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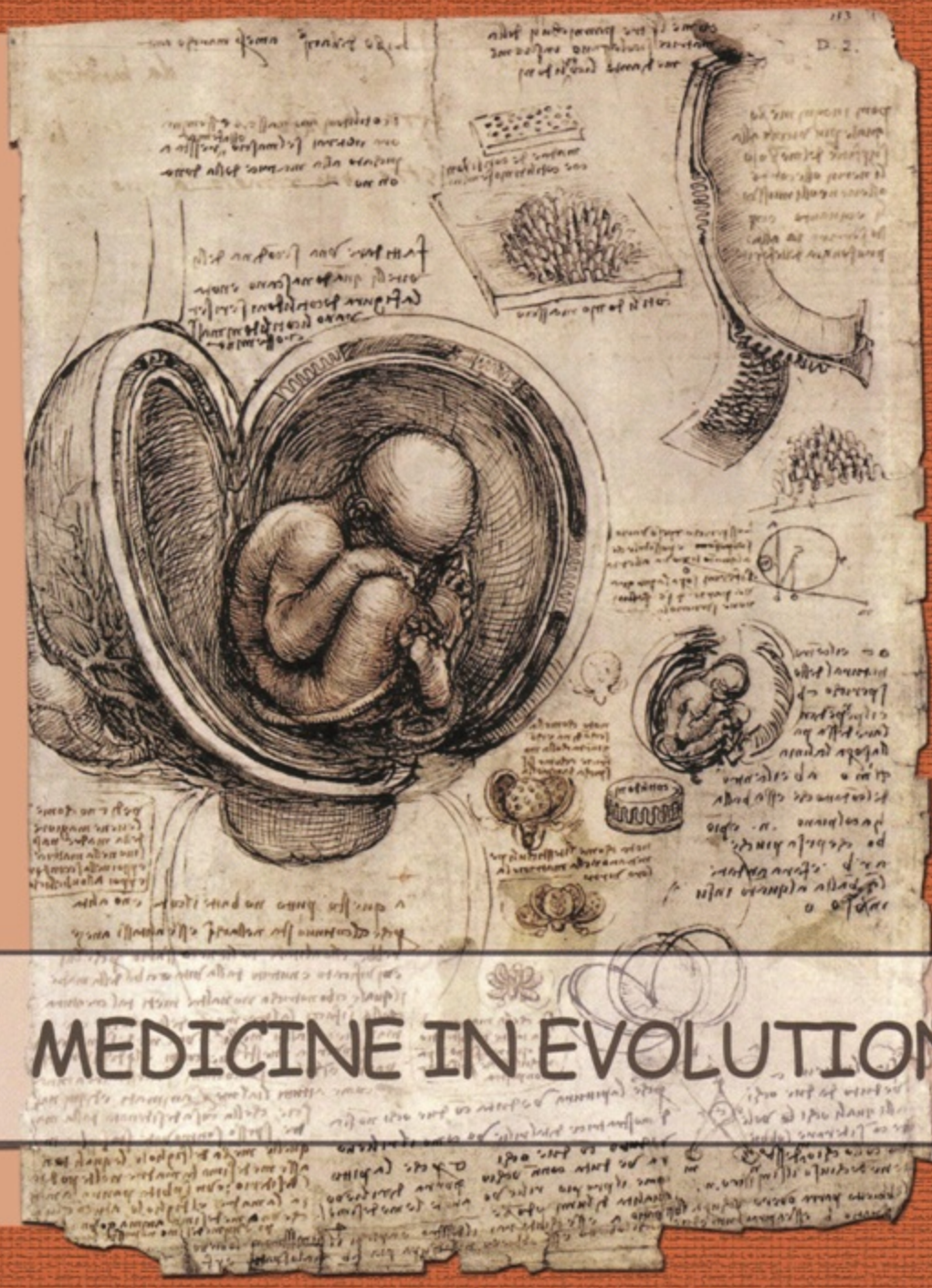

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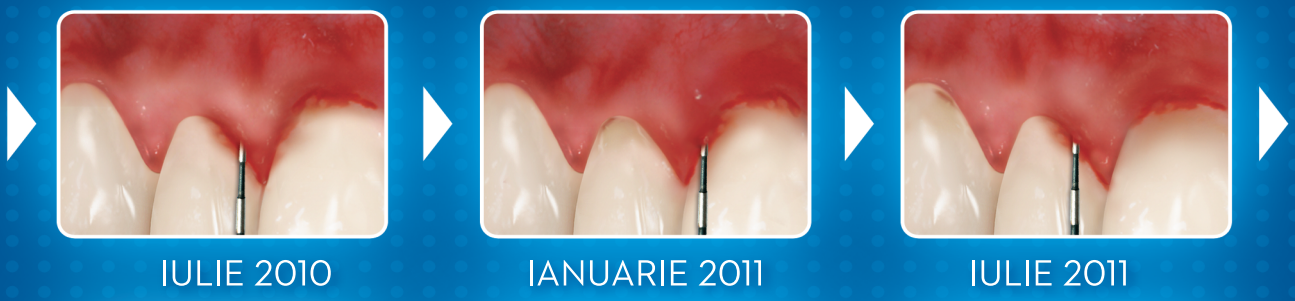

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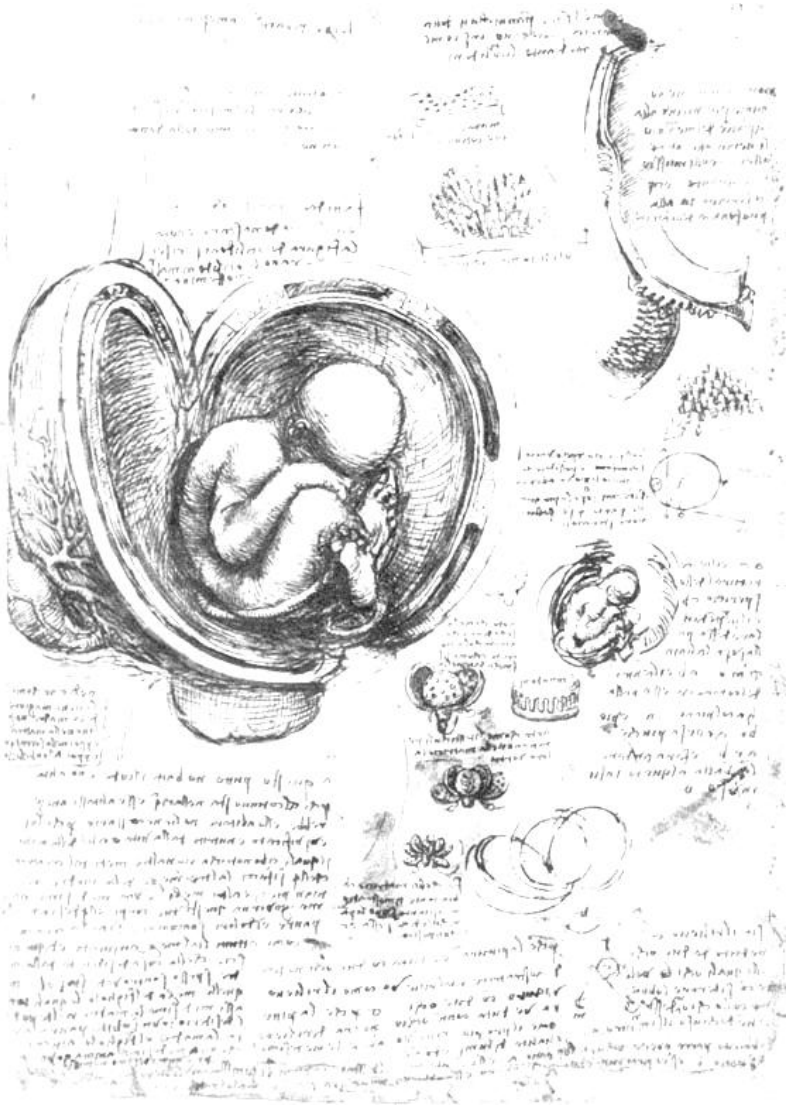

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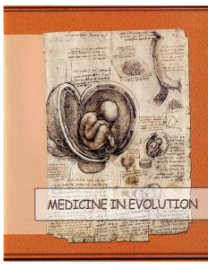
THE PRINCIPLES OF BASIC MEDICAL ATTENDANCE KEYS FOR THE DEVELOPMENT OF THE HEALTH SYSTEM MANAGEMENT



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ABSTRACT

The first part of the article there is a short history of the implementation of the social insurance laws (LASS) and the principles of the health insurance system in Romania, according to the Law of the social health insurance. It is emphasized the idea that in a democratic state it is stipulated the active participation of the society at the achievement of one of the fundamental rights of the individual: the right to health. This does not actually represents the voicing of a policy, but of the actions for the nation; the right of the patients express the wishes of each individual that are connected to the quality of the medical attendance that he receives or that he could receive, mirroring the two fundamental dimensions of quality: the tehnical quality and the interpersonal quality, the responsibility of the supliers and of the patients in the process of request and offer of health services.

Key words: *health, law, health assurance, health system, medical care, the rights of the patients in Europe*

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A HISTORY REGARDING THE GRANTING OF THE RIGHTS OF MEDICAL ATTENDANCE

In 1920, 8 years after the implementation of the law regarding the granting of medical attendance, in Great Britain there was launched the so – called"The white charta"(white paper) that refers to the organization of the system of medical attendance (1). In this document there were described 3 major levels for the health services: the primary health centers, the secondary health centers and the universitary hospitals; also there were mentioned their functions and the connections between these. Thus, we have the continuation of an idea of organising a system of services that was appointed to answer the different levels of medical needs that the population has, representing the starting point for the reorganisation of the health services in some countries. (2)

In the 30s, in China there was applied a project in the field of granting health services. This was developed in the countryside, in TING HSIEN, a village 150 kilometres close to Beijing.

The experiment was notable, fundamental for many projects form the health field all around the world.

By the help of this experiment it was underlined the fact that is possible to have comprehensive medical attendance, at a reasonable price (that the initiator of the project can afford) through the participation of the community and through the rationalizing and the demystification of the proffesional training, the diagnosis and the therapeutical procedures being based on scientific principles.

In this experiment, the work was done by the inhabitants from the health field in the villages, who were trained, and prepared to assure the basic attendance for their community, underlining the equality concept in the suppyling of the medical attendance. (2).

In 1975, the main executive of OMS. Dr. Halfdan Mahler launched the concept „Health for all until 2000"suggesting an immediate action for achieving in 25 years of a generation something that has not been achieved before".

In 1977, The General Meeting of OMS has decided, unanimously, the main purpose of the member countries, namely:"until 2000 all the people in the world should be reaching a health level that would allow them to have a prolific life, socially and economically speaking".

In 1978: the declaration from the Alma Ata – an international meeting that was organized by OMS and UNICEF, where the representatives from 134 governments had participated and 670 international organisations.

The conference from Alma Mata had expressed the neccesity of an urgent action from all the governments, of all the workers in the sanitary field and of the global community for health promotion to all the peoples of the world. (3)

The Declaration from Alma Mata has adopted the principles of the primary medical attendance as being the key elements of the developing of the health systems.

The health problems lead to needs for health. The need of health is given by the difference between the perfect state of health and the present state of health, that is established in that moment.

Thus, the need for health refers to what it should be done to solve the health problem that is identified at a certain point at the population. The need for health is measured through the estimation of the deviation from the normality. The greater is the deviation from normality, the greater is the need for health. The need for health gives birth to needs for health services and needs of resources of health.

Types of needs: classification (according to Bradshaw) (1)

a. Experienced needs – refer to the perception of a person's own health problems or to what that person would need connected to health services. The experienced needs have a subjective character.
b. Expressed needs – refer to the request for services and medical attendance that is offered to the population according to their needs.
c. Normative needs – are established by proffesionals (doctors, economists, sociologists, psychologists) according to certain norms, standards that are considered as being the ideal, the perfect situation.
d. Comparative needs – the need for medical attendance refers to the difference between the profylactic, treatment, recovering health services that exist and what si expected from these (the ideal) to obtain the desired state of health.

From a democratic European perspective, health represents a fundamental right of the individual and establishes personal and social political responsabilities. The discovery of the ecomomical, social, cultural, psychological etiologies of some diseases, of the colaboration of different pathogenic agents of different natures in the settling of a disease has moved the accent from the individual responsibility to the social one, regarding the preserving of the health and the avoidance of pathogeny. This is the suite of concepts which supports the health policies of the modern democratic states. In these policies a central part belongs to the promoting of health, as an actual *state of wellness* of several members of the society and as a *value* that must be kept, or for whose regaining, the greatest individual and social efforts are justified. (4).

THE DEVELOPMENT OF THE HEALTH INSURANCE SYSTEM FROM ROMANIA

The law of the social health insurance (LASS) was approved by the Senate in 1994 and by the Chamber of Deputies in July 1997. The implementing of the law of the health insurance was expected for the rise of the available resources for health (by the obligatory insurance bonus) and as an accelerator for the continuity of the reforms, including the improving of the efficiency of the immunitary system. The reform was thus promoted from different reasons: the Ministry of Finance, for example hoped for the growth of efficiency and in a control of the costs, while the doctors waited for higher salaries.

The law of the social health insurance was debated for the first time by the Romanian Parliament in 1994, it was voted and approved in the summer of 1997. It has initiated the transformations of the health system from a model sponsored by the state to a plural model, based on health insurance.

By adopting LASS the sponsorship based on general taxes is replaced with the first obligatory bonus for insurance. These are calculated by taking into account the income and they are paid equally by the employee (the insured person) and by the employer, through a fixed percentage from the income (from the salary and from the fund of salaries). This system allows the insured persons the access to health services and to medicines, as it is stipulated in the *frame contract* which includes: the list of the health services that are supplied by the sanitary institutions, the parameters of quality and efficiency, methods of payment, the period of hospitalization, criteria and medicines. The insured person has the right to choose the suppliers of the health services, and the personal doctor has the role to *control the access* in the system. The frame

contract is the basis of any contract between the insurance companies and the sanitary institutions: hospitals and the unities of ambulances, the centres of diagnosis and treatment centres, the health centres, a doctor's private office and so on.

The packages of services that are financed by CJAS do not include risk services and proffesional diseases, accidents at work, some highly specialized medical services, some dentist services and the luxury hotels. All these will be directly paid by the patient or by any other method of payment.

The law of the health insurance stipulates a serie of methods of payment for the suppliers, like the payment for the insured person, which is written on the doctor's chart; the payment for the specialized assistant on the ambulance; the global budget for the hospitals – that is calculated for different price lists (the hospitalized patient; health services and other forms that have been negociated).

Various documents and statements of the officials from the medical system, including the ones which belong to the nowadays systems of government have as main subjects the following principles and objectives, that were desired to be reached through the means of the social health insurance system.

In this respect, **the principles of the health insurance system** from Romania, according to the Law of the Social Health Insurances are the follwing:

- **the universality –** meaning that all the citizens are legally eligible for certain social goods and for certain services of medical attendance, partially and totally financed by the social health insurance.
- **the solidarity**, that is the contributions for the health insurances are based on a percentage from the income, irrespective of the income or of the state of health of the patient; the ones with high incomes can finance the sick people, the young ones can help the old ones and the developed counties can support the poor ones;
- **the subsidiarity –** meaning that certain entities (the retirement funds or other social funds from the state budget pay for the health insurance for the ones who are:
- incapable to pay (the poor ones) or
- for the staff that does not have to pay for the health insurance.
- **non – discrimination and the equality –** meaning equal access, irrespective of paying for certain goods and health services, or otherwise said: for equal health needs, equal medical needs.
- **the autonomy and the decentralization –** refers to the independence of the health insurance funds from the central government and from the interested parties as well as the taking of decisions as closer as possible to the place of their use.
- **the proffesional training-** that is the health insurance funds (the house, the houses) is a financial investment, specialized in the purchasing of goods and services of medical attendance.
- **the financial independence –** is paired with a growth of the transparency of the process of giving resources, geographically speaking and also between the different types of sanitary institutions (5).

THE RIGHTS OF THE PATIENTS

Having deep roots in the rights of the people, the rights of the patients express the wishes of any individual which are connected to the quality of medical attendance that a person receives or that he could receive. Thus,

it reflects the two fundamental dimensions of quality: the tehnical quality and the interpersonal quality, the responsibility of the suppliers and of the patients in the process of request and offer of the health services

In the conditions in which the health systems become more and more complex, the medical tehnology develops, the bureaucracy develops, often the medical practice tends to become closer to the people. On the other side, the patient does not have the same"profile"as in the past, when the doctor and his reccomendations were a tabu topic, judgeless, unverified, or contested. Then, the patient received without questioning whatever s/he was offered, sometimes as a mere favor. The patient form the present tends to claim his rights and to make them public; he tends to ask for them when they are ignored. From a simple patient he becomes a client of the system of health, from a"backup"an active agent of the system.

Because we cannot talk about quality in the health system, without realizing that this is focused on the patient, we cannnot speak about the assurance, about the improvement or about the manteinance of the quality if we do not have the patient's rights in mind.

There are two great types of rights for the patient:

- *the social rights*, that refer to the obligation of the state and of the health system to supply medical services, that are accesible and equal for all, that are protected from any type of discrimination, rights that are under the permanent influence of the political and of the economic sphera.
- *The individual rights*, which complete the social ones, expecially they refer to the access to medical care, to autonomy, to facilities.

At an international level there are some basic documents reffering to the rights of the patients which have been implemented in the majority of the European countries, aming which:

- The Declaration of the promotion of the patients' rights in Europe (OMS., 1994);
- The Charta of the reform of the medical care from *Ljubljana* (O.M.S., 1996);
- The Convention of the human rights and of the dignity of the human being in connection with the application of biology and medicine. (The European Council, 1997);
- The European Charta of the patients' rights (Active Citizenship Network)

The major chapters of the patients'rights comprise refferences to the following rights:

- The fundamental rights of the human being, reffer to the respect with which the patient is treated; his opinions, his convictions and beliefs, his values, his self determination are taken into account.
- His right to be informed upon, the patient has to receive a verbal or a written notification from his legal representatives at his leaving of the hospital. Then he has to receive a paper with all his problems, his affections, the complications, the side effects and the benefits of the treatment. Everything has to be clearly espressed.
- The consent, when the patient or his legal representatives are guaranteed the right to choose any medical intervention, the participation to the studies or to scientific research, in an informed way, in such a way as to fit the needs, the purposes and the lifestyle of the patient;
- The right to confidentiality and to the respect of the privacy, as for the patient to be sure that there will be no display of the nature of his condition, as long as it will surely not affect his public health;

- The right to attendance and to treatment, with the respect of the access to medical attendance, without being affected by obstacles or prejudices, the right to have this attendance, to confort, and to the continuation of the treatment as lons as it is neccesary.

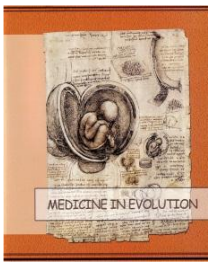
Additionally, to the large chapters of the patients' rights that are almost totally taken from the Declaration of promoting the patients' rights, the Romanian law of the patients' rights approaches the chapter of the patient in the field of the health of reproduction, that supports the right of the woman to choose to have babies, the right of the woman to choose her life and not her pregnancy when the pregnancy represents a major risk for her health and for her life, also it refers to the right of the patients to gather information, education, neccesary services, of family planning. (5,6)

"**Health is a fundamental right of the human being. The promoting of health is not an answer for the ones who want budget reduction. The invested money bring high benefits in time. There is a small risk for a big investment**"we can call this the managerial definition of promoting health, that was stated in a **Report of the European Committee for the International Union of Health Promotion (IUHPE)"The proof of the efficiency for promoting health"– The Shaping of Public Health in the new Europe. (5)**

REFERENCES

1. Vlădescu, Cristian (coord.), Sănătate publică şi management sanitar. Bucureşti: Editura Cartea Universitară, 2004.
2. Zanoschi, Georgeta, Sănătate publică şi management sanitar. Iaşi: Edit Dan, 2003.
3. Ramona Amina Popovici, Conexiunea educație-comunicare în managementul activităților de promovarea a sănătății orale. Lugoj: Editura Nagard, 2009.
4. Ramona Amina Popovici, Angela Codruța Podariu, Daniela Jumanca, Atena Găluşcan, Roxana Oancea, Ruxandra Sava Roşianu, Educația pentru sănătate oro-dentară. Managementul proiectelor educaționale. Timişoara: Editura Mirton, 2007.
5. Reinhardt Busse & colab., Sănătate publică şi management sanitar. Sisteme de sănătate. Centrul pentru Politici şi Servicii de Sănătate, Bucureşti, 2005.
6. Ramona Amina Popovici, Virgil Ciobanu, Angela Codruța Podariu, Mariana Pacurar, Ruxandra Sava Roşianu, Sănătate Publică Orală. Management, epidemiologie şi biostatistică medicală. Timişoara: Editura Mirton, 2014.

SOCIO-ECONOMIC ASPECTS IN THE CONTEXT OF ONCOLOGIC PATHOLOGY OF COLON CANCER



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ABSTRACT

The health of an individual *is defined by WHO as: „a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[1]. Health status is influenced positively or negatively by biological factors, by behavior, habits, economical, political, social and cultural factors.* ***Health as an individual notion*** *is the result of interaction between biological and genetic heritage of the human and environmental conditions, natural and social, of its life and activity.*

Lifestyle depends on the behavior and attitudes which in turn are conditioned by social factors, i.e. the lifestyle is the result of social factors and behaviors. [2]. The current trend is that the pattern of health to include the identification of the etiological factors, that are considered direct factors, and also of indirect factors influencing outcomes in health, because by preventing them it may lead to improving health, lower mortality, morbidity and to healing, contributing to the change in the quality of life, particularly in the case of malignant pathology, such as colon cancer.

Key words: *risk factors, lifestyle, behaviors, socio-economic factors, colon cancer*

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INTRODUCTION

From the statistical results, in Romania increased frequency of colon cancer is found in western counties, Transylvania and Bucharest. This frequency is on the third place among neoplastic morbidity being similar to the US and Western countries.

Colon cancer in terms of frequency and mortality, in Argentina is ranked second after breast and lung cancer.

There is in Romania a Monography of the National Cancer Commission comprising solid theoretical knowledge of the specialists involved in the diagnosis and treatment of colon cancer. [3]

This neoplastic localization, trough its high frequency, became a real public health problem.

Interdisciplinarity and modal treatment represents a milestone in colon cancer therapy. Thus, the complexity of diagnosis, diagnostic and therapeutic medical decision difficulty, are best when they are issued by a multidisciplinary commission in which the leading role belongs to the patient. Collaboration with a conscious patient involved and advised on all aspects involving the disease and treatment is an essential premise for the success of prevention and later of the therapy of colon cancer. [4,5]

Recently, Oncology commissions increased their competencies by cooptation of psychologists and specialists in communication.

Dr Alberto Gomez member of the Proctology team stated that: an early diagnosis can increase the possibility of cure rate up to 90%.

At the time of cancer diagnosis, nearly 65% of the cases have an advanced form of local or loco-regional dissemination.

The issue of colon cancer is permanent in the surgical field, the technical progress is successfully making visible its presence.

The prognosis of colon cancer, compared to other digestive segments, has a benign character, illustrated by the results both immediate and distant. [6,7]

Colon surgeries are well coded and can comply with the basic principles of oncological surgery, which explains the results obtained in this form of neoplasm. [8]

Colon cancer is the third malignant neoplasm in the world as frequency and secondary cause of death in the United States. [9,10]

Every year there are 150,000 new cases and 58 000 deaths, representing about 13-15% of cancer deaths.

Between 1973 and 1975 mortality from colon cancer has decreased from 20.5% to 7.4% in the US. [10]

The incidence is higher in men than in women. The corresponding mortality age is 26.3 for men and 18.5 for women. [11]

Only 6% of American adults believe they will manifest the disease during their lifetime. Age-specific incidence and mortality rate shows that most cases of colon cancer are diagnosed around the age of 50 years. [11]

Between 1985-1995, the incidence of colon cancer has dropped significantly to 1.8% per year, but stabilized between 1995 and 1999. In a span of 15 years the mortality rate will drop to 1.7% per year. Survival rate at 5 years is 62.1%.

The risk of cancer is doubled every next decade and continues an exponential growth.

Socio-economic factors

Colon cancer is common in Western Europe, the US and England with a ratio of 30: 100 000 inhabitants and very rare in Africa and South America with a ratio of 5: 100 000 inhabitants, the differences being related to the degree of industrialization and geographical and environmental factors. [10,11]

It is 2nd in frequency among all neoplastic diseases. It is estimated that every 30th man and every 25th woman are at risk of developing a colon carcinoma. There are epidemiological data that show, in immigrants from countries with low frequency of colon cancer, a significant increase in incidence equal to it in the country where the inhabitants are emigrating. [12]

Other data show that in high-risk populations, neoplastic lesions are more common in men and located in the sigmoid, and in population in which the neoplasm is endemic, the injury is more common in women on the right colon, this phenomenon has been described by Haenzel.

Nowadays, the frequency of colon cancer is increasing.

The most affected age group is 60-69 years, the incidence of the disease in general increases with age. A special attention is paid to this disorder in youth. [10]

The incidence neoplasm of the large intestine in people under 40 years, ranges between 2-4%. Most of these patients are aged between 20-40 years, under the age of 20 years being only sporadic cases. [10]

Bulow shows that in young colon cancer patients, it is most commonly located on the right side in men and on the left side in women, but this was not confirmed by others.

Sex and age: under 60 years, the gender distribution of cases is uneven, and over 70 years the neoplasm prevails in men. [10]

Table 1.

Age	**Colon**	**% total**
21-30	2	3.33
31-40	6	10.00
41-50	12	20.00
51-60	7	11.66
61-70	25	40,00
71-80	8	13.33
81+	1	1.66

Table 2. Location of cancer in 146 cases

Location	No. of cases	%cases
Colon	69	48,8

Table 3. Correlation with gender

Gender	Colon	% total
Male	31	46.26
Female	36	53.73

As seen, decades IV and VI are most commonly affected by the presence of this colon tumor. As for gender, there is a slight predominance of rectal localization in males and colon localization in women. [10]

Morbidity by colorectal cancer

Table 4. Number of new cases

Localization	1995	1996	1997
Malignant tumor of the colon	43	81	85
Malignant tumor of the rectal-sigmoid junction	48	56	40
Malignant tumor of the rectum	50	53	61
Malignant tumor of the anus and anal canal	4	5	3
Total	145	197	189

Table 5. Morbidity by colon cancer

Year	Morbidity in 100 000 inhabitants
1995	23.16
1996	31.47
1997	30.19

In Romania, by the *Minister of Health Order no. 219/1980* has been introduced mandatory nominal declaration of cancer patients, confirmed as such, thus creating the national cancer registry. [13]

Subsequently, this legislative provision is repealed and replaced by *Order of the Minister of Health nr.871 / 2002 regarding the mandatory declaring and nominal track of cancer patients*, which stated that from 1st January 2003 shall be updated the registers of cancer patients, institutional and territorial with population support, as well as the national cancer registry. [13] The units with competence for the diagnosis and treatment of cancer patients and which have in records over 500 new cases per year will hold the institutional register of cancer patients (which will work at the office of admissions), and will communicate the data to the county oncology office (by cancer patient statistical sheet ONC.1). The other units of cancer diagnosis and treatment will be controlled based on records at the office of admissions and records of outpatient consultations, in terms of reporting of new cases by cancer patient statistical sheet ONC.1.

Health care units with competencies for complex diagnosis and treatment must declare all of the detected cancer patients. Other health units are required to refer patients with suspected cancer by reference note (type MSF) or admission note (type MSF), as appropriate, for the diagnosis and establishment of therapeutic conduct, by accredited health units, respecting the rights of addressability of patients.

That legislative act is repealed and in force today is the *Order of the Minister of Public Health no.2027 / 2007 regarding the registration in population data bases of cancer patients and setting up regional cancer registries.* [13]

In Article 4 it is stated: a reportable case is any primary tumor newly diagnosed after the 1st of January 2008 for which, by clinical and / or laboratory methods, has been established a reportable diagnostic. Nominal reporting is mandatory for all primary tumors that are part of the list of reportable diagnoses. [13]

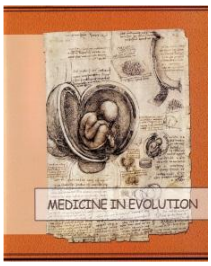
With all these legislative provisions, in the absence of a national registry of patients with oncological diseases, there is no clear evidence of cancer patients. According to estimates of Alliance of the chronic patients in Romania, in our country, 98,000 inhabitants receive treatment for oncological diseases. The same source says that the number of people suffering from different cancers would be much higher.

REFERENCES

1. VLADESCU C. – Sanatate Publica si Management Sanitar, Ed. Cartea Universitara, Bucuresti, 2005
2. POPOVICI RA, CIOBANU V, PODARIU A.C., PACURAR M., SAVA-ROSIANU R.- Sanatate Publica Orala. Epidemiologie si Biostatistica, Editura Mirton, Timisoara, 2015
3. IONESCU G., sub red. Chirurgia colonului.Ed. Cluj-Napoca, 1985
4. PROCA E., sub red. Tratat de patologie chirurgicala, Ed. Med. 1986, vol VI
5. PAUN R. sub red. Tratat de medicina interna. Bolile aparatului digestiv, partea I, Ed Medicala Bucuresti 1984
6. PATRASCU E., HIJAZI F., ORBAN F., Pregatirea mecano-enzimatica a colonului, Simpozion Cluj-Napoca, aprilie 1979

7. IONESCU G., CUCU A., BLAJ A.,Modalitati de pregatire a colonului in vederea interventiilor chirurgicale de exereza
8. PAPILIAN V., Anatomia omului, vol. III Ed.Didactica si Pedagogica Bucuresti 1982.pp110-114;122-156
9. SHIKE M., WINAWER SJ., GREENWALD PH.,et al: Primary prevention of colorectal cancer. The WHO Collaborating Center for the Prevention of Colorectal Cancer.Bull World Health Organ 68(3): 377-85, 1990
10. AMERICAN CANCER SOCIETY: Cancer Facts and Figures 2003 Atlanta. Ga: American Cancer Society, 2003
11. GOLDBOHN RA., VAN DEN BRADT PA., VAN VEER P., et al: A prospective cohort study on the relation between meat consumtion and the risk of colon cancer. Cancer Res, 1994
12. PHILLIPS RL. SHOWDON DA: Dietary relationship with fatal colorectal cancer among Seventh-Day Adventist, J.Natl Cancer Inst 1985
13. www.legis.ro

INSULAR CORTEX AND NEUROGENIC HEART DISEASE- A CASE PRESENTATION



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ABSTRACT

Recent studies begin to emphasize the idea of insular cortex involvement in the sympathetic-parasympathetic central control of the cardio-vascular system. The sympathetic- parasympathetic balance may be impaired by insular unilateral ischemic lesions, because of the existence of cortex lateralization that implies right hemispheric dominance for the sympathetic activity and left hemispheric dominance for the parasympathetic activity. The imbalance created is followed by cardio-vascular manifestations by tipping the balance towards one of the two influences- sympathetic or parasympathetic.

We present the case of a female patient suffering from an acute ischemic stroke affecting the right fronto-parietal and insular cortex, in whom the detection of a heart rhythm disturbance (rapid ventricular response atrial fibrillation), with no signs suggesting a chronic evolution, brings arguments for the existence of cortical lateralization in the sympathetic- parasympathetic control and also for cardio-vascular manifestations as a result of this balance impairment

Key words: *stroke, insular cortex, atrial fibrillation, neurogenic heart disease*

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INTRODUCTION

Cerebrovascular disease, along with cardio-vascular disease, represents the main cause of morbidity and mortality among adults worldwide[1]. Hence, this raises the concern for an accurate diagnosis and management of these patients. People suffering from cerebrovascular diseases may have, sometimes, unpredictable evolutions- from a full recovery of the deficits to death, which may be caused by associated disorders involving other organs than the nervous system. The complexity of non-neurologic pathological manifestations during a stroke, has led to the concept of"neurogenic heart disease"[2]. This resides in all the cardiac manifestations that may appear during a stroke and consists of various changes from electrocardiographic changes, to acute ventricular failure or malignant arrhythmias and even sudden cardiac death.

CASE PRESENTATION

We present the case of a female patient, 73 years old, brought by ambulance to The Psychiatry and Neurology Hospital of Brasov, presenting complete motor deficit of the left superior and inferior limbs. The symptoms started two hours before admission in the hospital.

Medical history of the patient consisted of high blood pressure (stage 3), diabetes mellitus (on diet control) and mixed anxiety- depression disorder. She stated daily alcohol intake and failure in following the anti-hypertensive treatment.

On clinical examination we found stage II obesity (BMI= 37kg/m2 and waist circumference= 110cm), altered general state with moderate orthopnea, pulmonary rales at the base of both lungs, arrhythmic and tachycardic cardiac sounds. Heart rate was 160 bpm. Blood pressure= 140/90 mmHg. Neurological examination revealed complete motor deficit of both left limbs, left central facial palsy, head and gaze left oriented, dysarthria.

Laboratory findings showed liver impairment (hepatic cytolysis and cholestasis), high levels of uric acid, CK and CKMB at the upper limit of normal range; normal values of lipids and blood sugar.

Cranial computed tomography examination found an ischemic stroke located in the fronto-parietal and insular region of the right hemisphere (Fig.1).

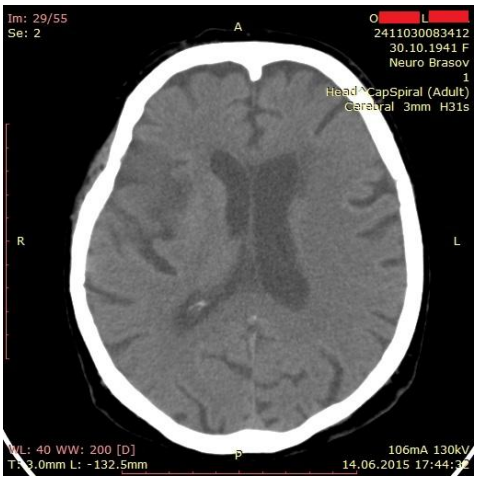

Figure 1. CT scan slice- hipodensity located in the fronto-parietal and insular region of the right hemisphere

The electrocardiogram at the admission revealed atrial fibrillation with a rate of 160 bpm, diffuse negative T waves and ST segment depression (1mm) on the inferior and anterior leads.

The Holter ECG monitoring performed during the first 24 hours since admission in the hospital, detected atrial fibrillation with a rapid ventricular response (Fig.2), diffuse negative T waves and ST segment depression on the inferior and anterior leads and rare isolate and coupled ventricular premature beats.

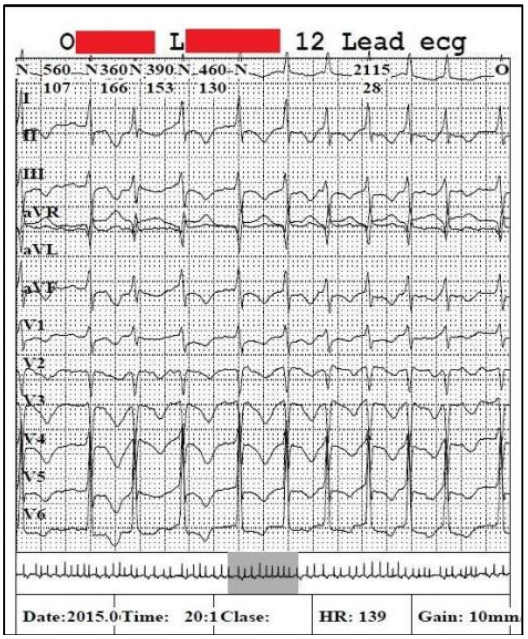

Figure 2. ECG Holter image- atrial fibrillation with a heart rate of 139 bpm

On the echocardiography exam, we noticed a normal sized left atrium (Fig.3), concentric left ventricular hypertrophy, a slightly hypokinetic inter-ventricular septum, a left ventricular ejection fraction of 50% and mild mitral, tricuspid and aortic regurgitations.

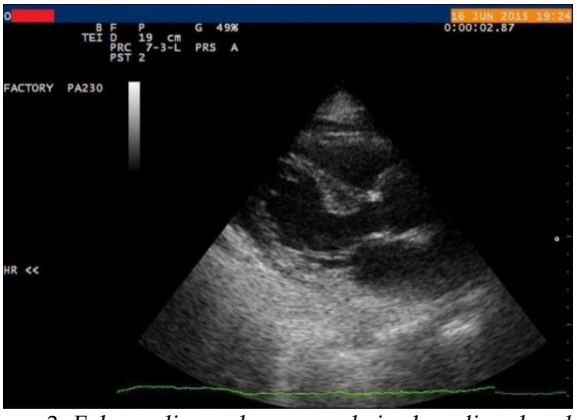

Figure 3. Echocardiography- normal sized cardiac chambers

During in-hospital stay, the patient was treated with anticoagulants, an anti-platelet agent, cholesterol- lowering drug, beta-blocker, digitalis, proton pump inhibitors and intravenous fluids. She also started kinetic-therapy. Clinical evolution was favorable with gradually partial recovery of the motor deficits and slight improvement of the dyspnea. The electrocardiogram at discharge showed atrial fibrillation with 120 bpm.

