins). The conversion monomer-polymer is never complete. Auto-polymerized materials are known for their lower degree of conversion and consequently higher residual monomer content (3 to 5%), compared to heat-activated resins (less than 1%). In case of last mentioned, MMA residual monomer content can be reduced by increasing the polymerization temperature and time.

The residual monomers stay trapped in the polymer net, affecting the mechanical properties of the materials, or can diffuse to the surrounding medium, causing biological responses and compromise the biocompatibility of the denture resins, since these compounds have been pointed out as cause of local chemical irritation, hypersensibility, signs of mucosal inflammation, vesiculation and ulceration, burning mouth sensation and systemic allergic reactions. The percentage of monomer release is dependent not only on the monomer chemistry or amount in the resin but also on the medium composition [11].

CONCLUSION

Long term deterioration of the polymeric complete dentures in oral environment is still an unsolved problem. It can be induced by the manufacturing technology, polymers' defects and distortions in hot and humid environment, material fatigue. Various aggression of external or internal environment, such as acids, alkalis, alcohol, tobacco, thermal variations and so on, but also the contact with water and salivary enzymes, fermented or not food residues, biological products excretion, oral swab system changes, contact with living tissues, bacteria, viruses and yeast should also be taken into account. An important role seems to have human saliva enzymes, namely hydrolases which are capable of causing a softening of the polymer surface [6].

Physicochemical and mechanical properties of the polymers can be affected by water absorption [11]. This can cause decrease of their mechanical resistance [11]. If there are areas where the fibers are not fully incorporated into the polymer matrix or pores formed during manufacture or polymerization technology, there will be goals that increase water absorption. Water immersion produces a plasticizing effect on resins through the process of water sorption and replacement of leached residual monomer with water molecules [10]. On the other hand, temperature compensates this plasticizing effect by increasing the rigidity of the material.

Ferracane [10] reveals that, fillers in a polymer network can affect properties such as solubility and hygroscopic effects. Fillers can generate particles or ions that can be released, in addition to free radicals resulting from the reaction of polymerization. These components are able to be dissolved from the polymer network, aspect that might be biologically alarming.

Evaluation of biodegradation aspects of acrylic based resins should be widened and considered not only as negative aspects regarding loss of mechanical properties and adverse toxic effects but can also be explored towards a positive interaction with the oral environment. The incorporation of products like antioxidant molecules intending to enhance the biocompatibility of the materials can be explored. The use of acrylic based resins as drug delivery polymer systems could be an innovative new strategy for extending the use of these materials in the clinical dental practice.

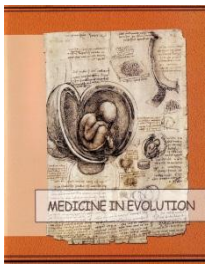
Some practical conclusions that can be drawn regard the importance of following exactly the polymerization protocol indicated by the manufacturer, the powder-liquid correct dosage in order to avoid changes in the polymers properties, the attention to be given to deflasking (to avoid possible cracks), and processing and polishing (avoiding overheating, which could also affect the mechanical properties). Important for the dentist and the patient is keeping of dentures' in distilled water - for 24 hours after completion - for volume stabilization after water absorption.

REFERENCES

1. Klaus D. Jandta, Bernd W. Sigusch, Future perspectives of resin-based dental materials; Dental Materials 25 (2 0 0 9) 1001–1006.
2. Smith LT, Powers JM. Relative fit of new denture resins polymerized by heat, light and microwave energy. Am J Dent. 1992 Jun;5(3):140-2.
3. Turk MD, Lang BR, Wilcox DE, Meiers JC. Direct measurement of dimensional accuracy with three denture-processing techniques. Int J Prosthodont. 1992 Jul-Aug;5(4):367-72
4. CM Bortun, A Cernescu, L Ardelean. Mechanical Properties of Some Dental Resins in Wet and Dry Conditions, Materiale Plastice 2012, 49 (1): 5-8
5. C Bortun, A Cernescu, N Ghiban, N Faur, B Ghiban, O Gombos, AC Podariu. Durability Evaluation of Complete Dentures Realized with "Eclipse Prosthetic Resin System", Materiale Plastice 2010, 47(4): 457-60
6. A.F. Bettencourt, C.B. Neves, M.S. de Almeida et all - ,,Biodegradation of acrylic based resins: A review'', Dental Materials, vol. 26, e171-e180, 2010;
7. Ardelean, L., Materiale în laboratorul de tehnicã dentarã, ed.Victor Babes, Timisoara, 2009

8. C Bortun, L Sandu, S Porojan. Tehnologia protezelor totale- Îndreptar de lucrări practice pentru tehnicienii dentari, Lito UMF Victor Babes Timisoara 2006.
9. L Ardelean, C Bortun, M Motoc, L Rusu. Alternative Technologies for Dentures Manufacturing using Different Types of Resins, Materiale Plastice 2010, 47(4):433-35
10. Ferracane J., L.: Hygroscopic and hydrolytic effects in dental polymer networks, Dental Materials 2006; 22:211–222
11. Ferracane Jl, Berge Hx, Condon Jr. In vitro aging of dental composites in water–effect of degree of conversion, filler volume, and filler/matrix coupling. Journal of Biomedical Materials Research 1998; 42:465–72.
12. Zappini G, Kammann A, Wachter W. Comparison of fracture tests of denture base materials, J Prosthet Dent 2003, 90:570-85
13. Niikura, K., Structural Deformation and Fracture Analyses of Complete Dentures: Part 2. Stress/Strain Parameters in a Complete Upper Denture, The journal of the Japan Prosthodontic Society 2001, **27**(1): 114
14. J.L. Drummond - ,,Degradation, fatigue and failure of resin dental composite materials'',J. Dent. Res., 2008;87:710-9;
15. MS Memon, N Yunus, AAA Razak. Some Mechanical Properties of a Highly Cross-Linked, Microwave-Polymerized, Injection-Molded Denture Base Polymer, The International Journal of Prosthodontics 2001, 14(3): 214-218.
16. Sideridou I, Tserki V, Papanastasiou G. Study of water sorption, solubility and modulus of elasticity of light-cured dimethacrylatebased dental resins. Biomaterials 2003;24: 655–65.
17. ASTM E647 (*Standard Test Method for Measurement of Fatigue Crack Growth Rates*.ASTM International. 2000).
18. A. Cernescu, N. Faur, C. Bortun, C. Nes, Fatigue crack growth rate in acrylic resins under variable amplitude loading, Theoretical and Applied Fracture Mechanics, 2011, 56(1): 58-61
19. MC Goiato, DM dos Santos, MF Haddad, AA Pesqueira. Effect of accelerated aging on the microhardness and color stability of flexible resins for dentures, Braz. oral res. vol.24 no.1 São Paulo Jan./Mar. 2010, nhttp://dx.doi.org/10.1590/S1806-83242010000100019
20. Villalta P, Lu H, Okte Z, Garcia-Godoy F, Powers JM. Effects of staining and bleaching on color change of dental composite resins. J Prosthet Dent. 2006 Feb;95(2):137-42.

THERAPEUTIC OPTIONS FOR DENTAL-MAXILLARY ABNORMALITIES IN PATIENTS WITH ORAL BREATHING



DANIELA JUMANCA[1], ATENA GALUSCAN[1], ANGELA PODARIU[1], ROXANA OANCEA[1], RAMONA POPOVICI[1], RUXANDRA SAVA-ROSIANU[1]

[1] University Of Medicine And Pharmacy "Victor Babes" , Department of Prevention, Community Dentistry and Oral Health, Faculty of Dentistry, Timisoara

ABSTRACT

Introduction: *The most frequent causes for the oral breathing syndrome are impermeability of the nasal cavity, adenoid vegetations, nasal septum deviation, tonsillar hypertrophy, bronchial asthma, allergies. Oral breathing syndrome is mainly characterized by the atrophy of the upper maxillary. Other characteristic signs include: atonic and short upper lip, vestibularized upper frontal teeth due to narrow maxillary and atonic upper lip, distalized mandible, sagital inocclusion and dental caries on the upper incisors.*

Material and method: *A total of 1071 patients - children aged between 6 and 12 years - were examined. Of these, 557 (52%) had dental-maxillary abnormalities (all types and various degrees) and only 45 were oral breathers (4.2%). The treatment applied in these patients aimed to decongest the nasal airways in order to achieve a normal physiological breathing and to correct the symptoms which characterize the oral breathing syndrome. They were devided in 3 groups and the following variants were chosen: group 1 – mobile orthodontic appliances, group 2 –disjunctor appliances and group 3 – myofunctional appliances.*

Results: *During the treatment period (between 1 year 7 months and 3 years 8 months), the gingival inflammation index decreased from 2.5 to 1.3 at the end of the treatment. Of the 3 selected orthodontic treatment options, the most effective results were obtained with disjunctors. On the oposite was the Herbst device.*

Conclusion: *Oral breathing influences the severity of microbial gingivitis and increases bacterial plaque deposits on all teeth but especially on the upper frontal group. Both the bacterial plaque index and the gingival inflammation index decrease with the elimination of oral breathing. Of the treatment options, the most effective proved to be the expansion screw disjunctor, the disjunction being followed by the correct alignment of teeth with the help of brackets.*

Key words: *oral breathing, maxillary compression, upper maxillary atrophy*

Correspondence to

Dr. Atena Galuscan, Department of Preventive, Community Dentistry and Oral Health, Faculty of Dentistry, University Of Medicine And Pharmacy "Victor Babes" Timisoara, Spl. Tudor Vladimirescu nr. 14A.
Tel.: 0256-204950,
e-mail: proiectetm@yahoo.com

INTRODUCTION

Inhaled air usually enters the nostrils. In case of sustained physical effort when the oxygen requirements are increased, breathing may be supplemented by oral inhaling. In such cases, oral breathing is physiological. When occuring outside these situations, oral breathing is considered to be pathological. The most frequent causes for the oral breathing syndrome are [1]: impermeability of the nasal cavity, adenoid vegetations, nasal septum deviation, tonsillar hypertrophy, bronchial asthma, allergies.

The pathological oral breathing may be intermitent or permanent (in severe cases).[2] The upper airways have been found to be extremely important for the occurence of oral breathing. Nevertheless, in many cases of oral breathing the otorhinolaryngeal (ORL) examination does not detect rhino-pharyngeal obstacles. Depending on the permeability of the upper airways there are two types of oral breathing: with and without rhino-pharyngeal obstacles, i.e. without an evident anatomic determinant.

This habit may occur after long lasting rhinitis, as anamnestic detection may not always be possible. Oral breathing as a harmful habit may persist even after permeabilization of the upper airways by ORL surgery. The return to nasal breathing requires functional reeducation. Oral breathing has extremely harmful effects upon the organism as a whole as well as on the development of the dental-maxillary apparatus. [3]

This oral breathing syndrome is mainly characterized by the atrophy of the upper maxillary.[4] The lack of the physiological stimulation represented by the airflow passing through the nostrils and by the permanent aeration of the maxillary sinuses will cause the atrophy of the upper maxillary. Following this atrophy, the midface appears retracted and the malar prominence is flattened. Also, maxillary compression occurs; due to the constantly open mouth, the tongue does not maintain contact with the palate, and the cheek muscles are in tension leading to a veritable maxillary compression. Other characteristic signs include: atonic and short upper lip, vestibularized upper frontal teeth due to narrow maxillary and atonic upper lip. The mandible is distalized to allow air to enter the oropharynx via the oral cavity; the lower frontal teeth are extruded because they do not find an antagonism with the upper vestibularized frontal teeth. [5]. Occlusion is distalized with a frontal sagital inocclusion. The extrusion of the lower frontal teeth causes the denivelation of the sagittal curve of Spee; the lower lip protrudes in the inocclusion space, aggravating the clinical picture of prognatism. Last but not least, oral breathers often present a high number of dental caries on the upper incisors which, being dry, are being deprived of the anticarious effect of saliva. [6].

MATERIAL AND METHOD

In this study we included for treatment 45 patients with oral breathing who were monitored by our dental practices. A total of 1071 patients - children aged between 6 and 12 years - were examined. Of these, 557 (52%) had dental-maxillary abnormalities (all types and various degrees) and only 45 were oral breathers (4.2%). The treatment applied in these patients aimed to decongest the nasal airways in order to achieve a normal physiological breathing and to correct the symptoms which characterize the oral breathing syndrome. The proportion between these cathegories is given in Fig. No. 1.

In certain situations surgical treatment was needed, and this was performed in collaboration with otorhinolaryngology surgeons. In most cases, the nonsurgical i.e. orthodontic treatment was sufficient.

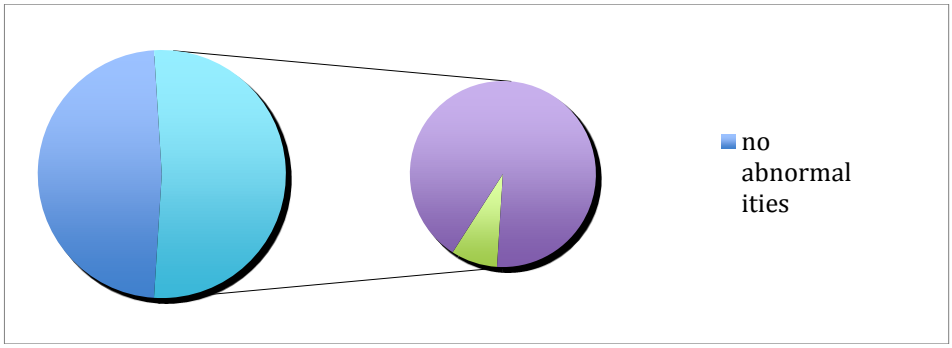


Fig. No. 1. Proportion of children with dental-maxillary abnormalities (DMA) and the report between oral and non-oral breathers

We monitored the evolution of the Quigley & Hein bacterial plaque index (revealing substances are used) and of the Silness and Loe gingival inflammation index (GI) from the beginning of treatment until correction of oral breathing. Concomitantly, we performed a comparative study on several orthodontic treatment options in order to conclude on the most effective one. The 45 patients were divided into 3 groups. They were all informed on possible treatment options and after consulting with family members, one of the folloowing variants were chosen: group 1 – mobile orthodontic appliances, group 2 –disjunctor appliances and group 3 – myofunctional appliances.

Group 1: Mobile appliances: 10 patients of whom 2 chose the Herbst and 8 the Positioner appliances, respectively. At present, of the available functional appliances, the Herbst appliances is considered an effective device to correct class II malocclusion. It is an incremental articular appliance based upon a bilateral telescopic mechanism which forces the mandible to adopt a protruded position. The appliance is worn 24/7 and the effects are achieved in around 6-12 months. The Herbst appliance allows the restoration of interarch relations, favouring an optimal occlusal adjusment. The tongue is directed frontally, the pharyngo-laryngeal airway is reopen providing a good nasal breathing. Positioner treatment is performed in stages, each stage requiring a specific type of positioner. The positioner is an elastomeric mouthguard. It is manufactured after a template constructed on a semiadaptable articulator which must be concordant to dental alignment cephalometric data and mandible cinematics. The appliance's indications are: interceptive therapy, actual orthodontic treatment, contention following orthodontic treatment, the same appliance being simultaneously usable for orthopedic, orthodontic and functional purposes.

Group 2: Disjunctors: 27 patients of whom 23 with expansion screw disjunctor and 4 with Quad-helix expander. Intermaxillary disjunction offers the possibility to achieve considerable widening of the upper arch, palate, nostrils and even of the face over a short period of time. By hemimaxillary displacement a similar change in the position of muscular insertions is achieved. It is characterized by opening the medio-palatine suture and distancing the two hemimaxillaries with the consecutive transversal increase of the upper maxillary. Due to its multiple indications, most patients chose this type of treatment. The major indication is represented by the severe narrowing of the upper arch with deep and narrow palate in subjects in whom the lower arch is normally developed or was previously developed by other means. Other indications are: oral or mixed breathing, with no otorhinolaryngeal (ORL) obstacles; retrognatisms and retroalveolism with or without oral breathing; class III abnormalities, improving the disfunction by correct tongue repositioning. Throughout this treatment we monitored 3 stages: opening

sutures, contention and consecutive orthodontic treatments.
Quad-helix is an orthodontic appliance for the upper dental arch which is cemented in the oral cavity. It is attached to the molars by two orthodontic braces and has four loops which act for widening the dental arch. The action mechanism consists of slightly opening the midpalatal suture. The active stage of the treatment lasts around 30 days. During this period, up to 2 adjustments will be performed depending on the aimed degree of expansion and the contention period is of 6 weeks. Activation of the posterior loops will lead to a transversal, predominantly anterior enlargement. If activation involves the anterior loops, the enlargement of the transversal perimeter will occur posteriorly. It is used in cases of upper maxillary retrognatism, upper maxillary compression and in correcting breathing, deglutition, as well as finger suckling induced disfunctions.
Group 3 – Myofunctional appliances – 8 patients. Myofunctional appliances are represented by the Myobrace Trainers devices. The trainer aims to stop the incorrect posture of the mouth and to induce deglutition. The tip of the tongue is trained to its correct upward position, on the palate. Deglutition may only be achieved with the tongue in the correct position due to the tongue tags of the trainer. The correct tongue position on the maxillary forces teeth into the right form on the arch. In the case the trainer is used, there is no compression on the temporo-mandibular joint. The activity of the lips is low and breathing occurs via the nostrils.
The types of treatment according to the chosen device are shown in Fig. No. 2.

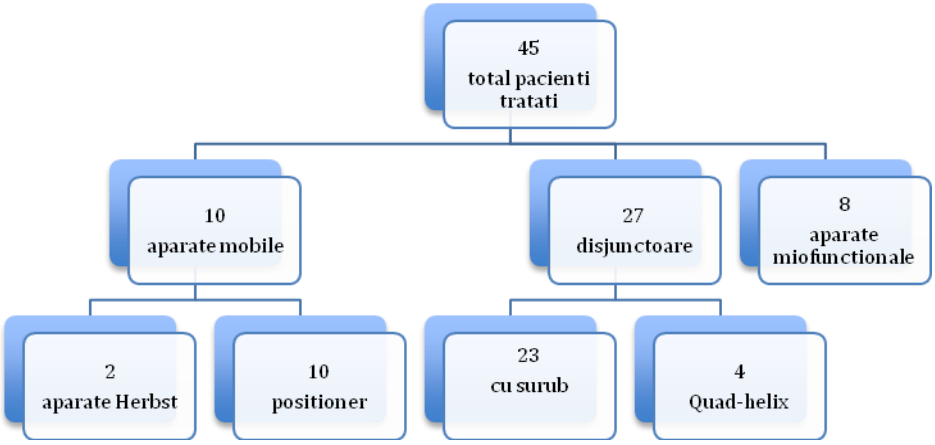


Fig. No. 2. Types of treatment.

RESULTS

The duration of the actual orthodontic treatment was between 1 year 7 months and 3 years 8 months. During the treatment, both the gingival inflammation index and the bacterial plaque index decreased both due to elimination of the oral breathing habit and to the oral-dental health education received throughout the entire treatment period. Even though orthodontic treatment involves the creation of new retention areas around the brackets, loops, etc. by education and patient motivation, oral hygiene improved in all these patients. The average bacterial plaque index calculated using the Miraton solution decreased from 3.7 in the beginning of the treatment to 3.1 at 6 months and to 1.9 at the end of the treatment. Also, the gingival inflammation index decreased from 2.5 to 1.3 at the end of the treatment.
Of the 3 selected orthodontic treatment options, the most effective results were

obtained with disjunctors. These appliances being cemented in the oral cavity acted constantly and optimal results were achieved if recommendations regarding the frequency of activations were adhered to. The oposite is true for the Herbst device. Patients complained on the discomfort and low tolerability. Due to these reasons, the duration of orthodontic treatment was considerably extended. Satisfactory results were also obtained with myofunctional devices. Still, in this case the results largely depended on patient's compliance. Through perseverence and by periodic assessments, all types of treatment led to satisfactory results.

CONCLUSION

By an accurate clinical examination and a thorough anamnesis, by a correct approach for each case and designing an appropriate treatment plan, by multidisciplinary collaboration (in cases also requiring ORL or oral surgery interventions) any oral breathing case with dental-maxillary abnormalities can be successfully solved.

After finalizing the treatment, the characteristic oral breathing facial aspect is much improved, the specific signs being visibly diminished.

Oral breathing influences the severity of microbial gingivitis and increases bacterial plaque deposits on all teeth but especially on the upper frontal group. Both the bacterial plaque index and the gingival inflammation index decrease with the elimination of oral breathing.

Of the treatment options, the most effective proved to be the expansion screw disjunctor, the disjunction being followed by the correct alignment of teeth with the help of brackets.

Oral breathing is a disfunction leading to facial alteration (the oral breather's face), various diseases affecting the already impaired and defective respiratory cycle, fonation changes, occurence and persistence of infantile deglutition; its treatment consists of surgical and orthodontioc correction or non-surgical correction of otorhinolaryngeal obstacles and of the causal abnormalities.

REFERENCES

[1]. Merck Manual Patients & Caregivers. Mouth and Dental Disorders. Symptoms of Oral and Dental Disorders. http://www.merkmanuals.com/home/mouth_and_dental_disorders.html

[2]. Wolfgang Schmidt-Nowara, Alan Lowe, Laurel Wiegand, Rosalind Cartwright, Francisco Perez-Guerra and Stuart Menn. Oral Appliances for the Treatment of Snoring and Obstructive Sleep Apnea: A Review. An American Sleep Disorders Association Review.

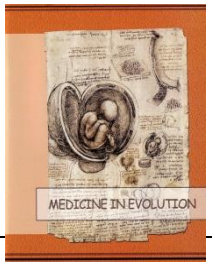
[3]. John Flutter BDS (London) Dental Surgeon. Brisbane Queensland.The negative effect of mouth breathing on the body and development of the child

[4]. Jefferson Y. Mouth breathing: adverse effects on facial growth, health, academics, and behavior. Gen Dent. 2010 Jan-Feb;58(1):18-25; quiz 26-7, 79-80.

[5]. A.C. Guyton, MD, The Textbook of Medical Physiology. How to Stop Mouth Breathing (Treatment).

[6]. Laurence J. Walsh. Dry Mouth: A Clinical Problem For Children And Young Adults. www.moderndentistry.com/sept_oct2007/walsh.pdf

SCHOOL TEACHERS' ABILITIES IN THE DETECTION OF DENTAL CARIES -A PILOT STUDY



ROXANA OANCEA[1], ANGELA CODRUȚA PODARIU[1], RAMONA AMINA POPOVICI[1], RUXANDRA SAVA-ROȘIANU[1], JUMANCA DANIELA[1], MELINDA ONEȚ[1]

[1] University Of Medicine And Pharmacy "Victor Babes", Department of Prevention, Community Dentistry and Oral Health, Faculty of Dentistry, Timisoara
[2] Faculty of Dentistry, West University "Vasile Goldiş", Arad

ABSTRACT

The aim *of this study was to analyze the ability of school teachers to identify dental caries among school children using minimal resources.*

Material and method

In 2011, 220 students aged between 6-14 years were examined by 9 teachers from 3 schools situated in underprivileged villages in Timis county and a dentist, after obtaining the informed consent of the parents. Each teacher examined his/her own class students in a single session. The teachers didn't undergo any training or calibration. They were instructed to indicate caries, regardless of the extent of the lesion and darkness of the teeth. The early stages of disease (white spot – according to WHO criteria) were not included because of the difficulty in detecting them. The results of the visual examination performed by the dentist served as a benchmark for comparing the findings of teachers. The visual examination procedure was made under natural light, with the observer facing the student, using standard examination equipment. Kappa (k) statistics were estimated to asses agreement between observers.

Results

The findings suggest satisfactory agreement with the dentist, with kappa values of 0.74 for teachers. The absence of cavities was easily detected (specificity = 97.8%). More caution is required in positive results indicated by teachers because they were not always confirmed subsequently (sensitivity 73.1%).

Conclusion

The results indicate that it is possible to collaborate with teachers in collecting data regarding dental caries in order to asses dental status within a community with little or no access to dental care.

Key words*: schoolteachers, dental caries, visual examination, children*

Correspondence to

Roxana Oancea.
Address: Splaiul T. Vladimirescu nr.14/A
Tel: 0256/ 204950,
E-mail: roancea@umft.ro

INTRODUCTION

There is no doubt that schools are ideal settings to educate children about the prevention of common oral diseases. Schools, with their special characters amongst other behaviour-affecting institutes, provide a big opportunity for promoting schoolchildren's health. School environment, curriculum, and extracurricular activity could all be utilized for promoting student's oral health and general health as well. They are also a suitable platform for organizing preventive program services that can be made available to all children, including those who, for a variety of reasons, might not be receiving professional care. The school years are a time where many elements of attitude, behaviour and life skills are still forming. School teachers, with their educational experience and contact with students, can actively contribute to student's health promotion, provided that they receive enough training and support to do so. Knowledge of oral diseases and more importantly about the fact that most of these diseases are preventable to a large extent is a major vehicle for improving the oral health of the children. School teachers have traditionally been considered as potentially important primary agents of socialization, with a capability of influencing the future, knowledge, attitude and behavior of school children.

Nowadays Romania still faces many challenges in addressing oral health-care needs.

In most countries, the targeted groups selected as oral health programme beneficiaries are children and adolescents on the assumption that early dental disease prevention and treatment can improve dental health in the future. At schools, such actions like health promotion, prevention and early detection of health related problems should be prioritized. This is the rationale for outreach programmes in health education and promotion, fluoride application and other initiatives.

In response to the World Health Organization (WHO), school teachers have been utilized as health-education agents for school children in many countries, where they serve as alternative personnel in primary health-care approach to fight preventable diseases.[1] School-based dental education is internationally recognized, and might play a role in increasing the knowledge of oral health and disease among school teachers.[2-10] Daily contact of schoolteachers with children provides teachers the opportunity to know them, to understand their needs and eventually enabling the observation of certain changes from normality before a specialist can detect the problem.

Since 1995 when a study was undertaken to describe the oral health behavior of schoolchildren in the first grade in order to assess the level of oral health knowledge and attitudes among the mothers, and to describe oral knowledge and attitudes to prevention among the schoolteachers in Romania, only dentists and trained personnel have conducted such studies and alternative of other professionals have been unexplored. That study pointed out that schoolteachers knew about the poor dental conditions in children and wanted to become involved in oral health education.[2]

The idea of involving teachers in evaluating the need for caries treatment became an important issue especially where no dental professional assistance is available and in order to implement a preventive programme the need to collect reliable data is very important.

The main purpose of this pilot study is to analyze the performance of public school teachers in identifying changes related to dental caries among school children.

MATERIALS AND METHODS

The study was performed in 2011 in 3 schools located in 3 underprivileged villages from Timis county, Romania. The schools had a total of 848 students aged 6-14 enrolled in the morning and afternoon shifts. The study was receiving the ethical approval of the Ethical Comitee of the University and the 3 school principals approved the study. 9 teachers agreed to take part in the research and volunteered themselves. The next phase

involved voluntary acceptance by students (of this 9 teachers) and the consent of their parents or guardians. A group of 220 children were selected as the sample.

Neither of the 9 teachers participating in the study underwent any kind of training or calibration. They were instructed simply to indicate the tooth (or teeth having cavities) without taking in consideration the extent of the lesion. Each teacher examined her/his own class students in a single session without previous communication. Each subject had all his or her teeth examined by the researcher dentist and the teacher.

Because the current status of the disease is the key target of this study, the agreement analysis of the examinations performed by teacher and the dentist and the validation of their findings considered only decayed and healthy elements. The notating used was 0 –for deciduous and healthy; 1-for deciduous and decayed and A -for permanent and healthy and B-for permanent and decayed. The results of the visual examination performed by the dentist serve as benchmark for comparing the obtained findings of teachers.

The early stages of disease (white spot – according to WHO criteria) were not included because of the difficulty in detecting them, which may lead to questionable reliability.

The diagnostic criteria adopted to define decayed teeth were when a pit, fissure, or smooth surface lesion presented with decay or loss of substance. The teeth requiring extraction were also included in the group of decayed teeth. Teeth with temporary restoration, fracturated or infiltrated, filled or restored with sealant were not considered for purposes of the agreement analysis and validation of examination performed by teachers because they require assessment of a trained professional dentist.

In order to ensure uniformity of the examination the environmental conditions were standardized and patient and examiner positioning were preset.

The visual examination was performed in the classroom under natural lighting with the observer facing the student to facilitate natural light to the oral cavity. Cleaning and drying of the teeth prior to the examination was not performed for simulating the condition under which most epidemiological surveys are conducted. All the examination took place in the morning because in the afternoon after lunch the examination could be modified because the absence of brushing teeth.The observers were masks, caps, disposable gloves and tongue blades to allow better visualization of tooth surfaces.

The obtained data were analyzed using tables consistent with measurement scales of the variable studied and the data collected were analyzed using SPSS software version17.

RESULTS

Table 1 shows the analysis of the prevalence of caries according to each of the observers (teacher and dentist) and between-observer agreement as regard indication for treatment, taking the individual as the unit of observation. The kappa value found was 0,74 indicating a satisfactory agreement concerning children's need for treatment.[Table 1]

Treatment indicated by theachers	**Total**		**Treatment indicated by dentist**					**p-value of McNemar**
			Yes		No		Kappa	
	n	%	n	%	n	%	(95%CI)	test
Teachers								
Yes	197	89.5	190	86.3	7	3.2	0.74	
No	23	10.5	4	1.9	19	8.6	(0.54-0.85)	0.549
Total	220	100.0	194	88.2	26	11.8		

Table 1. Treatment indication based upon visual examination performed by teachers compared to visual examination by dentist

The agreement between the examiners according to the healthy or decayed criteria is presented in table 2. Considering all teeth examined, kappa value indicate good response. [Table 2]

Visual evaluation by teachers	Total		Visual evaluation by dentist				
			Healthy teeth		Decayed teeth		
	n	%	n	%	n	%	Kappa
Teachers							
Healthy teeth	4572	88.8	4380	85.0	192	3.7	0.73
Decayed teeth	580	11.2	164	3.2	416	8,1	
Total	5152	100.0	4544	88.2	608	11.8	

Table 2. Tooth by tooth agreement between visual examination performed by teachers and those performed by the dentist

The absence of cavities was easily detected (specificity = 97.8%). More caution is required in positive results indicated by teachers because they were not always confirmed subsequently (sensitivity 73,1%).

DISCUSSION

Previous studies have compared the responses of simplified screening, outside dental offices and not performed by the dentists, with visual examination carried out by a dentist in the dental office. They found that differences were not statistically significant, thus providing a simple and easy alternative for the development of oral health programme. [11,12]

Thus, professional training includes a commitment to community health promotion, in general, and oral health, in particular. Our study also showed that inexperienced school teachers could be used in dental health programme, but if the aim is to utilize their potential, the dental profession should attempt to encourage the inclusion of knowledge about oral health, diseases, their methods of prevention, and oral health promotion within the school curriculum.

A similar study showed that school teachers, with their educational experience and contact with students, can actively contribute to students' health promotion, provided if they themselves receive sufficient training and support to do so. The study showed that, overall, school teachers in general have medium knowledge and experienced school teachers have more knowledge about dental decay, gum disease, and oral cancer. Factors among sociodemographic variables, such as education, sex and experience, also play a role. Prevention package should be implemented through school health schemes in different urban and rural areas. In addition, it chapters on oral health should be included in school textbooks at the third, fifth, and eighth grades.[13]

Regular oral health promotional activities in the form of health education, regular dental check-ups, demonstrations of brushing and rinsing techniques, and preventive and interceptive treatment can be undertaken at the school level.[14-16]

Teachers cannot contribute to nurturing well-informed students if they themselves remain uninformed. With respect to future oral health education programs, accurate information on preventive measures of common oral diseases is needed, since they have the potential to reach all children. This can further be improved by providing accurate knowledge about oral health and preventive measures, particularly to younger school teachers and those with just a basic educational degree. This is particularly important, since the major purpose of health education, as per the WHO, is that people

learn to control their own community's health environment.

The results found by the collected data indicate that is possible to develop a programme to identify tooth disease in communities with little or no access to dentist care. A limitation of the present study is that the sample is from Timis county, and is not a representative sample from Romania as a whole. However, it could be taken as an indicator to improve the system of education of school teachers and inclusion of health-related information in teachers' training at the national level through appropriate policy amendment.

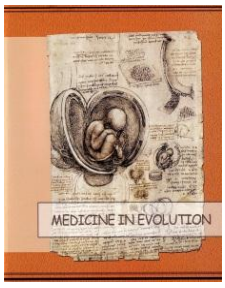
CONCLUSION

Teachers proved to be able to perform the first screening in such places, and the performance of such a programme would be enhanced by previous training of these groups. Training of teachers should aim at improving their level of knowledge on oral health. As a result, the patients could avoid future pain and costs and more the involvement of teachers in caries detection would bring dentistry closer to the school environment, facilitate dissemination of health promotion concepts.

REFERENCES

1. Primary Health Care: Report of International Conference on Primary Health Care, Alma-Ata, USSR, 6–12 September 1978. Geneva: World Health Organization, Health for All Series, No. 1.
2. Petersen PE, Danila I, Samoila A. Oral health behavior, knowledge, and attitudes of children, mothers, and school teachers in Romania in 1993. Acta Odontol Scand. 1995;53:363–368.
3. Kay EJ, Baba SP. Designing dental health education materials for school teachers: formative evaluation research. J Clin Pediatr Dent. 1991;15:195–198.
4. Peterson PE, Hadi R, Al-Zaabi FS et al. Participation, willingness and abilities of school teachers in oral health education in Tanzania. Community Dent Health. 1994;11:101–104.
5. Masters DH. The class room teacher. Effective dental health educator. J Am Soc Prev Dent. 1972; 2:38–49.
6. Petersen PE, Hadi R, Al-Zaabi FS et al. Dental knowledge, attitudes and behavior among Kuwaiti mothers and school teachers. J Pedod. 1990;14:158–164.
7. Mullins R, Sprouse W. Dental health knowledge of elementary school teachers in bowling green, Kentucky. J Am Soc Prev Dent. 1973;3: 60–65.
8. Loup MJ, Frazier PJ. Knowledge and attitudes of school teachers towards oral health programs and preventive dentistry. J Am Dent Assoc. 1983;107:229–234.
9. Giasrud PH, Frazier PJ. Future elementary school teachers' knowledge and opinions about oral health and preventive dentistry. J Publ Health Dent. 1988; 48: 74–80.
10. Peterson PE, Esheng X. Dental caries and oral health behavior situation of children, mothers and school teachers in Wuhan, People's Republic of China. Int Dent J. 1998; 48: 210–216.
11. Beltran ED, Malvitz DM, Eklund SA. Validity of two methods for assessing oral health status of populations. J Publ Health Dent. 1997;57(4):206-214.
12. Kwan SYL, Prendergast MJ, Willians SA. The diagnostic reliability of clinical dental auxiliaries in caries prevalence surveys- a pilot study. Community Dent Health. 1996;13:145-149.
13. Shodan M, Prasad K, Javali SB. School teachers' knowledge of oral disease prevention: a survey from Dharwad, India. J Investig Clin Dent. 2012;3: 62–67.
14. Hecksher AS, Luiz RR, Costa AJ, Moraes NM. Reliability analysis of visual examinations carried out by school-teachers and a dental assistant in the detection of dental caries. Community Dent Health. 2010 Jun;27(2):89-93.
15. Wierzbicka M, Petersen PE, Szatko F, Dybizbanska E, Kalo I. Changing oral health status and oral health behaviour of schoolchildren in Poland. Community Dent Health. 2002 Dec;19(4):243-50.
16. Petersen PE, Mzee MO. Oral health profile of schoolchildren, mothers and schoolteachers in Zanzibar. Community Dent Health. 1998 Dec;15(4):256-62.

CURRENT METHODS FOR IMAGISTIC EVALUATION OF ADULT PATIENTS WITH PERIODONTAL DISEASE UNDERGOING ORTHODONTIC TREATMENT. -A REVIEW PART I: COMBINED ORTHODONTIC - PERIODONTAL TREATMENT CONSIDERATIONS



JIANU ALEXANDRU[1], ONISEI DOINA[2], STRATUL STEFAN-IOAN[2]

[1] University of Medicine and Pharmacy "Victor Babes", Department of Orthodontics-Pedodontics, Timisoara
[2] University of Medicine and Pharmacy "Victor Babes", Department of Periodontology, Timisoara

ABSTRACT

Patients undergoing orthodontic treatment often have a certain degree of periodontal issues. Sometimes, adults are not even aware of their periodontal status and might seek orthodontic treatment for esthetic and functional purposes. It is the responsibility of the orthodontist to be fully aware of the periodontal status of patients undergoing orthodontic treatment. On the other hand, patients undergoing periodontal treatment might also need orthodontic care in order to resolve different tooth position problems. Such patients must be handled with care and the efficient collaboration between the periodontologist and orthodontist becomes essential.
Part I of this review debates the main issues of the combined orthodontic-periodontal treatment, its potential benefits and guidelines.
***keywords**: orthodontics, periodontal treatment, 3d imaging*

Correspondence to:

Dr. Alexandru Jianu.
Adress: Str.Nicolae Labis, Bl.3, ap.9, 300199 Timisoara, Romania
email: jianu.alexandru@gmail.com
tel. : +40-724-901943

INTRODUCTION

Orthodontic treatment may be an important adjunctive to contemporary periodontal therapy. These may resolve some malocclusions and positional pathologies resulted from the loss of periodontal support or loss of periodontaly-involved teeth: elongation, spacing, and proclination of incisors, rotation, and tipping of premolars and molars with collapse of the posterior occlusion, and decreasing vertical dimension. In addition, orthodontic tooth movement can also facilitate the management of several restorative and esthetic problems in adults, caused by subgingival fractured or lost teeth, tipped abutment teeth, excess spacing, inadequate implant space, over erupted teeth, narrow alveolar ridges that prevent implant placement, and other conditions.[1]

It is well known that most humans suffer from periodontal disease at some time in their lives, and the severity of the disease varies widely. Nearly all fixed orthodontic appliance patients will get gingivitis at some point during their treatment.[2] Gingival enlargement and inflammation are often temporary and solved within weeks after removing the orthodontic appliance.[3] Some studies have been suggesting that the contemporary use of bonded rather than banded orthodontic appliances bonds may result in less gingivitis.[4] Fixed orthodontic appliances cause an increase in bacterial activity around the bracket or the band. There is a decrease in facultative anaerobes and an increase in anaerobic rods, spirochaetes and other motile organisms.[5]

In addition, orthodontic tooth movement may be a substantial benefit to the adult periodontal patient in the perio-restorative phase. On the other hand, many adults who seek routine restorative dentistry have problems with tooth malpositions that compromise their ability to clean and maintain their dentitions. If these individuals are susceptible to periodontal disease as well, tooth malposition may be an exacerbating factor that could cause the premature loss of these teeth.[6]

The current trend is that orthodontic appliances become smaller, less noticeable, and easier to maintain during orthodontic therapy. Thus, many adults are taking advantage of the opportunity to have their teeth aligned improving the esthetics of their smiles and boosting their self confidence and social integration. If these individuals also have underlying gingival or osseous periodontal defects, these defects often can be improved during orthodontic therapy if the orthodontist is aware of the situation and applies the appropriate tooth movement.[7] The key element in the orthodontic management of adult patients with periodontal disease is to eliminate or reduce plaque accumulation and gingival inflammation.[8] Therefore, the periodontal patient with orthodontic appliances and the treating periodontologist have to put much emphasis on oral hygiene instructions.