DISCUSSIONS

Neurocardiology is a new medical field that studies the mechanisms of interaction between neurologic and cardio-vascular pathologies. Its main directions of study are: the effects of the neurologic diseases on the heart (neurogenic heart disease), the effects of the cardiac diseases on the brain (e.g. cardiac emboli as etiology for stroke) and neurocardiac syndromes[2].

Neurogenic heart disease, although it is a very important entity seeing its implications in the prognosis of the patients, still remains a medical field with many uncertainties. The literature mentions three pathophysiological ways that could explain the cardio-vascular disturbances that may appear in the context of a stroke. These are: the catecholamine systemic storm[3], excessive local catecholamine discharge (in the heart tissue)[4] and the sympathetic- parasympathetic imbalance that may appear in insular cortex lesions (island of Reil)[5]. In our patient the ischemic stroke involves the insular cortex of the right cerebral hemisphere (non-dominant hemisphere).

The insular cortex, along with the hypothalamus, is involved in the autonomic system control, with a role in maintaining the balance between the sympathetic and parasympathetic influences on the heart[5]. Recent studies outline the idea of an inter-hemispheric asymmetry of this control so that the left insular cortex modulates preferably the parasympathetic influence on the heart, while the right insula modulates mainly the sympathetic influence[5]. Thus, in our case, the ischemic lesion that affects the right insula involves a sympathetic-parasympathetic imbalance with excessive parasympathetic activity because of the loss of central sympathetic influence. Parasympathetic stimulation on the heart determines bradycardia. According to ONTARGET/TRANSCEND studies, resting low heart rates are associated with high incidence of atrial fibrillation[6]. Also, it is a well-known fact that an undamaged sinus node inhibits the exertion of spontaneous abnormal electrical activity in the atria (ectopic foci). In this situation, the marked parasympathetic stimulation of the heart induces sinus node inhibition which may lead to activation of ectopic pacemaker cells that take become the main heart rhythm generators. This may have happened in our case, the ectopic foci being the atrial fibrillation substrate. Also, in our case there are some clues that suggest a recent onset of the atrial fibrillation and make it less possible to be a chronic disturbance. These are represented by: the occurrence of dyspnea (sign of acute left ventricular failure) almost simultaneously with the stroke symptoms, a normal sized left atrium and a normal sized left ventricle seeing the fast heart rate which, in a long standing tachyarrhythmia, should lead to structural changes suggesting a tachycardiomyopathy. Thus, it raises the possibility of atrial fibrillation occurrence as a consequence of a stroke and not as its etiology.

Another theory implies that the right insular ischemic lesion may be an irritative type which would lead to sympathetic over-activity and, on a pre-existent atrial fibrillation with a moderate ventricular response, well tolerated (e.g. without dyspnea), it may exert an influence on the atrio-ventricular node by increasing the conduction at this level, thereupon a moderate frequency atrial fibrillation becomes a fast frequency atrial fibrillation with acute tachyarrhythmic left ventricular failure and probably,

subsequent morphologic changes in the ventricle.

This case presentation had as main purpose to highlight the existence of the possibility that a cardio-vascular disturbance may be the result of the functional impairment that comes from cerebrovascular lesions of structures involved in vegetative control, herein-the insular cortex.

Aknowledgement

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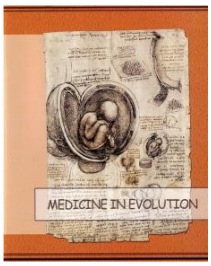
REFERENCES

1. World Health Organisation- Factsheet No. 310/ May 2014
2. Martin A. Samuels. The brain-heart connection. Circulation. 2007.116:77-84
3. Sahil Koppikar et al. Stroke and ventricular arrhythmias. International Journal of Cardiology. 2013, March.
4. Tamsin Gregory Martin Smith. Cardiovascular complications of brain injury. Continuing Education in Anaesthesia, Critical Care & Pain Advance Access published December 22, 2011.
5. Stephen Oppenheimer. Cerebrogenic cardiac arrhythmias: cortical lateralization and clinical significance. Clin Auton Res. 2006. 16:6-11
6. Böhm M, Schumacher H, Linz D, Reil JC, Ukena C, Lonn E, Teo K, Sliwa K, Schmieder RE, Sleight P, Yusuf S. Low resting heart rates are associated with new-onset atrial fibrillation in patients with vascular disease: results of the ONTARGET/TRANSCEND studies. J Intern Med. 2015 Apr 15. doi: 10.1111/joim 12373.

ADRENAL INCIDENTALOMA



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ABSTRACT

Different radiological technics (CT, MRI) frequently used in our days for diagnosis, made adrenal incidentaloma a common finding. Most of these kinds of tumors are benign, hormonally inactive, and asymptomatic, but, in a few cases, they may be hormonally active, associating hypersecretion symptoms. Paroxysmal increases in blood pressure may be caused by the high level of cathecolamines (as seen in pheochromocytoma), or a Cushing syndrome induced by hypercorticism). A subclinical hypercortisolism is observed in a significant percentage of patients with adrenal incidentaloma. The continuous secretion of cortisol may induce several effects, such as high blood pressure, dyslipidemia, decrease of the sugar tolerance or type 2 diabetes, osteoporosis with high risk of fracture. The tumor should be differentiated from the clinical silent pheochromocytoma and from adrenal cancer, conditions associated with a significant high mortality and morbidity, and a need for a specific therapy. For the evaluation of these masses a variety of diagnostic strategies has been developed. However, they are still controversial.The right diagnostic of an incidentaloma involves a careful evaluation, considering the general health and the patient`s preferences. In case of hormonally active masses as pheochromocytoma, adrenal carcinoma or adenoma, which produce an excess of glucocorticoids, mineralocorticoids, or sex steroids, there are several steps to follow in order to evaluate the patients.

Key words: *pheocromocytoma, adrenal incidentaloma, secondary tumor*

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INTRODUCTION

Adrenal incidentaloma (AI) is defined as an adrenal lesion mass > 1 cm in diameter, discovered occasionally, usually during an imagistic diagnosis for another condition, that have no relationship with the adrenal disease. This lesion`s prevalence varies between 3% and 7% in general population, meaning that it is not a rare disease [1]. These masses have been lately often discovered by the frequent use of imagistic examination for thorax and abdomen (computed tomography [CT], magnetic resonance imaging [MRI], ultrasound), Their incidence increased with age.

First case of AI was described 30 years ago [2]. Due to improved imagistic technics, AI became a common clinical problem, with a management dilemma [3]. The prevalence of adrenal incidentaloma in 87065 autopsies effectuated during 25 clinical studies was 5,9% [3]. The prevalence of suprarenal masses discovered by CT, MRI or ultrasound was smaller. Abecassis et al have examined 1459 de patients over two years and discovered in 63 (4,3%)of them adrenal masses [4].

Further, we are describing an adrenal incidentaloma case, a patient with complex pathology.

CASE REPORT

A female patient 71 years old was hospitalized for high blood pressure, retrosternal pain, dyspnea, and asthenia, symptoms which occurred episodically.

The medical history revealed that the patient was already diagnosed systemic arterial hypertension, , vulvar epidermoid carcinoma that was surgically treated, autoimmune chronic tiroiditis , old ischemic stroke, depression, gallstones, chronic venous insufficiency.

The patient presented episodic blood pressure jumps, these being the reason for an AI or pheocromocytoma suspicion. During the endocrinological investigations, ultrasonography and MRI detected a left adrenal mass of 30/31 mm (Fig.1).

The problem in this moment was to differentiate between AI, adrenal adenoma and a secondary tumor due to the gynecologic malignancy.

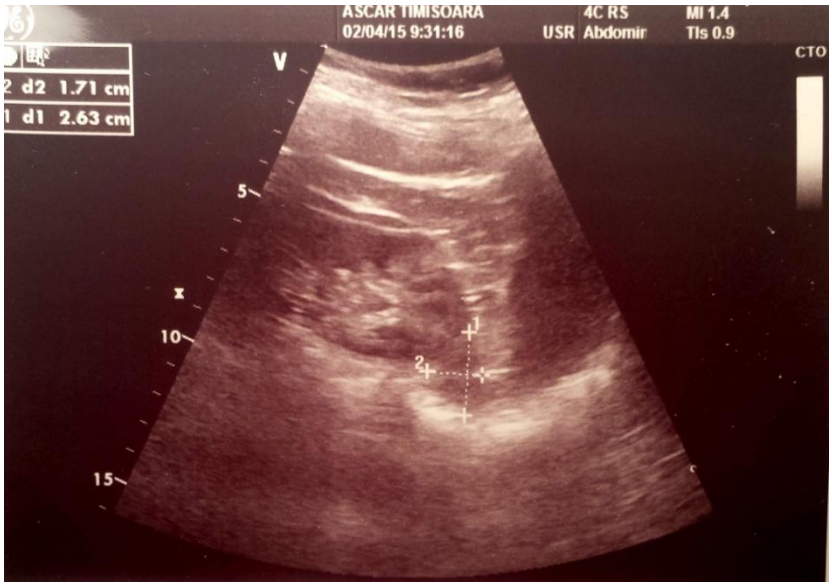


Figure 1. Abdominal ultrasound showing left adrenal incidentaloma

The laboratory analysis revealed:cortisol = 16,08 micrograms / dL ; dexamethasone suppression test (2 mg of dexamethasone) = 1,37 micrograms / dL ; urinary catecholamine methanephrine = 61 micrograms / 24h ; normethanephrine = 148 micrograms / dL ; 3- metoxi - thiramine = 87,6 mcg / dL ; serum potassium = 4,8 mEq / L. The oral glucose tolerance test was normal. The mineral bone density showed osteoporosis.

The laboratory results eliminated the suspicion of adrenal adenoma , but we still had to differentiate between an incidentaloma and a secondary adrenal tumor[5,6].

Echocardiography showed medium aortic stenosis(Fig 2,3).

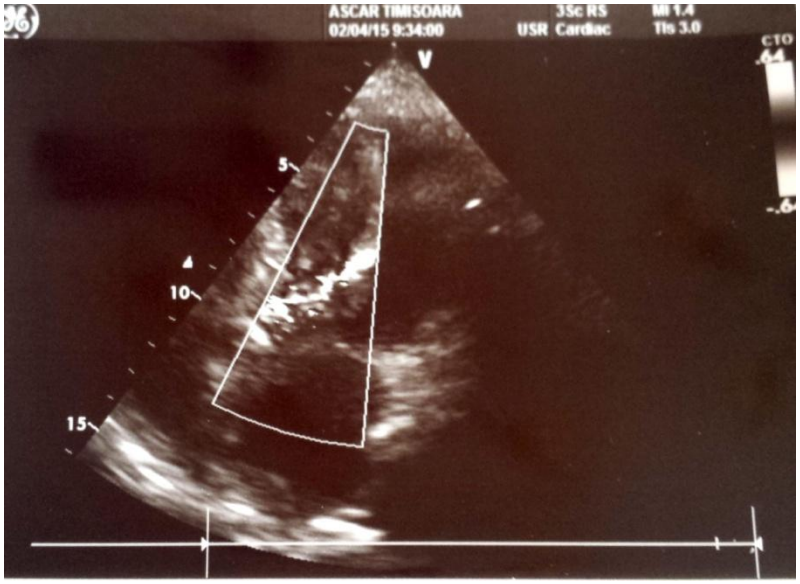


Figure 2. Two dimensional echocardiography showing aortic stenosis

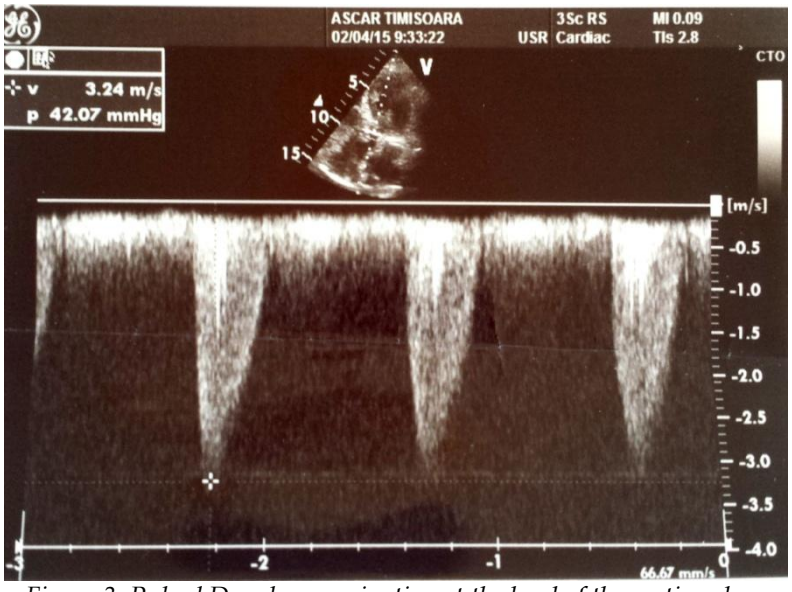


Figure 3. Pulsed Doppler examination at the level of the aortic valves

The patient had also a gynecological examination and a new MRI to evaluate a possible dynamic evolution as a secondary tumor. The diagnosis in this case was that of an incidentaloma, because the identified tumor was not a hormonally active tumor and not secondary to the gynecological malignant pathology previously diagnosed.

During the hospitalization the patient received perindopril and a selective beta blocker to control hypertension. The patient was

discharged at home and advised to continue this medication. Periodical evaluation of the aortic stenosis degree was recommended, as well as the monitoring of the gynecological malignancy. The adrenal tumor mass will be annually evaluated biologically and by MRI [7,8].

DISCUSSIONS

Nonfunctional adrenal masses are space-occupying lesions of the adrenal glands that have no hormonal activity. Symptoms, signs and treatment depend on the nature and size of the mass.

Although most AI have no significance beyond the anxiety they produce indirectly, some of them are clinically significant, and inadvertently leaving them not treated might damage the patient`s health.

It is recommended that all patients with an adrenal mass should have biochemical screening tests for pheochromocytoma, that include the determination of the 24-hour urinary excretion of vanil mandelic acid, metanephrines, or catecholamines. In addition, the serum potassium concentration should be measured in all hypertensive patients, to screen for primary hyperaldosteronism.

Even in oncologic patients with indeterminate adrenal tumors, MRI can provide accurate differentiation between metastasis and benign adenomas. Although new imaging modalities may be diagnostic, if the tumor is solid, of adrenal origin, and greater than 40 mm, it should be excised, because in such cases, imaging alone cannot always distinguish between benign and malignant tumors. Tumors of 20 mm to 40 mm in diameter are particularly difficult to deal with. If MRI does not suggest cancer and the hormonal functionsare not altered (normal electrolytes and metanephrines, no evidence of Cushing syndrome), it is reasonable to reevaluate periodically the patient with imaging studies, usually for 1 to 2 years[9,10,11].

In our patient, who had a history of malignancy, repeated biochemical and imagistic evaluation did not show an adrenal metastasis, adenoma or carcinoma. We decided to continue medical treatment for hypertension and to evaluate periodically the adrenal mass.

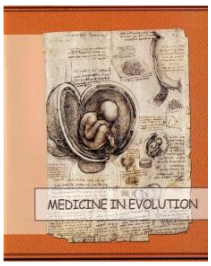
In conclusion, the presented case informs the physicians about increased incidence of adrenal incidentaloma during tests conducted for other reasons, and the importance of evaluating symptoms, signs and treatment depending on the nature and size of the mass.

REFERENCES

1. Young WF, 2000 Management approaches to adrenal incidentaloma. A view from Rochester, Minnesota.Endocrinol Metab Clin North Am 29: 159-185.
2. Geelhoed GW & Spiegel CT 1981 'Incidental'adrenal cyst: a correctable lesion possibly associated with hypertension. Southern Medical Journal 74 626–630
3. Aron DC 2002 Endocrine incidentalomas. Endocrinology and Metabolism Clinics of North America 29 1–238.
4. Abecassis M, McLoughlin MJ, Langer B & Kudlow JE 1985 Serendipitous adrenal masses: prevalence, significance and management. American Journal of Surgery 149 783–788.
5. Bertherat J, Mosnier-Pudar H & Bertagna X 2002 Adrenal incidentalomas. Current Opinion in Oncology 14 58–63.
6. Belldegrun A, Hussain S, Seltzer SE, Loughlin KR, Gittes RF & Richie JP 1986 Incidentally discovered mass of the adrenal gland. Surgery,

Gynecology and Obstetrics 163, 203–208.
7. Geelhoed GW & Spiegel CT 1981 'Incidental'adrenal cyst: a correctable lesion possibly associated with hypertension. Southern Medical Journal 74 626–630.
8. Geelhoed GW & Druy EM 1982 Management of the adrenal 'incidentaloma'. Surgery 92 866–874.
9. Herrera MF, Grant CS, van Heerden JA, Sheedy PF & Ilstrup DM 1991 Incidentally discovered adrenal tumors: an institutional perspective. Surgery 110 1014–1021.
10. Honigschnabl S, Gallo S, Niederle B, Prager G, Kaserer K, Lechner G & Heinz-Peer G 2002 How accurate is MR imaging in characterization of adrenal masses?: update of a long-term study. European Journal of Radiology 41,113–122.
11. Wajchenberg BL, Albergaria Pereira MA, Medonca BB, Latronico AC, Campos Carneiro P, Alves VA, Zerbini MC, Liberman B, Carlos Gomes G & Kirschner MA 2000, Adrenocortical carcinoma: clinical and laboratory observations. Cancer 88 711–736.

ANTI-INFLAMMATORY AND ANTITUMORAL MECHANISMS OF ACTION OF LUPEOL



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ABSTRACT

Lupeol is a pentacyclic triterpene with lupan skeleton, found in fruits, vegetables and medicinal plants, known to possess multiple pharmacological activities, including: anti-inflammatory, anticancer, antiarthritis, antimicrobial and hepato-protective. The anti-inflammatory and anticancer mechanisms of action of this natural compound are complex, involving several cellular signaling pathways. These features make lupeol a potent anticancer agent with significant therapeutic potential.

Key words: *lupeol, inflammation, cancer, signaling pathways*

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INTRODUCTION

Lupeol (lup-20(29)-en-3H-ol – $C_{30}H_{50}O$) is a pentacyclic triterpene of natural origin with lupan skeleton (Fig. 1), has been widely reported as triterpene with several curative properties in different pathologies, such as: inflammation, cancer, arthritis, diabetes, renal and hepatic injuries [1]. Moreover, it has also been reported that high doses of lupeol administered orally (2g/kg body weight), topically (2 mg/animal) or parenteral did not elicit adverse effects or systemic toxicity in animal models of experimental pathology [1].

Lupeol is widely spread in fruits (olive, red grapes, mango, strawberries and figues), vegetables (white cabbage, pepper, cucumber, tomato) as well as in various medicinal plants such as: American ginseng, Shea butter plant, *Tamarindus indica, Allanblackia monticola, Himatanthus sucuuba, Celastrus paniculatus, Zanthoxylum riedelianum, Leptadenia hastata, Crataeva nurvala, Bombax ceiba and Sebastiania adenophora* [1-3].

The lupeol chemical structure (Figure 1) is composed of four six-membered rings (that borrow chair conformations) and one five-membered ring (with an envelope conformation), all organized in trans conformation [4].

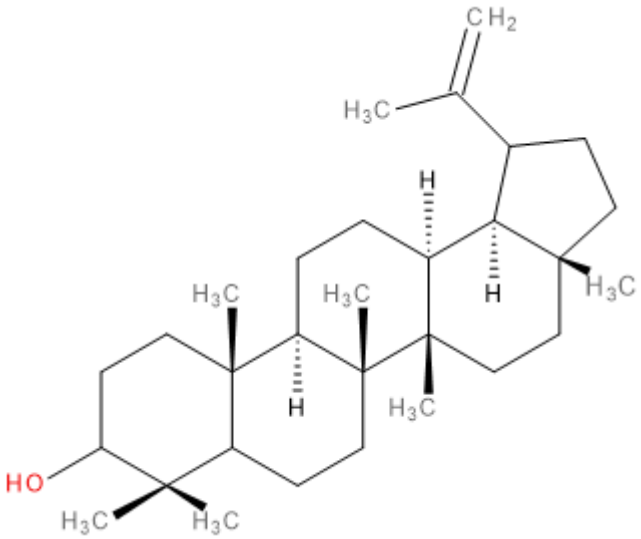


Figure 1. Chemical structure of lupeol

BIOLOGICAL EFFECTS OF LUPEOL

In the past decades, an increasing number of studies were focused on lupeol mechanisms of action due to the plethora of biological effects and its lack of toxicity both *in vitro* and *in vivo*. The beneficial effects of lupeol reported in the literature refers to: anti-inflammatory, anti-tumoral, antioxidant, hepato/gastro/renoprotective, and protection against the action of different noxious agents (e.g., benzoyl peroxide, 7,12-dimethylbenz[a]anthracene - DMBA) in experimental settings. The vast majority of papers addressed the anti-inflammatory and anti-tumoral potential of lupeol in order to elucidate the underlying mechanisms.

The present paper will briefly review the anti-inflammatory and anti-cancer mechanisms of action of lupeol.

The anti-inflammatory effect of lupeol was demonstrated in the mouse models of ear oedema induced by 12-0-tetradecanoyl-phorbol acetate (TPA)

[5], of paw swelling in adjuvant arthritis [6], of lipopolysaccharide (LPS)-induced neuroinflammation in the cortex and hippocampus of adult mice [7], and in ethanol-induced gastric lesions in mice [8].

ANTI-INFLAMMATORY MECHANISMS OF ACTION OF LUPEOL

Fernandez and co-workers showed that lupeol administered topically (0.5 and 1 mg/ear) was able to inhibit the ear oedema induced by 12-0-tetradecanoyl-phorbol acetate (TPA) by reducing the expression of myeloperoxidase, a neutrophil marker what led to the decrease of cell infiltration into affected tissues. We have also demonstrated that in the mouse model of ear inflammation that lupeol application had an anti-inflammatory comparable with the one obtained for indomethacin, a common non-steroidal anti-inflammatory drug. [5].

In another study developed on a mouse model of paw swelling in adjuvant arthritis it was shown that lupeol possessed an anti-inflammatory activity similar to indomethacin, but the mechanism of action involved is different since lupeol does not exhibit antinociceptive, anti-pyretic properties and is devoided of the ulcerogenic side-effects of indomethacin [6].

Ahmad *et al.*, reported that administration of different doses of lupeol per os (25, 50, 100 and 200 mg/kg) led to the inhibition of several pro-inflammatory cytokines: IL-2, IFN-gamma and TNF-alpha in the pleural exudate, with the most important effect being recorded at a dose of 100 mg/kg oral dose [9].

A recent study conducted by the Badshah and co-workers indicated that systemic treatment with lupeol inhibited the lipopolysaccharide (LPS)-induced neuroinflammation in the cortex and hippocampus of adult mice by decreasing the generation of pro-inflammatory cytokines, tumor necrosis factor (TNF)-α, inducible nitric oxide synthase (iNOS), and interleukin (IL)-1β. Cytokines elicited the phosphorylation of P38 mitogen-activated protein kinase (MAPK) and c-Jun N-terminal kinase (JNK) signaling pathways that were suppressed by lupeol treatment. Moreover, it was demonstrated that lupeol had an inhibitory effect on the LPS-induced activation of the mitochondrial apoptotic pathway, data that recommend lupeol as a therapy in diseases characterized by neuroinflammation [7].

ANTICANCER MECHANISMS OF ACTION OF LUPEOL

Another well-documented biological effect of lupeol is the anticancer one. Lupeol proved to be a very effective antitumoral agent both *in vitro* and *in vivo*. The anticancer effect of this natural compound was tested *in vitro* against a panel of tumor cell lines of different origin, including: human hepatocellular carcinoma cells (SMMC7721 and HepG2) [10-12] and HCCLM3 cells [13], human prostate cancer cells (CaP) [14, 15] and PC-3 [16], human melanoma cells (Mel 928, Mel 1241 and Mel 1011 melanoma cells) [17],human primarymelanoma cells WM35, and metastatic melanoma cells 451Lu [18],human pancreaticadenocarcinoma cells AsPC-1 [19], human epidermoid carcinoma - A431 [20], human colorectal cancer cells [21], human promyelotic HL-60 leukemia cells [22] and gallbladder carcinoma GBC-SD cells [23].

Administration of lupeol *in vivo* was associated with beneficial chemopreventive and anticancer effects in several animal models, such as: a mouse model of benzoyl peroxide-induced tumor promotion [24], on 7,12-dimethylbenz[a]anthracene (DMBA)-

induced alterations in the skin of Swiss albino mice [25], a mouse model of human gallbladder carcinoma [23], an animal model of oral carcinogenesis induced by administration of DMBA [26], a skin cancer mouse model [27], a human melanoma mouse model [28], a mouse model of head and neck squamous cell carcinoma [29], a highly aggressive human metastatic melanoma mouse model [18] and a human pancreatic carcinoma mouse model [30].

The *in vitro* anticancer activity of lupeol is attributed to its capacity to trigger apoptosis of cancer cells. In human hepatocellular carcinoma cell lines – SMMC7721 and HepG2, lupeol treatment determined inhibition of cells growth and the reduction of cell viability in a dose-dependent manner via induction of apoptosis by activation of caspase-3 and poly (ADP-ribose) polymerase (PARP)cleavage and the increase of the percentages of cells in S phase of the cell cycle [10]. These results were in concordance with the data obtained by Zhang *et al.*, who reported that lupeol treatment induced growth inhibition and apoptosis in SMMC7721 cells by down-regulating the expression of Death Receptor 3 [12].

In another study developed on the same type of hepatocellular carcinoma cell lines as the ones aforementioned, another putative intracellular mechanism of action of lupeol as anticancer agent was postulated. The signaling pathway involved was the PI3K/Akt pathway that plays a key role in various types of cancers, Akt being responsible for the protection of tumor cells against apoptosis. The results of the study showed that lupeol and S14161, a newly identified PI3-Kinase inhibitor, synergistically inhibited tumor growth without any adverse effects on body weight [11].

Lupeol was described as a proapoptotic agent *in vitro*, the compound being able to induce apoptosis in human promyelotic HL-60 leukemia cells [22].

Prasad *et al.*, showed in a study developed on human prostate and mouse prostate cancer cells that lupeol treatment determined the induction of apoptosis via mitochondrial pathway: loss of mitochondrial transmembrane potential and DNA laddering [31]. The antiproliferative and apoptogenic effects of lupeol were demonstrated in other study realized on human prostate cancer cells – PC-3, the intracellular mechanism of action being: inhibition of cell proliferation in a dose and time dependent manner, an increase in the G(2)/M-phase arrest via suppressing the cyclin B signaling pathway (down-regulation of cyclin B, cdc25C, and plk1 expressions). In addition, lupeol upregulated the expression of proapoptotic genes (bax, caspase-3, caspase-9 and apaf genes) and decreased the expression of antiapoptotic bcl-2 gene [16].

A similar mechanism of action of lupeol as the one described for the PC-3 cells was presented in the mouse model of skin cancer induced by application of 7, 12-dimethylbenz[a]anthracene (DMBA): lupeol-induced G2/M-phase arrest until 72 h, and these effects were induced viasuppression of the cyclin-B-regulated signaling pathway involving p53, p21/WAF1, cdc25C, cdc2, and cyclin-B gene expression. Furthermore, lupeolinduced apoptosis with upregulation of bax and caspase-3 genes and downregulation of anti-apoptotic bcl-2 and survivin genes [25].

Lupeol treatment induced inhibition of proliferation, migration and invasion of gallbladder carcinoma GBC-SD cells*in vitro*. *In vivo*, lupeol had similar effects and the mechanism of action involved was associated with the inhibition of EGFR/MMP-9 signaling [23].Zhang and co-workers proved in a study conducted on human hepatocellular carcinoma cells that that lupeol can suppress cell proliferation by inhibiting BDNF secretion and

phosphorylation of GSK-3β(Ser-9), cooperated with blockade of Akt/PI3K and Wnt signaling pathway [13].

A recent study developed by Liu et al., on human pancreatic cancer cells reported that lupeol inhibited cell proliferation in dose- and time-dependent manners and induced apoptosis as well as cell cycle arrest in G0/G1 phase by upregulating P21 and P27 and downregulating cyclin D1, p-AKT and p-ERK expressions [32].

Tarapore and collaborators proved that the mechanism of action underlying the anticancer effects of lupeol in melanoma cells involves the Wnt/β-catenin signaling pathway leading to a decrease in proliferation, viability and growth of melanoma cells and tumors in mice [17]. The Wnt/β-catenin signaling pathway is involved also in the anticancer effects of lupeol in colorectal cancer cells [21].

In a mouse model of two stage carcinogenesis it was demonstrated that topical treatment with lupeol before TPA (12-O-tetradecanoylphorbol-13-acetate) application inhibited the promotion of skin cancer. The mechanism of action of lupeol involved PI3K/Akt and NF-κB pathways. Topical treatment with lupeol before TPA application to mouse skin triggered a decrease inTPA-induced expression of PI3K and phosphorylation of Akt. It is known that NF-κB signaling pathway is activated by different stimuli, such as: growth factors, carcinogens and tumor promoters including TPA. The effect of lupeol on NF-κB pathway consisted in the suppression of TPA-induced NF-kB, IKKα activation, and phosphorylation and degradation of IkBα protein [27].

A protective effect of lupeol was described in a mouse model of skin cancer promotion induced by benzoyl peroxide application, effect characterized by an increase of glutation level and of the other antioxidant enzymes (catalase, glutathione peroxidase, glutathione reductase and glutathione S-transferase) and the susceptibility of cutaneous microsomal membrane to lipid peroxidation and hydrogen peroxide generation was significantly reduced [24].

CONCLUSIONS

The multiple pharmacological effects of lupeol and its lack of toxicity even at high doses make the triterpene compound a promising phytochemical in fighting against cancer. The different signaling pathways targeted by lupeol as anti-inflammatory and anticancer agent offer the possibility to avoid the resistance to therapy that occurs very often in the case of common anticancer therapies. Further studies are required to fully characterize the complex mechanisms of action of lupeol as anti-cancer and anti-inflammatory agent.

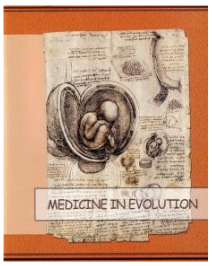
REFERENCES

1. Saleem M. Lupeol, a novel anti-inflammatory and anti-cancer dietary triterpene. Cancer Lett. 2009; 285(2):109-15.
2. Beveridge TH, Li TS, Drover JC. Phytosterol content in American ginseng seed oil. J Agric Food Chem 2002; 50:744–750.
3. Lima LM, Perazzo FF, Tavares Carvalho JC, Bastos JK. Anti-inflammatory and analgesic activities of the ethanolic extracts from Zanthoxylum riedelianum (Rutaceae) leaves and stem bark. J Pharm Pharmacol 2007; 59:1151–1158.
4. Corrêa RS, Coelho CP, dos Santos MH, Ellena J, Doriguetto AC. Lupeol. Acta Crystallogr C. 2009;65(Pt 3):97-9.
5. Minda D, Coricovac D, Panzaru I, Dehelean C, Borcan F, Muntean D. Lupeol is a potent anti-inflammatory agent in the acute inflammation mouse

ear model. Fiziologia/Physiology 2015 (in press).
6. Geetha T, Varalakshmi P.Anti-inflammatory activity of lupeol and lupeol linoleate in rats. J Ethnopharmacol. 2001; 76(1):77-80.
7. Badshah H, Ali T, Rehman SU, Amin FU, Ullah F, Kim TH, Kim MO.Protective Effect of Lupeol Against Lipopolysaccharide-Induced Neuroinflammation via the p38/c-Jun N-Terminal Kinase Pathway in the Adult Mouse Brain.J Neuroimmune Pharmacol. 2015.
8. Lira SR, Rao VS, Carvalho AC, Guedes MM, de Morais TC, de Souza AL, Trevisan MT, Lima AF, Chaves MH, Santos FA. Gastroprotective effect of lupeol on ethanol-induced gastric damage and the underlying mechanism. Inflammo-pharmacology. 2009; 17(4):221-8.
9. Ahmad SF, Pandey A, Kour K, Bani S.Downregulation of pro-inflammatory cytokines by lupeol measured using cytometric bead array immunoassay.Phytother Res. 2010;24(1):9-13.
10. He Y, Liu F, Zhang L, Wu Y, Hu B, Zhang Y, Li Y, Liu H. Growth inhibition and apoptosis induced by lupeol, a dietary triterpene, in human hepatocellular carcinoma cells. Biol Pharm Bull. 2011; 34(4):517-22.
11. Liu F, He Y, Liang Y, Wen L, Zhu Y, Wu Y, Zhao L, Li Y, Mao X, Liu H. PI3-kinase inhibition synergistically promoted the anti-tumor effect of lupeol in hepatocellular carcinoma. Cancer Cell Int. 2013; 13(1):108.
12. Zhang L, Zhang Y, Zhang L, Yang X, Lv Z. Lupeol, a dietary triterpene, inhibited growth, and induced apoptosis through down-regulation of DR3 in SMMC7721 cells. Cancer Invest. 2009; 27(2):163-70.
13. Zhang L, Tu Y, He W, Peng Y, Qiu Z. A novel mechanism of hepatocellular carcinoma cell apoptosis induced by lupeol via Brain-Derived Neurotrophic Factor Inhibition and Glycogen Synthase Kinase 3 beta reactivation. Eur J Pharmacol. 2015; 762:55-62.
14. Saleem M, Murtaza I, Tarapore RS, Suh Y, Adhami VM, Johnson JJ, Siddiqui IA, Khan N, Asim M, Hafeez BB, Shekhani MT, Li B, Mukhtar H. Lupeol inhibits proliferation of human prostate cancer cells by targeting beta-catenin signaling. Carcinogenesis. 2009; 30(5):808-17.
15. Saleem M, Murtaza I, Witkowsky O, Kohl AM, Maddodi N. Lupeol triterpene, a novel diet-based microtubule targeting agent: disrupts survivin/cFLIP activation in prostate cancer cells. Biochem Biophys Res Commun. 2009; 388(3):576-82.
16. Prasad S, Nigam N, Kalra N, Shukla Y. Regulation of signaling pathways involved in lupeol induced inhibition of proliferation and induction of apoptosis in human prostate cancer cells. Mol Carcinog. 2008; 47(12):916-24.
17. Tarapore RS, Siddiqui IA, Saleem M, Adhami VM, Spiegelman VS, Mukhtar H. Specific targeting of Wnt/β-catenin signaling in human melanoma cells by a dietary triterpene lupeol. Carcinogenesis. 2010; 31(10):1844-53.
18. Saleem M, Maddodi N, Abu Zaid M, Khan N, bin Hafeez B, Asim M, Suh Y, Yun JM, Setaluri V, Mukhtar H. Lupeol inhibits growth of highly aggressive human metastatic melanoma cells in vitro and in vivo by inducing apoptosis. Clin Cancer Res. 2008; 14(7):2119-27.
19. Saleem M, Kaur S, Kweon MH, Adhami VM, Afaq F, Mukhtar H. Lupeol, a fruit and vegetable based triterpene, induces apoptotic death of human pancreatic adenocarcinoma cells via inhibition of Ras signaling pathway. Carcinogenesis. 2005; 26(11):1956-64.
20. Prasad S, Madan E, Nigam N, Roy P, George J, Shukla Y. Induction of apoptosis by lupeol in human epidermoid carcinoma A431 cells through regulation of mitochondrial, Akt/PKB and NFkappaB signaling pathways. Cancer Biol Ther. 2009; 8(17):1632-9.
21. Tarapore RS, Siddiqui IA, Adhami VM, Spiegelman VS, Mukhtar H. The dietary terpene lupeol targets colorectal cancer cells with constitutively active Wnt/β-catenin signaling. Mol Nutr Food Res. 2013; 57(11):1950-8
22. Aratanechemuge Y, Hibasami H, Sanpin K, Katsuzaki H, Imai K, Komiya T. Induction of apoptosis by lupeol isolated from mokumen (Gossampinus malabarica L. Merr) in

human promyelotic leukemia HL-60 cells. Oncol Rep. 2004; 11(2):289-92.
23. Liu Y, Bi T, Shen G, Li Z, Wu G, Wang Z, Qian L, Gao Q. Lupeol induces apoptosis and inhibits invasion in gallbladder carcinoma GBC-SD cells by suppression of EGFR/MMP-9 signaling pathway. Cytotechnology. 2014.
24. Saleem M, Alam A, Arifin S, Shah MS, Ahmed B, Sultana S.Lupeol, a triterpene, inhibits early responses of tumor promotion induced by benzoyl peroxide in murine skin. Pharmacol Res. 2001; 43(2):127-34.
25. Nigam N, Prasad S, George J, Shukla Y.Lupeol induces p53 and cyclin-B-mediated G2/M arrest and targets apoptosis through activation of caspase in mouse skin.Biochem Biophys Res Commun. 2009; 381(2):253-8.
26. Manoharan S, Palanimuthu D, Baskaran N, Silvan S.Modulating effect of lupeol on the expression pattern of apoptotic markers in 7, 12-dimethylbenz(a)anthracene induced oral carcinogenesis.Asian Pac J Cancer Prev. 2012; 13(11):5753-7.
27. Saleem M, Afaq F, Adhami VM, Mukhtar H. Lupeol modulates NF-kappaB and PI3K/Akt pathways and inhibits skin cancer in CD-1 mice. Oncogene. 2004; 23(30):5203-14.
28. Tarapore RS, Siddiqui IA, Saleem M, Adhami VM, Spiegelman VS, Mukhtar H.Specific targeting of Wnt/β-catenin signaling in human melanoma cells by a dietary triterpene lupeol. Carcinogenesis. 2010; 31(10):1844-53.
29. Lee TK, Poon RT, Wo JY, Ma S, Guan XY, Myers JN, Altevogt P, Yuen AP.Lupeol suppresses cisplatin-induced nuclear factor-kappaB activation in head and neck squamous cell carcinoma and inhibits local invasion and nodal metastasis in an orthotopic nude mouse model. Cancer Res. 2007;67(18):8800-9.
30. Murtaza I, Saleem M, Adhami VM, Hafeez BB, Mukhtar H. Suppression of cFLIP by lupeol, a dietary triterpene, is sufficient to overcome resistance to TRAIL-mediated apoptosis in chemoresistant human pancreatic cancer cells. Cancer Res. 2009;69(3):1156-65.
31. Prasad S, Kalra N, Shukla Y.Induction of apoptosis by lupeol and mango extract in mouse prostate and LNCaP cells.Nutr Cancer. 2008;60(1):120-30.
32. Liu Y, Bi T, Wang G, Dai W, Wu G, Qian L, Gao Q, Shen G.Lupeol inhibits proliferation and induces apoptosis of human pancreatic cancer PCNA-1 cells through AKT/ERK pathways.Naunyn Schmiedebergs Arch Pharmacol. 2015; 388(3):295-304.