During orthodontic movement in patients, it is essential that all calculus is removed and plaque is minimized. In most patients, this can be accomplished with initial therapy and detailed oral hygiene instructions accompanied by the use of antibacterial agents such as chlorhexidine.[10] Failure to control these factors can lead to accentuation of gingivitis and even bone loss. The control of periodontal inflammation is so vital that in some severe periodontal affections such as furcation involvement, it may be necessary to use periodontal flap surgery to get access to the root surfaces so that root planning is completed before moving the teeth.[9-11]

To date, only a few well controlled studies have been published on groups of adults with advanced periodontitis, who have received comprehensive orthodontic fixed-appliance treatment.[12-14] To counteract the tendency of orthodontic appliances to increase the accumulation of plaque on the teeth, these authors recommend that attempts should be made to keep the appliances and mechanics simple, and avoid hooks, elastomeric rings, and excess bonding resin outside the bracket bases. The use of steel ligatures is recommended on all brackets where possible, because elastomere rings have been shown to be significantly more plaque attractive than steel ties.[15]

Renewed oral hygiene instruction and motivation is made after placement of the orthodontic appliances. During the orthodontic treatment period, professional tooth cleaning by a dental hygienist or periodontist may be performed at 3-month intervals, [2,12] or after regular examination updates at 6 and 12 month intervals, depending on the situation. In practice, shorter recall intervals may be recommended, depending on re-examination of the periodontal status. The re-examinations should include recordings of probing depths, the clinical attachment level (in order to detect false pockets), mobility, bleeding on probing, suppuration, gingival recessions, bone levels, altered relationships between the displaced roots and the oral plate etc. Professional scaling may be indicated during active intrusion of elongated maxillary incisors, since orthodontic intrusion may shift supra-gingival plaque to a sub-gingival location.[16, 17] The possibility of carrying an existing pocket in apical direction along with the intruded root should be also carefully evaluated.[18] In some points of the treatment, if efforts at maintaining an acceptable oral hygiene are unsuccessful, orthodontic treatment should be terminated because inflammation and high levels of plaque can have severe consequences when combined with orthodontic forces.[19] Also in cases where the patient has successfully kept a satisfactory oral hygiene and orthodontic treatment has been performed, it is recommended that after appliance removal, re-instruction in oral hygiene measures (re-enforced OHI) should be given, with care to avoid traumatic tooth brushing, that may increase the risk of subsequent labial gingival recession, since cleaning is now easier to perform.[20]

Many authors point at the fact that adults with a reduced periodontium represent different challenges for orthodontists than adolescents. [12,21-23] Worn or abraded teeth, missing papillae and uneven crown lengths are common problems, making therefore more difficult to obtain an esthetically optimal appearance of the teeth and gingiva after the bracket removal.[22]

Most incisor teeth in adults with malocclusions have some degree of worn incisal edges, which represent an adaptation to functional demands.[24] When the axial inclinations and rotations of such incisors are corrected, there is frequently a need for incisal grinding towards a more normal contour. Such grinding can be performed safely as long as the wear is limited, the overbite is adequate, and the patients display enough tooth material in conversation and on smiling. When the abrasion is more significant, however, cooperation with a restorative dentist is generally indicated. [25] The presence of papillae between the maxillary incisors is an important esthetic factor after orthodontic treatment. Teeth crowding with incisor overlap can be corrected through orthodontics in adults, but it is generally less likely to have an intact papilla.[26-28] Tuverson (1980) explains this phenomenon by the fact that the contact point becomes located too far incisally on the triangular crowns that have not had a normal interdental wear pattern.[29] Similarly, in patients with advanced periodontal disease and destruction of the crestal bone between the incisors, the papillae may be even absent, resulting in unesthetic gaps between the teeth after orthodontics. The author recommends as the best method of correcting this problem to have the the mesio-distal surfaces of the incisors during the orthodontic finishing stage recontoured, followed by the closing of the diastemata thus created. Thus, the roots of the teeth can come closer together, while the contact point is lengthened and moved apically, so there is a chance that the papillae can fill out the interdental space.[27] The modern periodontal treatment plan regarding malpositioned teeth must include an orthodontic treatment phase.

DISCUSSION

According to Newman and Carranza[30], orthodontic therapy can provide several benefits to the adult periodontal patient:

1. Aligning crowded or tipped maxillary or mandibular anterior teeth allows the adult
patient better access to clean all surfaces of their teeth adequately.

2. Vertical orthodontic tooth repositioning can improve certain types of osseous defects in periodontal patients. Often the tooth movement eliminates the need for osseous surgery.[31]

3. Orthodontic treatment can improve the esthetic relationship of the maxillary gingival
margin levels before restorative dentistry. Sometimes, aligning the gingival margins orthodontically avoids gingival surgery, which could require bone removal and exposure of the roots.

4. Orthodontic therapy may be useful to patients with severe fractured maxillary anterior teeth that require forced eruption to permit adequate restoration of the root, by allowing the crown preparation to have sufficient resistance form and retention.

5. Orthodontic treatment allows open gingival embrasures to be corrected to regain lost papillae. A combination of orthodontic root movement, tooth reshaping, and restoration may be used to additionally improve the esthetic appearance.

6. Orthodontic treatment could improve adjacent tooth position before implant placement.

CONCLUSION

Combined orthodontics – periodontics treatment can be a real benefit to the periodontal compromised patient as long as the right treatment plan is designed specifically for every individual and its periodontal status.

Furthermore, efficient collaboration between the orthodontist and periodontist is needed in order to prevent any harmful effects on the supporting structures of individual teeth. Patient oral hygiene is also essential to the success of treatment, plaque accumulation and inflammation must be kept under control at the lowest possible levels in order to prevent tissue breakdown and severe relapse. There is no guideline regarding the periodontal status and orthodontic treatment of adult patients, thus every case is a challenge and every patient must receive the proper treatment for his/her own needs.

It is safe to assume that, when performed properly, these two therapies can significantly improve the quality of periodontal compromised teeth, offer space for possible implants, efficient and satisfactory esthetics, stable occlusion and proper prosthesis abutments.

REFERENCES

1. Jan Lindhe , Niklaus P. Lang, Thorkild Karring. Clinical Periodontology and Implant Dentistry 5th edition. 2008; Blackwell Munksgaard Publishing; Oxford UK

2. Boyd RL, Baumrind S. .Periodontal considerations in the use of bonds or bands on molars in adolescents and adults. Angle Orthod. 1992 Summer;62(2):117-26

3. Alstad S, Zachrisson BU. Longitudinal study of periodontal condition associated with orthodontic treatment in adolescents. Am J Orthod. 1979 Sep; 76(3):277-86

4. Alexander SA. Effects of orthodontic attachments on the gingival health of permanent second molars. Am J Orthod Dentofacial Orthop. 1991 Oct;100(4): 337-40.

5. Willmot D. Orthodontic treatment and the compromised periodontal patient. Eur J Dent. 2008 Jan; 2(1):1-2.

6. Thilander B Infrabony pockets and reduced alveolar bone height in relation to orthodontic therapy. Semin Orthod. 1996 Mar; 2(1):55-61.

7. Wang SF, Leknes KN, Zimmerman GJ, Sigurdsson TJ, Wikesjö UM, Selvig KA. Intra- and

inter-examiner reproducibility in constant force probing. J Clin. Periodontol. 1995 Dec; 22(12):918-22.
8. Zachrisson BU. Clinical implications of recent orthodontic-periodontic research findings. Semin Orthod. 1996 Mar; 2(1):4-12.
9. Okamoto A, Ohnishi T, Bandow K, Kakimoto K, Chiba N, Maeda A, Fukunaga T, Miyawaki S, Matsuguchi T. Reduction of orthodontic tooth movement by experimentally induced periodontal inflammation in mice. Eur J Oral Sci. 2009 Jun; 117(3):238-47.
10. Deepa D, Mehta DS, Puri VK, Shetty S. J Combined periodontic-orthodontic endodontic interdisciplinary approach in the treatment of periodontally compromised tooth. Indian Soc Periodontol. 2010 Apr; 14(2):139-43.
11. Hayakawa H, Fujinami K, Ida A, Furusawa M, Nikaido M, Yamashita S, Saito A.
Clinical Outcome of Surgical Periodontal Therapy: A Short-term Retrospective Study.
Bull Tokyo Dent Coll. 2012;53(4):189-95.
12. Boyd RL, Murray P, Robertson PB. Effect of rotary electric toothbrush versus manual toothbrush on periodontal status during orthodontic treatment. Am J Orthod Dentofacial Orthop. 1989 Oct;96(4):342-7.
13. Nelson PA, Artun J. Alveolar bone loss of maxillary anterior teeth in adult orthodontic patients. Am J Orthod Dentofacial Orthop. 1997 Mar; 111(3):328-34.
14. Molon RS, Avila ED, Souza JA, Nogueira AV, Cirelli CC, Cirelli JA. Combination of orthodontic movement and periodontal therapy for full root coverage in a miller class iii recession: a case report with 12 years of follow-up. Braz Dent J. 2012; 23(6):758-63.
15. Forsberg CM, Brattström V, Malmberg E, Nord CE. Ligature wires and elastomeric rings: two methods of ligation, and their association with microbial colonization of Streptococcus mutans and lactobacilli. Eur J Orthod. 1991 Oct; 13(5):416-20.
16. Ericsson I, Thilander B, Lindhe J, Okamoto H. The effect of orthodontic tilting movements on the periodontal tissues of infected and non-infected dentitions in dogs. J Clin Periodontol. 1977 Nov; 4(4):278-93.
17. Ericsson I, Thilander B, Lindhe J. Periodontal conditions after orthodontic tooth movements in the dog. Angle Orthod. 1978 Jul;48(3):210-8. 18. Swed Dent J Suppl. 2011; (214):7-84.

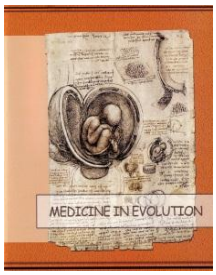
18. Stokland BL. On tooth movements and associated tissue alterations related to edentulous areas and bone defects. Swed Dent J Suppl. 2011; (214):7-84.

.19. Machen DE. Legal aspects of orthodontic practice: risk management concepts. A tale of two splints. Am J Orthod Dentofacial Orthop. 1990 Dec; 98(6):557-8.
20. Lalic M, Aleksic E, Gajic M, Milic J, Malesevic D. Does oral health counseling effectively improve oral hygiene of orthodontic patients? Eur J Paediatr Dent. 2012 Sep; 13(3):181-6.
21. Trulsson U, Engstrand P, Berggren U, Nannmark U, Brånemark PI. Edentulousness and oral rehabilitation: experiences from the patients' perspective. Eur J Oral Sci. 2002 Dec; 110(6): 417-24.
22. Mattick JS. The hidden genetic program of complex organisms. Sci Am. 2004 Oct; 291(4):60-7.
23. Craig RG, Pernat AM, Pecoits-Filho R, Levin NW, Kotanko P. Periodontal diseases and systemic inflammation. Semin Dial. 2013 Jan; 26(1):23-8.
24. Brown LJ, Albandar JM, Brunelle JA, Löe H. Early-onset periodontitis: progression of attachment loss during 6 years. J Periodontol. 1996 Oct; 67(10):968-75.
25. Helgeson MJ, Smith BJ, Johnsen M, Ebert C. Dental considerations for the frail elderly. Spec Care Dentist. 2002; 22(3 Suppl):40S-55S.
26. Eriksen EF, Steiniche T, Mosekilde L, Melsen F. Histomorphometric analysis of bone in metabolic bone disease. Endocrinol Metab Clin North Am. 1989 Dec; 18(4):919-54.
27. Tarnow DP, Magner AW, Fletcher P. The effect of the distance from the contact point to the crest of bone on the presence or absence of the interproximal dental papilla. J Periodontol. 1992 Dec; 63(12):995-6.

28. Sadhasivam S, Cohen LL, Szabova A, Varughese A, Kurth CD, Willging P, Wang Y, Nick TG, Gunter J. Real-time assessment of perioperative behaviors and prediction of perioperative outcomes. Anesth Analg. 2009 Mar; 108(3):822-6.
29. Tuverson DL. Anterior interocclusal relations. Part I.Am J Orthod. 1980 Oct; 78(4):361-70.

30. Michael G. Newman, DDS, Henry Takei, DDS, MS, Perry R. Klokkevold, DDS, MS and Fermin A. Carranza, Dr. ODONT. Carranza's Clinical Periodontology Expert Consult, 11th Edition. 2011; Saunders, an imprint of Elsevier Inc. ; Philadelphia USA.
31. Harpenau LA, Boyd RL. Long-term follow-up of successful orthodontic-periodontal treatment of localized aggressive periodontitis: a case report. Clin Orthod Res. 2000 Nov; 3(4):220-229.

CORRELATION OF PLASMA LEVELS OF ASYMMETRIC DIMETHYLARGININE WITH CAROTID INTIMA - MEDIA THICKNESS IN HYPERTENSIVE PATIENTS WITH ENDOTHELIAL DYSFUNCTION



MARIA SUCIU[1*], MINODORA ANDOR[2], CARMEN CRISTESCU[1], LIANA DRAGAN[3], LIANA SUCIU[1], MIRELA TOMESCU[2]

[1] University of Medicine and Pharmacy „Victor Babes", Faculty of Pharmacy, Department of Pharmacology and Clinical Pharmacy, Timisoara
[2] University of Medicine and Pharmacy „Victor Babes", Faculty of Medicine, Medical Semiotics Department, ASCAR Cardiology Clinic, Timisoara
[3] University of Medicine and Pharmacy „Victor Babes", Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Timisoara

ABSTRACT

Background: *Hypertension is one of the major risk factors in cardiovascular disease and the endothelial dysfunction in hypertensive patients is a major factor for cardiovascular complications. Asymmetric dimethylarginine (ADMA) has evolved in recent years as an important regulator of nitric oxide (NO) synthesis. The relationship between ADMA and essential hypertension is a rather new field of research. Carotid intima-media thickness (IMT) is an important marker in subclinical vascular lesion. An increased carotid IMT is considered by some authors a marker of subclinical atherosclerosis and blood pressure plays and important role in increasing the IMT.*

Aim: *This study is aiming to investigate the relationship between plasma ADMA levels and carotid IMT in essential hypertensive patients with / without endothelial dysfunction.*

Material and method*: The prospective present study was conducted during a period of 18 months and included a number of 62 patients with essential hypertension. They followed a series of clinical and laboratory investigations, including determination of plasma ADMA levels and respective carotid ITM Plasma ADMA levels were measured by high-performance liquid chromatography and carotid ITM by high-resolution ultrasonography system.*

Results: *Mean plasma ADMA levels were significantly higher in the premier group (0,96 ± 0, 06 µmol/L) in comparison with that second group (0, 67 ± 0, 11 µmol/L; $p < 0,001$) and the third group (0, 54 ± 0, 06; $p < 0,001$). In regards to the mean value of carotid IMT, its distribution in the study group is as follows: in the third group the mean value of carotid IMT was between normal limit (0,6 – 0,9; 0.73 ± 0,05), for the second group the mean value of carotid IMT were also between normal limit (0,7 – 0,9; 0,82 ± 0,03) but for the first group the mean value of carotid IMT was higher (1,0 – 1,3 mm; 1,15 ± 0,09). This value, for premier group, was significantly higher compared with the other two groups ($p < 0,001$).*

Conclusions*: Plasma ADMA levels are significantly high in mild – to – moderate hypertensive patients. Elevated ADMA levels are associated with endothelial dysfunction in these patients. High plasma ADMA levels was observed and significantly positively correlated with carotid IMT. The results obtained support the idea that, the correlation of the plasma ADMA levels and carotid IMT is maintained regardless of the degree of endothelial dysfunction.*

Key words: *hypertension, endothelial dysfunction, asymmetric dimethylarginine, carotid intima-media thickness*

Correspondence to

[*] Suciu Maria, doctorand afiliat UMF Timisoara
Adress: UMF "Victor Babes" Timisoara, Faculty of Pharmacy, Eftimie Murgu Square nr. 2 cod 300041
Phone: 004 - 0723319050
e-mail: suciu01maria@yahoo.com

INTRODUCTION

Hypertension is one of the major risk factors in cardiovascular disease, it accelerates the development of atherosclerosis and it affects 12% to 15% of the adult population. Ever since 1980, Furchgott[1, 2], has stated that the acetylcholine induced vascular relaxation is critically linked to an intact endothelium. Loss of vascular endothelium integrity in various heart diseases is associated with nitric oxide (NO) production. Physiologically, NO (Nitric Oxide) is synthesized within the endothelium, based on a reaction between the amino acid (L-arginine) and the corresponding nitric oxide synthase enzyme (NOS) [3].

Endothelial dysfunction is the earliest marker for vascular endothelial damage. Endothelial dysfunction in hypertensive patients is a major factor for cardiovascular complications. Primary prevention of cardiovascular disease, makes is a main target, to identify endothelial dysfunction by means of noninvasive clinical and laboratory methods.

Classical noninvasive assessment methods of endothelial dysfunction include tests such as: Doppler echocardiography (ultrasound flow mediated vasodilatation - ex. brachial artery ultrasound), circulating markers of endothelial dysfunction (asymmetric dimethylarginine) and vascular inflammation (high-sensitivity C-reactive protein and soluble cellular adhesion molecules) [4].

Carotid intima-media thickness (IMT) is an important marker in subclinical vascular lesion assessment and an independent predictor of future cardiovascular events in the general population[5]. An increased carotid IMT is considered by some authors a marker of subclinical atherosclerosis[6] while other studies show that and blood pressure plays and important role in increasing the IMT[7].

The relationship between ADMA and essential hypertension is a rather new field of research. During recent studies, repeated measurements of ADMA plasma concentrations have been found to be the higher in hypertensive patients [8, 9, 10] compared with normotensive healthy subjects[11], suggesting a systemic damage to the NO production levels[10].

Asymmetric dimethylarginine (ADMA) has evolved in recent years as an important regulator of NO synthesis. ADMA is an endogenous inhibitor of NOS. Many cell types, including human endothelial cells are able to synthesize and metabolize the ADMA. High levels by ADMA have been reported in cases that are associated with a high cardiovascular risk[12].

AIM AND OBJECTIVES

The present study is proposing to investigate the correlation between plasma levels by ADMA and carotid IMT, in patients with essential hypertension associated with / without endothelial dysfunction (ED).

MATERIALS AND METHODS

Patients

The prospective present study was conducted during a period of 18 months, 1 July 2011 – 31 December 2012, in ASCAR Cardiology Clinic of Timisoara, Romania and included a number of 62 patients. The criteria for study inclusion in the subjects have been: age, 18 +, diagnosis of essential hypertension and without cholesterol-lowering therapy within six months prior to inclusion. Prior to being admitted in the study, all patients completed a consent form, their participation was completely voluntary, and they were able to withdraw it at any point. We excluded the subjects presenting coronary artery disease, chronic heart failure, diabetes, chronic kidney or hepatic disease, stroke, asthma, peripheral

arterial circulatory failure, and acute or chronic inflammatory states.

We conducted a background check on their medical history, we ran physical exams, biochemistry checks (including the high-sensitivity C-reactive protein), electrocardiogram (ECG), echocardiography, Doppler echocardiography (flow mediated vasodilatation at brachial artery and carotid intima-media thickness (IMT). We used the baseline data of these patients for interpretations.

Sex distribution in the group was 30 (48, 39 %) men and 32 (51, 61 %) women. Mean age was 55 ± 3, with limits between 35 - 69 years. The presence of endothelial dysfunction has been confirmed / infirmed by high end investigation (including the high-sensitivity C-reactive protein and flow mediated vasodilatation at brachial artery).

Procedures

All patients were examined in a fasting state and in a temperature-controlled room. After 30 minutes of rest, blood pressure was measured in supine position at the right brachial artery and expressed as the mean value of 3 measurements over a period of 30 minutes. Mean arterial blood pressure was calculated as (2 diastolic pressure + systolic pressure) / 3.

Endothelium-dependent, flow-mediated vasodilatation (FMD) was determined by high-resolution ultrasound of the brachial artery and was performed, based on the literature data[13]. The diameter of brachial artery was measured with a 7.5 MHz transducer. Measurements were obtained at 09:00 AM — at baseline, after at least 20 min of resting in the supine position in a quiet room and 12 h without caffeine, smoking, food or any vasoactive drugs.

Longitudinal scans of the brachial artery were obtained approximately 5cm proximal of the antecubital fossa. The transmit focus zone was set at the depth of the anterior wall. A view of a 5-cm longitudinal section of the brachial artery was recorded on S-VHS for 30 s at baseline, before and during peak (1 min) reactive hyperemia (induced by deflation of a blood pressure cuff previously inflated to 50 mm Hg above the subject's systolic blood pressure point). Endothelium-dependent, flow-mediated dilation (FMD) was calculated due to percent change in diameter, 1 min after the cuff release and relative to the baseline diameter before cuff release. We considered that an endotheliun dependent FMD is "normal" when the reponse of the brachial artery is vasodilatation > 10% relative to baseline diameter and FMD to be "impaired" when vasodilatation is < 10%.

Carotid intima-media thickness (IMT) of the common carotid artery was determined as an index of atherosclerosis, at baseline in both carotid arteries, as agreed in the Mannheim consensus[14], with a GE medical system VIVID S6, high-resolution ultrasonography system, equipped with a 9 - Mhz linear array transducer. The carotid arterial scanning was performed by a certified sonographer. The subjects were examined in a supine position. The intima-media thickness was calculated online by built-in software of the ultrasound system. The mean IMT was calculated for each of the four measurements sites in each patient (fig.1).

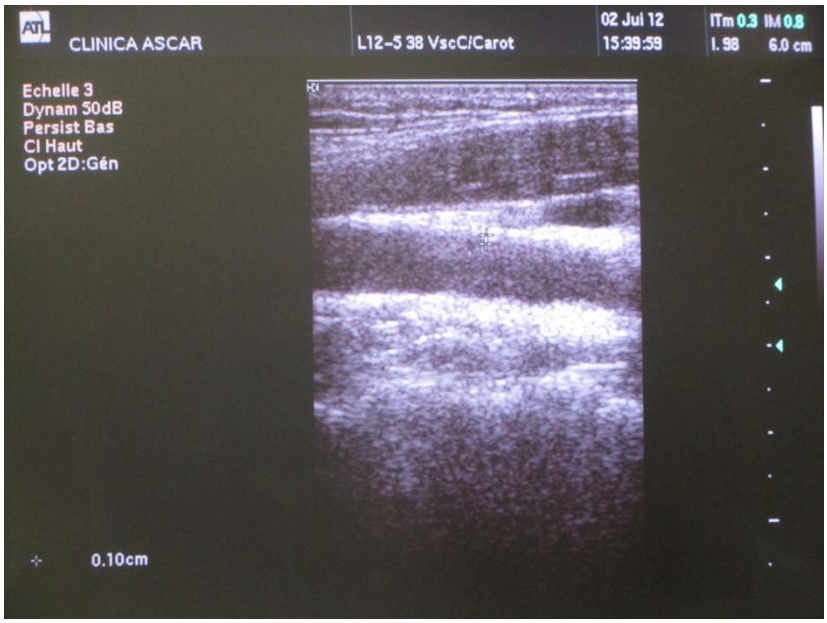


Fig. 1. Ultrasound measurement technique of the carotid intima-media thickness (IMT)

Laboratory analyses

The venous blood samples were collected after 15 minutes of rest, after an overnight fast (>12 hours since the last intake of food), immediately placed on ice and were drawn for glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides. All these analyses were measured by routine laboratory methods, inside the hospital. Total cholesterol > 200 mg/dL and triglyceride levels > 150 mg/dL were considered as dyslipidemia**.**

Plasma levels of high-sensitivity C-reactive protein (hs-CRP) were measured within the Laboratory Bioclinica SA, Timisoara through a highly sensitive quantitative immunoturbidimetric method, using a CRP Ultra kit, distributed by Abboth Diagnostics. The lowest detection limit for ultrasensitive method was 0, 01 mg / dL.

Plasma ADMA levels were measured in Labor Dr. Linbach Heidelberg by a simple and fast LC–MS–MS analytical method with fluorescence detection. Fluorescence was detected after solid phase extraxtion(SPE) whith carboxylic acid (CBA) cartridges online o-phtaldialdehyde (OPA) derivatization, and separation on a phenyl column (250 x 4,6 mm, Macherey-Nagel, Düren, Germany). For our laboratory, the reference value for ADMA: reference range of 0, 3 – 0, 8 µmol/L, for both sexes and all age groups over 18 years of age.

Statistical analyses

Continuous variables were evaluated using t – test and categorical variables using χ^2. Pearson correlation coefficient (r) test was used to calculate correlation coefficients. Linear regression analysis was performed to investigate the association between plasma ADMA levels and carotid IMT. Probability value < 0, 05 was considered significant (S) and p > 0, 05 was considered insignificant (NS).

RESULTS

During the initial phase, all patients were divided into three groups depending on the degree of endothelial dysfunction, the ADMA levels and respectively the values of carotid IMT: the first group consisted of 23 (37,10 %) hypertensive patients with endothelial dysfunction and elevated values of ADMA (> 0,8 µmol/L) and carotid IMT (> 0,9

mm), the second group consisted of 24 (38,71 %) hypertensive patients with endothelial dysfunction and normal values of ADMA (≤ 0,8 µmol/L) and carotid IMT (≤ 0,9 mm) and the last group consisted of 15 (24,19 %) hypertensive patients without endothelial dysfunction and normal values of ADMA (≤ 0,8 µmol/L) and carotid IMT (≤ 0,9), which represented the control group.

Table 1. *Baseline characteristics of the patients. Results are presented as mean + standard deviation for each group*

Patients characteristics	Group I HTA with ED and ADMA and carotid IMT increase	Group II HTA with ED and ADMA and carotid IMT normal	Group III HTA without ED and ADMA and carotid IMT normal	P value between group I and II
Sex				> 0,05
• male	10 (43,48 %)	11 (45,83 %)	9 (6 0%)	
• female	13 (56,52 %)	13 (54,17 %)	6 (40 %)	
Age years				> 0,05
• range	37 - 69	35 - 67	38 - 62	
• mean ± SD	53,45 ±	51,27 ±	52,74 ±	
Heart rate (beats / min)	74,6 ± 8,8	75,8 ± 9,7	73,9 ± 10,2	> 0,05
Systolic pressure (mmHg)				0,011
• range	150 - 190	145 - 180	145 - 165	
• mean ± SD	167, 85 ± 3,46	158,21 ± 2,65	153,64 ± 3,86	
Diastolic pressure (mmHg)				0,011
• range	95 - 115	90 - 110	90 - 105	
• mean ± SD	103,65 ± 1,01	96, 21 ± 2,87	93,43 ± 2,06	
Total cholesterol (mg/dL)				< 0,05
• range	205 – 260	190 - 230	175 – 220	
• mean ± SD	233 ± 6,5	210 ± 10,69	198 ± 13,11	
LDL (mg/dL), range	114 - 130	110 - 120	102 - 115	> 0,05
HDL (mg/dL), range	34 - 45	38 - 50	38 - 60	> 0,05
Triglycerides (mg/dL)	148	152	145	> 0,05
Glycemia (mg/dL)	98	102	99	> 0,05
Smokers %	15 (62, 5 %)	13 (56, 5 %)	9 (60%)	> 0,05
Plasma ADMA (µmol/L)				< 0,001
• range	0,9 – 1,1	0,5 – 0,7	0,3 – 0,7	
• mean ± SD	0,96 ± 0,06	0,67 ± 0,11	0,54 ± 0,06	
Flow-mediated vasodilatation (%)				< 0,001
• mean ± SD	6,53 ± 0,04	8,48 ± 0,03	14,67 ± 0,06	
Intima-media thickness (IMT) (mm)				< 0,001
• range	1,0 – 1,3	0,7 – 0,9	0,6 – 0,9	
• mean ± SD	1,15 ± 0,09	0,82 ± 0,03	0.73 ± 0,05	

In table 1 we are illustrated the baseline demographic, hemodynamic and humoral characteristics of the patients. There was no significant difference between the first two groups with respect to all demographic and blood pressure parameters (p> 0, 05).

Also, if we compare the three groups of patients, there are no significant statistical difference in their mean plasma levels to LDL-cholesterol, HDL-cholesterol, triglycerides and glucose (p> 0, 05).

There was no statistically significant difference between hypertension patients in the second and third group, in terms of all biomarkers tested, plasma ADMA levels and carotid IMT ($p > 0,05$), but there was a significant difference in terms of % FMD ($p < 0,01$).

Mean plasma ADMA levels were significantly higher in the first group (0, 96 ± 0, 06 µmol/L) in comparison with that second group (0, 67 ± 0, 11 µmol/L; $p < 0,001$) and the third group (0, 54 ± 0, 06; $p < 0,001$). There was no significant difference between the mean plasma ADMA levels of second and third group ($p>0$, 05). These results are represented in fig 2.

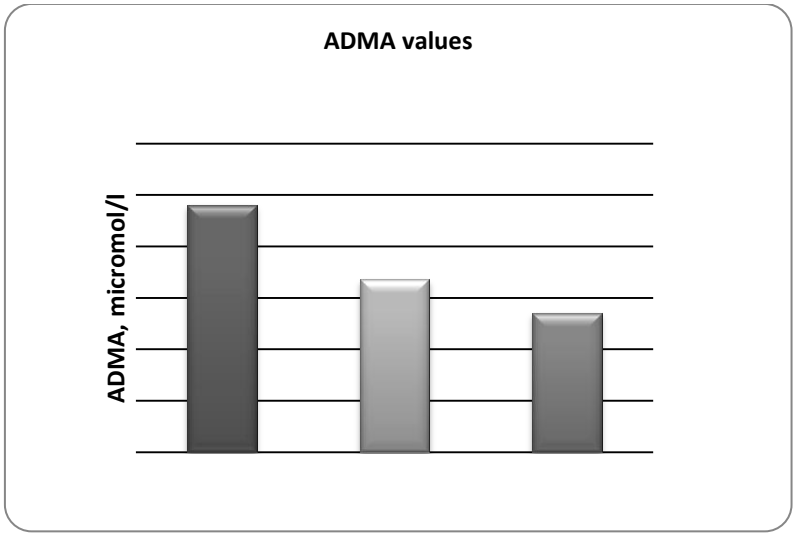


Fig. 2 *Mean plasma ADMA levels in the three patients groups*

Also show in table 1 the patients with plasma ADMA higher levels (the first group) had decreased % FMD (6, 53 ± 0, 04) in comparison to the patients with normal ADMA levels belonging to the second and the third groups (8, 48 ± 0, 03; 14, 67 ± 0, 06). So, we observed that there are a significant negative correlation between the plasma ADMA levels and the endothelium-dependent, FMD ($p < 0,001$).

By analyzing the data in the table, in the first and second group, we observed that there are a significant positive correlation between the plasma ADMA levels and blood pressure levels, systolic and diastolic, ($p = 0,011$).

In regards to the mean value of carotid IMT, its distribution in the study group is as follows: the third group of hypertensive patients, without endothelial dysfunction, the mean value of carotid IMT was between normal limit (0,6 – 0,9; 0.73 ± 0,05), for the second group of hypertensive patients with endothelial dysfunction the mean value of carotid IMT were also between normal limit (0,7 – 0,9; 0,82 ± 0,03) but for the first group of hypertensive patients with endothelial dysfunction the mean value of carotid IMT was higher (1,0 – 1,3 mm; 1,15 ± 0,09). This value, for premier group, was significantly higher compared with the other two groups ($p < 0,001$). But between the values of carotid IMT of groups 2 and 3 no there were significant differences ($p > 0, 05$). These results are represented in fig 3.

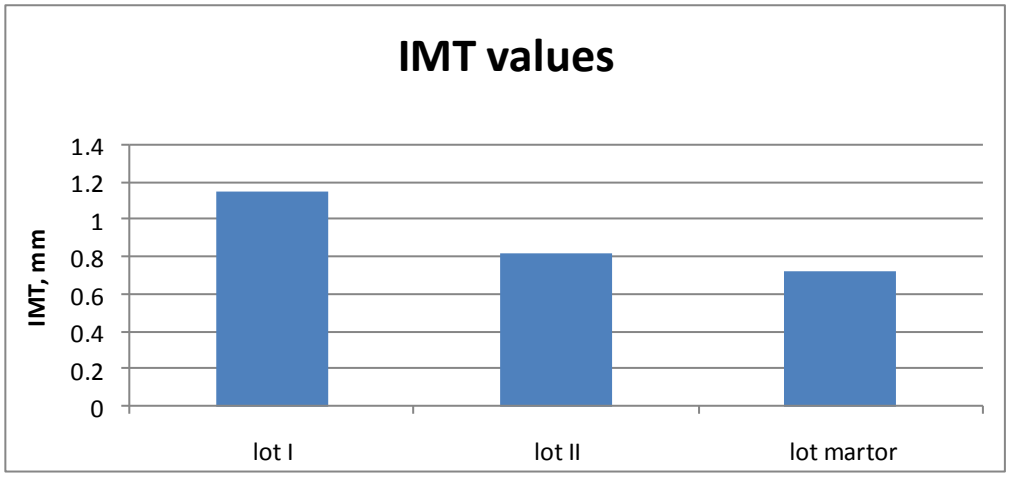


Fig. 3 *Mean carotid IMT in the three patients groups*

By analyzing the data in the table we observed that the hypertensive patients with increased carotid IMT (the first group) also have high plasma ADMA levels, demonstrating a positive powerful correlation between these two parameters ($p < 0,001$).

This aspect is also supported by the Pearson correlation coefficient r, which presented the following values in the two groups: in the first group the r coefficient was = 0.57, a value that sustains the existence of a positive correlation of the two parameters, ADMA and carotid IMT .A similar appearance was observed in the second group where the value of the r coefficient was = 0.67. The results obtained support the idea that, the correlation of these two parameters is maintained regardless of the degree of endothelial dysfunction.

Also show in table 1, that the both systolic and diastolic blood pressures had a significant positive correlation with carotid IMT ($p = 0,011$). Increasing the blood pressure levels, especially systolic blood pressure level, is associated with an increase in carotid IMT.

DISCUSSION

Hypertension is one of the major risk factors in cardiovascular disease and which contributes, as one of the most common causes of cardiovascular morbidity and mortality.

There are principal new findings in this study. First, the endothelial function was inversely associated with plasma ADMA – endogenous inhibitor of NOS. The plasma levels of ADMA were increased in a premier group of patients with essential hypertension and a reduced endothelium-dependent flow-mediated vasodilatation (the strongly negative correlations).

Second, plasma ADMA levels, in turn, were strongly and independently associated with carotid IMT, but not plasma hs-CRP.

Many authors have reported that concentrations of ADMA are increased in patients with essential hypertension[8, 15]. The cause which increased plasma ADMA levels in hypertension is still unknown. Increased shear stress can trigger the synthesis of ADMA and high ADMA levels in hypertension may be a consequence of high blood pressure and not a cause[8].

Thirdly, in our study the plasma ADMA levels were correlated with blood pressure levels in accordance to literature data[15]. There is a significant positive correlation between ADMA levels and systolic and diastolic blood pressures ($p = 0,011$).

Fourthly, in regards to the mean value of carotid IMT, this value, for premier group, was significantly higher compared with the other two groups ($p < 0,001$). But between the carotid IMT values of groups 2 and 3, with and without endothelial dysfunction, no there were significant differences ($p > 0, 05$).

Fifthly, the carotid IMT values were correlated with blood pressure levels in

accordance to literature data[16]. There is a significant positive correlation between carotid IMT and systolic blood pressures levels (p = 0,011).

Perspectives: because ADMA is relatively easily measured, not very expensive and because ADMA levels were independently and strongly related with carotid IMT, determination of ADMA would be not only a marker of atherosclerosis, but may also serve as a biomarker for carotid disease.

Study limitations

We studied a small and highly selected population of patients with essential hypertension which did not permit the establishment of a causal relationship of the described associations. Also, this study was not designed to analyze new mechanisms that link increased ADMA levels with atherosclerosis and essential hypertension.

CONCLUSION

Plasma ADMA - endogenous inhibitor of NOS – is significantly high in mild – to – moderate hypertensive patients, the first group, in comparison to the second group and control group. Also, plasma ADMA levels had a significant negative correlation to endothelial function as measured with classical methods.

The carotid IMT is significantly high in mild – to – moderate hypertensive patients, the first group, in comparison to the second group and control group.