CUTANEOUS MANIFESTATIONS IN RHEUMATOID ARTHRITIS



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ABSTRACT

Rheumatoid arthritis (RA) is an immune-mediated disease which usually affects joints. This systemic disease showed to have many manifestations, especially on skin. Most RA patients present subcutaneous lesions over 5-mm wide, and could be included into rheumatoid nodules as well as small-vessel vasculitis which present different clinical polymorphism. Pyoderma gangrenosum or Sweet's which can be distinguished from neutrophilic dermatoses which could be rarely seen in RA patients. The immunological mechanism of the different cutaneous manifestations of RA like rheumatoid nodules, rheumatoid vasculitis, neutrophilic dermatoses, and pyoderma gangrenosum are still unknown. In this regard, different outcome measures are required to perform further studies which will facilitate clinical and therapeutic studies.

Key words: *cutaneous, rheumatoid arthritis, nodules, vasculitis, therapeutic*

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INTRODUCTION

Rheumatoid arthritis (RA) is a disease that associates cutaneous involvement (1). Specific RA-associated cutaneous manifestations are characterized by the appearance of subcutaneous different lesions representing usually by classical nodules and/or vasculitis (2).

The immunological mechanism underlying the cutaneous manifestations of RA including rheumatoid nodules, rheumatoid vasculitis, neutrophilic dermatoses, and pyoderma gangrenosum are still unknown in the present. Whatsoever, immune complex of such deposition are still in debate.

RHEUMATOID NODULES

Subcutaneous lesions in the form of rheumatoid nodules are represented by more than 5-mm deep is the most common skin manifestatio in RA patients; usually affect the exterior part of the organism including forearms, the back of the arms, the occipital regions, including also other common regions. By a deeper search, it presents an intermediate area of macrophages and a peripheral area with many infiltrations (2).

In this case, elevated levels of tumor necrosis factor -α (TNF-α) with anti-inflammatory impact especially on the skin were observed (3).

If we are talking about treatment it is hard to believe that spontaneous regression could be seen, rather than a direct amelioration do to specific RA treatment administration. Many clinical studies found some promising answer in surgical excisions, and many patients are most treated in this way (2).

Another particular implication could be seen by the so called"accelerated rheumatoid nodules"which affect especially proximal interphalangeal joints. This are very hard to be distinguished by other nodules and surprisingly, they can be treated usually with drugs like methothexate, azathioprine, leflunomide, and TNF-α (4, 5).

RHEUMATOID VASCULITIS

Vasculitis represents another cutaneous lesion which is specific at RA patients. In this case, patients present usually a higher rheumatoid factor, elevated values of anti-citruline peptide antibody and erytrocite sedimentation rate, the skin being the most affected. The clinical picture shows a leukocytosis and polymorphism like ulcerative until occurrence of the necrotic area with eschars. This can be included into a systemic necrotizing vasculitis and/or urtical vasculitis (6) and is defined as benign manifestations involving a relevant and depicted mortality (7).

Usually the patients present an ulcerative-digital lesions into an advanced phase of the disease, with a clear clinically manifestations. It could be also seen necrosis of the vassal wall, perivasal inflammatory infiltration, suggesting the typical leukocytosis pattern including immunoglobulin perivasal deposits, predominantly IgG (8).

Many cutaneous infiltrations present a higher hypersensitivity involving the immune complex mechanism, in which cluster of differentiation (CD)4 plays an important role together with neutrophils. In this area direct implication of endothelium could be seen like damage till necrosis, activating the coagulation pathogenesis

cascade of the lesions (9). The treatment in the case of rheumatoid vasculitis includes corticoids and dapsone, cyclosporine and other chemical immunosuppresors used in this kind of lesions. However, cyclophosphamide and rituximab represents the best choice for systemic disease like rheumatic vasculitis.

NEUTROPHILIC DERMATOSES

Regarding the neutrophilic dermatoses, Marzano and contributors published a study in which neutrophilic dermatoses began to shows different shapes including epidermal, dermal, hypodermal, or mixed (10).

Neutrophilic dermatoses are usually characterized by neutrophil density at lesion from different parts of the body.

PYODERMA GANGRENOSUM

Another systemic dermatosis is represented by pyoderma gangrenosum which develop RA seropositive (11). This can be distinguished by an agglomeration of postules which began to develop into painful ulcers, having very deep shape and an erythematous-purple coloring (12). In these case where neutrophils are involved in predicting the affected skin, it's a rare condition which could be seen at patients which presented such manifestations. In this case, any organ of the body can be involved, especially joints affection.

Neutrophilic polymorphonuclear (PMNs) leukocytes could be found with seronegative destructive polyarthritis or acute monoarthritis. The systemic disease can also affect lungs (with PMNs), kidneys (by nephritic syndrome), bones (by chronic-recurrent multifocal osteomyelitis), central nervous system (aseptic meningitis or encephalitis), eyes (uveitis, episcleritis, ulcerative keratitis). Moreover, neutrophilic affection can also be associated with other aseptic abscesses affecting different organs, especially liver, spleen, and pancreas (13).

The pathological mechanism in neutrophilic affection has been only recently achieved and shows that this type of mutations can induce the neuthrophilic inflammation activating in the same time caspase-1, which is the enzyme determining the proteolitic clivage of inactive pro-interleukin-1-beta into interleukin-1-beta. Interleukin-1-beta is a cytokine which regulates a number of reactions like the stimulus to release chemokines. Moreover, this process is known as chemotactic recruitment of neutrophils which represent the central dogma of neutrophilic dermatoses. This could be also seen as an autoinflammation model applied usually to this kind of systemic disease (14).

Nuetrophilic dermatoses could also involve RA but its presentation is different, presenting many types of dermatoses. Some cases were reported showing an association at patients between pyoderma gangrenosum and Sweet's syndrome. Others like pyoderma gangrenosum and neutrophilic dermatitis. Some patients having RA coupling with pyoderma gangrenosum could be treated with anti-TNF-α, which has the ability to prevent the appearance of such dermatoses (15).

Another autosomic syndrome like Pyogenic sterile arthritis, Pyoderma gangrenosum acne (PAPA) could be seen and could be also involved in RA manifestation. In this case, two mutations in exons 10 and 11 from chromosome 15 have been showed and presented an abnormal

activation of the immunological response presented different immunopathological events. Another syndrome which should be mentioned is Synovitis, Acnee, Pustolosis, Hyperostosis, Osteomyelitis (SAPHO) in which an association of skin and rheumatoid manifestation could be seen together. This also could be trigger by the pain release on the anterior wall (15).

Another syndrome like PA-Pyodermqa gangrenosum, Acnee, Suppurative Hidradenitis (PASH) could be also presented by the combination of PAPA and PASH syndromes, with different immunological aspects and defined by a new mutation of exon 11 on the same chromosome (16).

Anti-TNF-α's which are inhibitors, could develop at many patients having RA an eruption, which could be distinguished from psoriasis in different many ways. The typically eruption involved drug cessation and may also interfere with other administered drugs (17).

CONCLUSIONS

In RA patients, different skin manifestations are often present. In this respect, the skin which is the easiest way to be observed will continue to enhance our understanding of this systemic disease. Together with the clinically picture of the patients a multidisciplinary outcome measures will enable the performance of the best diagnosis income in different clinical trials.

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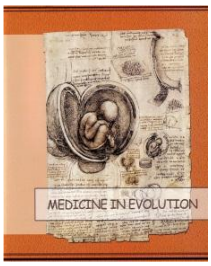
REFERENCES

1. Prete M, et al. Extra-articular manifestation of rheumatoid arthritis: An update.Autoimmun Rev. 2011 Dec;11(2):123–31.
2. Rozin A, Ygla M, Guralnik L et al., Rheumatoid lung nodules and osteopathy associatedwith leflunomide therapy, Clin Rheumatol 2006, 25: 384-388.
3. Chao J, Parker BA, Zvaifler NJ, Accelerated cutaneous nodulosis associated with aromatase inhibitor therapy in a patient with rheumatoid arthritis, J Rheumatol, 2009, 36: 1087-1088.
4. Stenn VD, Medsger TA Jr. Improvementin skin thickening in systemic sclerosis associated with improved survival, Arthritis Rheum 2001, 44: 2828-2835.
5. Sayah A, English JC, Rheumatoid arthritis: a review of the cutaneous manifestations, J Am Acad Dermatol, 2005, 53, 191-209.
6. Turesson C, Matteson EL, Vasculitis in rheumatoid arthritis, Curr Opin Rheumatol, 2009, 21: 35-40.
7. Puechal X, Miceli-Richard C, Mejjad O et al., Antitumor necrosis factor treatment in patients with refractory systemic vasculitis associated with rheumatoid arthritis, Ann Rheum Dis, 2008, 67: 880-884.
8. Kawakami T, Yamazaki M, Kawasaki K et al., Therapeutic effect of argatroban on rheumatoid vasculitis with antiphosphatidylserine-prothrombin complex antibody, Arch Dermatol, 2008, 144: 1075-1076.
9. Khanna D, Clements PJ, Furst DE et al., Recombinant human relaxin in the treatment of systemic sclerosis with diffuse cutaneous involvement: a randomized, double-blind, placebo-controlled trial, Arthritis Reum, 2009, 60, 1102-1111.
10. Marzano AV, et al. Neutrophilic dermatoses and inflammatory bowel

diseases.G Ital Dermatol Venereol. 2013 Apr;148(2):185–96.
11. Langan SM, et al. Incidence, Mortality, and Disease Association of Pyoderma Gagrenosum in the United Kingdom: a Retrospective Cohort Study. J Invest Dermatol. 2012;132:2166–2170.
12. Kawachi Y, Nakamura Y, Yoh K et al., Rheumatoid papules successfully treated with oral tacrolimus, J Eur Acad Dermatol Venereol, 2008, 22: 241-242.
13. Dourmishev LA, Dourmishev AL. Activity of certain drugs in inducing of inflammatory myopathies with cutaneous manifestations, Expert Opin Drug Sat 2008, 7: 421-433.
14. Marzano AV, et al. Role of inflammatory cells, cytokines and matrix metalloproteinases in neutrophil-mediated skin diseases. Clin Exp Immunol. 2010 Oct;162(1):100–7.
15. Wollina U, Hansel G, Koch A et al., Tumor necrosis factor-alpha inhibitor-induced psoriasis or psiriasiform exanthemata: first 120 cases from the literature including a series of six new patients, Am J Clin Dermatol, 2008, 9: 1-14.
16. Daoussis D, Liossis SN, Taamandas AC et al. Experience with rituximab in scleroderma: results from 1-year, proof-of-principle study, Rheumatology (Oxf), 2009.
17. Fiorentino DF. The Yin and Yang of TNF-alfpha inhibition, Arch Dermatol, 2007, 143: 233-236.



CYTOARHITECTONICS CHANGES ASSOCIATED WITH DIFFERENT AGES OF MYOCARDIAL INFARCTION

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ABSTRACT

Although myocardial infarction (MI) is a pathology that occurs in old people, young people can also suffer one acute cardiac event. Even in the absence of previous symptoms, some young patients can have coronary artery disease or chronic abnormalities that are not known. The objective of this study is to evaluate the preexistent chronic morphological aspects in young patients with myocardial infarction as the cause of death. We analyzed 212 forensic cases autopsied at the Bucharest National Institute of Legal Medicine"Mina Minovici"using necropsy reports and cardiac tissue samples for the pathological investigation. The study groups included patients with acute myocardial infarction (AMI), subacute myocardial infarction (SMI), patients that had a second myocardial infarction (reinfarction), others who had silent scared myocardial infarction and the control group without any known cardiovascular disease. Mild and moderate atherosclerosis was associated with subacute and scared MI, and severe lesions were associated with reinfarction. Severe myocardial fibrosis was highly associated with AMI and reinfarction, and its absents or mild form with myocardial scarring. Lipomatosis was correlated with old scarring myocardial infarct. Our study showed a correlation between chronic changes of the myocardium (fibrosis, lipomatosis and atherosclerotic lesions) and the occurrence of MI at different ages. Myocardial fibrosis leads to increased myocardial stiffness by promoting cardiac dysfunction.AMI associated mild atherosclerosis and lipomatosis with severe fibrosis, suggesting that people having the above mentioned chronic changes didn't have the resources for tissue remodeling to overcome the event, passing away in a shorter period of time compared with those who had more severe atherosclerosis, that subsequently allowed the formation of collateral circulation.

Key words: *myocardial infarction, cardiac fibrosis, young patients, atherosclerotic changes, lipomatosis*

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INTRODUCTION

Acute myocardial infarction represents an intensive studied pathology in clinical studies as well as in fundamental cellular research. Morphopathological changes represent the background for acute events in young and old patients. Atherosclerosis represents the main vascular inflammatory disease that leads to the alteration and remodeling of cardiac tissue, causing silent ischemic lesions whose initial manifestation can be sudden cardiac death (SCD). The disease can appear from the first years of life, its severity depends on multiple risk factors that don't always have a proportional histological expression(Murray CJL, 1997). In young people numerous studies concluded that SCD appears especially in individuals with intense physical activity, such as performance athletes (AHA, updated 2015). For individuals with a regular life style and activity, most of the changes are nonspecific, or are not sufficiently severe to explain the acute cardiac event that sometimes results in death. In some cases the cardiac lesions that are investigated through standard methods make it difficult to ascertain the cause of death with a high degree of certainty. Other chronic changes, such as fibrosis and lipomatosis, known as morphological expressions of chronic cardiac pathologies, appear even in young people with no symptoms.

Objectives

The aim of this study was to evaluate the preexistent chronic morphological aspects in young patients with myocardial infarction as the cause of death, without previous cardiac symptoms.

MATERIAL AND METHODS

Case selection for the study batch

We have retrieved from our database, in queue, in an interval between 1 Jan. 2010 – 31 Dec. 2013, 212 forensic autopsy cases from the National Institute of Legal Medicine"Mina Minovici"Bucharest using necropsy reports and cardiac tissue samples for the pathological investigation.

The study batch consisted of 171 male and 41 female patients (sex ratio M: F = 4,17: 1), with age between 18 and 50 years old. *The study groups* include: patients with acute myocardial infarction (AMI), patients with subacute myocardial infarction (SMI), patients that had a second myocardial infarction (reinfarction) and patients who had silent old myocardial infarction.

For the *study group* we used the descriptive microscopic assessment of myocardial infarction of different ages as a grading system. Myocardial infarction lesions of different ages were shown and split into groups based on the type of the infarction: acute, subacute, old and reinfarction. From the study batch were excluded the cases presenting age greater than 50 years old and sudden deaths with cardiac pathologies, but without acute cardiac infarction.

We selected the *control group* from consecutive cases of young patients that died in traffic accidents from cranial-cerebral trauma (TCC), without having any known cardiac pathologies. The inclusion criteria for the *control group* were: age between 18 and 50 years and the existence of a pathological exam that included the collection of cardiac fragments. The exclusion criteria: any traumatic cardiac injuries (cardiac rupture, aorta dissection, visible cardiac bruising).

The study has received ethical approval from the local ethics committee. Subsequently, tissue

samples for microscopy analysis were taken according to the law for medico-legal investigation, using a protocol approved by the local Bioethics Committee, in accordance to generally accepted international practice.

Tissue sampling and stains:

Tissue specimens were taken for histopathology investigation required at autopsy. The fragments were harvested from the left and right ventricles.

The selected tissue samples were fixed in 10% neutral buffered formalin (pH - 7) for 24–48 hours and paraffin embedded. Sections were cut at 5 µm and stained with standard HE and histochemical colorations (Lie, PTAH, van Gieson, Masson – in order to show the hypoxic areas or fibrosis areas).

Statistics:

In order to evaluate the data and to realize the statistical analysis, descriptive statistics were used for the uniformly distributed data of the study batch to calculate the mean, median and standard error. In order to study the associations between the qualitative variables we used the crosstab function with the parametric Pearson Chi square test. The non-parametric analysis was made with the Kendal-tau test. Statistical analysis was performed in SPSS–20 software, running under Windows 8.1. A value of $p<0.05$ was considered statistically significant.

RESULTS

The study batch included: 70 cases with AMI aged 3 weeks or less (33%), 31 cases (14.6%) with subacute myocardial infarction that occurred within 3-7 weeks from the subject's death, 49 cases (23.1%) with old myocardial infarction that was older than 7 weeks and 18 cases (8.5%) with reinfarction in the same area after a previous myocardial infarction. The control group was composed of 44 cases (20.8% of the total number of cases included in the study).

The mean age of the total batch was 39 years for men and 38 years for women. The median was 42 years in both cases. The mean age for the study group with MI (acute, subacute, reinfarction) was about 40 years, and for the group with old MI the mean age was 42 years. The control group, having been selected from consecutive cases, had the mean age of 35 years. The mean age for women from the study batch (41 cases – 19.34%) was smaller than the mean age for men (171 cases – 80.66%) by 2 years.

Within the study sample, women had predominantly more AMI, while the men were more evenly distributed. The sex ratio was very large in the case of subacute myocardial infarction (30:1) and in the case of reinfarction (18:0) while being very low in the case of AMI (1.9:1) Pearson Chi-Square value = 19.823 ($p<0.001$). (Chart.1)

Most of the patients with myocardial infarction (regardless of its type – acute, subacute, old or reinfarction) had atherosclerosis (ATS) in 59.1% of the cases. Patients from the control group had atherosclerosis in 15.9% of the cases, most of them not having this pathology. (Pearson Chi value = 70517 with $p<0.0001$). 70% (49 cases) of the deceased patients with AMI had atherosclerosis and 88.9% of the cases with reinfarction also had this condition. (Chart. 2)

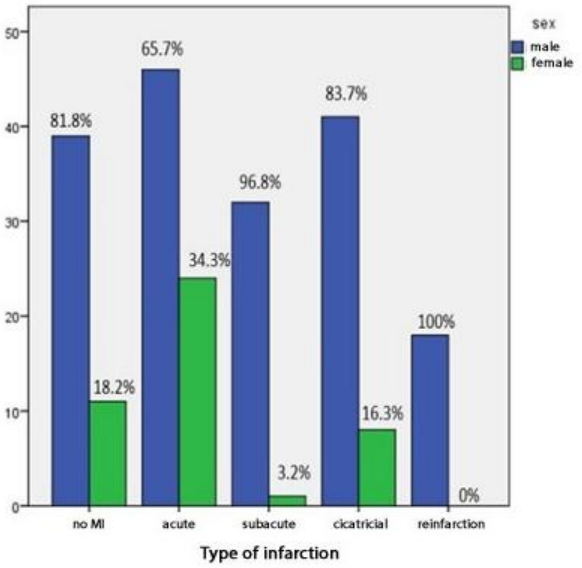

Chart 1. Myocardial infarction age by gender

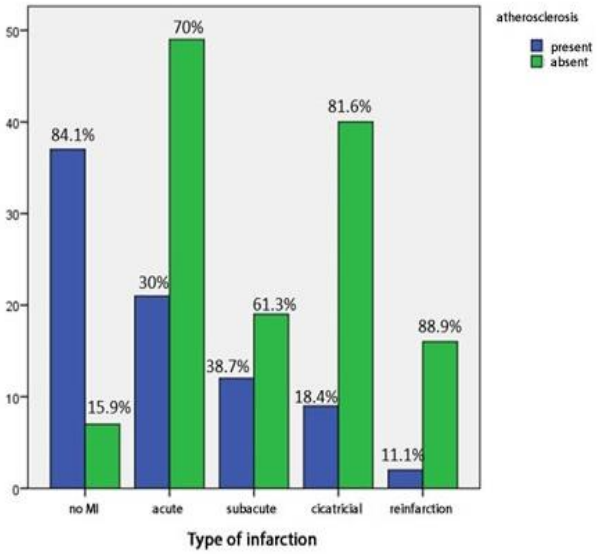

Chart 2. Myocardial infarction age with atherosclerosis

When analyzing the severity of atherosclerosis in terms of MI age, we noticed that the patients with AMI have predominantly mild and moderate or have no atherosclerosis while the ones with sub-acute MI have predominantly the absence of atherosclerosis, patients with scar MI have predominantly mild and moderate ATS, and the cases with reinfarction had predominantly severe ATS. The association between the severity of ATS and MI was statistically significant (Pearson Chi^2 value – 55.003, $p<0.001$) see table 1.

Table 1. *Cases with coronary atherosclerosis by myocardial infarction age*

Infarction type * Coronary atherosclerosis Crosstabulation

	Coronary atherosclerosis				Total
	Absent or unquantifiable	Mild	Moderate	Severe and complicated	
Without MI	37 (84.1%)	6 (13.6%)	1 (2.3%)	0 (0.0%)	44 (100.0%)
Acute	21 (30.0%)	18 (25.7%)	19 (27.1%)	12 (17.1%)	70 (100.0%)
Subacute	12 (38.7%)	4 (12.9%)	9 (29.0%)	6 (19.4%)	31 (100.0%)
Old MI	9 (18.4%)	14 (28.6%)	18 (36.7%)	8 (16.3%)	49 (100.0%)
Reinfarction	2 (11.1%)	3 (16.7%)	4 (22.2%)	9 (50.0%)	18 (100.0%)
Total	81 (38.2%)	45 (21.2%)	51 (24.1%)	35 (16.5%)	212 (100.0%)

In some cases coronary atherosclerosis determines a macroscopically visible narrowing of the artery, which was in correlation with the presence of MI. (Spearman r = 0.366, $p<0.001$ and Kendal-tau coefficient = 0.336 with $p < 0.001$). See table 2.

In our study 13 (18,6%) of cases with AMI and 6 cases (33,3%) of reinfarction cases presented intraluminal thrombosis.(Pearson Chi^2 value – 23.053, $p<0.001$).

Table 2. *Cases with luminal narrowing by grade of coronary atherosclerosis*

Coronary atherosclerosis * Arterial luminal narrowing Crosstabulation

		Arterial luminal narrowing		Total
		Without luminal narrowing	Luminal narrowing	
Coronary atherosclerosis	Absent or unquantifiable	74 (91.4%)	7 (8.6%)	81 (100.0%)
	Mild	40 (88.9%)	5 (11.1%)	45 (100.0%)
	Moderate	44 (86.3%)	7 (13.7%)	51 (100.0%)
	Severe and complicated	13 (37.1%)	22 (62.9%)	35 (100.0%)
Total		171 (80.7%)	41 (19.3%)	212 (100.0%)

Table 3. *Cases with intraluminal thrombosis by myocardial infarction age*

Infarction type * Intraluminal thrombosis Crosstabulation

	Intraluminal thrombosis		Total
	Absent	Prezent	
Without MI	44 (100.0%)	0 (0.0%)	44 (100.0%)
Acute	57(81.4%)	13 (18.6%)	70 (100.0%)
Subacute	28 (90.3%)	3 (9.7%)	31 (100.0%)
Old MI	48 (98.0%)	1 (2.0%)	49 (100.0%)
Reinfarction	12 (66.7%)	6 (33.3%)	18 (100.0%)
Total	189 (89.2%)	23 (10.8%)	212 (100.0%)

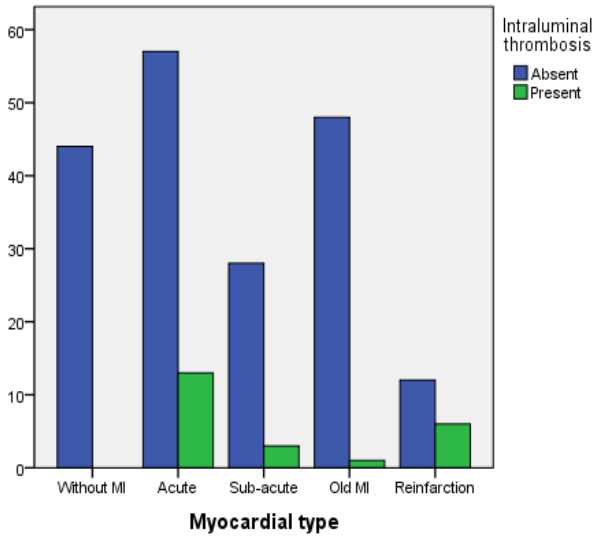

Chart 3. Myocardial infarction age with intraluminal thrombosis

During the statistical analysis we also noticed a strong correlation between the severity of myocardial fibrosis and the presence of atherosclerosis ($r = 0.239$, $p<0.001$). 40% (14 cases) of the ones with atherosclerosis also had severe myocardial fibrosis. From the cases with moderate and mild atherosclerosis, 33.3% (17 cases) and respectively 35.5% (16 cases) showed moderate forms of interstitial and

perivascular myocardial fibrosis. The more severe and complicated the atherosclerosis lesions were, the more they presented severe myocardial fibrosis. See details in table 4.

Table 4. *Association between coronary atherosclerosis and myocardial fibrosis*

Myocardial fibrosis* Coronary atherosclerosis Crosstabulation

		Coronary atherosclerosis				Total
		Absent or unquantifiable	Mild	Moderate	Severe and complicated	
Myocardial fibrosis	Absent	22 (27.2%)	28 (34.6%)	22 (27.2%)	9 (11.1%)	81 (100.0%)
	Mild	8 (17.8%)	16 (35.6%)	16 (35.6%)	5 (11.1%)	45 (100.0%)
	Moderate	5 (9.8%)	20 (39.2%)	17 (33.3%)	9 (17.6%)	51 (100.0%)
	Severe	3 (8.6%)	6 (17.1%)	12 (34.3%)	14 (40.0%)	35 (100.0%)
	Total	38 (17.9%)	70 (33.0%)	67 (31.6%)	37 (17.5%)	212 (100.0%)

The group with AMI predominantly had moderate and severe fibrosis. Patients who died after a subacute MI had mostly moderate fibrosis. For the cases with scarring myocardial infarction, the statistics show the predominance of mild fibrosis. Cases from the group with reinfarction presented moderate and severe fibrosis.

The absence of myocardial fibrosis or its presence in mild or moderate form it is almost similar in the control group (without MI). (Pearson $Chi^2 = 47.751$ with $p<0.0001$). See table 5.

Table 5. *Cases with myocardial fibrosis by myocardial infarction age*

	Interstitial myocardofibrosis				
	Absent	Mild	Moderate	Severe	Total
Without MI	12 (27.3%)	19 (43.2%)	12 (27.3%)	1 (2.3%)	44 (100.0%)
Acute	9 (12.9%)	14 (20.0%)	25 (35.7%)	22 (31.4%)	70 (100.0%)
Subacute	11 (35.5%)	8 (25.8%)	10 (32.3%)	2 (6.5%)	31 (100.0%)
Old MI	4 (8.2%)	27 (55.1%)	14 (28.6%)	4 (8.2%)	49 (100.0%)
Reinfarction	2 (11.1%)	2 (11.1%)	6 (33.3%)	8 (44.4%)	18 (100.0%)
Total	38 (17.9%)	70 (33.0%)	67 (31.6%)	37 (17.5%)	212 (100.0%)

Perivascular and interstitial lipomatosis was identified (in different stages) in 113 subjects (53.3%). From these cases, 17 (8%) presented moderate forms and 15 cases (7.1%) presented severe forms of lipomatosis. In the cases with death by AMI there was no correlation with the presence of lipomatosis in our groups with young people. In over 50% of these cases there was no lipomatosis. On the other hand, in cases with old MI we notice the presence of lipomatosis indifferent stages up to 80% of cases. (Pearson Chi2 = 50,012 with $p<0.001$)

Analyzing the severity of lipomatosis reported to the presence of atherosclerosis we notice the existence of a correlation between these changes. While the relationship between these values isn't proportional, it is nevertheless statistically valid with a Pearson $Chi^2 = 31.845$ with $p<0.001$ and Kendal-tau = 0.233 with $p<0.001$. Details in table 6.

Table 6. *Association between coronary atherosclerosis and lipomatosis*

Lipomatosis *CoronaryatherosclerosisCrosstabulation

		Coronary atherosclerosis				Total
		Absent or unquantifiable	Mild	Moderate	Severe and complicated	
Lipomatosis	Absent	49 (49.5%)	18 (18.2%)	22 (22.2%)	10 (10.1%)	99 (100.0%)
	Mild	25 (30.9%)	23 (28.4%)	21 (25.9%)	12 (14.8%)	81 (100.0%)
	Moderate	4 (23.5%)	1 (5.9%)	7 (41.2%)	5 (29.4%)	17 (100.0%)
	Severe	3 (20.0%)	3 (20.0%)	1 (6.7%)	8 (53.3%)	15 (100.0%)
Total		81 (38.2%)	45 (21.2%)	51 (24.1%)	35 (16.5%)	212 (100.0%)

We also evaluated other structural changes such as the presence of arteriolosclerosis, endocardial fibrosis, myofibrillar hypertrophy adjacent to the injured area, sub endocardium miocytolysis, granular vascular degeneration, presence of coagulation necrosis or of necrosis in coagulation bands, or the presence of myocardial bridging. There was no evidence for statistically significant correlations between these changes and the study samples that were taken into consideration.

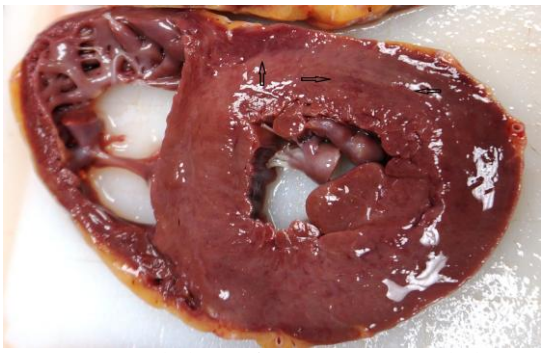

Figure 1. Gross pathology of an acute myocardial infarction located on the posterior wall of the left ventricle (1-3 days)

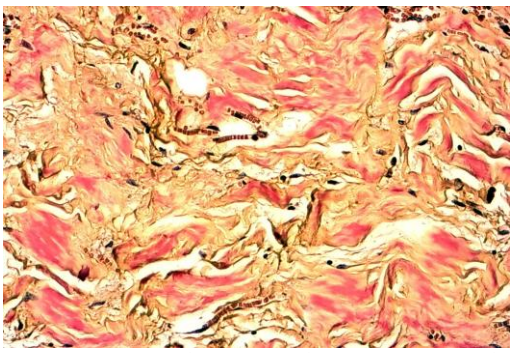

Figure 2. Acute hypoxic ischemia in myocardial fibers (focal reaction), Lie stain, 200x

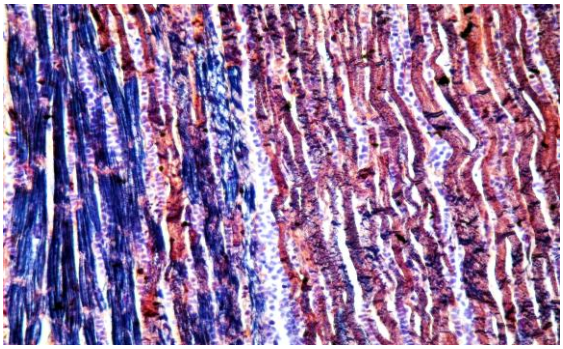

Figure 3. Cardiomyocytes with contraction bands necrosis (right), PTAH 400x

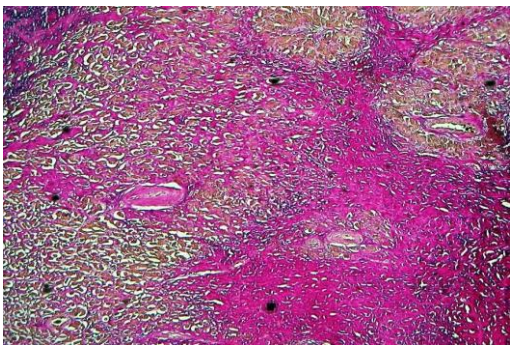

Figure 4. Old scared myocardial infarction about 4 – 6 weeks, VG stain 50x

DISCUSSIONS

In the study groups, patients with AMI predominantly, had moderate to severe myocardial fibrosis and showed mild lipomatosis. The severity of fibrosis increases with the severity of atherosclerosis, but the severity of lipomatosis is not directly related to the presence of atherosclerosis.

The present study revealed a higher presence of infarction in men than women. Women had predominantly more AMI, while the men's infarction lesions were more evenly distributed with acute, sub-acute, scarring myocardial infarction or reinfarction. While the presence of AMI in young women lead to sudden cardiac death in many cases, the number of cases with SCD was lower in men. In the male group there were many cases with late MI complications, as well as other causes of death unrelated with the myocardial scarring.

Coronary heart disease represents the main cause of death due to myocardial infarction in developed countries.(Klein LW, 2003) This pathology in young patients aged less than 40 years represented only 3% of all patients with coronary atherosclerosis.(Jaloweil DA, 1989) In the present study, this has frequently occurred in all investigated groups. Other studies have shown that atherosclerosis starts from the beginning of life, even in young people without cardiovascular disease. (Henry C McGill Jr, 2000, Strong JP, 1999). Otherwise the severity of atherosclerosis is not dependent only on age.(Z, 1991) Regardless of associated risk factors, patients with lethal IMA often had just mild and moderate atherosclerosis, without thrombus in situ or embolic parts of atherosclerotic plaque. This can be explained by the fact that the patient's death was not caused by a massive infarction, the actual cause being the malign rhythm disturbances that don't have a morphological expression. Also the collateral circulation plays an important role in the adaptation after myocardial infarction.(Gianmario Sambuceti, 1995) Atherosclerosis is the main cause of chronic ischemic cardiomyopathy(Hansson, 2005) through luminal narrowing(MJ, 1996). Collateral circulation can decrease the severity of an acute event. Our study showed that mild and moderate forms correlate with old infarction and severe forms are associated with reinfarction. In the CASS study, an increased number of cases with normal coronary arteries (up to 18%) and minor coronary artery abnormalities were found(Zimmerman FH, 1995). In our study batch we also had a lot of cases with normal arteries associated with AMI (30%) or sub-acute myocardial infarction (38,7%). These patients could have non-atheromatous coronary artery abnormalities such as congenital coronary artery anomalies(Cristina Basso, 2000) or myocardial bridging(Klues HG, 1997). Although the association between myocardial infarction and myocardial bridging wasn't statistically significant, in the study group we had 6 cases (2,8%) divided by the aging of the MI into 3 cases with AMI, 2 cases with sub-acute MI and 1 case with old infarction.

Thrombotic complications due to atherosclerosis plaque rupture is another important cause of mortality among people with coronary atherosclerotic disease. Plaque disruption depends on intrinsic factors (lipid and fibrotic content, cell population) and extrinsic vulnerability factors (circumferential mechanical stress, vasoconstriction or hemodynamic stress).(Zaman A.G., 2000) Thrombosis forms over atherosclerotic plaques following vessel injury(Farb A, 1997). In our study 18,6% of cases with AMI and 33,3% of reinfarction cases presented intraluminal thrombosis. The percentage in our findings is a lot bigger than other studies that found less than 10% (Michael John Davies, 1984). The thrombus recanalization were present in just 4 cases (1.9%) (2 patients with AMI and 2 with sub-acute MI).Other studies showed that reperfusion of reversibly or partial reversibly injured myocardium leads to structural improvement and reorganization.(Jutta Schaper, 1983)

Myocardial fibrosis, the morphologic expression of ischemic

cardiomyopathy, leads to increased myocardial stiffness by promoting cardiac dysfunction. The moderate and severe forms of interstitial myocardial fibrosis in patients who died due to AMI (or reinfarction) suggest that subjects with advanced pathology having an acute event did not have resources for tissue remodeling and rehabilitation to overcome the event, passing away in short time. Instead, young subjects who had an old infarction, tend to develop discrete fibrotic damage, which may suggest the importance of other complementary factors such as lifestyle (Murray CJL, 1997), metabolic syndrome (S. Pandey, 2009), undiagnosed and untreated essential hypertension (Maria Dorobantu, 2014), or substance abuse (El, 2006). Perivascular and interstitial severe fibrosis was seen in almost a half of cases with infarction, after an old event.

CONCLUSIONS

Our study showed a correlation between some chronic changes of the myocardium (as fibrosis, lipomatosis and also atherosclerotic lesions) and MI of different ages. Myocardial fibrosis leads to increased myocardial stiffness by promoting cardiac dysfunction.