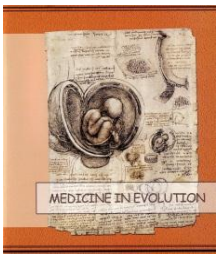
High plasma ADMA levels was observed and significantly positively correlated with carotid IMT. Higher plasma ADMA levels are associated with compromised endothelial function and an atherosclerotic lesion progression at carotid artery. The results obtained support the idea that, the correlation of the plasma ADMA levels and carotid IMT is maintained regardless of the degree of endothelial dysfunction.

REFERENCES

1. Furchgott RF, Zawadzki JV. The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. Nature 1980;288:373–6.
2. Furchgott RF. The role of the endothelium in the responses of vascular smooth muscle to drugs. Annu Rev Pharmacol Toxicol 1984;24:175–97.
3. Ignarro LJ, Buga GM, Wood KS, Byrns RE, Chaudhuri G. Endothelium-derived relaxing factor produced and released from artery and vein is nitric oxide. Proc Natl Acad Sci USA 1987;84:9265–9.
4. Andor Minodora, Tomescu Mirela. Endothelial dysfunction – Methods of assessment and pharmacological approach in cardiovascular disease. Timisoara Medical Journal 2005, vol 55, no 1, p 58 - 63
5. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. N Engl J Med. 1999;340:14 –22.
6. Mancini GB, Dahlof B, Diez J. Surrogate markers for cardiovascular disease: structural markers. Circulation. 2004;109:IV22–IV30.
7. Lakka TA, Salonen R, Kaplan GA, Salonen JT. Blood pressure and the progression of carotid atherosclerosis in middle-aged men. Hypertension. 1999;34:51–56.
8. Achan V, Broadhead M, Malaki M, Whitley G, Leiper J, MacAllister R, Vallance P. Asymmetric dimethylarginine causes hypertension and cardiac dysfunction in humans and is actively metabolized by dimethylarginine dimethylaminohydrolase. Arterioscler Thromb Vasc Biol. 2003 Aug 1;23(8):1455-9. Epub 2003 Jun 12.
9. Palloshi A, Fragasso G, Piatti P. Effect of oral L-arginine on blood pressure and symptoms and endothelial function in patients with systemic hypertension, positive exercise test, and normal coronary arteries. Am J Cardiol 2004;93:930–5.
10. Surdacki A, Nowicki M, Sandmann J. Reduced urinary excretion of nitric oxide metabolites and increased plasma levels of asymmetrical dimethylarginine in men with essential hypertension. J Cardiovasc Pharmacol 1999;33:652–8.
11. Calver A, Collier J, Leone A, Moncada S, Vallance P. Effect of local intra-arterial asymmetric dimethylarginine (ADMA) on the forearm arteriolar

bed of healthy volunteers. J Hum Hypertens 1993;7:193–4.
12. Anderssohn Maike, Schwedhelm Edzard, Lu¨ neburg Nicole. Asymmetric dimethylarginine as a mediator of vascular dysfunction and a marker of cardiovascular disease and mortality: an intriguing interaction with diabetes mellitus. Diab Vasc Dis Res 2010;7(2):105–18.
13. M. C. Corretti, T. J. Anderson, E. J. Benjamin et al., "Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the international brachial artery reactivity task force," *Journal of the American College of Cardiology*, vol. 39, no. 2, pp. 257–265, 2002.
14. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, Csiba L, Desvarieux M, Ebrahim S, Fatar M, Mannheim Carotid Intima-Media Thickness Consensus (2004 – 2006). An Update on Behalf of the Advisory Board of the 3rd and 4th Watching the Risk Symposium 13th and 15th European Stroke Conferences, Mannheim, Germany, 2004, and Brussels, Belgium, 2006. Cerebrovasc Dis. 2006; 23: 75– 80.
15. Matsuguma K, Ueda S, Yamagishi S, Matsumoto Y, Kaneyuki U, Shibata R, Fujimura T, Matsuoka H, Kimoto M, Kato S, Imaizumi T, Okuda S. Molecular mechanism for elevation of asymmetric dimethylarginine and its role for hypertension in chronic kidney disease. J Am Soc Nephrol 2006;17:2176–83
16. Arnett DK et al. Hypertension and subclinical carotid artery atherosclerosis in blacks and whites: The Atherosclerosis Risk in Communities Study. Arch Intern Med 1996; 17: 1983–1989

CORRELATION ANALYSIS BETWEEN BIOCHEMICAL, FUNCTIONAL AND STRUCTURAL MARKERS OF ENDOTHELIUM DAMAGE IN PATIENTS WITH ESSENTIAL HYPERTENSION



MINODORA ANDOR[1], MARIA SUCIU[2*], LIANA DRAGAN[3], LAVINIA VLAIA[4], MIRELA VOICU[2], LIANA SUCIU[2], RALUCA GRADINARU[2], MIRELA TOMESCU[1]

[1] University of Medicine and Pharmacy „Victor Babes", Faculty of Medicine, Medical Semiotics Department, ASCAR Cardiology Clinic
[2] University of Medicine and Pharmacy „Victor Babes", Faculty of Pharmacy, Department of Pharmacology and Clinical Pharmacy
[3] University of Medicine and Pharmacy „Victor Babes", Faculty of Pharmacy, Department of Pharmaceutical Chemistry
[4] University of Medicine and Pharmacy „Victor Babes", Faculty of Pharmacy, Department of Pharmaceutical Technology,

ABSTRACT

Aim: *The aim of this study was to investigate the correlation between biochemical, functional and structural markers of endothelium damage.*

Material and methods: *68 patients with essential hypertension were included in a prospective study. We studied biochemical markers respectively functional and structural evaluation.*

Results: *A higher mean values of sICAM-1 (380 respectively 334) and hs-CRP (4, 31 respectively 3, 32) was observed in the first two groups with endothelial dysfunction as compared with the control group (227 respectively 1, 91). The mean values of sP-selectin was higher for the first group (134) compared also with the second and the third groups (88 respectively 68, $p < 0,001$) with normal values.*

Conclusions*: High ICAM-1, P-selectin and hs-CRP plasma levels was observed and a significant correlation with structural changes and with functional changes in endothelium dependent FMD and could be used as a biochemical marker of endothelial dysfunction.*

Key words: *essential hypertension, ICAM-1, P-selectin, hs-CRP, endothelial dysfunction, carotid intima-media thickness*

Correspondence to

[*] ***Dr. MARIA SUCIU****,*
PhD Lecturer affiliated to the University of Medicine and Pharmacy „Victor Babes", Timisoara, Department of Pharmacology and Clinical Pharmacy,
Address: University of Medicine and Pharmacy „Victor Babes", Timisoara, Faculty of Pharmacy, Eftimie Murgu Square nr. 2 cod 300041
Corresponding author e-mail address: suciu01maria@yahoo.com

INTRODUCTION

In all developing countries[1], hypertension is the most important public health problem, because is one of the most important risk factors for cardiovascular disease who accelerated development of atherosclerotic process and its complications.

Endothelial cells integrity plays an important role in maintaining balance between humoral and cellular factors that are responsible for good function and structure of the endothelial wall. Endothelial cell dysfunction is considered to be a preclinical stage of atherosclerosis and is characterized by impaired vasodilatation mediated by endothelium (which depend in principal by the bioavailability of nitric oxide), increased adhesion and permeability of endothelial cells and structural changes of the vascular wall[2].

The pathophysiologic process potentially involved in initiation and development of hypertension was the both endothelial activation and chronic inflammation, aspects supported by numerous studies[3].

The endothelium clinical exploration is achieved either by use of noninvasive functional tests or by laboratory methods. The classical noninvasive assessment methods of endothelial dysfunction include tests such as: vascular echography (ultrasound flow mediated vasodilatation - ex. brachial artery ultrasound) [4]. Also, we used the vascular echography for assessing the vascular lesion by measuring the carotid artery intima-media thickness (IMT).

High plasma levels of inflammatory markers was demonstrated to be present by a number of studies both in healthy subjects with increased blood pressure[5] and hypertensive[6, 7, 8].

A several clinical studies was recognized in high sensitive C-reactive protein (hs-CRP), a pro-inflammatory marker in patients with cardiovascular disease, such us hypertension. Elevated hs-CRP levels can be used to predict the development of hypertension both in prehypertensive and normotensive patients[6, 9].

Cell adhesion molecules can be used as markers of endothelial cell activation, and their high plasma levels may have a role in initiation and development of atherosclerosis process in hypertensive patients[8, 10, and 11]. Endothelial dysfunction is associated with increased basic plasma levels of adhesion molecules of immunoglobulin family (ICAM-1, VCAM-1 and PECAM-1) and the selectin group (P-selectin and E-selectin) which mediates leukocyte rolling on vascular endothelial wall and leukocyte - platelet interaction respectively.

AIM AND OBJECTIVES

The present prospective study is proposing to investigate the correlation analysis between biochemical, functional and structural markers of endothelium damage in patients with essential hypertension associated with/without endothelial dysfunction.

MATERIALS AND METHODS

Patients

During a period of 18 months, between July 2011 and December 2012, in ASCAR Cardiology Clinic of Timisoara, Romania, a number of 68 patients were investigated in a prospective study, by using the following inclusion criteria: men and women aged over 18 years, diagnosis of mild and moderate essential hypertension defined as a blood pressure meeting the criterion of hypertension grade 1 and 2 of the World Health Organisation blood pressure classification (hypertension was defined by a clinic record of systolic blood pressure > 140 mmHg, a diastolic blood pressure > 90 mmHg, the absence of clinical or laboratory evidence of secondary hypertension) and without cholesterol-lowering therapy, six months prior to inclusion**.** The study was planned according to the ethical principles. The signed informed consent was obtained from each patient prior to being admitted in the study. The patients participating in the study was completely voluntary. They known, that they were able to

change their decision and withdraw at any point. For exclusion we used the following criteria: other cardiovascular disease (coronary artery disease in all forms and heart failure), chronic peripheral arterial circulatory failure, chronic kidney or hepatic failure, cerebrovascular disease, diabetes mellitus, chronic obstructive pulmonary disease as well as bronchial asthma, neoplasms, acute or chronic inflammatory disease, contraindication to statin treatment or used of cholesterol-lowering therapy six months prior to inclusion , therapy for essential hypertension with β-blockers (nebivolol) ACE-inhibitors and AT1-receptor antagonists, prolonged use of non - steroidal anti-inflammatory drugs, corticosteroids, alcohol and drug abuse and inability to comply with study procedures.

At the baseline visit, patients were undergoing anthropometric measurements, medical history, physical examination, laboratory assessment of cardiovascular risk factors [including the biochemical markers of endothelial dysfunction such as: of the inflammatory process (high-sensitivity C-reactive protein: hs-CRP), of cell adhesion (soluble intercellular adhesion molecule-1: sICAM-1) and of coagulation process (soluble P-selectin)]. Other cardiovascular investigations included: electrocardiogram (ECG), echocardiography and vascular echography (for determining the flow of mediated vasodilatation at the brachial artery and intima-media thickness at the carotid artery). The baseline data of these patients were used for interpretations.

The group of patient was composed of 38 (55, 88 %) men and 30 (44, 12%) women. Mean age was 51 ± 8, with limits between 35 - 67 years. We used the biochemical markers such as the hs-CRP and the endothelial dependent flow mediated vasodilatation (FMD) at brachial artery for confirmed / infirmed the presence of endothelial dysfunction in this patients.

Patients included in the study were selected according to the presence of essential hypertension associated or not with endothelial dysfunction.

Procedures

At baseline visit using standard protocols, all the patients were examined after 12 hours overnight in a fasting state and in a temperature-controlled room. Brachial blood pressure was measured in supine position at the right brachial artery, for each patient, after 30 minutes of rest, and expressed as the mean value of 3 measurements over a period of 30 minutes. Mean arterial blood pressure was calculated as (2 diastolic pressure + systolic pressure) / 3.

Endothelium-dependent, flow-mediated vasodilatation (FMD) was determined by high-resolution ultrasound of the brachial artery and was performed, based on the literature data[12]. We used for measured the brachial artery diameter a Philips ATL, HDI 3000 medical system, a high-resolution ultrasonography system, equipped with a 7.5 MHz transducer. Measurements of flow mediated vasodilatation were obtained at 09:00 AM — at baseline, after at least 20 min of resting in the supine position under the following conditions: a quiet room with the temperature between 21-23°C and 12 h without caffeine, smoking, no exercise, food or any vasoactive drugs, 12 hours prior to investigation**.**

We scanned the brachial artery transversal and then longitudinal. Measurements were obtained approximately 5cm proximal of the antecubital fossa. A view of a 5-cm longitudinal section of the brachial artery was recorded on S-VHS for 30 s at baseline, before and during highest value due to reactive hyperemia (induced by deflation of a blood pressure cuff previously inflated to 50 mm Hg over the patient's systolic blood pressure). Endothelium-dependent, flow-mediated dilation (FMD) was calculated using the maximum percent change in diameter, 1 min after the cuff deflation and relative to the first diameter measured before cuff deflation.

In accordance to the literature data[12], we considered that the vasodilation which depend of endothelium is "normal" when the response at the brachial artery was an vasodilatation > 10% relative to baseline diameter and the vasodilation which depend of endothelium is "impaired" when the response at the brachial artery was an vasodilatation < 10% relative to baseline diameter. Flow mediated vasodilatation was expressed as the relative increase in brachial artery diameter during hyperemia and was defined by a mathematical formula: [(diameter during peak reactive hyperemia – baseline diameter) / baseline diameter] x 100 %. Endothelium-dependent, flow-mediated vasodilatation was performed for each patient at baseline visit. For each patient we performed 2 measurements by a single dedicated physician.

Carotid intima-media thickness of the common carotid artery was determined as an index of structural lesion by atherosclerosis, at

baseline visit in both carotid arteries, as agreed in the Mannheim consensus[13], with a Philips ATL, HDI 3000 medical system, a high-resolution ultrasonography system, equipped with a 9 - Mhz linear array transducer. The carotid arterial scanning was performed by a certified sonographer. All the patients were examined in a supine position. The intima-media thickness was calculated online by built-in software of the ultrasound system. The mean values of carotid IMT was calculated for each patient of the four measurements sites.

For each patient we performed 2 measurements by a single dedicated physician. The reference values for carotid artery intima-media thickness were considered normal values if they were ≤ 0, 9 mm and the increased values for all carotid artery intima-media thickness value were > 0, 9 mm.

Laboratory analyses

Venous blood samples were taken with the each patient after 12 hours overnight fast, in the morning, in the supine position. Venous blood samples were collected after 15 minutes of rest immediately placed on ice and was drawn for glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides. All these laboratory analyses were measured by standard haematology and serum biochemistry tests, inside the hospital, using certified assays. Total cholesterol > 200 mg/dL, LDL-cholesterol > 140 mg/dL, HDL-cholesterol < 40 mg/dL and triglyceride levels > 150 mg/dL were considered as dyslipidemia**.**

Plasma levels of high-sensitivity C-reactive protein (hs-CRP) were measured within the Laboratory Bioclinica SA, Timisoara through a highly sensitive quantitative immunoturbidimetric method, using a commercial CRP Ultra kit, distributed by Abbott Diagnostics. For this ultrasensitive method the lowest detection limit was 0, 01 mg / dL.

We determinate in all of them the circulating cellular adhesion molecules (ICAM-1 and P-selectin) levels which were measured in duplicate by commercial ELISA kits (manufactured by R & D Systems Inc., Minneapolis, USA) according to the manufacture's instructions in the Laboratory Bioclinica SA, Timisoara. The references values for cell adhesion molecules were set at 98,8 – 320 ng/ml for sICAM-1 and 51 – 113 ng/ml for sP-selectin for both males and females and for all age groups (patients older than 18 years).

Statistical analyses

For each group, the results are expressed as mean ± standard deviation (SD). Pearson correlation coefficient (r) test was used to calculate correlation coefficients. Linear regression analysis was performed to investigate the association between plasma sICAM-1, sP-selectin and hs-CRP levels and respectively % FMD and carotid IMT for each group. An adjusted value of $p < 0, 05$ was considered to be statistically significant (S) and the value of $p > 0, 05$ was considered to be statistically insignificant (NS).

RESULTS

During the initial phase, depending on the severity of vascular damage and respectively the values of carotid IMT, the patients were divided into three groups: the first group consisted of 26 (38,24 %) hypertensive patients with endothelial dysfunction and elevated values of carotid IMT (> 0,9 mm), the second group consisted of 27 (39,71 %) hypertensive patients with endothelial dysfunction and normal values of carotid IMT (≤ 0,9 mm) and the last group consisted of 15 (22,05 %) hypertensive patients without endothelial dysfunction and normal values of carotid IMT (≤ 0,9), which represented the control group.

The demographic, hemodynamic and humoral data for all the patients at admission in study are reported in table 1. Related to all demographic and blood pressure parameters were no significant difference between the first two groups (p> 0, 05). Also, a similar situation if we compare the three groups of patients depending on their mean plasma levels to LDL-cholesterol, HDL-cholesterol, triglycerides and glucose, no significant statistical difference in (p> 0, 05).

Plasma levels of hs-CRP, ICAM-1 and P-selectin

By analyzing the data in the table, we observed that the patients in the first and the second groups had significantly higher mean values of sICAM-1 plasma levels (380 ± 29 respectively 334 ± 12) and hs-CRP (4, 31 ± 1, 13 respectively 3, 32 ± 0, 26) as compared with the control groups (227 ± 17 respectively 1, 91 ± 0, 20). If we analyze the mean values of sP-selectin plasma levels observed higher levels for the first group (134 ± 20) compared also

with the second and the third groups (88 ± 17 respectively 68 ± 15, p < 0,001) with normal values.

Endothelial function

If we compared the three groups of patients, at baseline, we observe that the patients in the first group, with increased values of carotid IMT, had a statistically significant decrease of endothelium dependent FMD (5, 6 ± 1, 8) in comparison to the patients belonging to the second and third groups (7, 15 ± 2, 3; 12, 8 ± 1, 6; p < 0,001), with values of carotid IMT normal.