Cases with acute myocardial infarction who had severe myocardial fibrosis also had mild and moderate atherosclerosis, which suggests that the luminal narrowing caused by atherosclerosis wasn't severe enough to create a hypoxic medium that would encourage the formation of collateral blood vessels. Given these conditions, when the myocardial infarction occurred, it lead to sudden death. This also suggests that patients with AMI had other asymptomatic pathologies (such as arterial hypertension, congenital cardiac diseases or channelopathies) that led to cardiac fibrotic remodeling.

Patients with old myocardial infarction, had mild and moderate associated cardiac fibrosis, which suggests that they didn't have severe fibrotic associated pathologies, instead they had diseases that caused the formation of collateral circulation that helped them survive the acute event.

In the case of patients with sub-acute myocardial infarction, many of the cases didn't have any atherosclerosis or myocardial fibrosis, or the present forms were mild or moderate.

Patients that had had a reinfarction showed severe forms of atherosclerosis and fibrosis.

Acknowledgments

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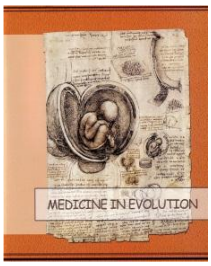
REFERENCES

1. AHA, AHA. Youths & Cardiovascular Diseases http://wwwheartorg/idc/groups/heart-public/@wcm/@sop/@smd/documents/downloadable/ucm_472920pdfupdated 2015.
2. Cristina Basso, BJM, Domenico Corrado, Gaetano Thiene. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. J Am Coll Cardiol. 2000;35(6):1493-501.

3. El, MAA. Drug-induced myocardial infarction secondary to coronary artery spasm in teenagers and young adults J Postgrad Med 2006;52(51-56
4. Farb A, BA, Malcolm GT, Liang Y, Mannan P, Smialek J, Virmani R. Coronary risk factors and plaque morphology in men with coronary disease who died suddenly New Engl J Med. 1997;336(1276–82.
5. Gianmario Sambuceti, OP, Assuero Giorgetti, Piero Salvadori, Mario Marzilli, Piero Dabizzi, Paolo Marzullo, Danilo Neglia, Antonio L'Abbate. Microvascular dysfunction in collateral-dependent myocardium. J Am Coll Cardiol. 1995;26(3):615-23.
6. Hansson, GK. Inflammation, Atherosclerosis, and Coronary Artery Disease. N Engl J Med. 2005;352(1685-95.
7. Henry C McGill Jr, CAM, Edward E Herderick, Gray T Malcom, Richard E Tracy, and Jack P Strong Origin of atherosclerosis in childhood and adolescence. Am J Clin Nutr 2000;72(5):1307-15.
8. Jaloweil DA, HJ. Myocardial infarction in young men and women. Cardiovasc Clin. 1989;20(197–206.
9. Jutta Schaper, WS. Reperfusion of ischemic myocardium: Ultrastructural and histochemical aspects. J Am Coll Cardiol. 1983;1(4):1037-46.
10. Klein LW, NS. Coronary artery disease in young adults. J Am Coll Cardiol. 2003;41(529-31.
11. Klues HG, SE, Vom Dahl S, et al. Disturbed intra coronary heamodynamics myocardial bridging: early normalisation by intra coronary stent placement. Circulation. 1997;96(2905–13.
12. Maria Dorobantu, O-FT, Ana Fruntelata, Lucian Calmac,Gabriel Tatu-Chitoiu et al. Hypertension and acute coronary syndromesin Romania: data from the ISACS-TC registry. European Heart Journal Supplements. 2014;16(A20–A27).
13. Michael John Davies, AT. Thrombosis and Acute Coronary-Artery Lesions in Sudden Cardiac Ischemic Death. N Engl J Med. 1984;310(1137-40.
14. MJ, D. Stability and instability: two faces of coronary atherosclerosis. Circulation. 1996;94(2013-20.
15. Murray CJL, LA. Alternative projections of mortality anddisability by cause 1990 – 2020: global burden of disease study. Lancet. 1997;349(1498 – 504.
16. S. Pandey, NB, S. Majhi, P. Acharya, P. Karki, S. Shrestha, B. K. L. Das, L. Chandra. Prevalence of the metabolic syndrome in acute myocardial infarction and its impact on hospital outcomes. Int J Diabetes Dev Ctries. 2009;29(2):52–55.
17. Strong JP, MG, McMahan CA, Tracy RE, Newman WP 3rd, Herderick EE, Cornhill JF. Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. JAMA. 1999;24:281(8):727-35.
18. Z, L. Atherosclerosis starts in childhood--fact, myth or insinuation? Z Gerontol. 1991;24(2):70-72.
19. Zaman A.G., HG, Worthley S.G., Badimon J.J. The role of plaque rupture and thrombosis in coronary artery disease. Atherosclerosis. 2000;149(251–66.
20. Zimmerman FH, CA, Fisher LD, et al. Myocardial infarction in young adults: Angiographic characteristics, risk factors and prognosis, coronary artery surgery study register (CASS). J Am Coll Cardiol. 1995;26(654.

VISUAL EVOKED POTENTIALS ABNORMALITIES IN ANKYLOSING SPONDYLITIS



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ABSTRACT

Aim and objectives: Neurophysiological abnormalities including visual evoked potentials (VEP) were reported in patients with ankylosing spondylitis (AS). This study aimed to investigate VEP abnormalities and its relation with clinical findings, laboratory tests and therapy in patients with AS.

Material and method: The study included 38 patients with AS. The control group was composed of 50 healthy subjects. BAEP were recorded for all subjects. Patients were assessed by clinical specific tests, inflammatory laboratory tests, Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and type of pharmacological therapy.

Results: The results have shown insignificant differences between the control group and the patients with AS in most of the wave latencies including p100. VEP are delayed in patients with AS, mostly in the group treated with TNF alpha blockers. Hip involvement and history of uveitis was significantly correlated with VEP abnormalities.

Conclusions: The physiopathology of these abnormalities is unknown and further studies should be done for interpreting delayed evoked potentials in AS. Demyelinating mechanism induced by TNF alpha blockers may be considered.

Key words: *ankylosing spondylitis, visual evoked potentials, TNF-alpha blockers, neurologic involvement*

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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease mainly affecting the axial skeleton. Progressive significant functional impairment is leading to spinal ankyloses which has an important impact on quality of life. Peripheral joint arthritis, enthesitis and extra-articular manifestations that involve eye, heart, lung, kidney and neurological system may be present. [1,]

AS may be associated with some neurological complications like cauda equina syndrome, atlanto-axial joint subluxation, discal hernia with nerve root or spinal cord compression, spinal fractures and monophasic myelopathy. Associations of AS and multiple sclerosis was also reported. [2,3,4,5]

Early diagnosis of AS and disease negative prognostic factors have been the main subject of research in the last decade, especially through the efforts of the ASessments in Ankylosing Spondylitis (ASAS) International Working Group.

The prognosis for patients with AS varies and it is influenced by the presence of hip arthritis, dactylitis, oligoarthritis, decreased range of motion of the lumbar spine, limited efficacy of NSAID, ESR>30mm/1h, early age of onset, masculine gender, extra-articular manifestations like uveitis, inflammatory bowel disease, and psoriasis.[6,7]

Aim and objectives

Neurophysiological abnormalities including visual evoked potentials (VEP) were reported in patients with AS. [4,8,9] A small number of studies recorded associations with multiple sclerosis. [3,10-14] Furthermore, neurologic complications may be associated with AS due to administration of anti TNF alpha biologic therapy. [15-20]

This study aimed to investigate VEP abnormalities and its relation with clinical findings and therapy used in AS.

MATERIAL AND METHODS

All patients have been assessed in Rheumatology Department and in Neurology Department, Clinical Rehabilitation Hospital Of Iasi, Romania. The study has been approved by the institutional review board. Prior to study inclusion, the informed consent was signed by all the patients.

The diagnosis of AS was made according to the modified New York criteria. [21] After detailed history and physical examination, all patients were assessed by clinical, biological and neurophysiological parameters.

We recorded the following parameters for each patient: age, sex, disease duration, axial or non-axial type of AS, history of uveitis or iridocyclitis, type of medication, presence of hip invlovment, clinical parameters such as Schober test, Ott index, chest expansion measurement; inflammatory tests: erythrocyte sedimentation rate (ESR), C reactive protein (CRP); indexes: Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The VEP patterns were described by the latencies and the amplitudes of the three waves: N 75, P 100 and N 145.

All parameters have been processed and analyzed using the Statistical Package for Social Sciences (SPSS), version 16.0 for Windows. Mann-Whitney U test was used to compare the average measurements. For the correlation test, p value of <0.05 was accepted to be statistical significant.

RESULTS AND DISCUSSIONS

The mean age of all the 38 patients, 28 males and 10 females, included in this study, was 41.95±11.06 years and the mean duration of disease of the patients was 12.39±8.32 years. BASDAI had a mean of 3,1±1.9 and BASFI was 4.1±1,1. Only 5 patients associated uveitis or iridocyclitis in the evolution of the disease. Half of the patients (n=19) associated hip involvement. Most of the patients (n=25) were taking NSAID or SSZ or the association between these medication, and 13 patients were treated with TNF-alpha blockers. For VEP, the recorded response signals have the amplitude up to 20 µV and frequencies between 1-300Hz. The values we recorded for N75, P100 and N 145 are presented in table1.

Table 1. *VEP results for all patients included in the study*

Indicator	n	$\bar{X}$	±s	s	V%	Min	Max
N75 R A1	38	81.26	4.675	28.818	35.463	45.6	177.9
N75 R A2	38	84.38	4.889	30.135	35.714	42.9	199.2
P100 R A1	38	109.58	4.572	28.185	25.721	55.2	210.6
P100 R A2	38	108.11	4.741	29.228	27.035	57.6	210
N145 R A1	38	143.5	5.226	32.216	22.451	70.2	222
N145 R A2	38	140.73	4.987	30.741	21.843	70.5	222
N75 L A1	38	81.51	3.856	23.768	29.162	56.1	174
N75 L A2	38	80.08	4.676	28.823	35.991	45.3	210.3
P100 L A1	38	109.49	4.987	30.743	28.079	74.7	244.2
P100 L A2	38	109.18	4.843	29.856	27.346	75.9	244.2
N145 L A1	38	138.41	5.336	32.892	23.764	87.3	272.4
N145 L A2	38	139.02	5.21	32.117	23.103	91.5	261.3

There was no significant change of VEP results observed in correlation with sex, duration of disease, chest expansion, BASDAI or BASFI. The results for VEP recorded in SA patients without TNF-alpha blokers are exposed in Tabel 2. For the patients treated with TNF-alpha blokers we present the results of VEP in Table 3.

Table 2. *VEP results for patients without TNF-alpha blocking therapy*

Indicator	n	$\bar{X}$	±s	s	V%	Min	Max
N75 DR A1	25	77.52	4.762	23.812	30.717	51.6	174.3
N75 DR A2	25	81.13	4.378	21.891	26.981	54	145.2
P100 DR A1	25	105.16	4.096	20.481	19.477	86.4	188.4
P100 DR A2	25	103.9	4.186	20.93	20.145	70.8	185.7
N145 DR A1	25	140.2	5.431	27.153	19.368	111.4	210
N145 DR A2	25	137.27	4.26	21.299	15.516	107.1	198.3
N75 STG A1	25	79.99	3.897	19.486	24.359	56.1	147
N75 STG A2	25	77.24	3.845	19.227	24.891	45.3	128.7
P100 STG A1	25	107.08	4.641	23.205	21.671	81.9	199
P100 STG A2	25	106.14	4.172	20.858	19.652	90.3	189.9
N145 STG A1	25	136.44	5.014	25.072	18.376	108.6	230.4
N145 STG A2	25	135.76	5.272	26.361	19.418	112.8	238.5

Correlation between the two groups, the one with biologic therapy and the one with other therapies showed no significant differences. However, all the waves were delayed in the group with TNF-alpha blocker therapy.

Table 3. *VEP results for patients with TNF-alpha blocking therapy*

Indicator	n	$\overline{X}$	±s	s	V%	Min	Max
N75 DR A1	13	88.45	10.158	36.625	41.405	45.6	177.9
N75 DR A2	13	90.62	11.693	42.16	46.523	42.9	199.2
P100 DR A1	13	118.08	10.711	38.618	32.703	55.2	210.6
P100 DR A2	13	116.22	11.265	40.616	34.949	57.6	210
N145 DR A1	13	149.84	11.298	40.735	27.186	70.2	222
N145 DR A2	13	147.39	12.195	43.97	29.832	70.5	222
N75 STG A1	13	84.42	8.632	31.122	36.867	61.2	174
N75 STG A2	13	85.55	11.679	42.108	49.223	45.9	210.3
P100 STG A1	13	114.12	11.773	42.449	37.198	74.7	244.2
P100 STG A2	13	115.02	11.839	42.685	37.113	75.9	244.2
N145 STG A1	13	142.2	12.573	45.331	31.878	87.3	272.4
N145 STG A2	13	145.29	11.522	41.545	28.594	91.5	261.3

Correlation between presence of unilateral or bilateral hip involvement and values of each wave was significant ($p < 0.05$).

Also Pearson Correlation showed that uveitis is significant correlated with the values of each wave. However, VEP reveals cortical and subcortical areas of response to the visual bright stimulation and informs especially about the integrity of visual pathways and less of cortical projection.

CONCLUSIONS

The results have shown differences between the control group and the patients with AS in most of the wave latencies including p100. The physiopathology of these abnormalities is unknown and further studies should be done for interpreting delayed evoked potentials in AS. Demyelinating mechanism induced by TNF alpha blockers may be considered.

Acknowledgement

This work received financial support through the"Program of excellence in multidisciplinary doctoral and postdoctoral research in chronic diseases"contract number POSDRU/159/1.5/S/133377, financed by the European Social Fund through"Human Resources Development"Operational Programme 2007-2013.

Disclosure statement

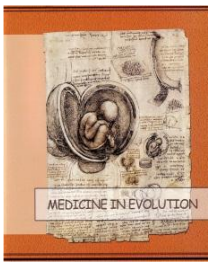
The authors have declared no conflicts of interest

REFERENCES

1. Gran JT, Husby G, The epidemiology of ankylosing spondylitis. Semin Arthritis Rheum 1993;22:319-34.
2. Ginsburg WW, Cohen MD, Miller GM, et al. Posterior vertebral body erosion by arachnoid diverticula in cauda equina syndrome: an unusual manifestation of ankylosing spondylitis. J Rheumatol. 1997;24:1417–20
3. Hanrahan PS, Russel AS, McLean DR. Ankylosing spondylitis and multiple sclerosis: an apparent association? J Rheumatol. 1988;15:1542–4.
4. Khedr EM, Rashad SM, Hamed SA, et al. Neurological complications of ankylosing spondylitis: neurophysiological assessment. Rheumatol Int. 2009;29:103
5. Gündüz OH, Kiralp MZ, Ozçakar L, et al. Nerve conduction studies in patients with ankylosing spondylitis. J Natl Med Assoc. 2010;102:243–6.
6. Boonen A, van der Linden S, The burden of ankylosing spondylitis. J Rheumatol Suppl 2006;78:4-11.
7. Olivieri I, van Tubergen A, Salvarani C, et al, Seronegative spondyloarthritides.

Best Pract Res Clin Rheumatol 2002;16:723-39.
8. Pillay N, Hunter T. Delayed evoked potentials in patients with ankylosing spondylitis. J Rheumatol. 1986;13:137–41.
9. Muharrem Cidem, Zerrin Sahin, Teoman Aydin, Fikret Aysal, Somatosensory Evoked Potential Findings in Ankylosing Spondylitis, Eurasian J Med. 2014 Feb; 46(1): 42–46. doi: 10.5152/eajm.2013.100
10. Libbrecht N, De Bleecker J. Ankylosing spondylitis and multiple sclerosis. Acta Clin Belg. 1999;54:30–2.
11. Calin A. Is there an association between ankylosing spondylitis and multiple sclerosis? Ann Rheum Dis. 1989;48:971–2.
12. Khan MA, Kushner I. Ankylosing spondylitis and multiple sclerosis: a possible association. Arthritis Rheum. 1979;22:784–6.
13. W Hitman G. J., K Han M. A. Unusual occurrence of ankylosing spondylitis and multiple sclerosis in a black patient. Cleve. Clin. J. Med., 1989, 56 (8): 819-822
14. C Ellerini M., G Abbrielli S., B Ongi S. M. Cerebral mag- netic resonance imaging in a patient with ankylosing spondylitis and multiple sclerosis syndrome. Neuroradiology, 2001 Dec, 43 (12): 1067-1069
15. M. Ramos-Casals, Roberto-Perez-Alvarez, C. Diaz-Lagares, M. J. Cuadrado, and M. A. Khamashta,"Autoimmune diseases induced by biological agents: a double-edged sword?"Autoimmunity Reviews, vol. 9, no. 3, pp. 188–193, 2010.)
16. K. Nozaki, R. M. Silver, D. E. Stickler et al.,"Neurological deficits during treatment with tumor necrosis factor-alpha antagonists,"The American Journal of the Medical Sciences, vol. 342, no. 5, pp. 352–355, 2011.
17. L. J. Mejico,"Infliximab-associated retrobulbar optic neuritis,"Archives of Ophthalmology, vol. 122, no. 5, pp. 793–794, 2004.
18. C. Faillace, J. R. de Almeida, and J. F. de Carvalho,"Optic neuritis after infliximab therapy,"Rheumatology International, vol. 33, no. 4, pp. 1101–1103, 2013.
19. P. Lozeron, C. Denier, C. Lacroix, and D. Adams,"Long-term course of demyelinating neuropathies occurring during tumor necrosis factor-a-blocker therapy,"Archives of Neurology, vol. 66, no. 4, pp. 490–497, 2009.
20. I. S. J. Shin, A. N. Baer, H. J. Kwon, E. J. Papadopoulos, and J. N. Siegel,"Guillain-Barré and Miller Fisher syndromes occurring with tumor necrosis factor α antagonist therapy,"Arthritis and Rheumatism, vol. 54, no. 5, pp. 1429–1434, 2006
21. . Goie The HS, Steven MM, van der Linden SM, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a comparison of the Rome, New York and modified New York criteria in patients with a positive clinical history screening test for ankylosing spondylitis. Br J Rheumatol. 1985 24(3):242-9.

THE IMPLICATION OF ROTAVIRUSES IN ACUTE DIARRHEA



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ABSTRACT

Introduction: *diarrhea represents a major public health problem, due to the diversity of etiologic agents, the intensity and the gravity of clinical manifestations, the endemoepidemic extensive disposition of the disease. The etiology of infectious diarrhea is very diverse, implying numerous pathogenic germs of bacterial, viral, parasitical, mycotic origin. The Rotavirus infection (RV) represents the most important cause of hospitalization for gastro-enteritis suffering children.*

Material and method: *the work includes a retrospective study, made on 120 patients admitted at Clinic II of"Victor Babeş"Infectious Diseases and Pneumoftiziogy Hospital Timişoara, diagnosed with Enterocolitis with Rotavirus, during may 2014 – april 2015.*

Objectives: *the analysis has been focused on the following aspects: the age groups structure of the cases, the place of the disease's outburst (hospital or familiar environment), subjective and objective symptomatology, the necesity of parental rebalancing, information regarding the progress of the disease.*

Discussions: *there has been identified a raised prevalence at the male gender, the period from the debut of symptomatology until the admittance has been, on average, of 48 hours. Of the total number of patients, 55% could be considered to have nosocomial infections. The average time of hospitalization has been of 5 days. The evolution has been favourable in all cases.*

Conclusions: *nosocomial infections constitute one of the major causes of morbidity amongst admitted patients. In this pathology, the implication of Rotaviruses is of great importance and extremely topical.*

Key words: *Rotavirus, acute diarrhea, nosocomial infections*

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INTRODUCTION

Diarrhea occupies an important position in infectious pathology, through the diversity of aethiologic agents, as well as through the extensiove endemo-epidemic character of the sickenings.

In 1943, Jacob Light and Horace Hodes proved that a filterable agent in the feces of children with infectious diarrhea caused a similar pathology in bovines. Three decades later, preserved samples of the agent proved to be Rotavirus. Ruth Bishop, through electronic microscopic image of the virus, proved its association with frequent gastro-enteritises admitted into hospital. Its name shows up a year later described by Flewett, who compares the partciles in Rotavirus's componence to a wheel (rota latin - rotation). In 1998 the first vaccine against Rotavirus enteritis is created.

Rotavirus infection represents the main cause of gastroenteritis in small children, being responsible for endemo-epidemic hot points, especially during the cold season and spring.

The specific diagnosis of the Rotavirus infection is achieved by determining the virus's antigen in the stool by latex-agglutination. There are 8 species of viruses, marked from A to H, but the most common ones, involved in the infection, are types A, B and C.

Rotavirus B infection is often met in countries like China and represents one of the importanta causes of diarrhea at adults, in epidemic forms, due to social-economical conditions in some suburbs, with transmission through contaminated drinking water.

In 2008, WHO declared a global crisis, due to the large number of Rotavirus enteritises, most cases being signaled in countries financially underdeveloped. Starting from 2009, WHO recommends adding the vaccine against Rotavirus enteritis to the list of mandatory vaccinations.

MATERIAL AND METHODS

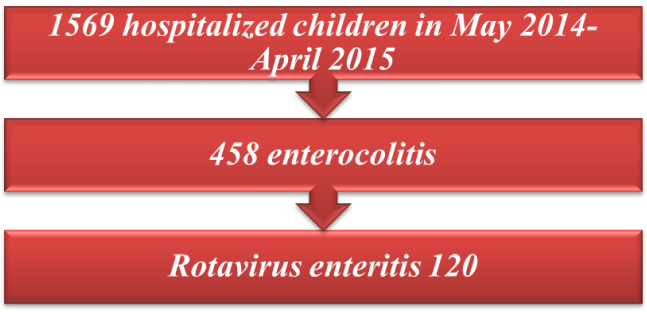
This work includes a retrospectiove, cross-observational study, performed on a number of 120 children admitted into Clinic II of Infectious Diseases Hospital"Victor Babeş"Timişoara, between may 2014-april 2015.

RESULTS

In the descriptive part of the work are presented a few general variables: age, gender, background.

The Rotavirus infection represented 26% (120 patients) of the total of diarrhea cases (458 patients), respectively 8% of the total of children (1569) admitted between may 2014-april 2015 – *table 1.*

Table 1. *General data*



Patients included in the study are aged between 4 months and 16 years, with and average of 6 months – *image 1.*

In the resulting casuistry we can notice a slight prevalence of the female gender in school age, with a morbidity apex 0-7 years in males (73 cases) – *image 2.*

66 children come from hospital environment (55%) – *image 3.*

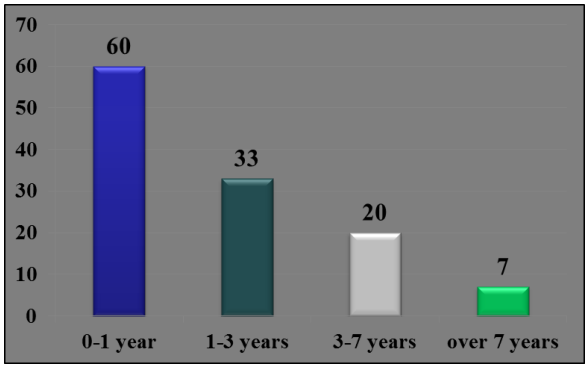


Figure 1. Age of the patients included in the study

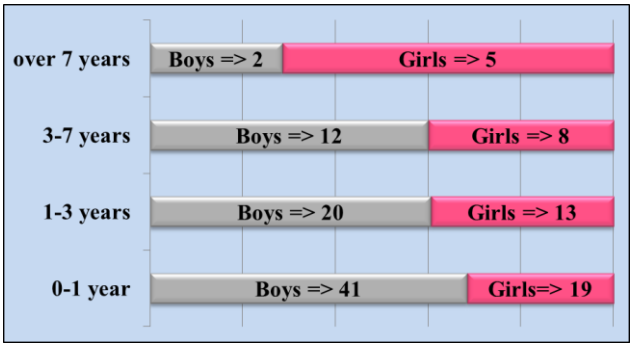


Figure 2. Age and gender group distribution of the patients

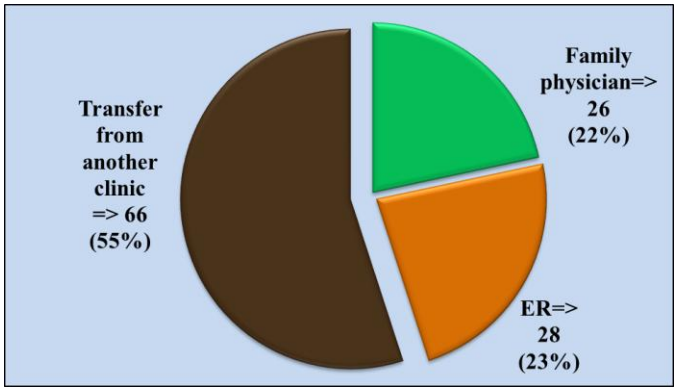


Figure 3. Adresability

The evolution of Rotavirus infection cases depends on the seriousness of the inflammation of the bowels episode, as well as on the patient's condition prior to the sickening. From seriousness scores, by prediction capacity and facility of its evaluation, Vesikari score stands out, most of the children (60-50%) presenting average forms of disease– *table 2.*

Table 2. *Vesikari score*

	Light form Vesikari score < 7	Average form Vesikari score < 7-10	Severe form Vesikari score > 10
May 2014-April 2015	**30**	**60**	**30**

The favourable evolution has been achieved in all cases and appears as secondary to pathogenic and symptomatic therapy quickly established, 90% of the children being in need of volemic and acido-basic parenteral re-balancing– *image 4.*

From the monthly incidence's analysis in the period of epidemic evolution results that the disease presents a high incidence in the cold season.- *image 5.*

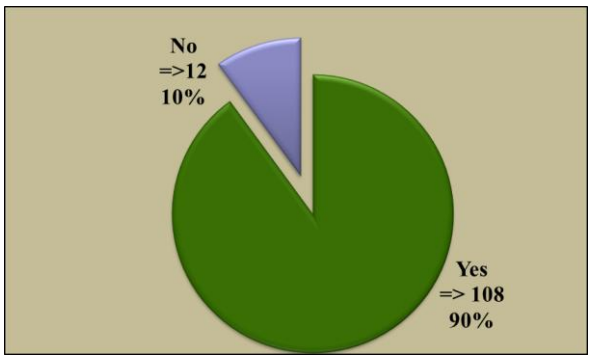


Figure 4. Volemic and acido-basic parenteral re-balancing

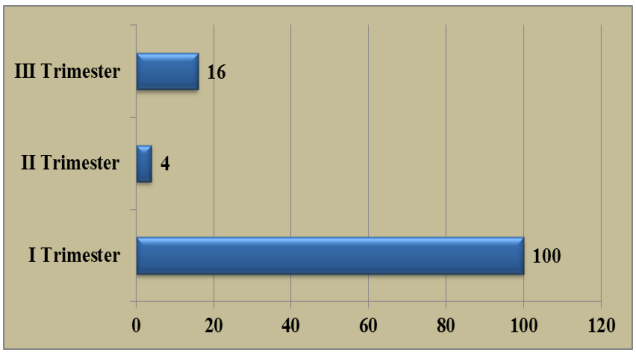


Figure 5. Disease's distribution on semesters

For the appreciation of the seriousness of the cases, the following have been taken into consideration: fever above 38,5°C, present in 48 patients, the number of vomiting, above 5 in 70 cases, stool number above 6, in 30 patients. Duration of stools after 6 days has been indentified at 10 patients. 92 children showed medium/severe dehydration syndrome– *table 3*.

Table 3. *Clinic parameters and parenteral re-balancing*

Parameter	**May 2014-April 2015**		
Nr. stools\day	1-3	4-5	Peste 6
	10	**80**	**30**
Diarrhea duration (days)	1-4	5	Above 6
	50	**60**	**10**
Vomit duration (days)	1	2	Above 3
	35	**70**	**15**
Fever (°C)	37.1-38.4	38.4-38.9	Above 39
	60	**48**	**12**
Acute dehydration syndrome	I Degree	II Degree	III Degree
	28	**72**	**20**
Parenteral rehydration(hours)	24 h	48 h	Above 72
	35	**60**	**25**

DISCUSSIONS

The presented data allow including the Rotavirus into the large group of causing agents of nosocomial infections.

Out of the 120 cases of Rotavirus bowel inflammation, most of the came from 52% rural environment to 48% urban area. Cases' assymetry emerges due to precarious socio-economical conditions in the rural area and also due to the virus's nosocomial character in the environment (community, family, drinking water).

In our casuistry, the aetiology's incidence has been significantly higher in the small age group (0-3 years, 93 cases). Male gender has been favoured as compared to the female one (2:1).

If we were to perform a comparative analysis with the cases admitted into Clinic II Infectious Diseases, we can mention the fact that in 2012 the morbidity apex was found also in the small age group (44 cases out of a total of 49), with prevalence of the male gender.

In 2012 the number of children admitted with Rotavirus bowel inflammation has decreased, with a ratio in the gender repartition much alike the one of the prior year.

As regards to the appearence of the patients to their family doctor it is to be highlighted the fact that most admitted patients did not perform the consult and came straight to the hospital, thus generating problems for sanitary units because of the large number of cases. Some infections in older children could be diagnosed, treated and supervised by the family doctor; of course this fact obliges to provide the family doctor's cabinet with a Pediatric profile also with kits for determining Rotavirus antigen in the stool, being an easily performed analysis.

Pathology has been epidemiologically classified as nosocomial infection in 66 cases (55%). The existence of epidemic hot points could not be proved.

The evolution of the cases under the imposed therapy was favourable with a short period of hospitalization. This can be explained by two aspects: Vesikari score, where prevalent clinic forms of the disease are average forms and patients' good adressability to the doctor.

CONCLUSIONS

Bowel inflammation with Rotavirus remains an up-to-date pathology through its nosocomial implication, being a virus that can easily contaminate contact areas, as well as through the possibility of a severe form of disease.

Currently, an aetiologic „turn"towards viral infections is being ascertained, probably due to:

- Lifestyle improvement;
- Diagnosis possibilities.

The true dimension of bowel inflammation with Rotavirus does not overlap with hospitalized cases, light clinical forms being treated at home and not aetiologically investigated.

The presented data allow including the Rotavirus into the large group of causing agents of nosocomial infections.

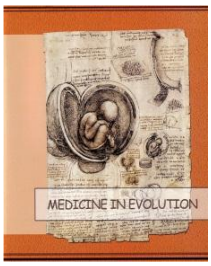
At the time, Rotarix, Rotateq or other vaccins continue to be the most efficient prophilactic method, but it still need to be analyzed in the vaccination calendar (since 2009, WHO recommends it on the list of mandatory vaccins).

Due to its contagiousness in small age groups and to difficulties in preventing transmission, bowel inflammation with Rotavirus will continue to represent a public health problem.

REFERENCES

1. Mandell L, Bennett J, Dollin R. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases.7th ed.Churchill Livingstone Elsevier:Philadelphia;2010.
2. Tortora GJ, Funke BR, Case CL.Microbiology-an Introduction.11th ed.Pearson Education, Inc.:USA;2013.Microbial Growth (6):160-161. Principles of Disease and Epideomiology(14):402-403. Microbial Diseases of the Digestive System (25):726.
3. Cohen J, Powderly WG, Opal SM, Calandra T, Clumeck N, Farrar J, et al, Infectious Disease.3rd ed.Mosby Elsevier:2010.vol I(35):381-388; vol II (173):1757-1776.
4. Lewis K, Vesikari Clinical Severity Scoring Sistem Manual, May 2011.

VASCULARY AND PARENCHYMALLY DISTRESSED PLURIETIOLOGIC HEPATIC CIRRHOSIS-CASE PRESENTATION



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ABSTRACT

Introduction: *Beside the long-known etiologies (A, B, C, D), during the last years new viral etiologies have been identified, respectively E, F, G, T, that can induce as well severe disease forms, including evolution in the direction of chronicization. Viral hepatitises continue to represent an important infectious pathology problem, due to the possibility of hepatic failure emergence resulting in death, in acute forms (especially as regards the B virus) as well as in chronic forms/B+D supra-infection, respectively chronic hepatitis C forms.*

Material and method: *We present the clinical case of a 72 year-old male patient, admitted into Clinic II of the"Victor Babeş"Hospital for Infectious Diseases and Pneumophtisiology, Timisoara, between 17.03-05.04.2015 with the following diagnosis:*

1. *Vasculary And Parenchymally Decompensated Plurietiologic Cirrhosis;*
2. *Chronic cerebral circulation insufficiency;*
3. *IInd degree essential arterial hypertension with moderate cardiovascular risk;*
4. *Hipertensive cardiopathy;*
5. *Diffuse cortical atrophy;*
6. *Cerebral organic psychosyndrome;*
7. *Prostate hyperplasia;*
8. *Non-resuscitable cardiac arrest.*

Discussions and conclusions: *The unfavourable evolution with multiple pluri-etiologic mechanisms (B, C, D hepatic viruses), joined with chronic alcohol consumption and combined with the patient's hemodynamic status have been predictive factors in the patient's later distress, with unfavourable evolution and death.*

Key words: *plurietiology, hepatic cirrhosis, hemodynamic status*

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INTRODUCTION

Worldwide, viral hepatitises still represent one of the most frequent causes for hepatic conditions, through the multitude of clinical forms of the disease. Known since the 18th century, viral hepatitises continue to represent an important infectious pathology problem, due to the possibility of hepatic failure emergence resulting in death, in acute forms (especially as regards the B virus) as well as in chronic forms/B+D supra-infection, respectively chronic hepatitis C forms. From the last reported data, Romania is amongst the first countries in Europe as regards hepatic viruses B and C morbidity, which represents an important public health problem and, due to the high treatment cost, according to the National Health Institution's program, only 1% of the patients are given anti-viral medication.

Under the circumstances, we consider relevant the presentation of the following case:

72 year-old male patient, admitted into Clinic II of the"Victor Babeş"Hospital for Infectious Diseases and Pneumophtisiology, Timisoara, between 17.03-05.04.2015 with the following diagnosis:

9. Vasculary And Parenchymally Decompensated Plurietiologic Cirrhosis;
10. Chronic cerebral circulation insufficiency;
11. IInd degree essential arterial hypertension with moderate cardiovascular risk;
12. Hipertensive cardiopathy;
13. Diffuse cortical atrophy;
14. Cerebral organic psychosyndrome;
15. Prostate hyperplasia;
16. Non-resuscitable cardiac arrest..

72 year-old male patient, affirmative chronic alcoholic, known by the Clinic of Infectious Diseases since December 2014, admitted then presenting the following complaints: diffuse pain in the right hypochondrium, nausea, vomiting, fatigue, dizziness. At the admission: patient with influenced general condition, conscious, cooperant, sclero-tegumentary jaundice, milklegs, cardio-pulmonary balanced (TA=130/65 mmHg, AV=62 b/min), abdomen vaguely sensitive to deep palpation, TI present, liver 4 cm below the costal rebord, spleen palpable 3 cm below the costal rebord, diuresis present, physiologic micturitions. No clinical signs of meninigeal irritation. From the patient's personal pathological antecedents, significant was the account of a possible non-staged HCV infection. Clinico-biological investigations are being performed – *table1.* During the admission, the patient's evolution has been slowly favourable, with alternate periods of psychomotor agitation, being discharged 10 days later with a relatively good general condition and with treatment recomendation.

Table 1. *Clinico-biological evaluation*

Hospital for Infectious Diseases and Pneumophtisiology"Victor Babeş", Timişoara December 2014	
Biologically	Leukocytes=4700/mm3↓ (N=75.6%, L=20%, M=4.4%)↓ Hemoglobin=12.2 g/L↓ Hematocrit=34.9 %↓ Red cells=3.530.000/mm3↓ Thrombocytes=61.000/mm3↓ TGP=92 UI/L↑ TGO=118 UI/L↑ BD/BT= 1.3 mg%/2.6 mg%↑ FA=112 U/L↑ GGT=98 U/L↑

	Urea=61 mg%↑ Creatinine=0.99 mg% Glycemia =85 mg/dl Ac anti HCV= POSITIVE PCR ARN-HCV=UNDETECTABLE Ag HBs=POSITIVE Ac Anti HBe=NEGATIVE Ag HBe=NEGATIVE PCR ARN-HBV=7925 UI/ml Ac anti Delta=POSITIVE PCR ARN-VHD=739.500 copies/ml ELISA HIV 1,2=NEGATIVE
Pulmonary X-ray	No active pleuro-pulmonary lesions
Abdominal ultrasound	Liver of irregular surface, showing in the Vith segment a discreet hypoechogenic formation of about 1.5 cm. Gallbladder with double thickened walls. RD and RS of normal dimensions and echostructure. Normal pancreas at the ultrasound. Ascites liquid in small quantity perihepatic and in the pouch of Douglas.
Abdominal MRI	Cirrhotic liver of reduced dimensions. Hepatic nodule of 16 mm, located in the Vith segment of the right hepatic lobe – requires IRM monitoring (cannot be etiopathogenically certainly classified)
CEUS	The formation described in the standard ultrasound seems to be discreetly with low uptake in the arterial stage but with the evolution of the uptake towards a two-beat neutral uptake aspect. Regeneration nodule.
Cranial CT	Diffuse cortical atrophy.
Gastroscopy	Esophagus with Iind degree esophageal varices. Stomach with light hypertensive gastropathy.
Pshychiatric consult	Depressive reaction. Slight organic cognitive disorder.

From the moment of discharge until the moment of the following admission, the patient has been non-adherent and uncooperant, not showing up for periodic consults, without respecting the doctor's indications before the discharge (according to the patient's daughter, he does not stop alcohol consumption).

On 17.03.2015, the patient comes to the Infectious Diseases Hospital with sclero-tegumentary jaundice, confusion, palpebral ecchymosis, diffuse abdominal pain, psychomotor agitation. At admission: gurney patient, with strongly influenced condition, confused, psychomotory agitated, cardio-pulmonary balanced TA=144/67 mmHg, AV=61 b/min, SaO2=57% without oxygen mask, weight=80kg. Abdomen loose of volume, tympanitic, TI absent (affirmative on the admission day), liver 4 cm below the costal rebord, spleen palpable 3 cm below the costal rebord, diuresis present, physiologic micturitions. Recurrent epistaxis. No clinical signs of meningeal irritation. Biological investigations are being performed – *table2*.

Table 2. *Biological investigations*

Hospital for Infectious Diseases and Pneumophtisiology "Victor Babeş", Timişoara 17.03-05.04.2015	
Biologically	Leukocytes=4700/mm3↓ (N=89.9%, L=3.9%, M=6.1%)↓ Hemoblobin=11.9g/L↓ Hematocrit=32.7 %↓ Red cells=3.150.000/mm3↓ Thrombocytes=43.000/mm3↓ TGP=73.7 UI/L↑ TGO=52.4 UI/L↑ BD/BT= 1.18 mg%/2.25 mg%↑ FA=72 U/L

GGT= 141.9 U/L↑
Urea=30.9 mg%
Creatinine=0.65 mg%↓
Glycemia =125 mg/dl↑
Protein electrophoresis:
- Albumin=38.4%↓
- α 1 globulins=1.5%
- α 2 globulins=6.4%↓
- β globulins=7.6%↓
- Gamma globulins=46.1%↑

PCR=6.31 mg/L↑
PSA=0.95 ng/ml
Urine summary:
- pH=6
- Density=1025
- Bilirubin
- Ketonic bodies Negative
- Ascorbic acid
- Proteins

Urinary sediment:
- 35-40 red cells/field, 30-35 white cells/field

Urine culture: bacteriuria (under 1000 UFC/ml)

Treatment: Has been established pathogenetic treatment, with Ampicilin (3x1 g/day, intravenous, for 5 days), Normix (200 mg cpr., 3x2 cp/day, for 15 days), Glucose 10%, physiologic serum 0.9%, diuretics (Furosemid), hepatoprotectors and ammonium fixators (Arginine, Hepamerz, Tiossen Turbo), gastroprotectors (Arnetin), hemostatics (Etamsilat, Fitomenadion, Adrenostazin – for 6 days), plasma for 6 days, corticotherapy (Dexamethazone, 16 days) and medication for cardiac and neurologic pathology (Carvedilol and Piracetam).

Evolution: Under the established therapy, the patient's symptomatology remained still, with waving general condition, until 31.03.2015, when the patient becomes psychomotory agitated, with strange behaviour, conscious but uncooperant, sometimes confused, which is why psychiatric consult has been reqested.

Psychiatric consult 01.04.2015: Toxic and vasculary founded cerebral organic psychosyndrome. Recommendations: supplementing the therapy with Haloperidol sol. (10-10-20, to maximum 40 drops/day when needed), Carbamazepin cpr. 250 mg (3x1/2 cpr/day).

On 03.04.2015, the patient's condition remains profoundly influenced, unconscious, uncooperant, not responding to any painful stimuli, I/II degree coma being declared, TA=116/60 mmHg, AV=58 b/min, SaO2=95% with O2 mask, condition which persists on 04.04 as well. On 05.04.2015, the patient gets hemodynamic unstable TA=86/40 mmHg, AV=62 b/min, SaO2= 86% with O2 mask. Cardiac support treatment is being tried, but the general condition remains profoundly influenced (unconscious, uncooperant, not responding to any painful stimuli, TA=60/45 mmHg, AV=52 b/min, SaO2=68% with O2 mask), the patient suffering irresuscitable cardio-respiratory arrest.

Case's peculiarities:

- Patient's age when diagnosed and the associated comorbidities;
- Pathology's plurietiology; the 3 viral entities B, C and D associated with chronic alcohol consumption;
- Patient's mental condition changes and psychomotor agitation alternated with confusion periods, owed to cirrhosis and chronic alcohol consumption with toxic products accumulation in the brain,

possibly, equally by decrease of cerebral flow (cerebral atrophy);

- Not cutting off alcohol consumption inspite the risk well known by the patient and the reccomendations suggested to relatives;

Severe thrombocytopenia which brings and additional risk to the patient by causing spontaneous bleedings or to minimum invasive methods; a small number of thrombocytes also represents a contraindication in Interferon treatment (especially in viral chronic hepatitis C).

DISCUSSIONS AND CONCLUSIONS

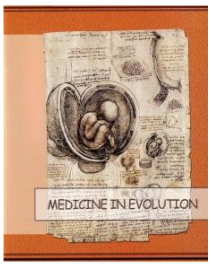
- The unfavourable evolution with multiple pluri-etiologic mechanisms (B, C, D hepatic viruses), joined with chronic alcohol consumption and combined with the patient's hemodynamic status have been predictive factors in the patient's later distress;
- From the anamnesis and the information from relatives, C virus infection was the former, afterwards being diagnosed with B and D viruses;
- Ineteresting to mention is the fact that, in december 2014, patient's hepatitis C viremia was undetectable, with HCV Ab positive, which would imply that at the time, according to specialty literature, the patient would have been healed;
- Highlighting the fact that the patient did not show extrahepatic manifestations due to well-know autoimmune mechanisms in HCV infection, which could be a supporting element for the previously mentioned thesis;
- B and D viruses infection was diagnosed afterwards, without managing to identify etiologic transmission ways;
- Chronic alcohol consumption as singular entity or associated with viral hepatic infection, as in our case, can certainly cause alcoholic hepatitis, cirrhosis, respectively hepatic failure;

Certainly, in this patient's case, the mechanisms have been multiple, complex and intricate, which inevitably led to unfavourable evolution and death.

REFERENCES

1. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: Part I. Diagnosis and evaluation. Am Fam Physician. 2006;74(5):756–762.
2. Kanwal F, Schnitzler MS, Bacon BR, Hoang T, Buchanan PM, Asch SM. Quality of care in patients with chronic hepatitis C virus infection: a cohort study. Ann Intern Med. 2010;153(4):231–239.
3. Garcia-Tsao G, Lim JK. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program [published correction appears in Am J Gastroenterol. 2009;104(7):1894]. Am J Gastroenterol. 2009;104(7):1802–1829.
4. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Biel AT. Hepatic encephalopathy—definition, nomenclature, diagnosis, and quantification: final report of the Working Party at the 11th World Congresses of Gastroenterology, Vienna, 1998. Hepatology. 2002;335(3):716–721.
5. McGee SR. Evidence-Based Physical Diagnosis. St. Louis, Mo.: Saunders-Elsevier; 2007:80.

ANTI-MEASLES VACCINATION – PRO AND AGAINST



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ABSTRACT

Introduction: *it is well known the fact that measles (also known as morbilli or rubeola) is an infectious-contagious disease, viral, endemoepidemic disease that can generate respiratory, ORL-related and neurological complications. It is a disease preventable by vaccination.*

Objectives:

- *The analysis of the incidence of measles in Timiş county in the last years.*
- *Comparison with other European countries' situation, as well as with the USA.*
- *The efficiency of the vaccination programs.*
- *Pro and against arguments regarding anti-measles vaccination.*

Material and methods: *we have made a retrospective study regarding measles' incidence in Clinic II Infectious Diseases of the Victor Babeş Hospital Timişoara during 2008-2014, compared to the situation in 1993, respectively 2004-2005 – age groups affected, complications, lethality.*

Results and conclusions:

1.In 1993 prevailed pulmonary and neurological complications, respectively encephalitisis, some with unfavourable evolution, resulting in high lethality rates.

2.During 2004-2005 there have been 309 cases in Timiş county with 219 admissions, mostly respiratory complications, small lethality rates.

3.There have been years – 2008, 2009, respectively 2013-2014 – with no misles cases in Timiş county.

4.In 2011/2012 has been registered an epidemic apex with 272, respectively 231 cases with especially pulmonary and ORL-related complications.

5.Rubeola continues to represent a problem, epidemic outbursts can emerge anytime: most recently, the USA example with over 100 declared cases.

6. Measles can be prevented by following the vaccination programs.

Key words: *vaccination, epidemic, incidence*

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INTRODUCTION

It is well known the fact that measles is a contagious infectious disease, endemo-epidemic viral, which can give respiratory, ORL and neurological complications; it is a disease which can be prevented by vaccination.

15 years ago, lots of countries, inlcuding France and USA, have established among their goals to eradicate measles. If we reffer to other diseases such as poliomyelitis, the General Assembly of WHO approved in 1998 a resolution regarding the eradication of poliomyelitis by 2000, decision that has not been respected globally. On the contrary, the international spread of wild polio virus strains has been noticed within the last two years, even with epidemic outbursts in some areas.

MATERIAL AND METHODS

We have performed a retrospective study regarding the incidence of measles in Clinic II of Victor Babes Infectious Diseases Hospital Timisoara in the period 2008-2014, compared to the situation of 1993, respectively the years 2004-2005, affected age groups, complications lethality.

RESULTS AND DISCUSSIONS

The authors have set to approach the following aspects:

- The analysis of measles' incidence in Timis county within the last years;
- Comparing with the situation in other European countries, respectively the USA;
- The efficiency of vaccination programmes;
- Pro/Against anti-measles vaccination arguments.

If we were to generally approach the history of anti-measles vaccine, different aspects of its evolution can be noticed: it has been used since 1960, it effectiveness has been proven in countless times, but unfortunately the scepticism with wich it has been treated led to epidemies with negative impact on the society - *image 1,2*. In our clinic, in 2004-2005 there have been admitted 219 patients with different respiratory or nervous (encephalitises) complications, due to measles – *image 3*.

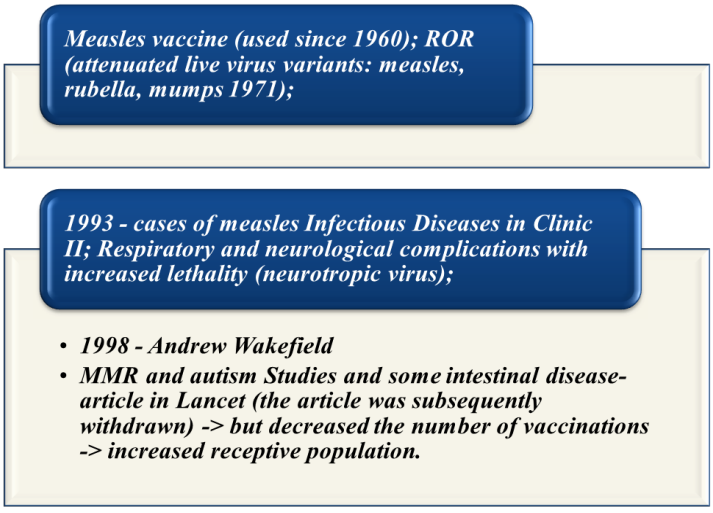


Figure 1. Generalities

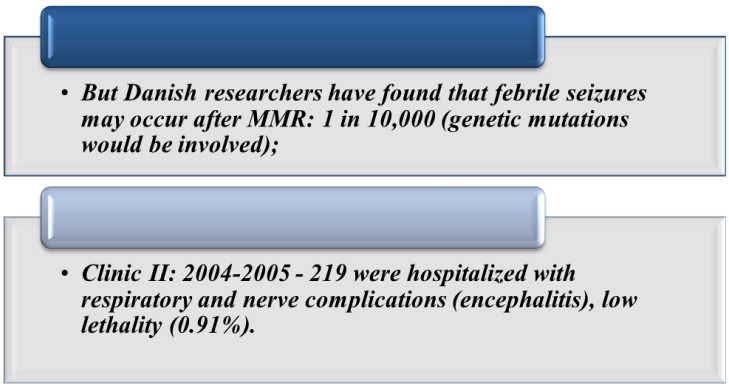


Figure 2. General aspects

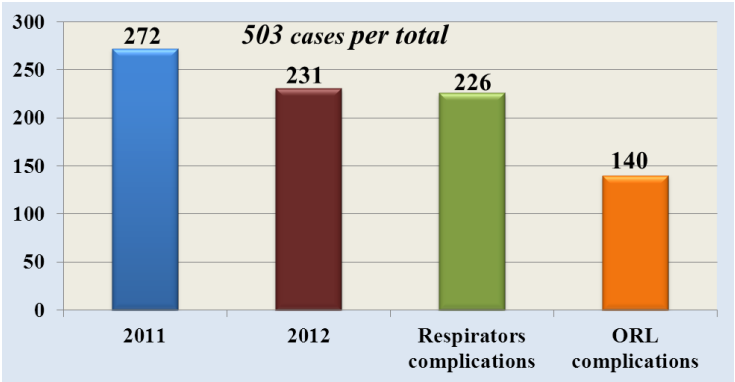


Figure 3. Distribution of measles and complications

In 2011, the number of cases of measles was 272 in Timis county. The morbidity apex of measles has been registered in Bihor county with 560 cases, followed by Cluj counting 462 cases – *image 4*. 2012 has brought to Timis county a symmetry of the number of cases, preserving the share of the previous year.

In Europe, in 2011, there have been 26.000 cases with 8 deaths in the 36 out of the 53 countries (mostly in France, Spain, Romania).

If we were to perform a statistic analysis of the years 2008-2014 as regards the measles' incidence, we could notice the two apexes of morbidity form 2011-2012, explained on the one hand by the disruption of the vaccination as a result of the dissent of the owners due to side effect, on the other hand by obsessive mass-media propaganda as regards this subject – *image 5*.

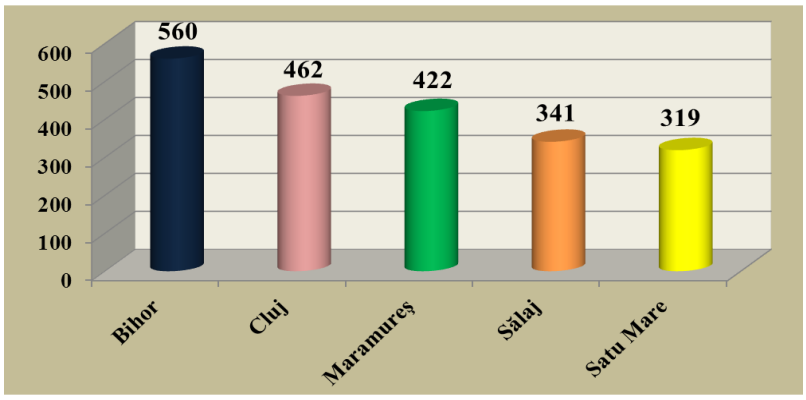


Figure 4. Distribution of measles (3270 cases per total)

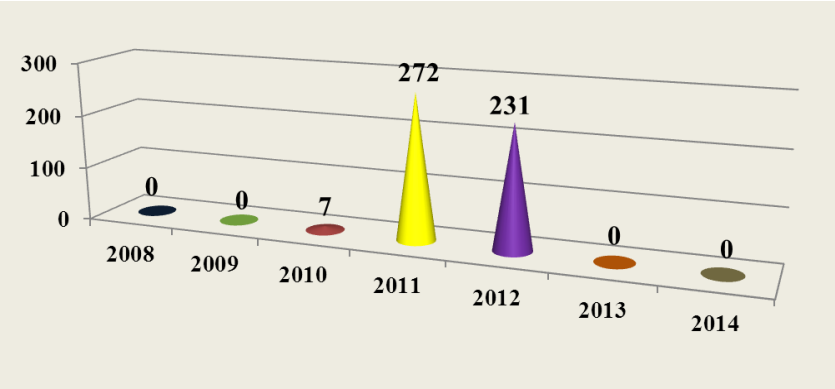


Figure 5. Distribution of measles on Clinic II

Reported to the last years, we can notice a significant increase of the number of measles cases, for instance USA (644 cases) and in general, in Europe there have been flagged 31.685 cases with a 378% increase compared with 2007. Alarming is the fact that these cases have appeared even in teenagers previously vaccinated, in young adults and sometimes in not immunized pre-schoolers – *image 6.*

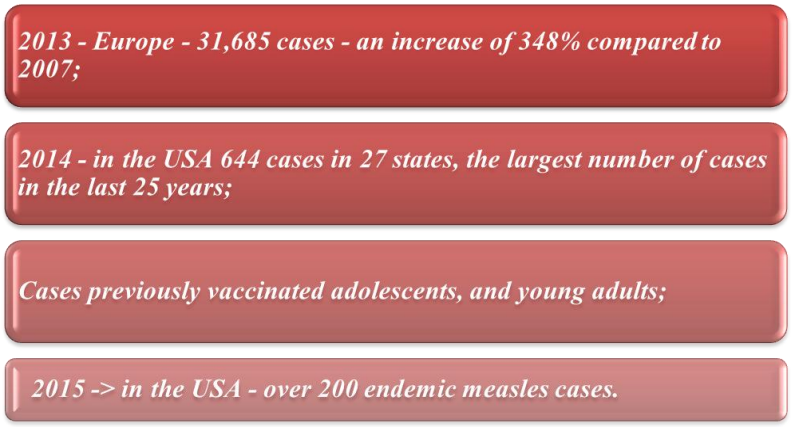


Figure 6. Measles' global evolution within the last 3 years

CONCLUSIONS

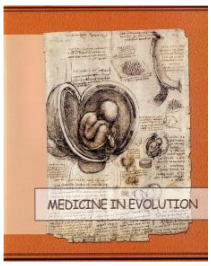
We consider very important the following aspects:

- European vaccination action plan under the protection of WHO against measles 2015-2020 (which Romania has joined too);
- Vaccinal Coverage in Romania was, 10 years ago, of 95% for diseases as diphteria, tetanus, measles, mumps, currently it is under 68% for some diseases;
- WHO experts have recommended mandatory vaccination for: diphteria, tetanus, poliomyelitis, measles, ruseola, pertusis, mumps. Furthermore, for meningococcus and pneumococcus, H. Influenzae, Papilloma, hepatitis B and tuberculosis – according to each country;
- In 1993 predominated pulmonary and neurologic complications of ruseola, respectively encephalitises, some with unfavourable evolution, with high lethality;
- Between 2004-2005 there have been 309 cases in Timis county with 219 admissions, complications being mostly respiratory, low lethality;
- There have been years – 2008, 2009, respectively 2013-2014 – without any measles cases in Timis county;
- In 2011/2012 there has been registered an epidemic apex of 272,

respectively 231 cases with complications mostly pulmonary and ORL-related;
- Measles continues to represent a problem, epidemic outbursts can emmerge anytime: the most recent example being the USA with over 200 reported cases;
- Measles can be prevented by respecting the vaccination programs.

REFERENCES

1. Mandell L., Bennett J., Dollin R. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. 7th ed. Churchill Livingstone Elsevier: Philadelphia; 2010.
2. Cohen J., Powderly WG., Opal S.M., Calandra T., Clumeck N., Farrar J., et al, Infectious Disease. 3rd ed. Mosby Elsevier: 2010.vol vol I; vol II.
3. Stanley A. Plotkin, Walter Orenstein, Paul A. Offit, Vaccines, 6th Edition, 2013



BACTERIAL MENINGOENCEPHALITIS. CEREBROVASCULAR ACCIDENT. ATRIAL FIBRILLATION. CEREBRAL ATROPHY – CASE PRESENTATION

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ABSTRACT

***Introduction**: Meningitis represents another important chapter of infectious pathology, which implies a quick, complex and correct diagnosis with an up-to-date treatment.*

***Material and method:** We present to you the clinical case of a male patient, 81 years old, admitted into the 2nd Clinic of Hospital for Infectious Diseases and Pneumophtisiology"Victor Babeş", Timişoara, between 30.08-12.09.2013 with the following diagnosis:*

1. Acute bacterial meningoencephalitis; 2. I/II degree coma; 3. Chronic bilateral mastoiditis; 4. Ischemic cerebrovascular accident; 5. Arterial hypertension with high cardiovascular risk; 6. Ischemic cardiopathy; 7. Permanent atrial fibrillation with average VA; 8. Inferior digestive haemorrhage; 9. Prostate adenoma; 10.Obesity; 11.Cerebral atrophy; 12.Hyponatremia.

***Discussions:** The diagnosis of meningoencephalitis of bacterial etiology was significantly supported by the anamnestic data, the cerebral CT (chronic mastoiditis and cerebral atrophy), proteinorachie and high lactic in the LCR exam.*

***Conclusions**: The sequence and selection of the biologic and poaraclinic investigation led to a specific diagnosis with the correct handling of therapy and the modification of the clinical status of the patient (from coma and worse status to a cooperative, conscious patient.*

***Key words:** acute meningoencephalitis, proteinorachie, lactic*

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INTRODUCTION

Meningitis represents another important chapter of infectious pathology, which implies a quick, complex and correct diagnosis with an up-to-date treatment. In the last years, the number of cases of bacterial meningitis that deviate from the classic, well-known pattern has increased, thus creating problems in medical practice.

In this context, we find it relevant to expose the following case:

Male patient, 81 years old, admitted into the 2nd Clinic of Hospital for Infectious Diseases and Pneumophtisiology"Victor Babeş", Timişoara, between 30.08-12.09.2013 with the following diagnosis:

1. Acute bacterial meningoencephalitis;
2. I/II degree coma;
3. Chronic bilateral mastoiditis;
4. Ischemic cerebrovascular accident;
5. Arterial hypertension with high cardiovascular risk;
6. Ischemic cardiopathy;
7. Permanent atrial fibrillation with average VA;
8. Inferior digestive haemorrhage;
9. Prostate adenoma;
10. Obesity;
11. Cerebral atrophy;
12. Hyponatremia.

Patient aged 81 with multiple comorbidities presented 4 days prior to the admission, namely on 27.08, fever and vomiting.

He was initially admitted into Lugoj Hospital during 27-30.08, being a cooperative patient, with no signs of meningeal irritation, pulmonary stetacoustic with subcrepitant rales. He followed a per os treatment with Ciprofloxacine 500mg 1 every 12 hours, Ampicilline 1g every 6 hours, Metoclopramide, Arnetin, hydroelectrolytic balancing solutions. In the first two days he maintains 38°C fever with some confusion episodes, then becomes uncooperative psychomotor agitated- *table 1.*

Table 1. *Clinical-biological evaluation of the patient prior to the admission into the clinic*

Lugoj Municipal Hospital (27-30.08)	
Biologically	Leukocytes=5900/mm3 (N=30%, L=17%, M=3%) Hemoglobin=15 g/L Hematocrit=45% Thrombocytes=149000/mm3 TGP=20 UI/L TGO=29 UI/L Glycemia=85 mg/dl Urea=44 mg% Creatinine=1.25 mg/dl
Pulmonary X-ray	Enlarged hilum. Interstitial vascular drawing, perihilar bilaterally emphasized with micronodules. Horizontal heart.
Abdominal ultrasound	Liver with a few microcalcifications.Homogeneous LD. Normal gallbladder volume, uninhabited. Normal CBP, VP. Non stasis RD. Nonstasis RS. Spleen 121 mm. Prostate 48/56/60.
Empty abdominal X-ray	No pneumoperitoneum. Average aerocoly.
Cranial CT	Conclusion: average cerebral atrophy.Symmetrical ventricles at the medial line. Extracerebral fluid spaces moderately enlarged diffusely. Chronic mastoiditis. No bone structure modifications.

Objective exam at the admission into Hospital for Infectious Diseases and Pneumophtisiology"Victor Babeş", Timişoara, Romania: gurney patient,

with intense psychomotor agitation, movement of the limbs, responds to stimuli, aphasia, discreet backhead stiffness, TA=143/80 mmHg, AV=86 b/min, T=37,8°C, saturation in O2=97-98% no oxygen mask, weight=90 kg. Clinical- biological investigations are being performed-*table 2.*

Table 2. *Clinical-biological evaluation on the first day of admission into the Hospital in Timisoara*

Hospital for Infectious Diseases and Pneumophtisiology"Victor Babeş", Timişoara **30.08 (first day of admission into the clinic)**	
Biologically	Leukocytes=13530/mm3 (N=87.6%, L=4.8%, M=7.5%) Hemoglobin=14.1 % Hematocrit=39.8% Thrombocytes=176000 mm3 VSH=20 mm Fibrinogen=2.66 g% CRP=53.28 TGP=16.7 U/L TGO=47.8 U/L BD/BT=0.35/0.98 mg% FAL=54.2 U/L Urea=33.6 mg% Creatinine=1.08 mg/dl Uric acid=5.61 mg% Glycemia=128 mg% Cholesterol=178 mg/dl Triglycerides=68 mg/dl Total of proteines =6.75 g/l Ionogramme/ASTRUP: ❖ Na=118.2/ K=3.71/ Lactic=12 mmol/l ❖ BE= - 0.5/ Ph= 7.424
Lumbar punction	LCR- slightly opalescent Pandy ++ Leucocytes=80 Hematii=100 Proteinorachie=97 mg/dl Lactic=39.07 mg/dl Glycorachie=51 mg/dl Direct protium- negative Culture on common environments= pathogen flora absent Hemoculture= sterile
Neurologic consult	Extremely agitated and confused patient, presents a slight backhead stiffness, no motor deficit, present ROT, RCP bilateral flexion, does not colaborate for coordination and sensibility. Cranial nervs in normal connection. Cranial CT – cerebral atrophy.

TREATMENT

And aetiologic antibiotic treatment with Meronem 2g every 8 hours, Vancomicine 1g every 12 hours has been instituted (pneumococcus has been interpreted as possible bacterial meningitis with the most frequent aetiology). Pathogenic treatment with Glucose 10%+Glucoze 33%, Manitol 20%, Dexamethazone 3x1 vial, Arnetin, Algocalmin + Cardiologic medication: Digoxine, Nebilet, Trombex.

EVOLUTION

Initially evolution towards aggravation, with the deepening of the coma from 01.09, sent again for a neurologic consult, performing a new cranial CT and cardiologic examination.

Neurologic re-evaluation on 02.09: uncooperant patient, backhead stiffness, coordination and sensibility cannot be evaluated. Shows RCP. Cranial nervs in normal connection. Cerebral CT – no changes since the previous CT.

Cardiologic evaluation 2.09: ECG with atrial fibrillation without acute ischemic modifications. TA=115/85 mmHg, AV=100 b/min. Echocardiography: small calcifications, no significant mitral-aortic valvulopathy, no pericardic fluid. Diagnosis: mixed ischemic and hypertensive cardiopathy; essential HTA IInd degree with high CV risk; Permanent atrial fibrillation. Recommendations: Digoxin 1/2/day, Nebilet 1/2/day, Trombex 1 tb/day, consult when needed.

On the 4.09, in the patient's evolution emerge melenic stools and gastroenterologic consult is requested.

Gastroenterologic consult 4.09: TA= 119/87 mmHg, AV=84 b/min, TR negative for melena or rectal bleeding (normal aspect of the stool in the rectal ampulla), hemoglobin stable in dinamics. It is not a gastroenterologic emergency at the moment of the examination.

Beginning from 4.09, patient's therapy is supplemented with Fitomenadion, Adrenostazin, Etamsilat and Controloc. Trombex administration is suspended.

In his evolution, the patient is conscious, difficult to handle, psychomotor agitated, hemodinamic balanced, being transfered on the section of Anesthesia and Intensive Care of the Hospital for Infectious Diseases and Pneumophtisiology"Victor Babeş", Timisoara.

On 11.09, a lumbar punction check is performed: LCR clear, Pandy negative, 12 elements, proteinorachie=0.5 g/l, lactic=17.95 mg/dl, glicorachie=79 mg/dl.

Ulterior evoluţia bolnavului fiind relativ bună fără semne obiective de iritaţie meningeană, cu unele perioade de confuzie, afebril, fără deficit motor. În data de 12.09, pacientul a fost externat cu recomandări de reevaluare urologică (pentru adenomul de prostată), cardiologică şi neurologică(atrofie cerebrală).

Later on, patient's evolution being relatively good with no objective signs of meningeal irritation, with some confusion episodes, afebrile, no motor deficit. On 12.09, the patient has been discharged with urologic (for the prostate adenoma), cardiologic and neurologic (cerebral atrophy) re-evaluation recommendations.

CASE'S PARTICULIARITIES

- Patient aged 81 with multiple comorbidities;
- Relatively small number of elements at the lumbar punction (80 elements), with proteinorachie and high lactic leads to a classification as a bacterial meningoencephalitis potentially pneumococcic (being the most frequent aetiology at seniors, combined with cranial CT – chronic mastoiditis);
- Initial worsening;
- Emergence of melenic stools (possibly related to the administration of Trombex);
- Marked psychomotor agitation condition (possibly connected to 3 intricate factors: post-meningoencephalitis status, the

ischemic vascular cerebral accident and the cerebral atrophy – elements described on the CT);

- Proteinorachie's modifications: in bacterial, tumoral, degenerative infectious processes. The proteins in LCR with triple aetiology: from plasma, through translocation, can be secreted by the small lymphocytes present in LCR or the nervous parenchyma (encephalitises) or can be produced by the cerebral parenchyma in surgeries, cranial trauma, degenerative pathologies, cerebral atrophies etc.

The presence of high lactic: it is important in the diagnosis of bacterial meningitis because once the bacteria enter, they multiply inside the LCR, causing the inflammation in the subarachnoid space. This inflammation is responsible for the majority of the physiopathologic consequences that contribute to the clinical syndrome of meningitis containing: high permeability of the hematoencephalic barrier, cerebral edema, high resistance to LCR circulation, cerebral vasculitis, high intracranial pressure, low cerebral sanguine flow and cortical hypoxia.

DISCUSSIONS

It is useful, besides determining total proteinorachia in LCR to perform the electrophoretic study of the protein profile in LCR as well. 5 LCR profiles are known:

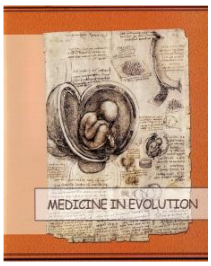
1. Habitual profile;
2. Inflammatory transudate;
3. Inflammatory profile;
4. Non-inflammatory transudate;
5. Local immune reaction transudate.

To be remembered and mentioned is the fact that minor clinc fluctuations of the average arterial pressure can have side effects at patients with meningitis, because autofixing can be altered, resulting in an increase of the risk of brain dammage due both to hypotension and tranzitory hypertension. Modifications of the sanguine flow can lead to regional hypoxia, increase of the lactic concentrations in the brain, secondary to the use of glucose by anaerobic means can be a precursor of encephalopathy.

REFERENCES

1. Durand ML, et al: Acute bacterial meningitis in adults. A review of 493 episodes. N Engl J Med 1993; 328(1): 21-8.
2. Scheld WM, et al: Pathophysiology of bacterial meningitis: mechanism(s) of neuronal injury. J Infect Dis 2002; 186 Suppl 2: S225-33.
3. Spanos A, Harrell FE, Durack DT: Differential diagnosis of acute meningitis. An analysis of the predictive value of initial observations. JAMA 1989; 262(19): 2700-7.
4. Quagliarello VJ, Scheld WM: Treatment of bacterial meningitis. N Engl J Med 1997; 336(10):708-16.

MICRORNAS AND DOWN SYNDROME PREGNANCY



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ABSTRACT

Down syndrome (DS) is the most frequent chromosomal aneuploidy and a common cause of mental retardation, determined in 95% of cases by the presence of three copies of chromosome 21. In spite of the intense research of the last 50 years, DS diagnosis is still based on invasive procedures and its pathogenesis is still blurred by multiple controversies. Here we describe the current knowledge on the possible use of microRNAs as novel biomarkers for differentiating between aneuploid and euploid pregnancies. Furthermore, we evidence the few data pointing towards an important role for microRNAs in the pathogenesis of DS anomalies.

Key words: *Down syndrome, microRNA, antenatal diagnosis, fetal development*

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INTRODUCTION

Down Syndrome (DS) is the most frequent chromosomal aneuploidy (about 1 in 750 live births), with an incidence that directly correlates with the maternal age and varies between different populations. John Langdon Down first described the clinical features in 1896, but it was only after 1950 that its etiopathology was linked to the existence of an extra copy (total or partial) of the chromosome 21. In 95% of Down syndrome cases, the genetic underlying mechanism is a meiotic nondisjunction and in only a few cases a chromosomal translocation, (usually involving chromosomes 14 or 15) could be documented[1,2].

DOWN SYNDROME: DIAGNOSTIC AND PATHOGENESIS

The standard methods for diagnosis of DS either in the prenatal or postnatal period are cytogenetic analysis of the karyotype, and (nowadays more and more often), Quantitative Fluorescence PCR (QF-PCR)[3]. In the case of prenatal diagnosis, these tests are applied on biological samples harvested during invasive procedures like amniocentesis and chorionic villus sampling, performed on women considered (according to the first or second trimester screening) at risk for aneuploid pregnancies. The first trimester screening combines the ultrasound measurement of nuchal translucency with the blood tests for human chorionic gonadotropin beta (β-hCG) and pregnancy-associated plasma protein A (PAPP-A). The second trimester screening combines the tests for estriol, β-hCG (double test), α-fetoprotein (triple test) and inhibin-α (quadruple test). However, it is the integrated test (which combines the quadruple test with the first trimester screening) that has the highest detection rates, although with the same incidence of false positive results[4-7].

DS patients present variable phenotypes, associating cognitive impairment and craniofacial characteristics to higher risks of seizures, Alzheimer disease (after age of 40), congenital heart defects (especially atrial-ventricular canal defect) and leukemia[2,8-11].

There are two major hypotheses aiming to correlate the genotype and the phenotype of DS patients, the gene dosage effect and the amplified developmental instability, both based on the assumption that the presence of an extra copy of chromosome 21 would lead to a 1.5 fold upregulation of the corresponding genes. However, only 9% of the genes mapped on chromosome 21 were found significantly overexpressed while 45% were significantly underexpressed on a trisomy 21 mouse model[3,12]. This rather puzzling result calls for alternative etiopathogenic models, involving epigenetic mechanisms among which the microRNA regulation of gene expression shows promising results[11].

MICRORNAS: BIOGENESIS AND FUNCTION

First described in 1993, the microRNAs are endogenous, small (22-25 nucleotides) non-coding RNAs, known to be involved in the regulation of gene expression at posttranscriptional level[13,14].

The human genome contains approximately 2000 individual or clustered microRNA genes, of which 1881 have been included in the miRBase (as of June 2014)[15,16]. MicroRNA transcription is performed mainly by RNA Polymerase II, and

(less commonly) RNA Polymerase III and is regulated by similar transcription factors that control protein-coding genes transcription, or by DNA methylation[17,18].

All mature microRNAs are synthesized from larger precursors that get through multiple processing steps of different maturation pathways. Most microRNAs follow the two steps canonical way of maturation. First, the primary transcript (pri-miRNA) is cleaved in the nucleus to precursor microRNA (pre-miRNA) by the RNaseIII endonuclease Drosha with the help of the double-stranded RNA binding domain protein Pasha/DGCR8 (DiGeorge critical region 8). Pre-miRNA is further exported into the cytoplasm by exportin (XPO5), where is processed to mature microRNA by the RNaseIII enzyme Dicer; the mature product is further loaded onto the RISC complex and exerts its function. The strand that is not incorporated into RISC, known as passenger strand (microRNA*), is normally degraded, although there are some cases when it associated with AGO proteins and acquired regulatory functions[19].

In addition to the classical maturation pathway, there are two alternative ways to process microRNAs, independently of Drosha/DGCR8 or Dicer. The Drosha-independent ways include the mirtron way and microRNA formation by snoRNA and tRNA processing; the Dicer-independent ways are represented by simtron way, microRNA formation by pre-tRNA processing and pre-miR-451 synthesis[20].

The main function of microRNAs is posttranscriptional regulation of gene expression through direct interaction with mRNAs. For microRNA to recognize the target mRNA, its seed region (nucleotides 2-8) have to base pair with the target mRNA. MicroRNAs are able either to inhibit translation or to degrade mRNA, depending on the complementarity with the target mRNA sequence: perfect complementarity induces mRNA cleavage and degradation, while an incomplete one inhibits translation[21].

MICRORNAS AND DOWN SYNDROME

It is now accepted that the presence of an extra-copy of chromosome 21 has important morphological and physiological impact on the fetus, which could be suspected as early as the first and/or second trimester through ultrasound and biochemical measurements; however, the actual diagnosis is being established through genetic testing after invasive procedures. Given the 1% risk of pregnancy loss during these invasive procedures, there is a great deal of interest for the discovery of non-invasive diagnostic tests, among which, cell free fetal-DNA (cffDNA) and placental mRNA/miRNA detection in maternal blood show the most promising results[22,23].

The increased stability of miRNAs in blood makes them attractive candidates as biomarkers for the non-invasive diagnosis of Down syndrome[24]. Several recent studies evaluated the presence of fetal microRNAs in cord blood, maternal plasma and amniotic fluid in aneuploid pregnancies relative to the normal ones.

MicroRNAs of placental and fetal origin can be found in maternal circulation either incorporated in exosomes, or in association with proteins like lipoproteins or RNA-binding proteins. The exact mechanism through which these microRNAs are released in maternal blood is not clear, both the passive or active mechanisms being possible[24].