Table 1. *Demographic, hemodynamic and humoral data of patients*
Results are presented as mean ± standard deviation for each group of patients

Patients characteristics	Group I HTA with ED and carotid IMT increase	Group II HTA with ED and carotid IMT normal	Group III HTA without ED and carotid IMT normal
No	26	27	15
Sex			
• male	15 (57, 69%)	15 (55, 55%)	8 (53, 33%)
• female	11 (42, 31%)	12 (44, 45%)	7 (46, 67%)
Age years			
• range	35 - 67	47 - 65	38 - 66
• mean ± SD	51 ± 7	56 ± 6	52 ± 8
Heart rate (beats / min)	78 ± 6	72 ± 5	78 ± 5
Systolic pressure (mmHg)			
• range	150 - 179	141 - 169	141 - 159
• mean ± SD	164 ,5 ± 5,61	155,00 ± 4,33	150,05 ± 3,67
Diastolic pressure (mmHg)			
• range	95 - 115	90 - 110	90 - 105
• mean ± SD	105,30 ± 4,15	103,10 ± 3,55	97,50 ± 3,05
Total cholesterol (mg/dL)			
• range	210 - 240	210 – 230	180 -220
• mean ± SD	223 ± 5,55	218 ± 4,85	200 ± 3,15
LDL (mg/dL), range	115 - 125	110 - 120	110 - 115
HDL (mg/dL), range	35 - 45	42 - 55	56 - 60
Triglycerides (mg/dL)	133 - 145	131 - 140	112 - 130
Glycemia (mg/dL) mean ± SD	88 ± 5,5	82 ± 3,16	78 ± 6,21
Smokers %	25%	12%	7%
hs-CRP (mg/L)			
• range	3 - 10	1 - 5	1 - 3
• mean ± SD	4,29 ± 1,18	3,47 ± 0,52	1,91 ± 0,25
sICAM-1 (ng/mL)			
• mean ± SD	387,23 ± 19,40	341,74 ± 14,24	227,33 ± 12,59
sP-selectin (ng/mL)			
• mean ± SD	134,23 ± 9,09	89,41 ± 9,40	68,13 ± 9,66
Flow-mediated vasodilatation %			
• mean ± SD	5,6 ± 0,93	7,14 ± 1,03	12,63 ± 1,12
Intima-media thickness (IMT) (mm)			
• range	1,0 – 1,3	0,6 – 0,9	0,5 – 0,8
• mean ± SD	1,15 ± 0,09	0,75 ± 0,09	0,63 ± 0,11

Carotid artery structure

Related the carotid artery structural changes, the mean values of carotid IMT, its distribution in the study group is as follows: in the third group of hypertensive patients, without endothelial dysfunction, the mean value of carotid IMT was between normal limit (0,5 – 0,8 mm; 0,56 ± 0,04), for the second group of hypertensive patients with endothelial dysfunction the mean value of carotid IMT were also between normal limit (0,6 – 0,9 mm; 0,75 ± 0,14) but for the first group of hypertensive patients with endothelial dysfunction the mean value of carotid IMT was higher than normal value (1,0 – 1,3 mm; 11,15 ± 0,22). This value, for the first group, was significantly higher compared with the other two groups ($p < 0,001$). For the mean values of carotid IMT of groups 2 and 3 were no significant differences ($p > 0, 05$).

Correlations

Comparing the sICAM-1 plasma levels in all three groups with %FMD, at baseline, was observed a high negative correlation between these parameters for all the groups (for the first group r = - 0, 8591, being higher for second group r = -0, 9579 and for the third group r = - 0, 9763) (fig 1).

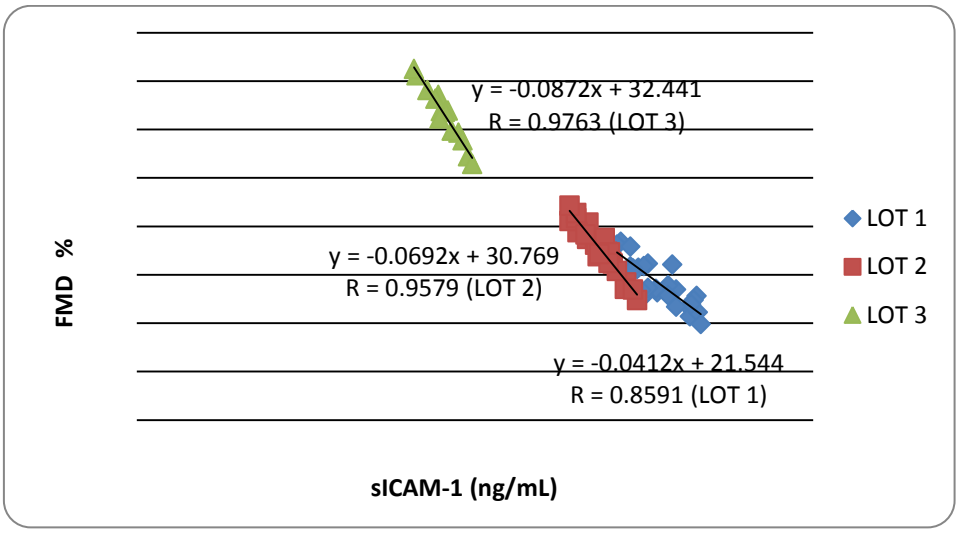


Fig. 1. Correlations between ICAM-1 plasma levels and % FMD at baseline in all groups

If we compared the sICAM-1 plasma levels in all three groups with the values of carotid IMT, at baseline, was observed a high significantly correlation between these parameters for all the groups (for the first group r = 0, 9267, being higher for second group r = 0, 8787 and for the third group r = 0, 9041) (fig 2).

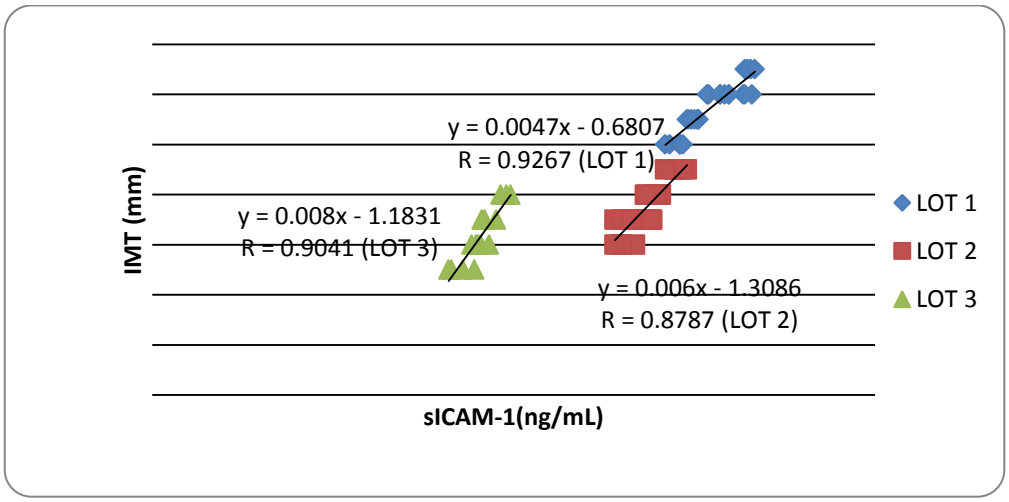


Fig. 2. Correlations between ICAM-1 plasma levels and carotid IMT at baseline in all groups

Comparing the sP-selectin plasma levels in all three groups with %FMD, at baseline, was observed a high negative correlation between these parameters for all the groups (for the first group r = - 0, 7331, being higher for second group r = - 0, 9316 and for the third group r = - 0, 9460) (fig 3).

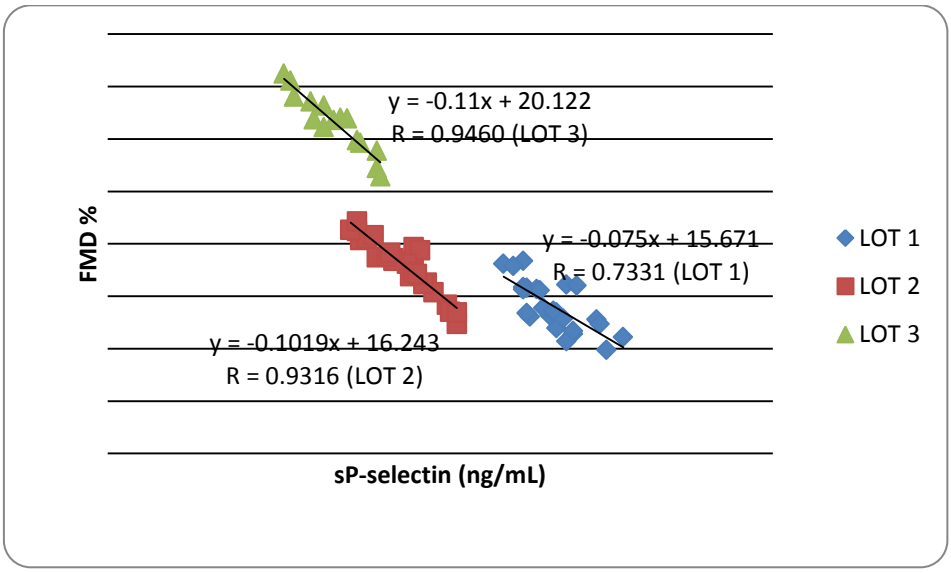


Fig. 3. Correlations between P-selectin plasma levels and %FMD at baseline in all groups

If we compared the sP-selectin plasma levels in all three groups with the values of carotid IMT, at baseline, was observed a high significantly correlation between these parameters for all the groups (for the first group r = 0, 8314, being higher for second group r = 0, 9171 and for the third group r = 0, 9188) (fig 4).

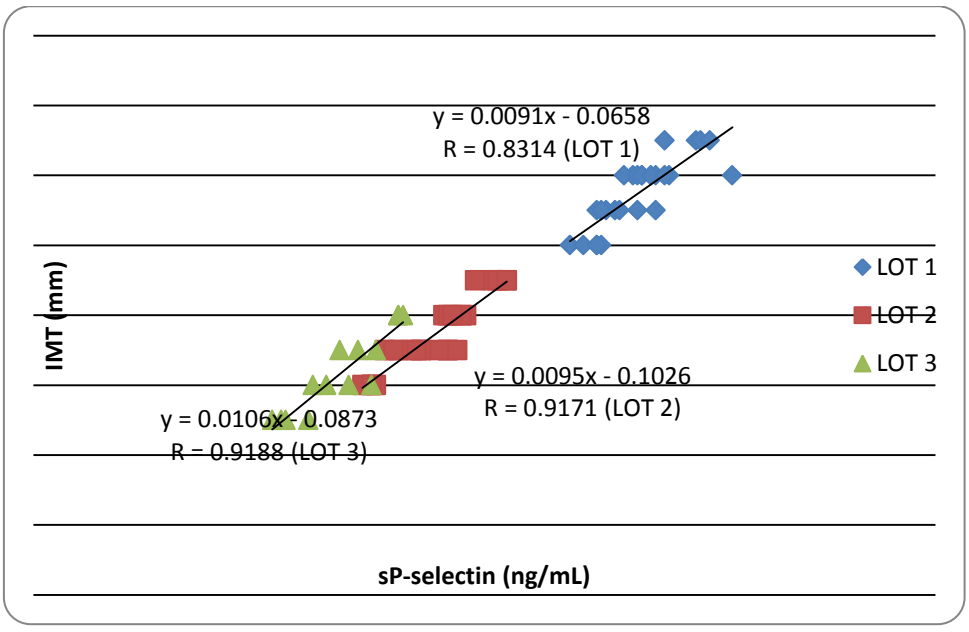


Fig. 4. Correlations between P-selectin plasma levels and carotid IMT at baseline in all groups

Comparing the hs-CRP plasma levels in all three groups with %FMD, at baseline, was observed a high negative correlation between these parameters for all the groups (for the first group r = - 0, 8668, being higher for the second group r = - 0, 9117 and for the third group r = - 0, 9421) (fig 5).

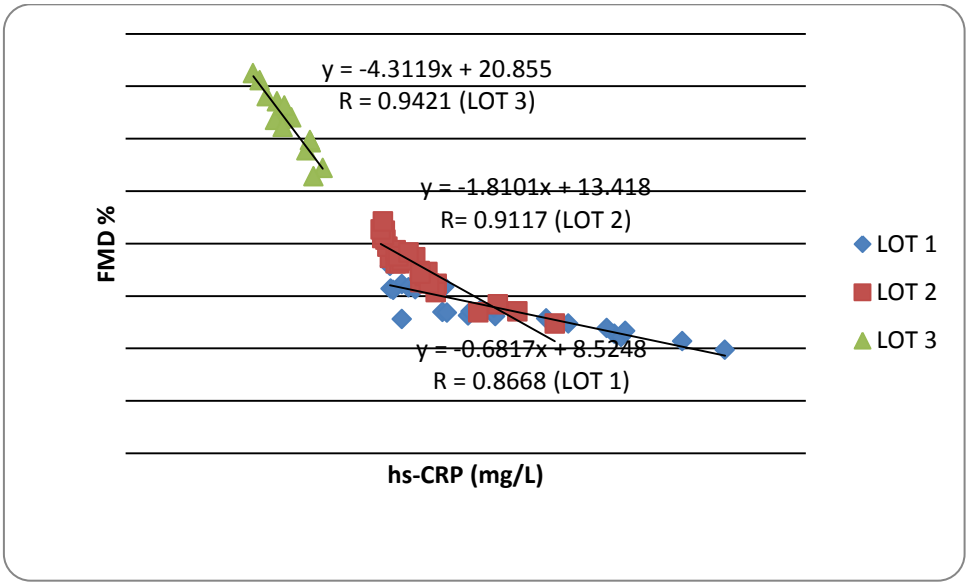


Fig. 5. Correlations between hs-CRP plasma levels and % FMD at baseline in all groups

If we compared the hs-CRP plasma levels in all three groups with the values of carotid IMT, at baseline, was observed a high significantly correlation between these parameters for all the groups (for the first group r = 0, 6543, for second group r = 0, 8467 and for the third group r = 0, 7964) (fig 6).

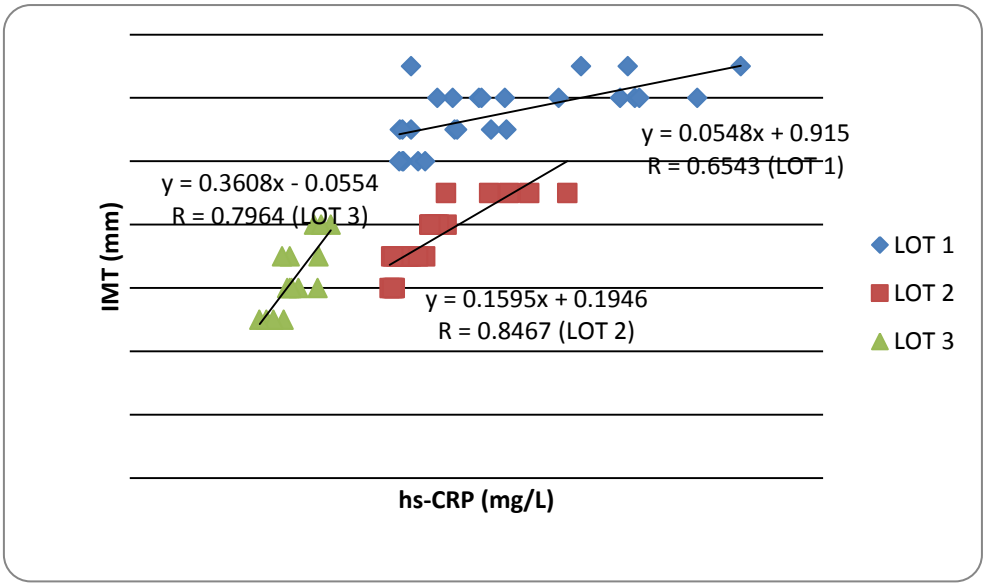


Fig. 6. Correlations between hs-CRP plasma levels and carotid IMT at baseline in all groups

DISCUSSION

There are principal new findings in this study. For the first time, this study has simultaneously evaluated indices of endothelium function and carotid artery structure and their relationship with circulating levels of adhesion molecules. A significant negative correlation between ICAM-1 plasma levels and %FMD and respectively a significant positive correlation with carotid artery IMT were observed, thus suggesting the presence of inter-relations between adhesion molecules and early functional and structural changes in all arterial territories. That relationship makes it possible to reveal the clinical consequences in terms of evolution the atherosclerotic lesions. These results were in according to literature data[14].

Secondly, evaluating the endothelial production of ICAM-1 observed that the mean values of ICAM-1 plasma levels was negatively correlated with endothelial dependent FMD, possibly direct leading to vascular damage in mild – to – moderate hypertensive patients.

Thirdly, in our study we demonstrated that the plasma levels of P-selectin were significantly elevated in patients with high degree of endothelial dysfunction and high changes in carotid artery structure, the first group, which confers an thrombogenic status on these hypertensive patients. The increased levels of soluble P-selectin is also been associated with the progressive vascular damage in hypertensive patients, in according to literature data[15].

Fourthly, evaluating the endothelial production of P-selectin observed that the mean values of P-selectin plasma levels was significantly and positively correlated with morphological and functional parameters of atherosclerosis process, in according to literature data[16].

Fifthly, in the study the mean values of hs-CRP were significantly increased in the patient of the first and the second groups signifying the presence of a mild – to – moderate grade of inflammatory process. Our findings are in according by Sesso et al results[17], which showed that there is a link between elevated CRP and increased risk of developing hypertension with all complication related to this.

Study limitations

We studied a small and highly selected population of patients with essential hypertension which did not permit the establishment of a causal relationship of the described associations. This limit could be seen in our very strong correlation result between inflammatory parameters and values of parameters of endothelial dysfunction. In the further study we are planning to evaluate a large number of patients, in order to have the same correlation value with a high sensibility of p values.

CONCLUSION

Patients with mild – to – moderate essential hypertension and without other risk factors of atherosclerosis have been show to have elevated plasma levels of intercellular cell adhesion molecule-1, P-selectin and hs-CRP. Increased levels of ICAM-1 and P-selectin acts as markers of endothelial dysfunction in patients with essential hypertension.

High ICAM-1, P-selectin and hs-CRP plasma levels was observed and significantly positively correlated with structural changes in carotid IMT and negatively correlated with functional changes in endothelium dependent FMD, in mil – to – moderate essential hypertension

Conflict of interest: none

REFERENCES

1. Whelton PK. Epidemiology and the Prevention of Hypertension. J Clin Hypertens 2004; 6: 636-42

2. Maria Suciu. The role of nitric oxide (NO) and statins in endothelial dysfunction and atherosclerosis. Farmacia, 2009; vol 57, 2 : 131-140

3. LI Jian-jun. Inflammation in hypertension: primary evidence. Chin Med J 2006; 119: 1215-21.

4. Andor Minodora, Tomescu Mirela. Endothelial dysfunction – Methods of assessment and pharmacological approach in cardiovascular disease. Timisoara Medical Journal 2005, vol 55, no 1, p 58 - 63

5. Chae CU, Lee RT, Rifai N, Ridker PM. Blood pressure and inflammation in apparently healthy men. Hypertension 2001;38:399–403.

6. King DE, Egan BM, Mainous AG 3rd, Geesey ME. Elevation of Creactive protein in people with prehypertension. J Clin Hypertens (Greenwich) 2004; 6: 562-8

7. Bermudez EA, Rifai N, Buring J, Manson JE, Ridker PM. Interrelationships among circulating interleukin-6, C-reactive protein, and traditional cardiovascular risk factors in women. Arterioscler Thromb Vasc Biol 2002;22:1668 –73.

8. Lu Wang, JoAnn E. Manson, J. Michael Gaziano, Simin Liu, Barbara Cochrane, Nancy R. Cook, Paul M Ridker, Nader Rifai, and Howard D. Sesso. Circulating Inflammatory and Endothelial Markers and Risk of Hypertension in White and Black Postmenopausal Women. Clinical Chemistry 57:5, 729–736 (2011)

9. Chrysohoou C, Pitsavos C, Panagiotakos DB, Skoumas J, Stefanadis C. Association between prehypertension status and inflammatory markers related to atherosclerotic disease: The ATTICA Study. Am J Hypertens 2004; 17: 568-73.