According to miRBase, 29 microRNAs map to chromosome 21, however, only 5 of them (has-miR-99a, has-miR-125b-2, has-let7-c, has-miR-155, has-miR-802) have been experimentally confirmed. Kotlabova et al analyzed the maternal blood level of these five microRNAs in order to evaluate their possible use as biomarkers for Down syndrome diagnosis. Although all five microRNAs were found to be overexpressed in cultured amniotic fluid cells derived from Down syndrome pregnancies, when quantified in maternal plasma, they failed to distinguish between aneuploid and euploid pregnancies[25].

Kamhieh-Milz et al used a high-throughput quantitative Real Time PCR array method to identify in maternal plasma the circulating microRNAs associated with Down syndrome pregnancies. Out of the 1043 extracellular microRNAs analyzed, 695 were present in the maternal plasma but only 36 (18 overexpressed, 18 underexpressed) were associated with the aneuploid pregnancy[24]. Interestingly, none of these mapped to chromosome 21.

A study that analyzed the microRNA expression profile directly from fetal cord blood samples showed different results: 181 novel and 395 known microRNAs were identified using a high-throughput sequencing method, of which 149 known microRNAs were significantly differentially expressed (143 underexpressed and 6 overexpressed). Four of the microRNAs mapped on chromosome 21 (has-miR-99a, has-miR-125b-2, has-let7-c, has-miR-155) were found downregulated in DS fetuses. Surprisingly, the members of let-7 family had among the most increased expression levels of expression, an important finding knowing their implication in development and neurological processes[26,27]. The validation of these results using real time PCR not only confirmed the downregulation of the 4 microRNAs, but also revealed an overexpression by at least 50% of miR-802, also a chromosome 21-derived micro-RNA. Out of the 181 novel microRNAs identified by small RNA sequencing, 2 of them originate from the *DS critical region* and only 13 microRNAs measure more than 10 tags per million, questioning nit only their importance in DS, but also their mere existence[28].

Although extremely heterogeneous, these results suggest that microRNAs could be used to distinguish between DS and euploid pregnancies; however, the present results are far from being conclusive in this respect.

Initially ignored by the scientific community, miRNAs turned out to be major regulators of gene transcription: every single miRNA can target multiple mRNAs and every single mRNA can be targeted by several miRNAs. In mammals, miRNAs control the expression of approximately 64% of the genes, and are involved in the regulation of multiple biological pathways[29]. A simple run of the chromosome 21-derived miRNAs through any of the miRNAs target prediction programs would yield at least 2000 target mRNAs. It is thus understandable why the recent efforts of many labs have been directed towards understanding the possible involvement of miRNAs in Down syndrome phenotype.

Using the Diana mirPath prediction program, Kamhieh-Milz et al found that the 36 extracellular miRNAs found overexpressed in maternal plasma of mothers bearing DS fetuses interact with and possibly modulate 46 molecular pathways. A further, in depth pathway union approach identified 5 distinct pathways (mucin type O-glycan, glycosaminoglycan biosynthesis, ECM-receptor interaction, TGF-β signaling, and endocytosis), known to be involved in DS anomalies and

potentially impacted by miRNAs. Glycosaminoglycan biosynthesis and TGF-β signaling pathways have been associated with neurological disorders (mental retardation, respectively Alzheimer's disease) commonly found in Down syndrome patients[24].

In a similar approach, but using the miRecord tool, Yong Xu et al found that the microRNAs from the fetal cord blood of DS patients could impact on pathways known to be involved in neural development (i.e. BDNF, CDK5R1) and immunological processes (i.e. SOD1, MXD4, PBX1, BCLAF1, FOXO1). Among the newly identified fetal cord blood microRNAs, the two that map on chromosome 21 target 211, respectively 101 genes, among which MECP2, a gene known to be involved in cognitive development. Interestingly, MECP2 is also a (theoretical) target of the other chromosome 21-derived miRNAs (has-miR-802, has-miR-125b-2, has-let7-c and has-miR-155), which outlines the importance of understanding the link between the abnormal expression of the microRNAs and DS pathology[28]. Further studies are needed to clarify whether microRNAs could be used as possible biomarkers for DS diagnosis, as prognosis predictors for DS anomalies or are simple players in the DS etiopathogenesis puzzle.

CONCLUSIONS

Despite of the heterogeneous character of the preset results, microRNAs clearly hold the potential for becoming valuable markers for DS diagnosis and prognostic predictors. Furthermore, it has become obvious that the modern understanding of DS pathogenesis should include microRNAs abilities to modulate the fate of thousands of target mRNAs.

Acknowledgement

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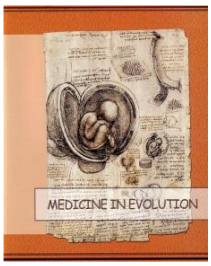
REFERENCES

1. O'Connor C. Trisomy 21 Causes Down Syndrome. Nat Educ [Internet]. 2008; Available from: http://www.nature.com/scitable/topicpage/trisomy-21-causes-down-syndrome-318
2. Wiseman FK, Alford K a, Tybulewicz VLJ, Fisher EMC. Down syndrome--recent progress and future prospects. Hum Mol Genet. 2009;18(R1):R75–83.
3. Antonarakis SE, Lyle R, Dermitzakis ET, Reymond A, Deutsch S. Chromosome 21 and down syndrome: from genomics to pathophysiology. Nat Rev Genet. 2004;5(10):725–38.
4. Pavarino ÉC, Biselli JM. Down Syndrome: Clinical and Genetic Aspects, Genetic Counseling and Prenatal Screening and Diagnosis. 2013;3–20.
5. Bianchi DW, Parker RL, Wentworth J, Madankumar R, Saffer C, Das AF, et al. {DNA} Sequencing versus Standard Prenatal Aneuploidy Screening. N Engl J Med [Internet]. 2014;370(9):799–808.
6. AHRQ guidelines for screening for fetal chromosomal abnormalities. http://www.guideline.gov/content.aspx?id=10921
7. Anderson CL, Brown CEL. Fetal chromosomal abnormalities: Antenatal screening and diagnosis. Am Fam Physician. 2009;79(2):117–23.
8. Weijerman, ME; de Winter J. Clinical practice. The care of children with Down syndrome. Eur jour8 nal Pediatr. 2010;169(12):1445–52.
9. Down syndrome and Alzheimer's disease. Available from:

www.alz.org/dementia/downloads/topicsheet_downsyndrome
10. Patterson D, Costa ACS. Down syndrome and genetics - a case of linked histories. Nat Rev Genet. 2005;6(2):137–47.
11. Elton TS, Sansom SE, Martin MM. Trisomy-21 gene dosage over-expression of miRNAs results in the haploinsufficiency of specific target proteins. RNA Biol. 2010;7(5):540–7.
12. Lyle, R., Gehrig, C., Neergaard-henrichsen, C., Deutsch, S. & Antonarakis, S. E. Gene Expression From the Aneuploid Chromosome in a Trisomy Mouse Model of Down Syndrome Gene Expression From the Aneuploid Chromosome in a Trisomy Mouse Model of Down Syndrome. Most 2004;1268–1274.
13. Lau NC, Lim LP, Weinstein EG, Bartel DP. An abundant class of tiny RNAs with probable regulatory roles in Caenorhabditis elegans. Science 2001;294:858–62.
14. Lagos-Quintana M, Rauhut R, Lendeckel W, Tuschl T. Identification of novel genes coding for small expressed RNAs. Science 2001;294:853–58.
15. Sun W, Julie Li Y-S, Huang H-D, Shyy JY-J, Chien S. microRNA: a master regulator of cellular processes for bioengineering systems. Annu Rev Biomed Eng. 2010;12:1–27.
16. Winter J, Jung S, Kelle S, Gregory RI, Diederichs S. Many roads to maturity: microRNA biogenesis pathways and their regulation, Nature Cell Biology 2009;11, 228 - 234.
17. Davis-Dusenbery BN, Hata A. Mechanisms of control of microRNA biogenesis, J Biochem. Oct 2010; 148(4): 381–392.
18. Amaia Lujambio, George A. Calin, Alberto Villanueva et al. A microRNA DNA methylation signature for human cancer metastasis, PNAS 2008;105(36): 13556-13561.
19. Okamura K, Chung WJ, Lai EC. The long and short of inverted repeat genes in animals microRNAs, mirtrons and hairpin RNAs, Cell Cycle. 2008;7(18): 2840–2845.
20. Helen J. Curtis, Christopher R. Sibley, Matthew J. A. Wood. Mirtrons, an emerging class of atypical miRNA, WIREs RNA 2012; 3:617–632.
21. Tarang S, Weston MD. Macros in microRNA target identification A comparative analysis of in silico, in vitro, and in vivo approaches to microRNA target identification, RNA Biology 2014;11:4, 324–333.
22. Mersy E, Smits LJM, Winden L a a P V, Die-Smulders CEMD, Paulussen a. DC, Macville MVE, et al. Noninvasive detection of fetal trisomy 21: Systematic review and report of quality and outcomes of diagnostic accuracy studies performed between 1997 and 2012. Hum Reprod Update. 2013;19(4):318–29.
23. Go, A. T. J. I., van Vugt, J. M. G. & Oudejans, C. B. M. Non-invasive aneuploidy detection using free fetal DNA and RNA in maternal plasma: Recent progress and future possibilities. Hum. Reprod. Update 2011;17, 372–382.
24. Kamhieh-Milz J, Moftah RFH, Bal G, Futschik M, Sterzer V, Khorramshahi O, et al. Differentially Expressed MicroRNAs in Maternal Plasma for the Noninvasive Prenatal Diagnosis of Down Syndrome (Trisomy 21). Biomed Res Int [Internet]. 2014;2014:1–9.
25. Kotlabova K, Doucha J, Chudoba D, Calda P, Dlouha K, Hromadnikova I. Extracellular chromosome 21-derived microRNAs in euploid & aneuploid pregnancies. Indian J Med Res. 2013;138(DEC):935–43.
26. Schulman BRM, Esquela-kerscher A, Slack FJ. Reciprocal Expression of lin-41 and the microRNAs let-7 and mir-125 During Mouse Embryogenesis. Dev Dyn. 2005;234(4):1046–54.
27. Wulczyn FG, Smirnova L, Rybak A, Brandt C, Kwidzinski E, Ninnemann O, et al. Post-transcriptional regulation of the let-7 microRNA during neural cell specification. FASEB J. 2007;21(2):415–26.
28. Xu Y, Li W, Liu X, Ma H, Tu Z, Dai Y. Analysis of microRNA expression profile by small RNA sequencing in Down syndrome fetuses. Int J Mol Med. 2013;32(5):1115–25.
29. Friedman RC, Farh KKH, Burge CB, Bartel DP. Most mammalian mRNAs are conserved targets of microRNAs. Genome Res. 2009;19(1):92–105.

PRIMITIVE SARCOMAS OF THE UTERINE CORPUS: 12 CASES ANALYSIS



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ABSTRACT

Uterine sarcomas are a rare, aggressive, heterogeneous group of tumors with unexpected clinical course and poor prognosis. They are classified into three main histological subtypes: leiomyosarcomas, endometrial stromal sarcomas and"other entities". The pathological type demands an adapted treatment approach. Surgical resection is regarded as the gold-standard treatment with total hysterectomy and bilateral salpingo-oophorectomy representing the usual choice. Pelvic and para-aortic lymph node dissection is also recommended in some cases. Uterine sarcomas usually exhibit aggressive clinical behaviour, with a high incienceof local recurrence and distant spread. Due to their rarity and lack of a preinvasive stage, there is no consensus for screening these neoplasms. Also there is a relative limited amount of literature concerning uterine sarcomas due to their low incidence and aggressive clinical course. In this paper, we present our experience regarding 12 cases of uterine sarcomas.

Key words: *leiomyosarcoma, endometrial stromal sarcomas, uterine sarcoma*

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INTRODUCTION

Primitive sarcomas of the uterine corpus are uncommon neoplasm with an incidence ranging between 1% to 3% of all malignancies of the uterine corpus [1,2]. The most common histhological types are leiomyosarcomas and endometrial stromal sarcomas. Rare histotypesare occasionally encountered such asembryonalrhabdomyosarcoma, Ewing sarcoma, angiosarcoma and pleomorphic rhabdomyosarcoma but the absence of significant accumulated experience with these histotypes may raise diagnostic and patient management difficulties [2]. Most uterine sarcoma were observed in postmenopausal women except a subset, including embryonalrhabdomyosarcoma, alveolar soft part sarcoma, and PEComaswich is more common inpremenopausal females. Staging is carried out using the updated FIGO/aJCC system for uterine sarcomas, taking into account that uterine sarcomas are different from endometrial cancer [3].

Multimodal therapeutic approaches have resulted in significantly improved outcomes [4]. Unfortunately, most of uterine sarcomas have been associated with rapid tumor progression and negative patient outcomes. The differential diagnosis for uterine sarcomas is often extensive and varies by histotype, but their accurate diagnosis fundamentally requires immunohistochemical characterization, morphometric analysis and, in some cases molecular genetic techniques.

MATERIAL AND METHODS

A three years retrospective study (2012-2014) was performed. Cases of primitive uterine corpus sarcomas were searched in the archives of the University Emergency Hospital from Bucharest. Clinical data were obtained from patients' charts. Information regarding gross examination were found in the files of the Pathology Department of the same hospital. Hematoxylin-eozin and van Gieson stained slides were examined. For immunohistochemical study we used Vimentin, Actin, Desmin, CD-34, CD-10, S100, CD117, Myogenin, Ck19 and Ki-67.

RESULTS

We found 12 cases of primitive uterine corpus sarcomas. Eight cases were leiomyosarcomas (almost 66, 66%) and four were endometrial stromal sarcomas (almost 33,33%). The patients'age varied between 46-64 years old (mean age: 55).The age of the patients with leiomyosarcomas varied between 50-64 years old (mean age: 55) and the age of the patients with endometrial stromal sarcomas varied between 46-62 years old (mean age: 55).

Signs and symptoms that suggested the presence of a tumoral mass were: metrorrhage, abdominal mass, abdomnial paint. Clinical and echographic examination revealed the tumoral processes of the uterine corpus. All patients underwent total hysterectomy with bilateral oophorectomy.

Grossly, leiomyosarcomas presented as solid whitish-yellow masses, nodular in shape, not well demarcated and with an intramural location. Only two cases presented as polipoid masses. In one case mucoid areas were observed in the intramural nodule.Also, 7 cases presented areas of hemorrhage and necrosis. Maximum diameter of the tumors varied between 3- 21 cm (mean: 9,7 cm). The two

polipoid masses measured 3, respectively 5 cm.

Microscopic examination revealed, in all 8 cases of leiomyosarcoma, proliferation of spindle cells arranged in fascicles, with eosinophilic cytoplasm, indistinct membranes, nuclear pleomorphism, nuclear atypia and mitotic activity. 7 cases were conventional leiomyosarcoma and one was myxoidleiomyosarcoma.

Regarding the histologic grading, 5 cases were moderately-differentiated, two were poorly differentiated and one was well-differentiated.

Five cases were limited to the myometrium, one showed invasion in the serosa of the uterus, one metastasized to the ovary and one to the toracal vertebras (T8-T10).

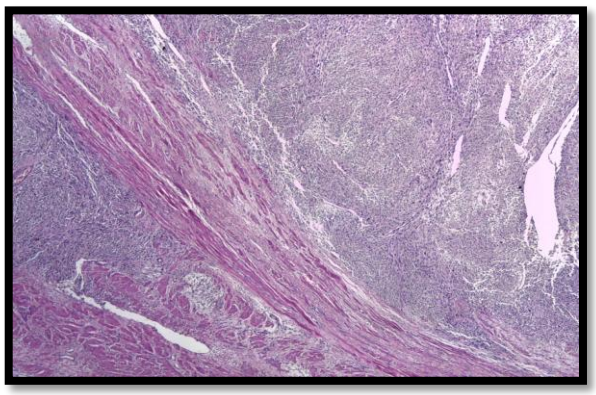

Figure 1. Spindle cell proliferation in a leiomyosarcoma infiltrating the smooth muscle cells of the myometrium (Hematoxylin-eozin, ob.4X)

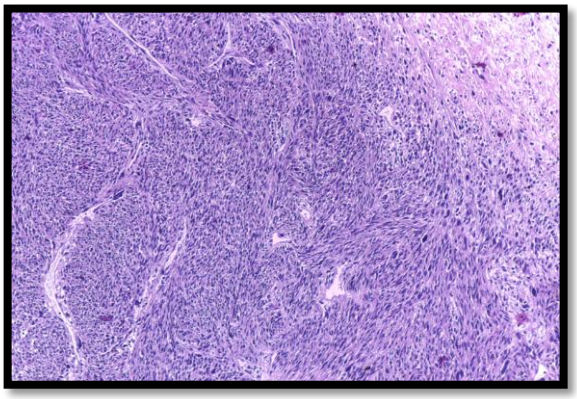

Figure 2. Highly cellular spindle cell proliferation in a leiomyosarcoma with area of necrosis in the right corner (Hematoxylin-eosin, 10X)

Grossly, endometrial stromal sarcomas presented as solid exophytic masses originating from the endometrial surface and with the tendency to invade the miometrium. Maximum diameter of the tumor varied between 5,3 - 16 cm (mean: 9,2 cm).

Microscopic examination revealed proliferation of oval medium-sized cells with a compact arrangement.

One case showed low-grade malignancy aspects and the other 3 cases showed high-grade malignancy aspects.

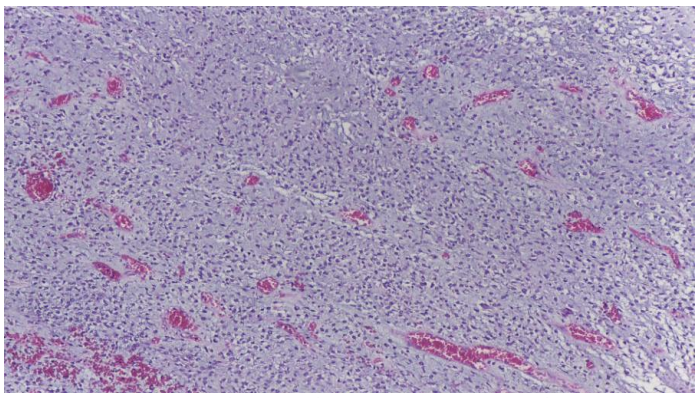

Figure 3. Endometrial stromal sarcoma (Hematoxylin-eozin, 10X)

In one case the tumorinvaded the inner-half of myometrium and extended to the cervix, the second case showed invasion into the outer-half of the myometrium, the third case showed invasion in the cervix and ovarian metastasis, in the fourth case the tumor had spread to the lung.

On immunohistochemistry, leiomyosarcoma showed positive

staining for vimentin, actin, desmin and caldesmon. Ki-67 immunopositivity varied between 35-70%. CD-34, CD 117, Ck-19, CD-10 and S-100 were negative in the tumoral cells of leiomyosarcomas. Endometrial stromal sarcomas showed CD-10 and vimentin immunopositivy in the tumoral cells, while Actin, desmin, Cd-34, S-100, AE1-AE3 were negative and mean Ki-67 immunopositivy was higher than 50%.

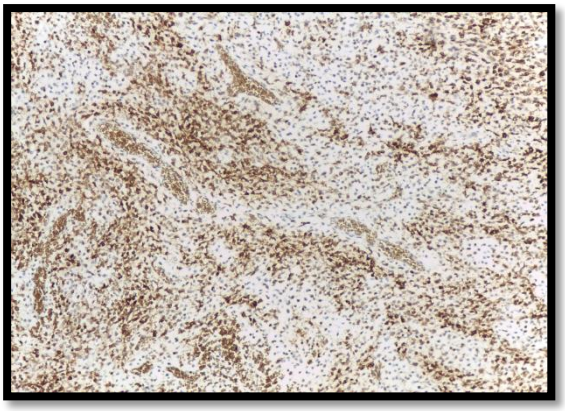

Figure 4. CD10 immunopositivetumoral cells in endometrial stromal sarcoma (ob.10X)

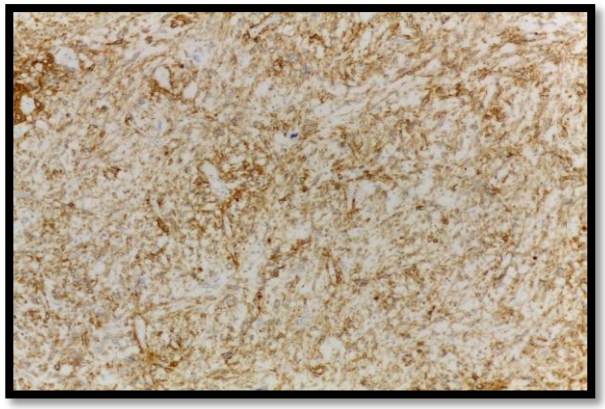

Figure 5. Positive immunostain for Actin in a leiomyosarcoma (ob.10X)

DISCUSSIONS

Uterine sarcomas are rare tumors that account for 3% of all uterine cancers [5]. Leiomyosarcomas are malignant smooth muscle tumors, mostly composed of spindle cells, but occasionally can show epithelioid or myxoid morphology, with vascular space invasion identified in 10-20% of cases [2]. They are the most common uterine sarcomas, with an incidence of 0,3-0,4/100000 women per year, that occur in female patients > 50 years old and present as nodular masses with irregular margins, typically large (mean diameter of 10 cm), either solitary or multiple, with tan fleshy appearance, often with necrosis and hemorrhage [2]. The tumor often has spread locally, regionally or at distance, the most often site for hematogenous dissemination being the lung [2]. Being smooth muscle derivated malignancies, they are positive for immunohistochemistry markers such as: desmin, smooth muscle actin, HDAC8, h-caldesmon, especially the spindle cell component, EMA, in 30-40% of cases ER+, PR+ and sometimes CD117+, even if c-kit mutations have not been identified [2, 6].

The prognosis for leiomyosarcomas is poor, they are considered high-grade malignancies, even when confined to the uterus (15-70% 5-years survival rate, depending on the tumor stage)[2]. Tumor size, tumor grade and stage are major prognostic parameters.For tumors confined to the uterine corpus, diameter < 5cm is associated with better survival rates[2].

In our case, the smallest leiomyosarcoma, that presented as a polipoid mass, has also showed a well differentiated aspect (G1), predicting a better outcome.

An important problem is the tumor recurrence after treatment, witch in spindle cell pattern are detected within 2 years, while in other variants later [2].

Endometrial stromal sarcomas are malignant tumors derived from mesenchymal stromal cell of the endometrium; they are generally divided in low-grade and high-grade endometrial stromal sarcomas [2]. The

low-grade type has a spindle cell pattern, of tongue-like growth in the myometrium and lymphovascular spaces, usually with low mitotic activity index (< 5/10HPF), but a high mitotic index does not exclude this diagnosis; the low-grade endometrial sarcomas can present, along with the typical pattern with smooth muscle differentiation in nodules with central hyalinization, fibromyxoid change, sex cord-like structures or endometrioid type glands[2, 5].

Mean age for diagnosis is 52 years and are the second most common sarcomas diagnosed [2].

They present as polypoidintracavitary or intramural masses, with ill-defined borders, apx 5-10 cm in diameter, tan-yellow fleshy cut surface, but hemorrhage or necrosis are only occasionally seen; metastasis to ovary or lung can be the initial presentation [2].In our study, all cases of endometrial stromal sarcomas had an exophyticaspect, while 2 cases of leomyosarcomas presented as polipoid masses and 6 cases as intramural nodules. Absence of necrosis in our cases of endometrial sarcomal sarcomas may be due to the smaller size of this tumors in comparison to leiomyosarcomas' size.

The high-grade type of endometrial sarcomas show a round cell morphology, sometimes in association with low grade spindle cells; mean age for diagnosis is 50 years, they are also polypoid masses, medium diameter of 7,5cm, often with extrauterine extension at the time of diagnosis [2]. Macroscopically, they resemble their low-grade counterparts. Microscopically, they have a more infiltrative and destructive growth, often involving the outer half of the myometrium, with high mitotic activity (> 10/10HPF) and lymphovascular invasion is typically seen compared to leiomyosarcomas [2, 5]. The higher aggressiveness of endometrial stromal sarcomas in comparison to leiomyosarcomas is well proven by the fact that all cases of endometrial stromal sarcomas showed invasion beyond the myometrium (cervix, ovary, lung), unlike the leiomyosarcomas' cases, where only 3 patients presented invasion to the uterus, ovary and toracal vertebras.

Endometrial stromal sarcomas usually strong positive for CD10, cyclin D1, negative for HDAC8 and h-caldesmon, occasionally positive for smooth muscle actin and desmin in areas of smooth muscle differentiation, ER and PR positive and may express CD117 but with no evidence of c-kit mutations [5, 6, 7].

Studies show that CD10 is a valuable marker in distinguishing between endometrial stromal sarcomas and uterine smooth muscle tumors [8].

Compared to leiomyosarcomas, low-grade endometrial stromal sarcomas have a better prognosis (5-years survival rate of 50-90%) [2]. Although high-grade endometrial sarcomas and leiomyosarcomas have similar prognostic rates, the risk for recurrences is higher for the first category (<1 year) [2].

As for treatment in advanced cancer stages, there are different new directed therapies, for advanced leyomiosarcomas including gemcitabine, docetaxel, trabectedin, whereas for endometrial stromal sarcomas hormonal therapies appear to be more useful [9].

CONCLUSIONS

Uterine sarcomas are rare highly malignant tumors. The two most common entities are leiomyosarcomas and endometrial stromal sarcomas, with a ratio of 2:1. Leiomyosarcomas tend to present as intramural nodules, while endometrial stromal sarcomas present as exophytic masses. They both are highly aggressive, but endometrial

stromal sarcomas are more prone for local and distal invasion.

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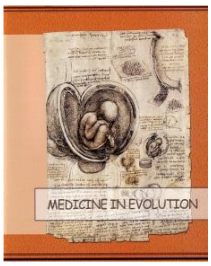
REFERENCES

1. Kurman RJ, Carcangiu ML, Herrington S, Young RH. Who Classifiction of Tumors of female Reproductive Organs, 4th Edition.Lyon; IACR, 2014.
2. Harlow BL, Weiss NS, Lofton S: The epidemiology of sarcomas of the uterus.J Natl Cancer Inst 1986, 76:399-402
3. Raut CP, Nucci MR, Wang Q, Manola J, Bertagnolli MM, Demetri GD, Morgan JA, Muto MG, Fletcher CD, George S. Predictive value of FIGO and AJCC staging systems in patients with uterine leiomyosarcoma, Eur J Cancer. 2009 Nov;45(16): 2818-24. doi: 10.1016/j. ejca 2009.06.030. Epub 2009 Jul 3
4. ZagouriF, DimopoulosAM, FotiouS, Kouloulias V, Papadimitriou CA. Treatment of early uterine sarcomas: disentangling adjuvant modalities, World Journal of Surgical Oncology 2009, 7:38, doi:10.1186/1477-7819-7-38
5. D'Angelo E, Prat J. Uterine sarcomas: A review. Gynecologic Oncology, January 2010; 116(1):131–139.
6. Koivisto-Korander R, Butzow R, Koivisto AM, Leminen A. Immunohistochemical studies on uterine carcinosarcoma, leiomyosarcoma, and endometrial stromal sarcoma: expression and prognostic importance of ten different markers. Tumor Biology, June 2011; 32(3):451-459.
7. Masand RP, Euscher ED, Deavers MT, Malpica A. Endometrioid stromal sarcoma: a clinicopathologic study of 63 cases. Am J SurgPathol. 2013; 37(11):1635-47.
8. Chu P, Arber D, Weiss L, Chang K. Utility of CD10 in Distinguishing between Endometrial Stromal Sarcoma and Uterine Smooth Muscle Tumors: An Immunohistochemical Comparison of 34 Cases. Mod Pathol 2001; 14(5):465–471.
9. Seddon B, Davda R. Uterine sarcomas—Recent progress and future challenges. European Journal of Radiology, April 2011; 78(1):30–40.



MULTICENTRIC UNILATERAL INVASIVE DUCTAL AND LOBULAR BREAST CARCINOMA - A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

The incidence of multicentric or multifocal breast cancer has been reported to be less than 2% [1]. However, synchronous, multicentric unilateral invasive ductal carcinoma and lobular carcinoma are rarely described. The biological understanding, the clinical implication of multifocal and multicentric breast cancers and the choice of proper treatment for these particular pathological entities are still debated. Multiple tumours may increase lymph node involvement compared with unifocal tumours, and some current statistics imply that multifocal or multicentric breast cancer is more aggressive and carries worse prognoses. The impact of multiple breast cancer has been poorly studied, and the requirement of specific adjuvant treatment in order to prevent the likely negative effect of multifocality is still a subject of research. We present a case of a 46 year old Caucasian woman with palpable invasive lobular carcinoma who was later found to have a synchronous invasive ductal carcinoma on further investigation. This case highlights the importance of careful evaluation of coexisting breast lesions in the presence of an existing carcinoma.

Key words: *breast cancer, invasive ductal carcinoma, lobular carcinoma, multicentric*

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INTRODUCTION

Multifocal and multicentric breast cancer are described as two or more synchronous ipsilateral malignant neoplasms, separated by benign tissue placed within the same quadrant or different quadrants of the breast [1,2]. The main difference between multifocal and multicentric breast cancer is based on the different anatomical position [3]. Multiple foci located in the same quadrant are classified as multifocal, whereas multicentric breast cancer is present in more than one quadrant. Some authors also distinguish multifocal from multicentric breast cancer based on the supposition that multifocal breast cancer originates within the same duct collecting system, while multicentric breast cancers arise in different duct collecting systems. This means that multifocal breast cancer is considered monoclonal, while multicentric breast cancer is not [4-6]. Some authors grouped multicentric and multifocal breast cancer together, due to ill-defined anatomical borders between different breast quadrants and the difficulty in estimating the proper area between tumours [1,4].

With the widespread use of mammographic screening and enhanced sensitivity of imaging techniques, the detection of multifocal and multicentric breast cancer is likely to increase in the near future [6]. The reported prevalence of these pathological entities varies extensively ranging from 9% to 75%, mostly due to the inadequate standardization of the gross examination and definition of multicentric and multifocal breast cancer. [3,8].

The American Joint Committee on Cancer (AJCC) defines multiple cancers as those that are grossly or macroscopically distinct. 0.5 cm is considered the minimum distance required between two macroscopic cancer foci to define them as multiple cancers; anything closer than 0.5 cm likely represents a single tumour with a complex shape that come in sight as multi-focal. If there is suspicion for multiple ipsilateral primary cancers, additional sampling of tissue in between the two foci should be done to confirm that there is no microscopic tumour connecting the two foci. If the microscopic invasion is proved, the tumour should be managed as a single, unifocal cancer and measured across the entire range of all foci. AJCC also states that the tumour size (pT) should be based only on the single, largest tumoral mass.

Clinical significance of multiple tumours within the same pT category remains to be studied. There is much controversy as to whether multifocal or multicentric cancers may predict the involvement of axillary nodes. Survival does not appear to be affected by multiple synchronous breast cancers in comparison to unifocal breast cancer [6,8].

It is not clearly defined if the assessment of ER/PR/HER2 should be done on all foci of multiple cancers in a single breast. Some studies found equivalent ER/PR/HER2 profiles in all tumour foci, as well as equivalent morphologic features [9] and other recent studies found mismatches in immunohistochemical features [10]. Generically if the morphology and pathological gradeing appears to be similar in all tumoral foci, performing prognostic markers on the largest or two largest is feasible; however if the morphologies or grades are clearly different, it may be cautious to test each distinct tumoral focus.

A 46-year-old Caucasian woman presented with a painful right breast lump. There was no family history of breast carcinoma. On examination, there was a 1.7 cm palpable lump at the right lower inner quadrant with right axillary lymphadenopathy. The overlying skin and the nipple showed no modification. Another 1.5 cm lesion was palpated at the right upper inner quadrant.

Bilateral mammogram revealed two large spiculated, high density lesions in the upper and lower inner quadrants, close to the chest wall associated with massive right axillary lymphadenopathy. There were no signs of invasion of the underlying pectoralis muscle. The mammographic examination was highly suspicious for carcinoma. Excisional biopsy for the larger mass was performed and revealed an invasive lobular carcinoma. A right modified radical mastectomy with axillary nodes clearance was performed.

The mastectomy specimen was sent for histopathological examination. Histopathological test revealed two different pathologies. The smaller tumoral mass in the upper midline was confirmed to be an invasive ductal carcinoma (NST-no special type) measuring 1.5 cm. On microscopic examination the neoplastic cells showed moderate tubule formation (approx. 60%), moderate to severe nuclear pleomorphism and about 8-11 mitotic figures/HPF. The tumour scored 6 points (grade 2 of differentiation) according to the Nottingham scoring system (the Elston-Ellis modification of the Bloom-Richardson grading system) with evidence of extensive lymphovascular and perineural invasion. The larger tumour found in the lower inner quadrant measured 1.7 cm and showed individual, noncohesive, malignant, small, uniform cells, round with minimal pleomorphism, evenly dispersed chromatin and no nucleoli arranged in a single-file pattern. The mitotic index revealed about 10-12 mitotic figures per 10 high-power fields. Immunohistochemical investigations were performed to assess the phenotype and provide a definitive diagnosis. The E-cadherin stain was negative, except for a few benign entrapped glands that stained positive. These findings were consistent with the diagnosis of invasive lobular carcinoma. Hormone receptor statuses for both tumours were positive for oestrogen receptor, diffuse positivity (about 70%) for progesterone receptor and cerbB-2 was not overexpressed.

The mastectomy specimens revealed that both lesions were approximately 5.0 cm apart, with infiltration of the lobular carcinoma within the apical and axillary nodes (9 nodes out of 22 examined). Based on these findings the final diagnosis was of multicentric unilateral invasive ductal and lobular breast carcinoma pT1c(m2)N2aMx, stage IIIA breast cancer.

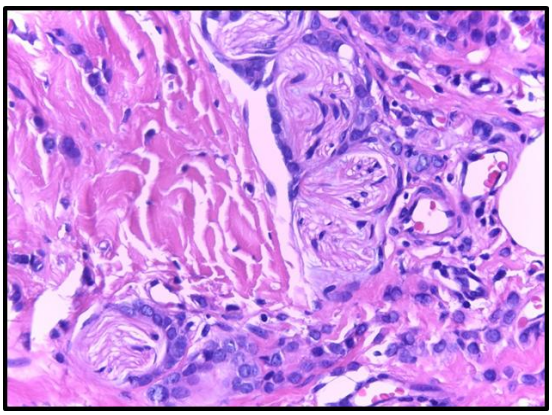
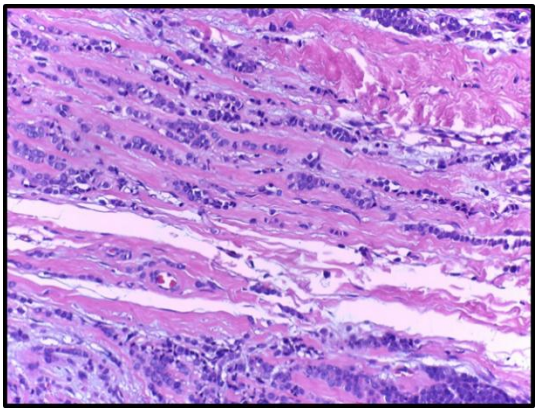


Figure 1.



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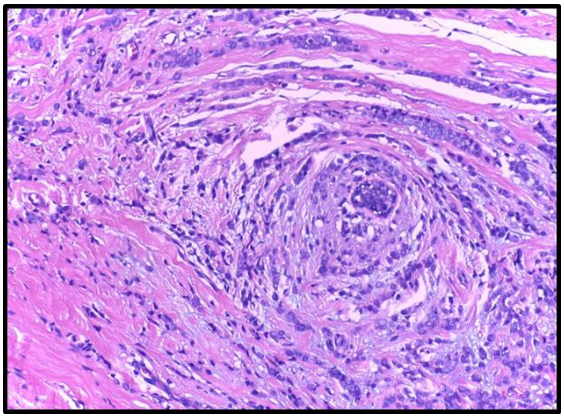

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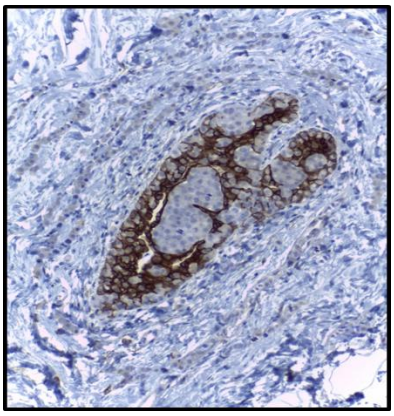
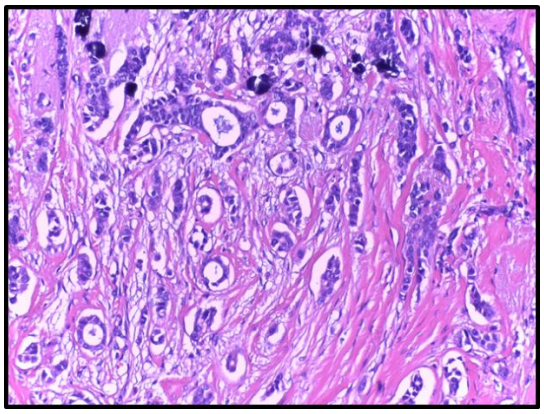


Figure 4.

Invasive lobular carcinoma (Fig. 1-4):

Round, small tumoral cells with minimal pleomorphism, noncohesive, encircling distorted ducts in a targetoid-like pattern (Fig.1, H.E. ob.x10), linearly arranged/indian file or loosely dispersed throughout fibrous stroma (Fig.2, H.E. obx10). Tumoral cells occasionally show perineural invasion (Fig.3, H.E. obx20). Invasive lobular carcinoma with no E-cadherine immunoreactivity. An invaded and distorted terminal ductal-lobular unit serves as an internal positive control (Fig.4, obX10).



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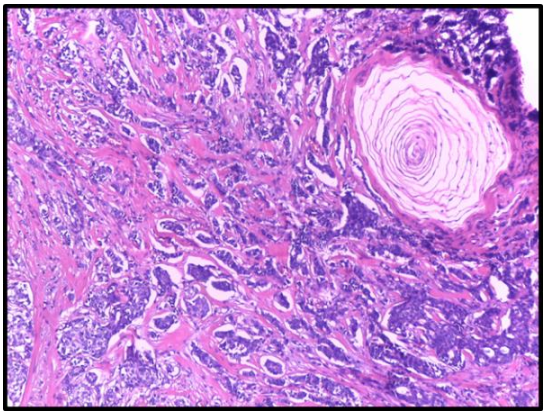

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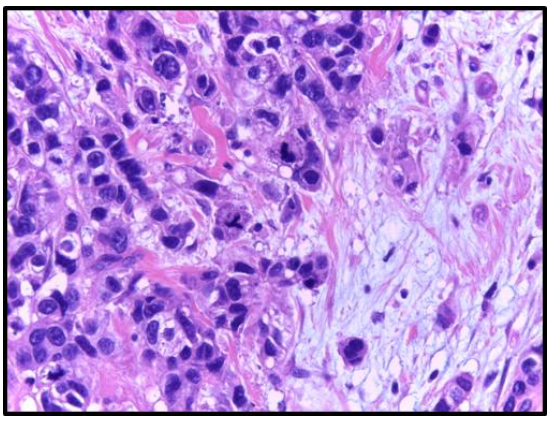

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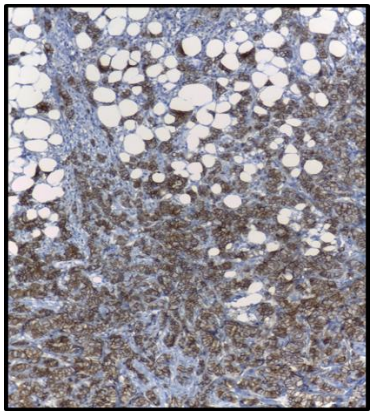

Figure 8.

Invasive ductal carcinoma (NST) (Fig. 5-8)

Haphazard arrangement of glands/tubules, along with gland variability in size and shape with desmoplastic stromal reaction and microcalcification (Fig.5 H.E. obx10). Tumoral cells show perineural invasion - here, a pacinian body (Fig.6 H.E. obx10). Pleomorphic tumoral cells with no sign of tubule formation and prominent atypical mitoses. Also stromal elastosis can be seen. (Fig 7. H.E. obx40). The E-chaderin immunostain is strongly positive (Fig. 8. obx10)

DISCUSSIONS

Some authors prefer the terms multifocal breast cancer and multicentric breast cancer, though the AJCC uses the term "multiple carcinomas" [13]. These terms have not been used constantly by many authors and some have even interchanged them. The distinction between multifocal and multicentric breast cancer is based on the site and anatomic distribution of the tumoral foci attributive to a breast quadrant. Tumoral foci within a single quadrant are called multifocal whereas tumours involving different breast quadrants are considered multicentric [11]. Also, multifocal breast cancers are described as tumoral masses no more than 5 cm apart from each other in the same quadrant [13].

The variation of description and terminology reside upon precise measurements and accurate dissection of the specimens to exclude microscopic cancer connecting different tumoral foci. The biological background for the discrimination between multifocal and multicentric breast cancer is suggested by some studies but remains to be cleared up. Some studies which focus on clonality suggest that multifocal tumours are biologically connected [11,12]. As mentioned above, there is controversy regarding the clinical significance of multiple synchronous carcinomas and more studies are needed. Our patient's condition was consistent with the above mentioned definition of synchronous multicentric cancer and details the rare occurrence of a synchronous unilateral invasive ductal carcinoma and an invasive lobular carcinoma. Mammographically, both lesions presented as spiculated masses with architectural distortion and asymmetry. A comparative analysis on the mammographic presentation of invasive ductal carcinoma and invasive lobular carcinoma showed that spiculated masses with or without microcalcifications were the most common finding in both entities [14]. Also the distortion of the breast parenchyma is a regularly reported feature.

Due to the histological aggressiveness and extensive nature of the invasive lobular carcinoma on excisional biopsy, our patient underwent a modified radical mastectomy. It was only on gross and histological examination that the presence of a second malignancy with different histological features was revealed. It is crucial that in the presence of an existing carcinoma, any other suspect lesion found in the breast needs circumspect assessment. In addition, magnetic resonance imaging is helpful in detecting contralateral breast disease and further ipsilateral malignant lesions, which can occur in up to 30% of cases of invasive lobular carcinoma [15].

Our patient's tumoral aggressiveness was also illustrated by the extensions of the disease to the axillary lymph nodes. Yerushalmi et al. reported that the multicentric or multifocal breast cancer patients are more likely to have axillary nodal involvement, compared to that of a unifocal group of patients [16]. Recently some studies [17] implied that women with multicentric or multifocal breast cancer were more likely to be less than 50 years old, have nodal tumoral extension, a larger tumor size which suggests that MMBC is more biologically aggressive than unifocal breast cancer.

The surgical treatment for multicentric multifocal breast cancer has changed over the past years. Some authors used to consider that multicentric and multifocal breast cancer patients should be treated with mastectomy due to the attested high rates of loco-regional recurrence. In some early trials, the recurrence in multicentric or multifocal breast cancer in women treated with breast conservation techniques ranged from 23% to 40% at a 5-year follow-up [18]. These studies concluded that the overall risk of loco-regional recurrence for the patients with multicentric or multifocal breast cancer was too high and hence, more radical approaches were recommended. In contrast, more recent studies have advised breast-conserving surgery as the principles of negative margins, appropriate chemotherapy, radiotherapy and acceptable reconstruction [19]. These studies reported a range of local and regional recurrence from 3% to 5% at 6-year follow-up patients with multicentric or multifocal breast cancer which underwent breast conservation surgical treatment. Therefore, breast-conserving surgery seems to be safe and adequate for these particular patients. Also, appropriate integrated adjuvant therapy after surgery has become an international consensus for the patients with multifocal or multicentric breast cancer.

CONCLUSIONS

Further case reports that describe the clinical experience and therapeutic outcomes in this very aggressive variant of breast cancer would help clarify its definition and may highlight new, more proper classification. Furthermore it will be easier to rapidly diagnose and treat these patients in order to achieve the most favourable outcome possible.

Conflict of interests: none to declare. *We undersign, certificate that the procedures and the experiments we have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2000 (5), as well as the national law.*

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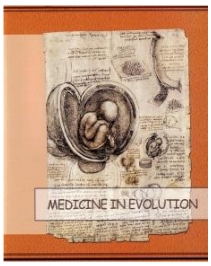
REFERENCES

1. Boyages J, Jayasinghe UW, Coombs N. Multifocal breast cancer and survival: each focus does matter particularly for larger tumours. Eur J Cancer 2010;46:1990-6.
2. Bozzini A, Renne G, Meneghetti L, Bandi G, Santos G, Vento AR, et al. Sensitivity of imaging for multifocal-multicentric breast carcinoma. BMC Cancer 2008;8:275.
3. Lopez JK, Bassett LW. Invasive lobular carcinoma of the breast: spectrum of mammographic, US, and MR imaging findings. Radiographics 2009; 29:165-76.
4. Gokalp G, Topal U. A typical invasive ductal carcinoma: Two cases. Eur J Raiol Extra 2009; 71:19-22.
5. Mann RM, Kuhl CK, Kinkel K, Boetes C. Breast MRI: guidelines from the European Society of Breast Imaging. Eur Radiol 2008; 18:1307-18.
6. Yoo JL, Woo OH, Kim YK, et al. Can MR Imaging contribute in characterizing well-circumscribed breast carcinomas? Radiographics 2010; 30:1689-702.
7. Bauman L, Barth RJ, Rosenkranz KM. Breast conservation in women with multifocal-multicentric breast cancer: is it feasible? Ann Surg On¬col 2010;17 Suppl 3:325-9.
8. Rezo A, Dahlstrom J, Shadbolt B, Rodins K, Zhang Y, Davis AJ, et al. Tumor size and survival in multicentric and multifocal breast cancer. Breast 2011;20:259-63.
9. Middleton LP, Vlastos G, Mirza NQ, Eva S, Sahin AA. Multicentric mammary carcinoma: evidence of monoclonal proliferation. Cancer. 2002 Apr 1;94(7):1910
10. Boros M, Ilyes A, Nechifor Boila A, Moldovan C, Eniu A, Stolnicu S. Morphologic and molecular subtype status of individual tumor foci in multiple breast carcinoma. A study of 155 cases with analysis of 463 tumor foci. Hum Pathol. 2014 Feb;45(2):409-16. doi: 10.1016/ j.humpath.2013.10.006. Epub 2013 Oct 18
11. Jain S, Rezo A, Shadbolt B, Dahlstrom JE. Synchronous multiple ipsilat¬eral breast cancers: implications for patient management. Pathology, 2009 Jan;41(1):57-67
12. Noguchi S, Aihara T, Koyama H, Motomura K, Inaji H, Imaoka S. Dis¬crimination between multicentric and multifocal carcinomas of the breast through clonal analysis. Cancer 1994;74:872-7.
13. American Joint Committee on Cancer. Breast. In: American Joint Committee on Cancer, editor. AJCC Cancer Staging Manual. 6th ed. New York: Springer; 2002. p.223-40.
14. Cornford EJ, Wilson AR, Athanassiou E, et al. Mammographic features of invasive lobular and invasive ductal carcinoma of the breast: a comparative analysis. Br J Radiol 1995; 68:450-3.
15. Macura KJ, Ouwerkerk R, Jacobs MA, Bluemke DA. Patterns of enhancement on breast MR images: interpretation and imaging pitfalls. Radiographics 2006; 26:1719-34
16. Yerushalmi R, Kennecke H, Woods R, Olivotto IA, Speers C, Gelmon KA. Does multicentric/multifocal breast cancer differ from unifocal breast cancer? An analysis of survival and contralateral breast cancer incidence. Breast Cancer Res Treat 2009;117:365-70.
17. Neri A Marrelli D, Megha T, Bettarini F, Tacchini D, De Franco L, Roviello F. Clinical significance of multifocal and multicentric breast cancers and choice of surgical treatment: a retrospective study on a series of 1158 cases BMC Surgery 2015, 15:1 doi:10.1186/1471-2482-15-1
18. Kurtz JM, Jacquemier J, Amalric R, Brandone H, Ayme Y, Hans D, et al. Breast-conserving therapy for macroscopically multiple cancers. Ann Surg 1990;212:38-44.
19. Gentilini O, Botteri E, Rotmensz N, Da Lima L, Caliskan M, Garcia-Etienne CA, et al. Conservative surgery in patients with multifocal/multicentric breast cancer. Breast Cancer Res Treat 2009;113:577-83.

MINI-REVIEW: CYTOKERATIN 7 AND CANCER



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ABSTRACT

Cytokeratin 7 (CK7) is a type II cytokeratin expressed in simple epithelia of the gallbladder, pancreatic and hepatic ducts, ovaries, endometrium, uterine tube, renal tubules, respiratory mucosa and the transitional epithelium of the renal pelvis mucosa, ureter and urinary bladder. CK7 is also expressed in endothelia and in mammary luminal glandular epithelial cells. Expression of CK7 uses for the immunohistochemical diagnosis of tumors and to discriminate the origin of metastases. A CK7 positive phenotype is associated with poor prognosis for patients with stage I/IIA/IIB of squamous cell carcinoma of the esophagus, adenocarcinoma of the lung and hepatocellular carcinoma.

Key words: *CK7; intermediate filaments; cancer; epithelial–mesenchymal transition*

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INTRODUCTION

Cytokeratins are a class of intermediate filaments of the cytoskeleton. The family of intermediate filaments is composed of vimentin, desmin, glial fibrillary acidic protein, neurofilaments and twenty subtypes of cytokeratin with a different molecular weight and variable tissue related expression (Bayrak et al., 2012).

The intermediate filaments are known as some of the most stable cellular components and are implicated in the distribution of cytoplasmic organelles, transduction, cellular polarity and gene modulating. Cytokeratins are proteins witch are involved in the development and differentiation of the epithelial cells. Therefore, they are essential for the good functionality and for maintaining the tissue structure. They are relatively resistant to degradation and show highly specific phenotypic expression depending on the type and differentiation of the epithelial cells. Therefore, different types of epithelial cells present different specific expressions for CK. Indifferent of the malign transformation, the tumors and metastasis keep the CK expression of the original tissue (Jasik, 2012).

CK can be divided in two classes: type I, acidic which contain CK9-CK20. Type I CK have small molecular weight. The type II CK, which are neutral-basic and have high molecular weight contain CK1-CK8. Type I and II CK are combined in a 1:1 ratio in no-covalent heteropolymers, assembled in keratin filaments (Weng et al., 2012, Cîmpean et al., 2008).

Keratinized epithelium of the skin is highly differentiated and expresses the larger CK: CK1 and CK10. The smaller CK – CK7, CK8 and CK18 are expressed in simple epithelia such as nasal epithelium and in the glandular epithelia (Guo et al., 2006, Dale et al., 1990).

CK7 EXPRESSION

CK7 is a polypeptide with a molecular weight of 54 kDa. It is encoded by the KRT7 gene localized on the 12Q13:13 (Bragulla and Homberger, 2009).

CK7 is distributed in the simple epithelia of the gallbladder, pancreatic and hepatic ducts, ovaries, endometrium, uterine tube, renal tubules, respiratory mucosa and the transitional epithelium of the renal pelvis mucosa, ureter and the urinal bladder (Iwatsuki and Suda, 2010). It is also present in the developmental stage of the teeth in the enamel (Bragulla and Homberger, 2009).

In the endometrium the CK7 expression is high in the secretory faze but low in the proliferative faze. The mesothelium and the endothelial cells (fig.1) express CK7. The luminal cells of the salivary ducts have an immune phenotype intensely positive for CK7 (Nikitakis et al., 2004). CK7 has not been identified in the hepatocytes, distal and proximal renal tubes and the squamous epithelia (Jasik, 2012).

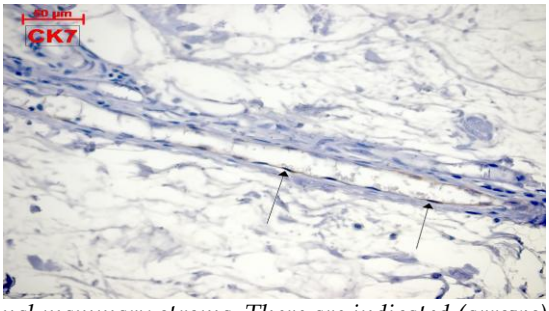

Figure 1. CK7 labelling of normal mammary stroma. There are indicated (arrows) CKT-positive endothelial cells

CK7 is a marker for progression of primary biliary cirrhosis. In hepatocytes, aberrant expression of CK7, a biliary ducts cytokeratin, is a marker for primary biliary cirrhosis and is related to metaplastic potential of destroyed hepatocytes (Chatzipantelis et al., 2006, Van Eyken et al., 1989).

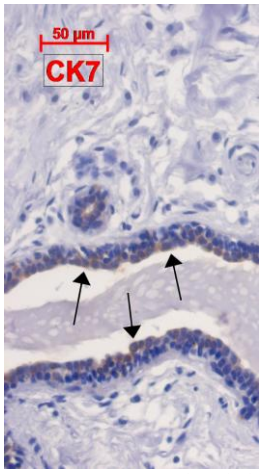

Figure 2. CK7 labelling of normal mammary tissue. Glandular/luminal cells express CK7 (arrows)

In normal mammary epithelia three main cell types are distinguished: luminal or glandular, basal or myoepithelial, and stem cells (Mohammadizadeh et al., 2009). Myoepithelial and luminal epithelia can be distinguished by their different cytokeratin expression patterns, CK5/6 being basal and CK7 – luminal (fig.2) (Mohammadizadeh et al., 2009). Expression of CK7 in stromal mammary cells suggested us an epithelial origin of stem/progenitor stromal cells (fig.3). On normal mammary tissues we sample in figures 1-3 was applied a primary antibody for cytokeratin 7 (clone RCK105, Abcam, Cambridge, UK, 1:1000).

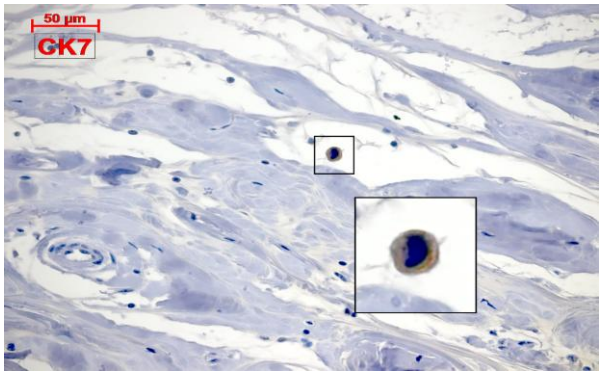

Figure 3. CK7 labelling of normal mammary stroma. There is presented a stromal cell, seemingly in a proliferative status, which express CK7 (inset, magnified detail)

CK7 AND CANCER

Recently, cytokeratins are evaluated to investigate the epithelial–mesenchymal transition (EMT). EMT is a process in which the cell phenotype is modified. The epithelial cells loosen desmosomes and adherens junctions and change their cytoskeleton: intermediate filaments typically switch from cytokeratins to vimentin (Savagner, 2010, Fortier et al., 2013). Thus, the epithelial cell acquire a mesenchymal phenotype (Walia et al.,

2012, Bonnomet et al., 2010), such as in breast cancers (Jang et al., 2015, Zeng et al., 2014, Choi et al., 2013, Imbert et al., 2012, Zeng et al., 2012, Mostert et al., 2012). EMT is a process with many implications in cancer progression: it is associated with tumor growth and invasion but also with a high metastatic capacity (Samatov et al., 2013, Gos et al., 2009). EMT is associated with a high metastatic potential of circulating tumor cells (Haslehurst et al., 2012). Also, it was established that the co-expression of vimentin and CK in tumoral breast cancer cells is associated with lower survival rates (Shioiri et al., 2006).

Although CK7 is hardly expressed in the adult intestinal tract, CK7 is present in the gastric epithelia of the fetus (Tatsumi et al., 2005, Ramaekers et al., 1990). Conversely, CK20 expression is restricted to gastrointestinal epithelium, Merkel cells of the epithelium and umbrella cells of the urothelium (Moll et al., 1992). Thus, correlated expression of CK7 and CK20 is very useful to establish the exact origin of uncertain metastasis (Table 1) (Centeno, 2006).

Table 1. *Cytokeratin 7 and 20 co-expression patterns (Centeno, 2006, Gyure and Morrison, 2000)*

CK7+/CK20+	CK7+/CK20-	CK7-/CK20+	CK7-/CK20-
Urothelial carcinoma	Ductal and lobular breast carcinoma	Colorectal	Prostate
Pancreatic adenocarcinoma	Lung	Gastric adenocarcinoma (variable)	Renal cell carcinoma
Biliary tract	Esophagus	Merkel cell carcinoma	Hepatocellular carcinoma
Cholangiocarcinoma	Stomach		Adrenal cortical carcinoma
Esophagus	Pancreas		Thyroid carcinoma
Gastric adenocarcinoma	Biliary		Small cell carcinoma of lung
Mucinous carcinoma (ovarian, colon, bronchoalveolar)	Cholangiocarcinoma		Squamous cell carcinoma of esophagus, lung, skin
Transitional cell carcinoma	Ovary (nonmucinous)		
	Endometrial adenocarcinoma		
	Malignant mesothelioma		

CK7 is a possible marker for transient dedifferentiation of gastritis lesions, metaplastic transformation, dysplasia and cancer (Kirchner et al., 2001). Some authors reported that CK7 is not expressed in normal gastric mucosa and most of gastric cancer, but intestinal metaplasia and dysplasia are CK7 positive. Knowing that fetal stomach express CK7, these authors evidenced that transient expression of CK7 in gastric cancer and gastric metaplasia describe a fetal-like, dedifferentiated phenotype (Stosiek et al., 1991).

Recent studies demonstrated that CK7 expression is associated with poor prognosis in patients with stage I/IIA/IIB of squamous cell carcinoma of the esophagus (Yamada et al., 2008), adenocarcinoma of the lung (Gharib et al., 2002) and hepatocellular carcinoma (Uenishi et al., 2003).

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Conflicts of interests

None.

Contribution of authors

All authors have equally contributed to this work.

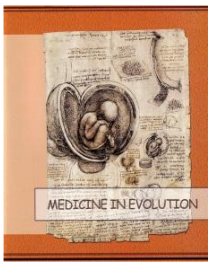
REFERENCES

1. Bayrak R, Haltas H, Yenidunya S. The value of CDX2 and cytokeratins 7 and 20 expression in differentiating colorectal adenocarcinomas from extraintestinal gastrointestinal adenocarcinomas: cytokeratin 7-/20+ phenotype is more specific than CDX2 antibody. Diagn Pathol. 2012;7:9.
2. Jasik A. Cytokeratin 7 and 20: INTECH Open Access Publisher; 2012.
3. Weng Y-R, Cui Y, Fang J-Y. Biological functions of cytokeratin 18 in cancer. Molecular Cancer Research. 2012;10(4):485-93.
4. Cîmpean AM, Suciu C, Ceausu R, Tatucu D, Muresan AM, Raica M. Relevance of the immunohistochemical expression of cytokeratin 8/18 for the diagnosis and classification of breast cancer. Rom J Morphol Embryol. 2008;49(4):479-83.
5. Guo JH, Maltha JC, He SG, Krapels IP, Spauwen PH, Steegers-Theunissen RP, Von den Hoff JW. Cytokeratin expression in palatal and marginal mucosa of cleft palate patients. Arch Oral Biol. 2006;51(7):573-80.
6. Dale BA, Salonen J, Jones AH. New approaches and concepts in the study of differentiation of oral epithelia. Critical Reviews in Oral Biology & Medicine. 1990;1(3):167-90.
7. Bragulla HH, Homberger DG. Structure and functions of keratin proteins in simple, stratified, keratinized and cornified epithelia. J Anat. 2009;214(4):516-59.
8. Iwatsuki H, Suda M. Seven kinds of intermediate filament networks in the cytoplasm of polarized cells: structure and function. Acta Histochem Cytochem. 2010;43(2):19-31.
9. Nikitakis NG, Tosios KI, Papanikolaou VS, Rivera H, Papanicolaou SI, Ioffe OB. Immunohistochemical expression of cytokeratins 7 and 20 in malignant salivary gland tumors. Mod Pathol. 2004;17(4):407-15.
10. Chatzipantelis P, Lazaris AC, Kafiri G, Papadimitriou K, Papathomas TG, Nonni A, Patsouris ES. Cytokeratin-7, cytokeratin-19, and c-Kit: Immunoreaction during the evolution stages of primary biliary cirrhosis. Hepatol Res. 2006;36(3):182-7.
11. Van Eyken P, Sciot R, Desmet VJ. A cytokeratin immunohistochemical study of cholestatic liver disease: evidence that hepatocytes can express 'bile duct-type' cytokeratins. Histopathology. 1989;15(2):125-35.
12. Mohammadizadeh F, Naimi A, Rajabi P, Ghasemibasir H, Eftekhari A. Expression of basal and luminal cytokeratins in breast cancer and their correlation with clinicopathological prognostic variables. Indian J Med Sci. 2009;63(4):152-62.
13. Savagner P. The epithelial–mesenchymal transition (EMT) phenomenon. Annals of Oncology. 2010;21(suppl 7):vii89-vii92.
14. Fortier A-M, Asselin E, Cadrin M. Keratin 8 and 18 loss in epithelial cancer cells increases collective cell migration and cisplatin sensitivity through claudin1 up-regulation. Journal of Biological Chemistry. 2013;288(16):11555-71.
15. Walia V, Yu Y, Cao D, Sun M, McLean JR, Hollier BG, Cheng J, Mani SA, Rao K, Premkumar L, Elble RC. Loss of breast epithelial marker hCLCA2 promotes epithelial-to-mesenchymal transition and indicates higher risk of metastasis. Oncogene. 2012;31(17):2237-46.
16. Bonnomet A, Brysse A, Tachsidis A, Waltham M, Thompson EW, Polette M, Gilles C. Epithelial-to-mesenchymal

transitions and circulating tumor cells. J Mammary Gland Biol Neoplasia. 2010;15(2):261-73.
17. Jang MH, Kim HJ, Kim EJ, Chung YR, Park SY. Expression of epithelial-mesenchymal transition-related markers in triple-negative breast cancer: ZEB1 as a potential biomarker for poor clinical outcome. Hum Pathol. 2015.
18. Zeng Q, Zhang P, Wu Z, Xue P, Lu D, Ye Z, Zhang X, Huang Z, Feng J, Song L, Yang D, Jiang T, Yan X. Quantitative proteomics reveals ER-alpha involvement in CD146-induced epithelial-mesenchymal transition in breast cancer cells. J Proteomics. 2014;103:153-69.
19. Choi Y, Lee HJ, Jang MH, Gwak JM, Lee KS, Kim EJ, Kim HJ, Lee HE, Park SY. Epithelial-mesenchymal transition increases during the progression of in situ to invasive basal-like breast cancer. Hum Pathol. 2013;44(11):2581-9.
20. Imbert AM, Garulli C, Choquet E, Koubi M, Aurrand-Lions M, Chabannon C. CD146 expression in human breast cancer cell lines induces phenotypic and functional changes observed in Epithelial to Mesenchymal Transition. PLoS One. 2012;7(8):e43752.
21. Zeng Q, Li W, Lu D, Wu Z, Duan H, Luo Y, Feng J, Yang D, Fu L, Yan X. CD146, an epithelial-mesenchymal transition inducer, is associated with triple-negative breast cancer. Proc Natl Acad Sci U S A. 2012;109(4):1127-32.
22. Mostert B, Kraan J, Sieuwerts AM, van der Spoel P, Bolt-de Vries J, Prager-van der Smissen WJ, Smid M, Timmermans AM, Martens JW, Gratama JW, Foekens JA, Sleijfer S. CD49f-based selection of circulating tumor cells (CTCs) improves detection across breast cancer subtypes. Cancer Lett. 2012;319(1):49-55.
23. Samatov TR, Tonevitsky AG, Schumacher U. Epithelial-mesenchymal transition: focus on metastatic cascade, alternative splicing, non-coding RNAs and modulating compounds. Mol Cancer. 2013;12(1):107.
24. Gos M, Miloszewska J, Przybyszewska M. [Epithelial-mesenchymal transition in cancer progression]. Postepy Biochem. 2009;55(2):121-8.
25. Haslehurst AM, Koti M, Dharsee M, Nuin P, Evans K, Geraci J, Childs T, Chen J, Li J, Weberpals J, Davey S, Squire J, Park PC, Feilotter H. EMT transcription factors snail and slug directly contribute to cisplatin resistance in ovarian cancer. BMC Cancer. 2012;12:91.
26. Shioiri M, Shida T, Koda K, Oda K, Seike K, Nishimura M, Takano S, Miyazaki M. Slug expression is an independent prognostic parameter for poor survival in colorectal carcinoma patients. Br J Cancer. 2006;94(12):1816-22.
27. Tatsumi N, Mukaisho K, Mitsufuji S, Tatsumi Y, Sugihara H, Okanoue T, Hattori T. Expression of cytokeratins 7 and 20 in serrated adenoma and related diseases. Dig Dis Sci. 2005;50(9):1741-6.
28. Ramaekers F, Van Niekerk C, Poels L, Schaafsma E, Huijsmans A, Robben H, Schaart G, Vooijs P. Use of monoclonal antibodies to keratin 7 in the differential diagnosis of adenocarcinomas. Am J Pathol. 1990;136(3):641.
29. Moll R, Löwe A, Laufer J, Franke W. Cytokeratin 20 in human carcinomas. A new histodiagnostic marker detected by monoclonal antibodies. Am J Pathol. 1992;140(2):427.
30. Centeno BA. Pathology of liver metastases. Cancer Control. 2006;13(1):13-26.
31. Kirchner T, Müller S, Hattori T, Mukaisyo K, Papadopoulos T, Brabletz T, Jung A. Metaplasia, intraepithelial neoplasia and early cancer of the stomach are related to dedifferentiated epithelial cells defined by cytokeratin-7 expression in gastritis. Virchows Archiv. 2001;439(4):512-22.
32. Stosiek P, Brautigam E, Kasper M. Expression of cytokeratin 7 in human glandular epithelium of fetal stomach. Acta Histochem. 1991;91(1):21-3.
33. Yamada A, Sasaki H, Aoyagi K, Sano M, Fujii S, Daiko H, Nishimura M, Yoshida T, Chiba T, Ochiai A. Expression of cytokeratin 7 predicts survival in stage I/IIA/IIB squamous cell carcinoma of the esophagus. Oncol Rep. 2008;20(5):1021-7.
34. Gharib TG, Chen G, Wang H, Huang CC, Prescott MS, Shedden K, Misek DE, Thomas DG, Giordano TJ, Taylor

JM, Kardia S, Yee J, Orringer MB, Hanash S, Beer DG. Proteomic analysis of cytokeratin isoforms uncovers association with survival in lung adenocarcinoma. Neoplasia. 2002;4(5):440-8.
35. Uenishi T, Kubo S, Yamamoto T, Shuto T, Ogawa M, Tanaka H, Tanaka S, Kaneda K, Hirohashi K. Cytokeratin 19 expression in hepatocellular carcinoma predicts early postoperative recurrence. Cancer Sci. 2003;94(10):851-7.
36. Centeno BA. Pathology of liver metastases. Cancer Control. 2006;13(1):13.
37. Gyure KA, Morrison AL. Cytokeratin 7 and 20 expression in choroid plexus tumors: utility in differentiating these neoplasms from metastatic carcinomas. Modern Pathology. 2000;13(6):638-43.

DISSOCIATED PAIN PERCEPTION



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ABSTRACT

Although dissociation has many definitions and conceptualizations, it is often referred to as a pathology or a pathological process. However, as it will be shown below, it is often linked to pain conditions, and there is evidence that it can serve as a protective mechanism against pain. This review discusses conceptualizations of dissociations relevant to the present topic, the existing evidence linking dissociation to pain perception, and the possibility of dissociation as a defense against pain.

Key words: *dissociation, pain, analgesia, hypnotic analgesia*

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INTRODUCTION

Dissociation is most often referred to as a *separation* of psychological functions that are otherwise normally associated. Most of the existing definitions revolve around the aforementioned concept. Thus, dissociation is the separation of one mental process from any other mental process. Another widely used term is *lack of integration*, which bears the same core concept. That is, a mental process is not homogeneously integrated with other processes or the psychic system as a whole, leading to yet another commonly used word in definitions of dissociation: a *disruption*. For examples of definitions, see (1, 2, 3, 4).

Dissociation is viewed both as a disorder and a day-to-day experience. This conceptual contradiction is solved by the Dissociative Continuum Theory, which states that a small amount of dissociation explains day-to-day dissociative experiences (such as being absorbed in thought to the point that getting off the bus is forgotten), while a large amount of dissociation is responsible for dissociative disorders (5). Although this is a good theoretical approach, and moreover, a comprehensive and easy to understand model, it may not be the most useful tool in clinical settings. There is evidence in scientific literature of a taxon model, a pathological dissociation, a fracture in the continuum theory (6, 7). The two perspectives could form, in a complementary way, a three dimensional image of dissociation.

Psychoanalysts use the term *cleavage* to refer to the separation or partition of the self when facing dangerous and/or anxiety inducing situations (8). An extreme form of cleavage is a fracture of personality that happens when a part of the self separates from the whole. Later, Hillgard (9) postulated, in what is known as the Neodissociative Theory, that we all have parts of our cognitive structures we are not aware of, which lookout over us as"guardians"or hidden observers. Since then, contemporary theories state that dissociation can also act as a defense mechanism, separating us from overwhelming experiences.

However, dissociation does not only involve the mind, but also the body. Somatoform dissociation refers to dissociative symptoms that involve the body such as motor inhibitions, anesthesia, pain symptoms, sensory alterations, convulsions, etc. (10, 11). Although there still are debates about whether somatization disorders have a dissociative nature, the majority of authors consider that somatization is indeed a dissociative phenomenon. From this perspective, the body bears the burden of the psychological trauma. Thus, not only can dissociation affect the body, but also, it would seem that conversion disorders and somatoform disorders are related.

Up until now dissociation has been described as a mechanism. However, both ICD10 and DSM V recognize dissociation as a psychiatric disorder. DSM 5 describes Depersonalization/derealization disorder (the feeling that a person's own body or environment is strange or unusual), dissociative amnesia (memory gaps, inability to recall personal information, usually linked to a traumatic event) and dissociative identity disorders (characterized by the presence of two or more personality states in a person). ICD 10 describes with few exceptions such as Ganser syndrome (approximate answers) basically the same disorders. However it also includes under the same category of *dissociation*, conversion disorders such as: dissociative motor disorders, dissociative convulsions (former hysterical convulsions), dissociative anesthesia and sensory loss.

Although it is a highly polyvalent construct, the text above is a synthesized version of the most common conceptualizations.

Dissociation should not be viewed as a single sided or one-dimensional construct. We could state that all of the above explanations are true, but in different situations, or better yet we can see all these as different facets of the same complex phenomena.

Pain is most often defined as"an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"(12). As it can be observed in the definition above, one can identify two components of pain. On the one hand, pain presumes a sensorial component - the body's system of signaling tissue damage, which represents the perceptual element of pain. On the other hand, suffering is another element, representing the affective component (13).

DISSOCIATION AND TRAUMA

A strong connection can be found between dissociation and trauma. It seems that as a reaction to trauma (especially sustained/repeated trauma), a brutal and total defense is needed. The vast majority of authors claim that dissociation is a reaction to trauma, however, not all authors agree (14, 15).

The fantasy process and false memory models state that dissociative patients are more prone to fantasizing and false memories or iatrogenic trauma. This would mean that the fact that the vast majority of dissociative patients report traumatic events in the past could be either fiction or induced/suggested stories. In the attempt to clarify this, Dalenberg and colleagues in 2012 conducted an extensive review concluding that the trauma-dissociation model is the strongest (16). Also, studies suggest that peritraumatic dissociation is predictive for post-traumatic stress disorder (17).

Besides a developmental point of view according to which childhood trauma leads later on to dissociative disorders, it seems that trauma can cause dissociation at the moment of the stressful event, called peritraumatic dissociation (17). More precisely, dissociation can occur during the traumatic event, most likely to protect the victim from the emotional impact.

DISSOCIATION AND CHRONIC PAIN

Chronic pain is found to be in co-occurrence with a wide variety of mental disorders (18). There is no need for evidence in stating that chronic pain bares a great deal of psychological distress, not only due to the unpleasant experience of pain, but also due to the functional impact, economic impact and in some cases due to the realization of what a degenerative disease implies.

One aspect which has to be taken into consideration is the deterministic factor. Two major points of views can be taken into account when talking about the link between pain and psychopathology. Firstly, the pain itself is a factor of great distress. Furthermore, as we know from the vulnerability-stress model of psychopathology (19), stress can be a triggering factor (at least) in almost every kind of mental illness. Thus, anxiety, depression, dissociation, etc. in this context would be a result of the physical suffering, basically the emotional result of the physical pain. Secondly, mental illness, or clinical mental processes can be linked to pain. In an organicist view, we talk of

psychosomatic symptoms, such as headaches caused by stress or anxiety or pain due to deconditioning caused by depression. A more psychological approach indicates that due to the unbearable nature of some psychological content, we live the psychological pain as physical pain, because it is easier to bare and thus the body becomes a projective screen for the mind.

Nevertheless, there is also a middle ground. There are complex integrationist models of chronic pain outlining the reciprocal influence between pain and anxiety for example, circling into a downward spiral such as the bio-behavioral model, the Glasgow model, the fear avoidance model and the diathesis-stress model (20, 21, 22, 23).

Although there is a lack of experimental research linking dissociation to pain syndromes, there is an abundance of non-experimental studies on the subject. For example, Walker, Katon, Neraas, and Jemelka (24) found that chronic pelvic pain patients were prone to use dissociation as a coping mechanism. Fishbain, Cutler, Rosomoff, and Rosomoff (25) described six patients with chronic pain and co-occurring dissociative disorders. Both the onset and the evolution of the dissociative disorders correlated with the onset and evolution of the pain. Leavitt, Katz, Mills, and Heard (26) found an overexpression of dissociative symptoms in fibromyalgia patients and suggested that it may play a role in the amplification of pain symptoms. However, since the study was non-experimental by nature, such conclusions may be hazardous, since the opposite may be just as true.