10. Claudio Ferri, Giovambattista Desideri, Marco Valenti, Cesare Bellini, Mehtap Pasin, Anna Santucci and Giancarlo De Mattia. Early Upregulation of Endothelial Adhesion Molecules in Obese Hypertensive Men. Hypertension. 1999;34:568-573

11. Kavita K Shalia, Manoj R Mashru*, Jagdish B Vasvani*, Rajashree A Mokal, Shilpa M Mithbawkar and Priti K Thakur. Circulating levels of cell adhesion molecules in hypertension. Indian Journal of Clinical Biochemistry, 2009 / 24 (4) 388-397

12. M. C. Corretti, T. J. Anderson, E. J. Benjamin et al., "Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the international brachial artery reactivity task force," *Journal of the American College of Cardiology*, vol. 39, no. 2, pp. 257–265, 2002.

13. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, Csiba L, Desvarieux M, Ebrahim S, Fatar M, Mannheim Carotid Intima-Media Thickness Consensus (2004 – 2006). An Update on Behalf of the Advisory Board of the 3rd and 4th Watching the Risk Symposium 13th and 15th European Stroke Conferences, Mannheim, Germany, 2004, and Brussels, Belgium, 2006. Cerebrovasc Dis. 2006; 23: 75– 80.

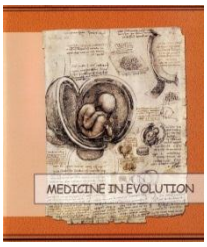
14. van der Meer I et al. Inflammatory mediators and cell adhesion molecules as indicators of severity of atherosclerosis. Arterioscler Thromb Vasc Biol 2002; 22: 838–842.

15. Verhaar MC, Beutler JJ, Gaillard CA, et al: Progressive vascular damage in hypertension is associated with increased levels of circulating P-selectin. J Hypertens 1998; 16: 45−50.

16. Hidenori Koyama, Takaaki Maeno, Shinya Fukumoto et all. Platelet P-Selectin Expression Is Associated With Atherosclerotic Wall Thickness in Carotid Artery in Humans. *Circulation.* 2003;108:524-529;

17. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-Reactive Protein and the Risk of Developing Hypertension. JAMA 2003; 290: 2945-51.

PHARMACOECONOMICS EVALUATION AS A MEANS OF MANAGING THE HEALTH CARE SYSTEM



LIANA SUCIU[1*], MIRELA TOMESCU[2], CARMEN CRISTESCU[1], MARIA SUCIU[1], MIRELA VOICU[1], RALUCA GRĂDINARU[1]

[1] University of Medicine and Pharmacy "Victor Babes", Faculty of Pharmacy, Department of Pharmacology-Clinical Pharmacy, Timișoara
[2] University of Medicine and Pharmacy "Victor Babes", Faculty of Medicine, Department of Internal Medicine, Timișoara

ABSTRACT

The pharmacoeconomics is a field of economy specific to the health care system that assesses costs, available for various types of drug therapies in relation to benefits.
It helps the decision makers to choose a regimen upon two criteria not taken into account in clinical trials: efficiency and the "well-being" as perceived by the patient.

This paper aims at covering the pharmacoeconomical analysis methods with the specific features of each method, their practical applicability, potential benefits afforded by these tests, with certain extents where they should be improved.

We conclude that these tests help health fund providers (Ministry of Health, National Health Insurance Fund, etc.), drug manufacturing companies, medical professionals and not least patients who should receive effective, safe, affordable medication for quality of life improvement.

Keywords: *pharmacoeconomics, costs, QALY, modeling, discount rate, uncertainty assessment*

Correspondence to:

Dr. Liana Suciu, Drd. UMF Timișoara
Adresa: str.Bujorilor, nr.132 A, 300431, Timișoara, Romania
Email: lianads@yahoo.com

INTRODUCTION

Providing medication to population is a priority for the Romanian Government due to the social importance of this area, and the very important impact played in the national economy.

The entry on the Romanian market of the international product providers, put pressure on expenditure on medicines and it has increased every year in order to reach the European level of health care available in other EU member states.

During 1995-2005, the countries of the Organization for Economic Cooperation and Development (OECD) met an annual average increase per capita in health of 4%, exceeding the economic growth of only 2.2% on the same period. (Steven Simoens Health Economic Assessment: A methodological primer Int. J. Environ. Res. Public Health 2009, 6, 2950-2966). [1]

This growing phenomenon has objective causes. Consumption of drugs is influenced by several factors:

- The current state of knowledge on diseases' treatment;
- Habits of the population on the use of drugs;
- Economic power of society and the individual;
- The organizational structure of the hospital;
- The medical staff available within the health unit or territory. Besides these factors, whose influence is difficult to quantify others are added, standing for the two main "arms" of competitors in the fight for funding:

- The drug industry, strongly oriented towards profit, is using access to the medical information as the main marketing tool;
- The people in charge for managing public funds within the health care system (Health Insurance Fund, Ministry of Health and Ministry of Finance). They have the opportunity to gauge distribution and drug prescribing activity and especially to control the health care system.

After years of increasing financial expenses related to the drug product, 2011 was the first year to record a "drop" in growth below a 10% threshold. Romanian Government has introduced several measures in recent years aimed at reducing these costs. The most notable of these were:

Price cuts imposed on import drugs (basically the EU minimum level);

- Amendment of margins;
- Negotiation of margins charged by pharmacies on drug products prescribed within national programs;
- Introducing reference price on therapeutic classes.

The data show that these measures have failed - the drug industry managed to sell more than the amounts allocated from public funds for this type of expenditure, exceeding the imposed threshold. [1]

Definition of pharmacoeconomics

"Pharmacoeconomics" – stands for implementation of economic assessment methods of health programs for interventions that include pharmaceutical products. [2, 3]

"Economic evaluation" includes:

1) comparative analysis of therapeutic protocols in terms of costs and consequences;
2) a set of quantitative formal methods used to compare each alternative medical strategies included in a therapeutic protocol.

A pharmacoeconomic study aims to:

a) Implementation and development of methods of economic evaluation in the health care field by using sound
and transparent criteria for different treatment regimens;

b) Validation of clinical trials. Currently, clinical trials are based on assessing the efficacy and safety of the treatment, but over time, data on costs and the amount to be refunded before the product is released will be required by the assessment entities. Modeling programs allow evaluation shortened, the financial investments being lower for those conducting clinical trials.

c) Assessment of patient needs by:

- Assessing the acceptability of a therapeutic strategy recommended by doctors;
- Assessment of the impact of a therapeutic protocol on a patient's comfort level (by assessing the number of years of life saved or quality of life years gained from following medical procedures).

d) Establishment of treatment algorithms including a pharmacoeconomic analysis;
e) Development of economic evaluation guidelines to facilitate pharmacoeconomic analyses. [4, 5]

Types of costs used in the pharmaeconomical analyzes

A pharmaeconomical analysis is initially conceived to assess costs. They should be valued according to the mobilization of financial, material and human resources. The payer may be: the health insurance fund, the patient or costs can be measured from society's point of view. The payer's "point of view" should be noted before initiating cost assessment.

Classically we can distinguish the following types of costs:

1. ***Direct costs*** include the total amount of amounts consumed directly for the care of a patient. They are:

• *Direct medical costs*, include costs related to:

- hospitalization;
- medical and paramedical care granted;
- prevention and rehabilitation services;
- investigations performed;
- special equipment;
- prescribed drugs for therapeutic, prophylactic or correction purpose, and all that entails prevention and treatment of unwanted effects, dose formulation and administration, supervision of therapy.

• *Direct non-medical costs* include:

- patient transportation costs towards sanitary locations;
- patient's home adaptation costs in the event of disability;
- expenses related to care provided by the family, childcare sickness

2. ***Indirect costs*** refer to the economic consequences due to the loss of employment or cessation of professional activity of the patient.

3. ***Total cost*** stand for to the sum of direct and indirect costs.

4. ***Intangible costs*** are those costs incurred on human and psychological perspective with negative impact on the wellbeing of the patient of as result of the existence of a condition. Following a chronic illness they may lead to a state of anxiety, depression, family disorganization, physical and / or social dependence, etc.These costs are difficult to assess and return.

5. ***Incremental costs*** are additional costs incurred as a result of therapeutic intervention or medicinal pharmacotherapy that is required in place of another. Additional cost characterizes an additional effect, a result or an advantage achieved through the new intervention. This type of cost provides another way to assess the pharmacoeconomical impact of a medical service or of a treatment option. [3, 6, 7]

6. Types of pharmacoeconomical analyses

a) Cost of illness

This assessment identifies and estimates the total cost of a disease for a well-defined sample population. It involves measuring the direct and indirect costs that correspond to specific pathologies. For example in the U.S., costs for diabetes, mental illness, cancer have already been estimated. By identifying the costs of a disease one can determine the relative value of treatment or disease prevention strategy.

This type of analysis is not used to compare alternative regimens of the same pathology but to provide an estimate of costs of the disease. This evaluates the financial value of prevention and treatment strategies versus cost of the disease.

b) Cost-minimization analysis of the disease

The analysis involves assessing the cost of several therapeutic strategies in order to identify the cheapest one. In this case, the types of drug strategies must be equivalent in efficacy and safety. The costs are to be compared in monetary units.

It is the simplest form of economic evaluation and it applies to two or more equivalent therapeutic agents or to compare different doses of the same drug. This type of analysis is used on the market due to the existence of a large number of medicines called "me too", which belong to the same class of drugs, being different active substances produced by different drug plants, but with similar pharmacological properties or due to the emergence of a variety of generics on the pharmaceutical market.

c) Cost-advantage analysis

In this type of analysis, both costs as well as consequences of therapeutic strategy are measured in monetary terms.
Although favored by economists, using this type of analysis in health care is problematic because it is difficult to assign to a monetary value a clinical consequence, such as avoiding a heart attack or appearance of a major physical disability.
The Cost-advantage analysis can be used for setting macroeconomic policies relating to health programs. For example, an immunization program conducted at national level can be assessed in terms of costs by assessing the resources used to conduct this program. Later, results will be compared with data on mortality and morbidity arising from the implementation of this program on a specific area of the pathology.
This type of analysis can evaluate therapeutic strategies with different goals because all benefits are converted into monetary value.

Table1. *Example of cost – advantage analysis*

	Drug A	Drug B
Costs:		
• Costs of purchasing D and medical devices	300	400
• D Administration	50	0
• Monitoring drug therapy	50	0
• Prevention and treatment of adverse effects post medication	100	0
Subtotal	500	400
Advantages:		
• Number of days of work earned (dollars)	1000	1000
• Months of Life gained (dollars)	2000	3000
Subtotal	3000	4000
Cost – advantage report	3000/500=6:1	4000/400=10:1
Net Benefit	2500	3600

Cost-effectiveness analysis aims at comparing two or more drug strategies that have the same clinical outcome measured in physical units, eg: number of years of survival gained, number of avoided physical handicaps or rate of eradication of a bacterial germ.
Two medical strategies considered being similar in terms of availability and clinical tolerability can be selected depending on the financial costs of the therapeutic procedure.
Cost-effectiveness analysis examines the costs associated with obtaining a defined health care outcome. These outcomes can be: removed symptoms of dizziness or vomiting, reducing pain, and cost-effectiveness analysis often uses life years derived from a treatment as a measure of success of a particular program. From here we get a method to compare the costs associated to two or more interventions.
Cost-effectiveness analysis is useful because it provides information to support drug policy, helps prepare documents supporting a patient's medical record and therefore decisions on treatment regimens.
This type of analysis is used indeed to make prescribing guidelines that already exist in countries like UK, Canada, Australia, Italy

***Table 2**. Example of cost effectiveness analysis*

	Drug A	Drug B
Costs:		
• Purchasing costs	300	400
• Administration costs	50	0
• Monitoring	50	0
• Adverse Effects	100	0
Subtotal	500	400
Results measured in years of life gained	1.5	1.6
Cost – effectiveness report	500/1.5=333 dollars per year of life gained	400/1.6=250 dollars per year of life gained

Another method of measuring the impact of health care intervention introduces the concept of utility.

Cost - utility studies are aimed at comparing the costs of a drug strategy to the advantages gained. The advantages or utilities are expressed by the patient's comfort level and preference for the use of a new drug. For example, if a pharmaceutical lab markets an oral insulin drug, with the same efficiency as conventional insulin administered parenterally, it is likely for the diabetic patients to prefer the oral formulation.

Usefulness of certain health conditions are associated with time spent in that state. The number of years spent in that state of health is such calculated. QALY is calculated using utilities derived from health assessment tools. The most used tools to assess health are: EQ-5D and SF-6D. They differ in sensitivity variation of impact on various health issues affecting the individual's quality of life.

The patient's preference is measured by an index that ranges between 0 and 1, where 0 (representing death) and 1 (representing perfect health state). The efficiency of a treatment is measured indeed by the number of years of life gained from therapy applied.

The utility product and years of life gained provide the concept of "quality adjusted life year", so called QALY (Quality Adjusted Life Year)

***Table 3**. Example for computing QALY*

For therapy A Estimating survival =10 years Estimating the quality of life in relation to the state of ideal health = 0.7 QALY's = 10x0.7 = 7.0	For therapy B Estimating survival = 5 years Estimating the quality of life in relation to the state of ideal health = 0.5 QALY's = 5x0.5 = 2.5
QALY gained for therapy A = 7-2.5 = 4.5 QALY's	

If the price of therapy A is of $ 18,000 and of therapy B is $ 4000 per QALY, the price per QALY gained is of 18000/4.5 = $ 4,000 / year of life gained by therapy A. [6]

The main result of cost-utility analysis is the cost per year of quality life gained or ICER (incremental cost-effectiveness report). ICER computes the expected cost difference for two types of treatment or interventions divided by

the difference in years of life gained for such intervention.
The results obtained from this analysis were compared with a threshold value of ICER. If, by the payer's point of view these have a value less than or equal to the respective investment threshold these may be taken into account, but if these are above this threshold it is not a worth taking investment. [2, 3, 6, 7, 9, 10, 11].

Cost-effectiveness incremental report = (the costs of therapy A - the costs of therapy B)

(Advantages of therapy A - advantages of therapy B)

The modeling is based on sketchy descriptions of reality the so called "models". Increasingly widely used, modeling allows the formulation of complex problems such as a history of a chronic disease under a certain treatment and its evolution according to the treatment used.

A Modeling is useful when:
• The study of population is impossible as it requires a large number of subjects and a long time (decades);
• Repeated simulations are needed to verify the impact of a single factor (environmental, dependent on the patient or his affection) on therapeutic outcome;
• The need for fast results for decision taking without being able to afford to wait for the findings of a prospective study.

Examples of modeling: Markov chain method or Monte Carlo method. [2, 3, 9].

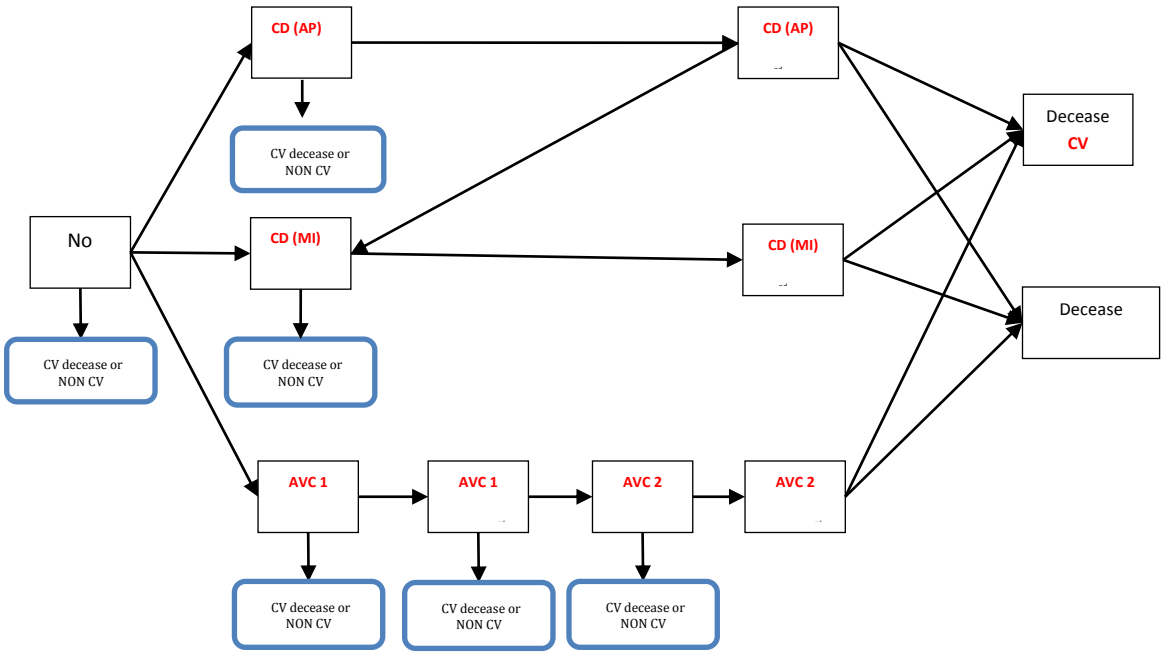


***Fig.1 Markov** prediction model of coronary heart disease*
CD: Coronary Disease; AP: angina pectoris; IM**:** myocardial infarction**;** AVC: stroke

5. The discount rate

All benefits and costs that are assessed at a particular moment in time should be adjusted to reflect the monetary value that can be compared over time. This can be done by converting the time value of money into a present value using an interest rate called the "discount rate".

Because there is always a time difference between investing resources in health care and benefits showing up, all expenses must be discounted to equalize the effects of inflation over a long period of time.

NICE (National Institute for Health and Clinical Excellence, UK) recommends a discount rate of 6% for costs if the assessment exceeds one year timeframe and for benefits a discount rate of 1.5%. [6, 11].

6. Evaluation of uncertainty

The clinical trials' main objective is to determine the efficacy and safety of a therapeutic protocol. Health economy is more interested in evaluating the effectiveness of therapeutic protocol, meaning what benefits and costs are associated with the administration of new therapies, or how it is used in practice where patients are often difficult to monitor and frequently, comparative parameters are not those used in clinical studies.

So far we have little data on the effectiveness of a therapeutic protocol and we are forced to make assumptions in the absence of concrete informations.

Economic studies are testing these assumptions through sensitivity analysis. The analysis assesses the limits where a conclusion is dependent on an assumption, e.g. a study assumes that a coronary accident rate is 5% for high blood pressure and coronary artery disease patients in a year. What happens if this rate is different in practice? This could change the outcome of the study.

These assumptions must be reasonable and transparent in order to be valued in practice and for the assessment results to be robust despite changes in assumptions. [2, 6].

7. Advantages and limitations of a pharmacoeconomical analysis

The advantages we expect from an intervention can be measured in terms of units:

a) *Natural units*, that are years of life saved, prevented strokes, healing of certain diseases (gastric or duodenal ulcers, skin diseases, eradication of serious infections, etc.);

b) *Utility units*: usefulness translated in economic terms is reflecting satisfaction or welfare of a patient, it assesses the quality of his life and not just the number of years of life gained. Expected utilities can be obtained by direct measurement or by evaluating and comparing them with the literature or expert opinion. The concept of "Quality Adjusted Life Years" - is the most common measure that aims to integrate both quality and quantity of life years lived by a certain person. [6, 8]

The pharmacoeconomical analysis of therapeutic strategies will influence:

A. Medical research by:

• Using modeling methods (Markov, Monte-Carlo, etc) that will allow rapid assessment of the impact the effectiveness of a long term administered therapy but the assessment of the cost / quality of life year (QALY) indeed;

• Forecasting results of clinical trials will lead to shortened clinical research and therefore shortened costs;

B. *Medical practice by***:**

• Understanding the advantages and disadvantages of each method of analysis used for the economic evaluation of therapeutic strategies (cost-advantage analysis, cost-effectiveness, cost-convenience analysis, etc.);

• Improve capacity for objective evaluation of a type of pharmaeconomical analysis with favorable impact on improving and streamlining the analysis models used;

• Facilitate health care team's choice of an economic evaluation protocol based on the patient's clinical context;

C. *The public health system* **by:**

• A judicious and dynamic allocation of financial funds on various fields of pathology, eg oncology, metabolic diseases, HIV, TB infection, etc;

• Preparation and implementation of prescribing guidelines for the entire health system that takes into account not only the

therapeutic efficacy and safety, but also the economic and human aspects;
• Justification of means used to maximize results gained with resources assigned to the health care units;

D. Society

• The openness to new therapeutic strategies;
• By creating a new image of the medical system, which will monitor and advise the patient and his care takers on the implications of therapeutic interventions in human and financial terms.

A pharmacoeconomical analysis may, however, have certain limitations:
• Wrong choice of comparison parameters can lead to uncertainties in the analysis because of the way the prediction model is constructed or the procedures for reporting results;
• Allocate funds for health care directed mainly to short-term investments at the expense of long-term investments that prove most effective in terms of cost;
• Erroneous equivalence of a pharmacoeconomic study by specialist staff with rationalization of costs which leads to rejection of the use of these types of studies by ethical considerations;
• Difficulty in monetary equivalence of the years of life gained as a result of therapeutic interventions;
• Evaluation, often subjective, of the 'wellbeing' by the patient, which can influence the final result;
• Momentary lack of explicit guidelines for pharmaeconomical analysis, implementation and evaluation of it in the medical and pharmacotherapeutic fields.

CONCLUSION

Following the evaluation of the advantages and limitations posed by a pharmacoeconomic study we can conclude that:
Implementation of economic evaluation methods are needed and welcome for the healthcare system decision-makers because they provide a financial analysis of therapeutic interventions;

Pharmacoeconomical studies allow decision makers (pharmaceutical industry, Health Insurance Funds, medical professionals) to choose a new therapeutic strategy by clarifying its importance in a particular therapeutic indication, to a specific targeted population, with certain costs;
Certain pharmacoeconomical analyzes contribute to the clinical stages of research through modeling, determining the degree of uncertainty and the impact therapy has on health which is directly evaluated by the patient through specific questionnaires.
Pharmacoeconomical studies alongside the ones examining the clinical efficacy and safety of medical interventions enable comprehensive evaluation of a therapeutic protocol.

Pharmacoeconomics must be seen as a way of rationalizing expenditures on health care and optimization of therapeutic strategies;
As in Romania today there are still insufficient pharmacoeconomical studies additional training for health practitioners in this field is recommended, in order to rationally implement pharmacoeconomical analysis in a therapeutic protocol.

REFERENCES

1. Paveliu S., Aprovizionarea cu medicamente a populatiei - de la contentia costurilor la evaluarea eficacitatii, Eu Ro Comunitatea Medicala, septembrie, 2012;
2. N Arnold R.J.G., Pharmacoeconomics from theory to practice, CRC Press, 2009;
3. Clinical Pharmacy and Therapeutics, Walker R. And Whittlesea C., fourth edition, Churchill Livingstone Elsevier, 2007, Pharmacoeconomics by Cooke J.;
4. Bootman J.L., Townsend R.J., McGhan W.F., Principles of pharmacoeconomics, second edition, 1996;
5. Pradelli L., Wertheimer A., Pharmacoeconomics: Principles and Practice, Kindle Edition, 2013
6. Walley T., Pharmacoeconomics and Economic Evaluation of drug Therapies,
7. Christopher McCabe, What is cost-utility analysis, 2009;
8. Braizer JE, Ratcliffe J, Tsuchiya A, Salomon J. Measuring and Valuing Health benefits for Economic Evaluation;Oxford: Oxford University Press, 2007;
9. McCabe C, Claxton K, Culyer A. The NICE cost-effectivness threshold: what it is and what that means. Pharmacoeconomics 2008; 26: 733-744
10. Fujikawa Keita, Hasebe N., Kikuchi Kenjiro and NICE-Combi study group, Cost-effectiveness analysis of hypertension treatment: controlled release nifedipine and candesartan low dose combination therapy in patients with essential hypertension – The Nifedipine and Candesartan Combination (NICE-Combi) study, Hypertension research 2005, 28, 585-591;
11. Paveliu S., Radu C-P, Tudose F., Tudose C., Arsene A. L., Cost-effectiveness analysis and the concept of quality adjusted life year (QALY) in Romania, Farmacia, 2011, vol.59-3, 304-320.
12. National Institute for Clinical Excellence 2004, Guide to the methods of technology appraisal, London

Digital perfection

Planmeca sets new standards with world's first dental unit integrated intraoral scanner for open connectivity to various CAD/CAM systems.

We would like to invite you to explore the dentistry in new dimensions – see the perfect combination of digital intraoral scan, CBVT and 3D facial photo datasets in one 3D image. This digital perfection enables you to study patient's complete anatomy in detail, plan and utilise open interface with modern CAD/CAM systems according to your needs. Now you can be one of the pioneering specialists, whether you are an implantologist, endodontist, periodontist, orthodontist or maxillofacial surgeon. The new era of dentistry is reality. It's your decision.

Planmeca Oy, Asentajankatu 6, 00880 Helsinki, Finland
tel. +358 20 7795500, fax +358 20 7795 555, sales@planmeca.com, www.planmeca.com

PLANMECA

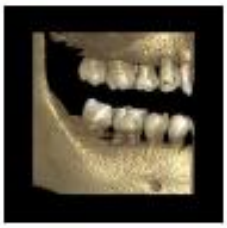
Planmeca ProMax 3D

All volume sizes

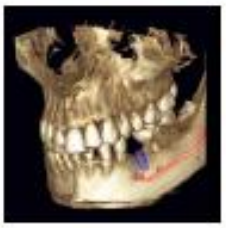
The Planmeca ProMax concept offers a full range of imaging volumes providing detailed information on patient anatomy. The comprehensive Planmeca ProMax platform complies with every need in dental radiology, offering digital panoramic, cephalometric, and 3D imaging as well as 3D face photo together with advanced imaging software.

At the heart of the concept is the robotic SCARA technology: the unique robotic arm enables any movement pattern required by existing or future program, eliminating all imaging restrictions. With the Planmeca ProMax concept superior maxillofacial radiography can be performed with a single platform, today and in the decades to come.

All volume sizes



Planmeca ProMax 3D S
Ø42 x 42 mm–90 x 60 x 110 mm



Ø34 x 42 mm–140 x 105 x 190 mm

Planmeca ProMax 3D

Planmeca ProMax 3D Mid
Ø34 x 42 mm–Ø160 x 160 mm

Planmeca ProMax 3D Max
Ø42 x 50 mm–Ø230 x 260 mm

Planmeca Oy, Asentajankatu 6, 00880 Helsinki, Finland
tel. +358 20 7795 500, fax +358 20 7795 555
sales@planmeca.com, www.planmeca.com

PLANMECA

INSTRUCTIONS FOR AUTHORS

The journal publishes general reviews, studies and clinical, epidemiological, experimental and laboratory research, clinical case presentation, papers from the history of medicine, reviews, scientific and technical state-of-the-art articles, medical informations and opinions. Only papers which have not been published or sent for publishing in other journals are accepted.

The authors are responsable for the opinions expressed in the papers.

The paper must be edited both in Romanian and in English; the English version will be supervised by our collaborator Dana Brehar-Cioflec, MD, PhD; typed on white A_4 paper (fonts - Times New Roman 12, Romanian characters, line spacing 1.5, upper and lower margins 2cm, left border 3cm, right border 2cm) and on CD, DVD or Memory Stick.

Manuscripts will not exceed:

- general reviews: 6-8 pages
- studies and research: 5-7 pages
- case presentations: 2-4 pages
- reviews, scientific and technical state-of-the-art articles, medical information and opinions: 1-2 pages.

The paper will be edited according to international editing rules for manuscripts. The title will be written in capital letters and it will be followed by the name and surname of the author (authors), followed by their place of work (place where the paper has been written). Studies and research will be preceded by a brief abstract, followed by 3-4 key-words.

The body of the paper will be structured in the following sections: introduction, aim, objectives, material and method, results, discussions, conclusions. The references will be presented alphabetically and in conformity to the Vancouver Convention, including:

- for articles: name of the authors and surname initials, title of the article in the original language, title of the journal according to the international abreviation system, year of issue, volume, number, pages;
- for books: name of the authors and surname initials, volume, publisher (editors), city of publishing, year of issue.

Citation of references inside the body of the paper will be put between brackets, Harvard style (author, year) or Vancouver style (number by number in square brackets or superscript). Cited reference titles will be selected, maximum 6 for studies and case presentations and 12 for general reviews. Acceptance, rejection or the need of alterations in sent materials, or in iconography, will be comunicated to the authors in due time. For this, the authors will indicate the person and address for corespondence (phone number, e-mail address). Given the less pleasant experience of the editorial board with some articles being rejected because they did not meet publishing criteria, we decided to support those who intend to publish in this journal by detailing the way such a paper should be elaborated, as well as our requirements.

Except some particular aspects concerning this journal, the following details are general requirements asked or imposed by other journals as well. Conditions to be met in order to propose a paper for publishing. The main author has the responsability to make sure the article has been approved by all the other authors. The journal will have copyright for papers accepted for publishing. The editorial board reservs the right to change the style and dimensions of an article (major changes will be discussed with the main author) and to decide the date of issue.

2. FIRST PUBLICATION

The editorial board will not consider a paper already reported in a published general review or described in a paper proposed to or accepted by another journal. This does not exclude papers which have been rejected by other journals. Also, papers which have been presented at a scientific meeting will be accepted for discussion if they have not been entirely or partially published in a similar publication. „Multiple" publishing of the same study is seldom justified. One of the possible justifications is publishing in a second language but only if the following conditions are met:

- Editors of both journals involved are fully informed;
- Priority of the initial publication will be respected by a minimum publishing interval of two weeks;
- For the second publication, a shortened version will suffice;
- The second version strictly reflects data and interpretations in the first;
- A footnote may state: „This article is based upon a study initially published in [title of the journal]".

3. PATERNITY

Paternity must reflect the common decision of the coauthors. Each author must have participated enough to take public responsability for the content. A paper with collective paternity must have a key person responsable for the article.

4. COPYRIGHT

In order to reproduce materials from other sources, written agreement from the copyright owner must be obtained:

- photographer – for unpublished photographs;
- hospital where the photographer (physician) is employed – for unpublished photographs performed during the employment period;
- initial publisher – for a table, picture or text which have previously been published elsewhere.

5. ETHICAL ASPECTS

Do not use name of patients, initials or hospital observation charts numbers. If a photograph of a body part which could allow direct or deductive recognition of the patient needs publishing, then the paper must be accompanied by the written consent of the patient and clinician, as well.

6. PRESENTING THE MANUSCRIPT

For the journal *„Medicine in evolution"*, the manuscript must be typed double spaced, on white A_4 paper – 210 x 297mm, on one side (2.5cm upper and lower borders, 3cm left and 2cm right border, respectively), in clear characters, no further corrections or addings. It is advisable that articles are presented on CD or other data transfer methods, in Word format, 12 Times New Roman fonts - using Romanian characters – respecting the same page order, accompanied by a printed version. Graphs – black and white or coloured – may be generated in MS Excel or MS Graph, inserted in the body of the paper or presented in a different file.
Infected materials will not be used.

6.1. FIRST PAGE (TITLE PAGE)

Together with the title and names of the authors, the first page must include the affiliation, professional and university degree (if applicable), marked by asterisc for every author; it is advisable to give at least a phone and/or fax number or e-mail address of the first author who may be contacted by the editors for additional recommendations or explanations.

6.2. ABSTRACT OF THE PAPER

6.2.1 Recommendations for original studies

Original studies must include a structured abstarct of maximum 150 words, containing the following titles and informations:

- Aim and objectives;
- Material and methods;
- Results;
- Conclusions;

- Key words: give 3-5 key words;
- The abstract will be translated into an international circulation language.

6.3 CONTENT OF THE PAPER

6.3.1 For original articles

The text will usually be divided into sections:

- Introduction – presentation of general aspects, in the context of the approached theme
- Aim and objectives – Define the aim of the article. Briefly expose the rationale of the presented study or observation. Make strictly pertinent referals and do not exhaustively review the subject. Do not include data or conclusions from the paper.
- Material and methods – Describe the selection of observations or subjects for the experiment (including controls). Identify methods, equipments (with the name and address of the manufacturer in brackets) and give sufficient details on procedures. Give references for the selected methods, including statistical methods; offer details and brief descriptions for previously published methods which are not well known; describe new or substantially modified methods, justify their use and assess their limitations. Precisely identify all used drugs and chemicals, including generic names, dosage and administration ways. Describe statistical methods with sufficient details for reported results to be verified. Whenever possible, quantify discovered aspects and present them with appropriate measurement indicators for the uncertainty or error of measurement (such as confidence intervals).
- Results – Present results in a logical succession as text, tables and illustrations. Emphasize or briefly describe only important observations.
- Discussions – Underline new, important aspects of the study. Do not repeat in detail data which have been presented in previous sections. Include implications of revealed aspects and their limitations, including implications for future studies. Connect your observations to other relevant studies. Relate the results to the aim proposed for the study.
- Conclusions – organize conclusions which emerge from the study. In the end state: a) contributions to be acknowledged but which do not justify paternity right; b) thanks for technical support; c) thanks for financial or material support.

6.3.2 Indications for case reports

Themes may be selected from all medical fields. Manuscripts which offer a special gain for daily activity will have priority. The title must be clearly, precisely stated. It may be completed by a subtitle. It is advisable to include in the key words of the title the main message, the special element which may be

observed from the case evolution. The content of a case report must be divided into three parts:

- Introduction – It must include a maximum of 15 typed rows (half page). Here, the main medical problem is summarized in order to place the case in a specific domain.
- Case report – It contains essential specific information on the case.
- In order to make a logical, chronological and didactical case report the following 5 chapters are needed:
  I. Anamnesis;
  II. Clinical examination data;
  III. Laboratory data;
  IV. Additional paraclinical investigations;
  V. Treatment and evolution.
- Discussions – The reason for the case report must be stated. The report must be patient-centered. Occasional deviations from typical (characteristic) evolutions, nosologically important facts must be presented in such a manner to expose the clinical picture as completely as possible. The case report must not appear as an appendix of a general review. Dimensions of a case report: maximum 6-8 typed pages, 30 rows of 60 characters/page.

6.4. MEASUREMENT UNITS, SYMBOLS, ABREVIATIONS

All measurements must be expressed in International System (IS) units. Abreviations must be fully explained when first used.

6.5. TABLES

Tables are noted with Roman figures and they will have a brief and concise title, concordant with their content.

6.6. ILLUSTRATIONS

Number all illustrations in Arabic figures in a single succession. Apply a label on the back side of every illustration, containing its number and an arrow indicating the upper side. Coloured illustrations may be accepted but it is the choice of the editors, according to particular technical abilities of each journal issue, or it may involve a fee in special cases.

6.7. EXPLANATIONS FOR DRAWINGS AND GRAPHS

Explanation for drawings and graphs must be clear and in readable dimensions, considering the necessary publishing shrinkage.

6.8. PHOTOGRAPHS

Offer glossy, good quality photographs. Any annotation, inscription, etc. must contrast with the ground. Microphotographs must include a scale marker.

6.9. ILLUSTRATION LEGENDS

Include explanations for each used symbol, etc. Identify the printing method for microphotographs.

6.10. REFERENCES

A numbered list of references must be provided at the end of the paper. The list should be arranged in the order of citation in the text of the publication, assignment or essay, not in alphabetical order(according to the Vancouver rules). List only one reference per reference number. It is very important that you use the correct punctuation and that the order of details in the references is also correct.

- Books - Standard format - #. Author of Part, AA. Title of chapter or part. In: Editor A, Editor B, editors. Title: subtitle of Book. Edition(if not the first). Place of publication: Publisher; Year. p. page numbers.
- Journal Articles - Standard format - #. Author of article AA, Author of article BB, Author of article CC. Title of article. Abbreviated Title of Journal. year; vol(issue):page number(s).
- E-Books - Standard format - #. Author A, Author B. Title of e-book [format]. Place: Publisher; Date of original publication [cited year abbreviated month day]. Available from : Source. URL.
- E-Journals - Standard format - #. Author A, Author B. Title of article. Abbreviated Title of Journal [format]. year [cited year abbreviated month day];vol(no):page numbers[estimated if necessary]. Available from: Database Name (if appropriate). URL.
- Internet Documents - Standard format - #. Author A, Author B. Document title. Webpage name [format]. Source/production information; Date of internet publication [cited year month day]. Available from: URL.

7. COPIES FOR PUBLISHING

In order to accelerate publishing, the main author will send a set of printed sheets presenting the final version of the paper, as it will appear in the journal. It is really helpful that texts to be also sent on electronic support, diacritic characters mandatory.

8. REJECTION OF PAPERS

If a paper does not meet publishing conditions, whatever these may be, the editors will notify the first author on this fact, without the obligation of returning the material. Original photographs or the whole material will be returned only if the author comes to the editor and takes them.

Papers submitted for publishing will be addressed to:

Prof. Angela Codruta Podariu, DMD, PhD

Journal Medicine in evolution
Department of Preventive, Community Dental Medicine and Oral Health
Splaiul Tudor Vladimirescu no. 14 A
300041, Timişoara
Phone: 0256-204950
Email: proiectetm@yahoo.com

Dana Brehar-Cioflec, MD, PhD

Institute of Public Health *"Prof. Dr. Leonida Georgescu"* Timişoara
Bd. Victor Babeş no. 16
300226, Timişoara
Phone: 0256-492101
Email: danabreharcioflec@yahoo.com

Order form

☐ Rate 38 Euro (Outside Romania)

☐ Rate 160 Ron(Inside Romania)

The money will be pay in the account: RO80 ABNA 3600 264 1000 89 288 opened at RBS BANK, Timisoara

Name_____

Speciality _____

Adress _____

Phone _____Fax _____Email _____

.....

Order form

☐ Rate 38 Euro (Outside Romania)

☐ Rate 160 Ron(Inside Romania)

The money will be pay in the account: RO80 ABNA 3600 264 1000 89 288 opened at RBS BANK, Timisoara

Name_____

Speciality _____

Adress _____

Phone _____Fax _____Email _____