A study carried out on 200 gynecological patients found a strong association between somatoform dissociation and female sexual dysfunctions (27). A study involving 14 dissociative disorder participants showed more (expressed as number of symptoms) headaches, abdominal pain, joint pain and pain in the extremities than the matched, non-dissociative, psychiatric, inpatient group (28).

DISSOCIATION AND ACUTE PAIN

In this chapter, acute pain should not necessarily be understood as a toothache or as the effect of dissociation on a broken leg, but rather as an experimental pain induced in a laboratory (thus acute).

Even if information on dissociative mechanisms involved in real live tissue injury is valuable, it is, however, highly questionable from an ethical standpoint. Therefore, when studying the effect of dissociation on pain perception in a laboratory setting, the most common types of pain are induced by pressure on the finger, an arm introduced in ice water, pain induced by a progressively heated metal plate, pain induced *via* electrical stimulation, injecting capsaicin under the skin, etc.

Upon reviewing studies using pain elicitation, evidence can be found for a desensitizing (29, 30), sensitizing (31) and lack of effect (32) of dissociation on pain perception both in experimental and non-experimental settings.

A study conducted on 12 patients suffering from borderline personality disorder showed both in calm and distressed states, but mainly in distressed states, reduced pain perception in borderline patients (33). Although the study did not specifically target dissociation, borderline personality patients very often reported dissociative experiences. Another study revealed that borderline personality patients who did not feel pain while conducting self-injurious behavior reported higher ratings of

dissociative symptoms than did borderline patients who felt pain while conducting self-injurious behavior (34). It also seems that physical/sexual abuse is related to dissociation (35), and, most often, physical and sexual abuse causes physical pain.

In addition, there are many cases of trauma victims who report not feeling any pain during a traumatic event. However, in this instance, there is a debate concerning the analgesic effect of dissociation versus the analgesic effect of stress-induced analgesia, since there is a situational overlap between the two concepts (36).

On the other hand, one of the most important intra-hypnotic mechanisms is dissociation (37). Besides the fact that surgeries are performed with the use of hypnosis as the sole anesthetic, scientific literature consistently shows the efficacy of hypnosis for pain management (38, 39, 40).

CONCLUSIONS

From the literature reviewed, it is clear that there is a relationship between dissociation and pain. Since experimental investigations studying the dissociation-pain relationship are scarce, and the few existing studies show contradictory results, it is difficult to say if dissociation is an unpleasant side effect of pain, a cause of pain or a protective factor against it.

Firstly, since dissociation is proven to be related to psychological distress (41), and as described above dissociation is related to chronic pain, it is conceivable that the stress of pain could cause a pathological dissociative reaction; thus, dissociation would be a secondary condition of pain. This is a promising direction for further research, and more so, for therapeutic approaches. A treatment plan could be conceived, treatment that specifically targets the stress caused by pain for managing dissociative symptoms.

Secondly, somatoform disorders are physical symptoms with a psychological cause. Since, as described above, somatoform disorders could be related to dissociative conditions, it is possible the pain is caused by dissociation. It is also possible that, using a dissociative mechanism, the mind converts psychological pain into physical pain.

Thirdly, although there are minor exceptions, it seems dissociation, when related to pain, serves as a protective factor or as a defense mechanism, most likely separating/distancing the patient from the physical pain. According to the existing literature, this seems to be the strongest hypothesis. As mentioned previously, there is strong evidence supporting the effectiveness of hypnosis in pain management. According to Hilgard (9), highly hypnotizable subjects use dissociation to block information from reaching conscientiousness (e.g. pain).

Although the three apparently opposing explanations were listed, they are not necessarily mutually exclusive. It is possible that, in the case of moderate pain, dissociation is a protective factor, which in time, or in the case of overwhelming pain, could develop into a dissociative disorder.

Future studies should explore the dissociation-pain link in a naturalistic approach. A good research direction would be an emergency room setting or accompanying an ambulance. Also, studies should account for stress induced analgesia and endogenous analgesics. Moreover, a distinction should be made between the effect of fear, and the effect of dissociation on pain perception.

Regarding somatoform disorders, there is a need to clarify whether they are dissociative disorders or not. If the pain indeed is a dissociative substitute for the traumatic event, the recall or priming of the event should in theory

trigger the physical pain. Thus, a design could be conceived in which patients suffering from somatoform disorders are either primed for their traumatic event (if it can be identified) or simply they are asked to read a list of common traumas to see if they start having more physical pain.

Since dissociation is a wide and polyvalent concept, one form of dissociation could alleviate pain, while another form could cause physical pain.

The term dissociation is utilized as ability (ex. for actors), as defense, as hypnotic phenomenon, as pathological entity. Dissociation can happen between emotion and reason, between global psychological functioning and memory, between body and mind, and many more. Precisely for this reason caution is advised when using the term since its vague definition is a source of great methodological vulnerability (42).

The fact that both dissociation and pain are wide and multifaceted concepts is among the greatest difficulties in treating this subject. Studies should be carried out targeting different conceptualizations of pain in different types of pain conditions.

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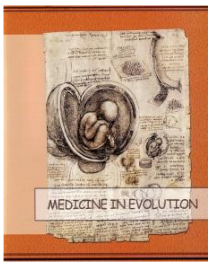
REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, (DSM-5). American Psychiatric Pub; 2013. p. 820.
2. Dell, PF, O'Neil JA. Dissociation and the dissociative disorders: DSM-V and beyond. Routledge; 2010. p. xxi.
3. Spiegel D. Hypnosis and traumatic dissociation: Therapeutic opportunities. J Trauma Dissociation. 2003; 4(3):73-90.
4. Putnam, FW, Helmers K, Trickett PK. Development, reliability, and validity of a child dissociation scale. Child Abuse Negl. 1993; 17(6):731-741.
5. Brown RJ. Different types of"dissociation"have different psychological mechanisms. J Trauma Dissociation. 2006; 7(4):7-28.
6. Waller N, Putnam FW, Carlson EB. Types of dissociation and dissociative types: A taxometric analysis of dissociative experiences. Psychol. Methods. 1996; 1(3):300.
7. Waller N, Ross CA. The prevalence and biometric structure of pathological dissociation in the general population: Taxometric and behavior genetic findings. J. Abnorm. Psychol. 1997; 106(4):499.
8. Ionescu Ş. Les mécanismes de défense: théorie et clinique. Armand Colin; 2003. p.162.
9. Hilgard ER. Divided consciousness: Multiple controls in human thought and action, New York: Wiley. 1977.
10. Nijenhuis ERS. Somatoform dissociation: Major symptoms of dissociative disorders. J Trauma Dissociation. 2001; 1(4):7-32.
11. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
12. Merskey HE. Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms. Pain. 1986; 3:226.
13. Barabasz A, Watkins JG. Hypnotherapeutic tecniques. Brunner-Routledge; 2005.
14. Merckelbach H, Muris P. The causal link between self-reported trauma and dissociation: A critical review. Behav Res Ther. 2001; 39(3):245-254.
15. Candel I, Merckelbach H. Peritraumatic dissociation as a predictor of post-traumatic stress disorder: A critical review. Compr Psychiatry. 2004; 45(1):44-50.
16. Fullerton CS., Robert JU, Richard SE et al. Peritraumatic dissociation following motor vehicle accidents: Relationship to prior trauma and prior major

depression. J Nerv Ment Dis. 2000; 188(5):267-272.
17. Dalenberg, Constance J., Bethany L. Brand, David H. Gleaves et al. 2012."Evaluation of the evidence for the trauma and fantasy models of dissociation."Psychological bulletin 138 (3): 550.
18. Marmar, Charles R., Daniel S. Weiss, and Thomas J. Metzler. 1998."Peritraumatic dissociation and posttraumatic stress disorder."Trauma, memory, and dissociation 229-252.
19. Demyttenaere K, Bruffaerts R, Lee S, Posada-Villa J, Kovess V, Angermeyer MC. Mental disorders among persons with chronic back or neck pain: Results from the world mental health surveys. Pain 2007; 129:332–342.
20. Ingram, R. E., & Luxton, D. D. (2005). Vulnerability-stress models.Development of psychopathology: A vulnerability-stress perspective, 32-46.
21. Waddell, G. (1992). Biopsychosocial analysis of low back pain. Clinical Rheumatology, 6, 523–557.
22. Vlaeyen, J. W. S., & Linton, S. J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. Pain, 85, 317–332.
23. Turk, D. C. (2002). A diathesis-stress model of chronic pain and disability following traumatic injury. Pain Research and Management, 7, 9–19.
24. Gordon J. G. Asmundson & Kristi D. Wright (2004) in Hadjistavropoulos, T., Craig, K.D. (2004). Pain. Psychological perspectives. Lawrence Erlbaum Associates, p.51.
25. Walker E, Katon WJ, Neraas K, Jemelka RP, Massoth D. Dissociation in women with chronic pelvic pain. Am. J. Psych. 1992; 149(4):534-537.
26. Fishbain DA, Cutler RB, Rosomoff HL, Rosomoff RS Pain-determined Dissociation Episodes. Pain Med. 2001; 2(3):216-224.
27. Leavitt F, Katz RS, Mills M, Heard AR. Cognitive and dissociative manifestations in fibromyalgia. J. Clin. Rheumatol. 2002; 8(2):77-84.
28. Benedetto F, Mazzotti E, Pasquini P, Mantione MG. Somatoform and psychoform dissociation among women with orgasmic and sexual pain disorders. J Trauma Dissociation. 2011; 12(5):526-534.
29. Saxe GN, Chinman G, Berkowitz R et al. Somatization in patients with dissociative disorders. Am. J. Psych. 1994; 151(9):1329-1334.
30. Ludäscher P, Valerius G, Stiglmayr C et al. Pain sensitivity and neural processing during dissociative states in patients with borderline personality disorder with and without comorbid posttraumatic stress disorder: a pilot study. J. Psychiatry Neurosci. 2010; 35(3):177-184.
31. Ludäscher P, Bohus M, Lieb K, Philipsen A, Jochims A, Schmahl C. Elevated pain thresholds correlate with dissociation and aversive arousal in patients with borderline personality disorder. Psychiatry Res. 2007; 149(1):291-296.
32. Horowitz JD, Telch MJ. Dissociation and pain perception: An experimental investigation. J. Trauma. Stress. 2007; 20(4):597-609.
33. Varga ŞS, Dafinoiu I, Rusu A, Bredicean C. Correlates of Pain Perception: Anxiety and Dissociation. Annal. Al. I. Cuza. Univ. Psych. Ser. 2013; 2:75-85.
34. Martin B, Limberger M, Ebner U et al. Pain perception during self-reported distress and calmness in patients with borderline personality disorder and self-mutilating behavior. Psychiatry Res. 2000; 95(3):251-260.
35. Kemperman I, Russ MJ, Shearin E. Self-injurious behavior and mood regulation in borderline patients. J Pers Disord. 1997; 11(2):146-157.
36. Nijenhuis ERS, Van der Hart O. Forgetting and re-experiencing trauma. In: Goodwin J. Splintered reflections: Images of the body in trauma. Basic Books; 1999. p. 39-65.
37. Giesbrecht T, Smeets T, Merckelbach H. Dissociative experiences on ice-Peritraumatic and trait dissociation during the cold pressor test. Psychiatry Res. 2008; 157(1):115-121.
38. Dafinoiu I, Vargha JL. Hipnoza clinica. Polirom; 2003. p. 99.
39. 38) Montgomery GH, DuHamel KN, Redd WH. A meta-analysis of hypnotically induced analgesia: How effective is hypnosis?. Int J Clin Exp Hypn. 2000; 48(2):138-153.
40. Stoelb BL, Molton IR, Jensen MP, Patterson DR. The efficacy of hypnotic analgesia in adults: A review of the

literature. Contemp Hypn. 2009; 26(1):24-39.
41. Accardi MC, Milling LS. The effectiveness of hypnosis for reducing procedure-related pain in children and adolescents: a comprehensive methodological review. J. Behav. Med. 2009; 32(4):328-339.
42. Ozer EJ, Best SR, Lipsey TL, Weiss DS. Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis. Psychol. Bull. 2003; 129(1):52-73.
43. Varga ŞS, Dafinoiu I, Ile LI, Bredicean C, Răduț RO. The terminological relativism of dissociation: A literature review. Rom J Psychiat. 2013; 15(1):6-11



CORRELATION BETWEEN MORTALITY AND GLYCEMIC LEVELS IN ACUTE STROKE AND AFTER 24 HOURS IN PATIENTS ADDMITED IN THE INTENSIVE CARE UNIT. A RETROSPECTIVE STUDY

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ABSTRACT

New data appeared in the recent years that have changed the critical care management of acute ischemic stroke, particularly in the area of glycemic control.

Hyperglycemia in the acute phase after ischemic stroke is common, occurring in most all the patients with a history of diabetes mellitus and in one-third to one-half of nondiabetic patients.[3] A major goal of the acute stroke management is resuscitation of the ischemic penumbra. If reperfusion of the penumbra occurs, neurons recover and the patient improves. In the setting of acute stroke, hyperglycemia may be deleterious to the ischemic penumbra by permitting anaerobic metabolism with the creation of local lactic acidosis [3].

In this study were enrolled 162 patients admitted in the Intensive Care Unit between January 2014 and December 2014. Inclusion criteria were: documented diagnostic of stroke, ischemic or hemorrhagic, blood sugar level at admission in ICU (G1), and after 24 hours (G2), men and women aged 25 to 80 years old and who had monitored blood glucose level. Patients details included: age, sex, type of stroke, associated diabetes mellitus, length of ICU stay, blood glucose level at admission in the intensive care unit (G1) and after 24 hours (G2).

Preexisting hyperglycemia is found commonly in patients presenting with acute stroke and worsens clinical outcome. The risk is higher in non-diabetic patients compared with patiens already diagnosed with diabetes; women had a higher risk as well.

Key words: *ischemic stroke, hemorrhagic stroke, hyperglycemia, mortality, diabetes mellitus*

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INTRODUCTION

The goal for the acute management of patients with stroke is to stabilize the patient and to complete initial evaluation and assessment, including imaging and laboratory studies, within 60 minutes of patient arrival [1].

New data appeared in the recent years that have changed the critical care management of acute ischemic stroke, particularly in the area of glycemic control. Hypoglycemia and hyperglycemia need to be identified and treated early in the evaluation. Not only can both produce symptoms that mimic ischemic stroke, but they can also aggravate ongoing neuronal ischemia.

Administration of glucose in hypoglycemia produces profound and prompt improvement, while insulin should be started for patients with stroke and hyperglycemia. Ongoing studies will help to determine the optimal level of glycemic control [2].

Hyperglycemia in the acute phase after ischemic stroke is common, occurring in most all the patients with a history of diabetes mellitus and in one-third to one-half of nondiabetic patients.

Early hyperglycemia is associated with larger infarct volume in experimental stroke models. In humans, hyperglycemia on admission is associated with increased cerebral edema volume, higher rates of hemorrhagic transformation and worse neurologic outcome [3].

Neurons die within few minutes of oxygen deprivation. Thus, some neuronal death occurs in areas of no blood flow within minutes of stroke onset. Around such areas of necrosis exist regions of hypoperfused, electrically silent tissue that barely receives enough blood flow to keep neurons alive. This tissue area is called ``the ischemic penumbra``. A major goal of acute stroke management is resuscitation of the ischemic penumbra. If reperfusion of the penumbra occurs, neurons recover and the patient improves. In the setting of acute stroke, hyperglycemia may be deleterious to the ischemic penumbra by permitting anaerobic metabolism with the creation of local lactic acidosis [3].

Martini and Kent suggest that, even if an occluded vessel causing stroke is recanalized, effective reperfusion may not be established in patients with hyperglycemia [4].

Parsons et al used magnetic resonance imaging (MRI) and magnetic resonance spectroscopy in patients with hyperglycemic stroke and reported that the detrimental effect of hyperglycemia may be due to metabolic acidosis in the infarcted brain parenchyma [5]. However, earlier animal studies suggested that hyperglycemia has a detrimental effect on the cerebral vascular tree [6,7].

Despite the differences in clinical presentation between hemorrhagic and ischemic strokes, no collection of clinical features has sufficient predictive value to forego brain imaging. Computed tomography (CT) is the key of the initial diagnostic because it clearly differentiates hemorrhagic from ischemic stroke. Intracerebral hemorrhage is more than twice as common as subarachnoid hemorrhage and is much more likely to result in death or major disability than cerebral infarction or subarachnoid hemorrhage [8]. High blood glucose on admission predicts an increased risk of mortality and poor outcome in patients with and without diabetes and intracerebral hemorrhage [9,10,11].

MATERIAL AND METHODS

This study presents a retrospective analysis of data from the Intensive Care Unit of the Emergency County Hospital Timisoara. Data correlation and utilizing was approved by the Ethic Committee from our hospital: informed consent was waived because of the retrospective nature of the study.

Patients and inclusion criteria

In the study were enrolled patients admitted in the Intensive Care Unit between January 2014 and December 2014. Inclusion criteria were: documented diagnostic of stroke, ischemic or hemorrhagic, blood sugar level at admission in ICU (G1), and after 24 hours (G2), men and women aged 25 to 80 years old and who had monitored blood glucose level. Imaging diagnosis was made by CT scans and MRI scans and were analysed by neurologist, radiologist and ICU doctor.

Data Collection and Processing

Patients details included: age, sex, type of stroke, associated diabetes mellitus, length of ICU stay, blood glucose level at admission in the intensive care unit (G1) and after 24 hours (G2).

Statistical analysis

Results are reported as mean ± standard deviation. For comparison of the variables t test was used. Statistical significance was defined as $p < 0.01$. Analysis was performed with Microsoft Office Excel for Mac 2011 v.14.4.7. (Microsoft Corporation) and Prism 6 for Mac OS X v.6.0. (GraphPad Software, Inc.)

RESULTS AND DISCUSSIONS

During January 2014 and December 2014, 194 patients were admitted in the Intensive Care Unit of the Emergency Clinical County Hospital Timisoara with a documented diagnostic of acute stroke. Only 83,5% (162 patients) of them had measured both G1 and G2 and they were included in the study. 18% (29 patients) had ischemic stroke (ISCH) and 82% (133 patients) had hemorrhagic stroke (HEM).

From the lot of patients with ISCH, 72%(21 patients) were with hyperglycemia at the time of admission (G1 nonN) with a mortality rate of 50%(12 patients) compared with 75%(6 patients) mortality from the ISCH group with normal levels of blood glucose at the time of admission (G1N), equal with a number of 8 patients.

From the lot of patients with HEM, 82%(109 patients) were with hyperglycemia at the time of admission (G1 nonN) with a mortality rate of 60%(66 patients) compared with 33%(8 patients) mortality from the HEM group with normal levels of blood glucose at the time of admission (G1N) equal with a number of 24 patients.

The aim of this research in the followings is to study the mortality related to both normal and higher values of blood glucose levels at 24 hours from admission for the ISCH and the HEM groups, where G2 represents the blood glucose level at 24 hours from admission.

Table 1. *G1 for the improved patients has a mean value of M=141.54 (SD=48). For de deceased patients G1 was greater, M=170.02 (SD=87.19). The differences were tested with t test on independent samples and revealed that average pointer between G1 in improved patients and the average pointer G1 in deceased patients had significant differences t(147)=2.64, p<0.01.*

Group Statistics

	STARE	N	Mean	Std. Deviation	Std. Error Mean
G1	Improved	70	141.54	48.000	5.737
	Deceased	92	170.02	87.199	9.091

Table 2. *G2 for the improved patients has a mean value of M=122.83 (SD=41.93). For de deceased patients G2 was greater, M=154.03 (SD=77.91). The differences were tested with t test on independent samples and revealed that average pointer between G2 in improved patients and the average pointer G2 in deceased patients had significant differences t(146)=3.26, p<0.01*

Group Statistics

	STARE	N	Mean	Std. Deviation	Std. Error Mean
G2	Impreved	70	122.83	41.935	5.012
	Deceased	92	154.03	77.916	8.123

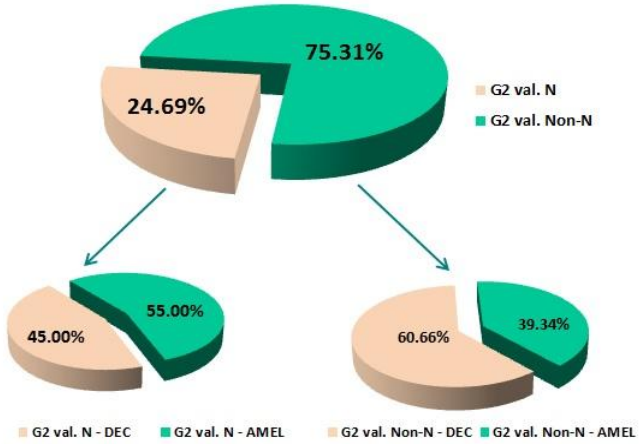

Figure 1. Mortality rate in patients with stroke and with normal and high levels of blood glucose after 24 hours from admission

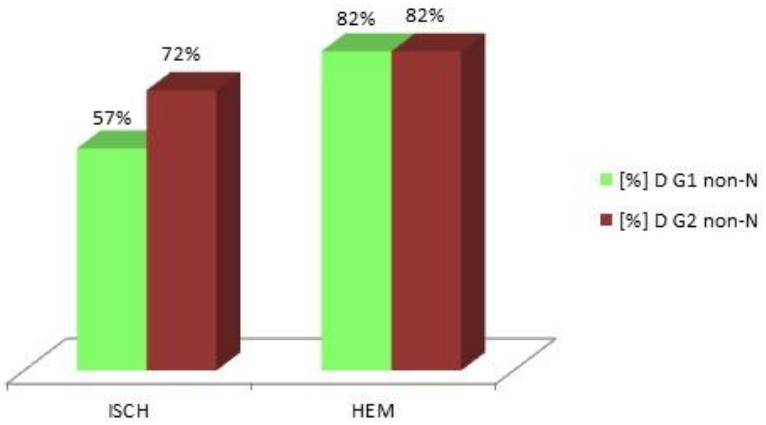

Figure 2. Mortality in both ISCH and HEM groups related to the glycemic levels at the time of admission and after 24 hours

Figure 1 shows that from the total of 162 patients from the study only aproximatively 25% had a normal blood glucose level after 24 hours from admission (G2 N). The mortality rate in this subgroup was 45%. From the patients with hyperglycemic levels after 24 hours from admission (G2 non-N) the mortality rate was aproximatively 61%.

In figure 2 we can see that the mortality is very high in the HEM group compared to the ISCH group. The higher survival rate is in the ISCH group with hyperglycemia at the onset of stroke.

It was a small difference in the mortality rate in the HEM group associated with diabetes (moratality DZ) of 50% vs 48% in the HEM group with no diabetes (mortality non-DZ) in women and 65% mortality DZ vs 64% mortality non-DZ in men. In the ISCH group things aredifferent. If in the men

subgroup there was a small difference, 63% mortality DZ vs 60% mortality non DZ, in the women subgroup the mortality DZ was 100% compared to 50% mortality non DZ. (Figure 3). So, gender remains a high risk factor. (Figure 4).

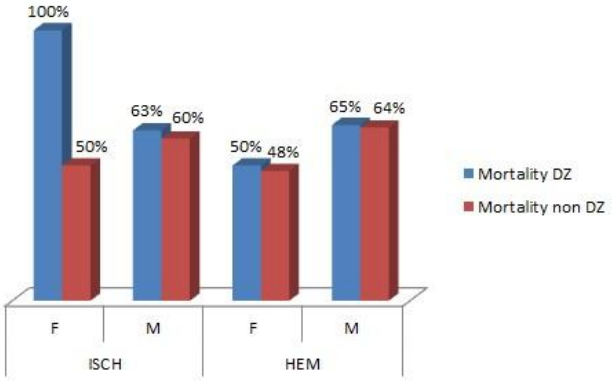

Figure 3. Mortality rate in the ISCH and HEM groups corelated with the presence of diabetes melitus and sex

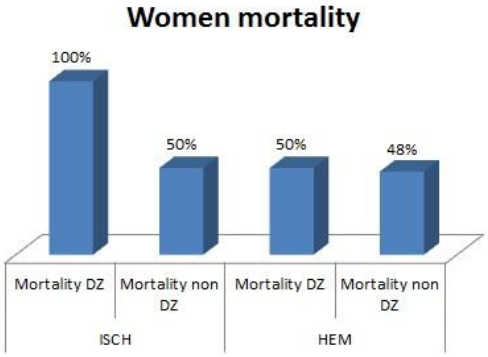

Figure 4. Women mortality in ISCH and HEM groups in patients with or without diabetes

From the ISCH group, 72% had hyperglycemia at admission and 48% had no diabetes. 57% from the group died and 5% developed cerebral edema. In the HEM group, 82% had hyperglycemia at the time of admission in ICU, but only 8% were with no diabetes. Mortality rate was of 61%, and cerebral edema was present in 19% of cases.(Figure 5).

After 24 hours, from the ISCH group still 72% of patients had hyperglycemia and 38% had no diabetes. 67% from the group died and 5% had cerebral edema. In the HEM group, after 24 hours, 76% of patients had hyperglycemia and 11% had no diabetes. The mortality rate was 59% and 21% of patients developed cerebral edema.(Figure 6).

From the patients with hyperglycemia at the admission in ICU, 75% from the ISCH group had normal blood glucose level after 24 hours, respectively 50% from the HEM group.(Figure 7).

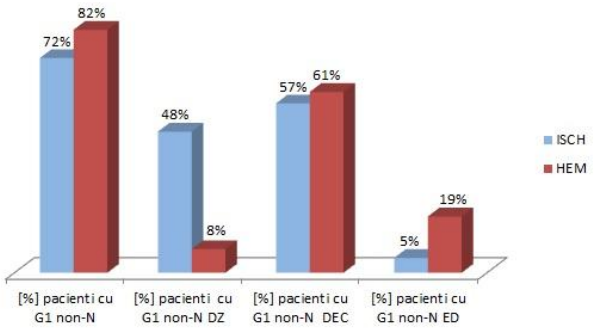

Figure 5. Mortality in non-diabetic patients with hyperglycemia at the admission in ICU

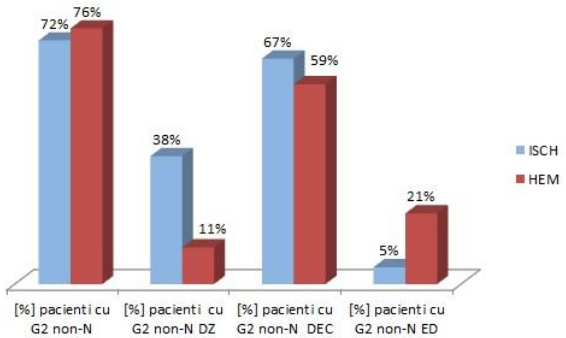

Figure 6. Mortality in non-diabetic patients with hyperglycemia after 24 hours from admission in ICU

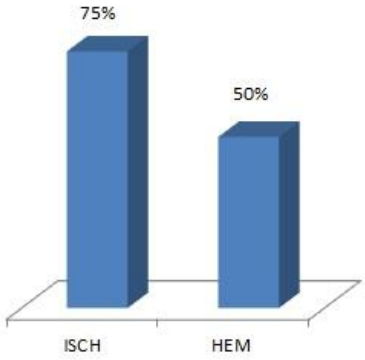

Figure 7. Transition from hyperglycemia to normoglycemia in the ISCH and HEM groups

DISCUSSIONS

This retrospective single center study shows a higher mortality rate in the ISCH group in patients with normal glucose values at admission compared with the HEM group were the mortality rate was higher in patiens with hyperglycemia at the admission time. This data was not correlated with the presence of diabetes mellitus.

This finding is supported by studies showing higher mean admission glucose level in nonsurvivors of stroke compared with survivors [12-18]. It is also supported by multivariate analyses of data from 2 large studies, in wich admission glucose level was a significant predictor of mortality [19] or poor functional recovery [20] after stroke independent of other prognostic factors.

Few explanations will account for the observed association between hyperglycemia and poor prognosis after ischemic stroke. First of all, hyperglycemia may be directly toxic to the ischemic brain. Even if the mechanism is not completely understood, accumulation of lactate and intracellular acidosis in the ischemic brain (produced through anaerobic cerebral glucose metabolism) [21] mai contribute. Intracellular acidosis may accelerate ischemic injury by enhancing lipid peroxidation and free radical formation [22], allowing accumulation of intracellular calcium [23] (a key component of the glutamate-dependent excitotoxicity seen inischemic neurons [24]), and impairing mitochondrial function [25]. These neurotoxic effects may be important in the ischemic penumbra. In an animal model of stroke, hyperglycemia facilitated the developement of cellular acidosis in the ischemic penumbra and resulted in a greater infarct volume compared with insulin-treated hypoglycemic animals [25].

On the other side, hyperglycemic patients can be deficient in insulin, resulting in both reduced peripheral uptake of glucose (increasing the amount of glucose vailable to diffuse into brain) and increased circulating free fatty acids. Free fatty acids may impair endothelium-dependent vasodilation [26] and promote calcium overload and arrhytmias [27] in patients with acute myocardial infarction.

Another point of view is that patients without a diagnosis of diabetes who develop stress hyperglycemia are likely to have dysglycemia (just a little above the normal range) or undiagnosed diabetes when not stressed. Patients with dysglycemia or undiagnosed diabetes have a higher risk of vascular disease than patients with normal blood glucose level [28]. These patients may present more ischemic damage at the time of infarction as a result of more extensive underlying cerebral

vasculopathy compared with those who do not develop stress hyperglycemia. Stress hyperglycemia may be a marker of the area of ischemic damage in patients with stroke.

Hyperglycemia may disrupt the blood-brain barrier [29] and promote hemorrhagic infarct conversion [30].

There are not to many studies who followed the survival rate taking in consideration the evolution of blood glucose levels.

Taking in consideration the presence of diabetes mellitus and related to patient`s gender, in the HEM group there are not big differences in mortality in women with diabetes mellitus (50%) compared with mortality in women without a previous diagnosis of diabetes mellitus (48%), and in men with diabetes mellitus (65%) versus men without it (64%). In the ISCH group, mortality was a little bit higher in men with diabetes mellitus (63%) compared with men without a previous diagnosis of diabetes mellitus (60%), but in women differences are critically high: women with a previous diagnosis of diabetes mellitus had a mortality rate of 100% compared with mortality in women without a diagnosed diabetes mellitus of 50%.

In the ISCH group, 72% from the patients had hyperglycemia at the addmission time in ICU and after 24 hours; from the patients with hyperglycemia at the addmission time, 52% had diabetes mellitus, while from the patients with hyperglycemia after 24 hours, 62% were with diabetes mellitus. Mortality rate in patients with hyperglicemia at the addmission time was 57% and 67% for the patients with hyperglycemia after 24 hours.

5% from the ISCH group had cerebral edema.

In the HEM group, 82% from the patients had hyperglycemia at the addmission time in ICU and a lower percent after 24 hours (76%); from the patients with hyperglycemia at the addmission time, 92% had diabetes mellitus, while from the patients with hyperglycemia after 24 hours, 89% were with diabetes mellitus. Mortality rate in patients with hyperglicemia at the addmission time was 61% and 59% for the patients with hyperglycemia after 24 hours.

Aproximatively 20% from the HEM group developed cerebral edema.

CONCLUSIONS

In patients with hyperglycemia after 24 hours from admission and no history of diabetes melittus, mortality was higher in the ISCH group and lower in the HEM group. Even so, diabetes melitus still remains a high risk factor, especially in women with ischemic stroke.

Preexisting hyperglycemia is found commonly in patients presenting with acute stroke and worsens clinical outcome. The risk is higher in non-diabetic patients compared with patiens already diagnosed with diabetes.

These results highlight the need for further research to determine whether glucose lowering at the time of stroke and after 24 hours from admission in the Intensive Care Unit can improve outcomes.

Compliance with Ethical Requirements

Lavinia Anca Mozos and Liviu Matcau declare that they have no conflict of interest. For the study we have the approved form to use the clinical and demographic data of the patient from the Ethical Committee of Emergency County Hospital Timisoara.

REFERENCES

1. [Guideline] Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Stroke. May 2007;38(5):1655-711.[Medline].
2. Bruno A, Kent TA, Coull BM, Shankar RR, Saha C, Becker KJ, et al.Treatment of hyperglycemia in ischemic stroke (THIS):a randomized pilot trial. Stroke. Feb 2008;39(2):384-9.[Medline].
3. Benavente O, Hart RG. American Family Physician: Management of Acute Ischemic Stroke, 1999;59:2475-82.
4. Martini SR, Kent TA. Hyperglycemia in acute ischemic stroke: a vascular perspective. Journal of Cerebral Blood Flow and Metabolism.2007;27:435-451.
5. Parsons MW, Barber PA, Desmond PM, et al. Acute hyperglycemia adversely affects stroke outcome: a magnetic resonance imaging and spectroscopy study. Ann Neurol. Jul 2002;52?(1):20-8.[Medline].
6. Kawai N, Keep RF, Betz AL. Hyperglycemia and the vascular effects of cerebral ischemia. Stroke. Jan 1997;28(1):149-54.[Medline].
7. Quast MJ, Wei J, Huang NC, et al. Perfusion deficit parallels exacerbation of cerebral ischemia/reperfusion injury in hyperglycemic rats. J Cereb Blood Flow Metab.May 1997;17(5):553-9.[Medline].
8. Broderick J, Brott T, Tomsick T, Miller R, Huster G. Itracerebral hemorrhage is more than twice as common as subarachnoid hemorrhage. J Neurosurg. 1993;78:188-191.[Medline].
9. Kimura K, Iguchi Y, Inoue T, Shibazaki K, Matsumoto N, Kobayashi K, Yamashita S. Hyperglycemia independently increases the risk of early death in acute spontaneous intracerebral hemorrhage. J Neurol Sci.2007;255:90-94.
10. Passero S, Ciacci G, Ulivelli M. The influence of diabetes and hyperglycemia on clinical course after intracerebral hemorrhage. Neurology. 2003;61:1351-1356.
11. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, et al. Intensive insulin therapy in the critically ill patients. N Engl J Med.2001;345:1359-1367.
12. Woo E, Chan YW, Yu YL, Huang CY. Admission glucose level in relation to mortality and morbidity outcome in 252 stroke patients. Stroke.1988;19:185-191.
13. Czlonkowska A, Ryglewicz D, Lechowicz W. Basic analytical parameters as the predictive factors for 30-day case fatality rate in stroke. ActaNeurol Scand. 1997;95:121-124.
14. Tracey F, Crawford VLS, Lawson JT, Buchanan KD, Stout RW, Hyperglycemia and mortality from acute stroke. Q J Med. 1993;86:439-446.
15. Mase G, Zorzon M, Biasutti E, Tasca G, Vitrani B, Cazzato G. Immediate prognosis of primary intracerebral hemorrhage using an easy model for the prediction of survival. Acta Neurol Scand. 1995;91:306-309.
16. Murros K, Fogelholm R, Kettunen S, Vuorela A-L, Valve J. Blood glucose, glycosilated hemoglobin, and outcome of ischemic brain infarction. J Neurol Sci. 1992;111:59-64.
17. Poungvarin N, Viriyavejakul A. Spontaneous supratentorial intracerebral hemorrhage: a prognostic study. J Med Assoc Thai. 1990;73:206-210.
18. M`Buyamba-Kabangu J-R, Longo-Mbenza B, Tambwe MJ, Dikassa LN, Mbala-Mukendi M. J-shaped relationship between mortality and admission blood pressure in black patients with acute stroke. J Hypertens. 1995;13:1863-1868.
19. Moulin T, Tatu L, Crepin-Leblond T, Chavot D, Berges S, Rumbach L. The Besancon Stroke Registry: an acute stroke registry of 2500 consecutive patients. Eur Neurol. 1997;38:10-20.
20. Bruno A, Biller J, Adams HP, Clarke WR, Woolson RF, Williams LS, Hansen

MD, for the TOAST Investigators. Acute blood glucose level and outcome from ischemic stroke. Neurology. 1999;52:280-284.
21. Levine SR, Welch KM, Helpern JA, Chopp M, Bruce R, Selwa J, Smith MB. Prolonged deterioration of ischemic brain energy metabolism and acidosis associated with hyperglycemia: human cerebral infarction studied by serial 31P NMR spectroscopy. Ann Neurol. 1988;23:416-418.
22. Siesjo BK, Bendek G, Westerberg E, Wieloch T. Influence of acidosis on lipid peroxidation in brain tissues in vitro. J Cereb Blood Flow Metab. 1985;5:253-258.
23. Ou Yang YB, Mellergard P, Kristian T, Kristianova V, Siesjo BK. Influence of acid base changes on the intracellular calcium concentration of neurons in primary culture. Exp Brain Res. 1994;101:265-271.
24. Choi DW, Rothman SM. The role of glutamate neurotoxicity in hypoxic-ischemic neuronal death. Ann Rev Neurosci. 1990;13:171-182.
25. Anderson RE, Tan WK, Martin HS, Meyer FB. Effects of glucose and PaO2 modulation on cortical intracellular acidosis. NADH redox state, and infarction in the ischemic penumbra. Stroke. 1999;30:160-170.
26. Steinberg HO, Tarshoby M, Monestel R, Hook G, Cronin J, Johnson A, Bayazeed B, Baron AD. Elevated circulating free fatty acid level impair endothelium-dependent vasodilation. J Clin Invest. 1997;100:1230-1239.
27. Oliver MF, Opie LH. Effects of glucose and fatty acids on myocardial ischemia and arrhytmias. Lancet. 1994;343:155-158.
28. Coutinho M, Gerstein HC, Wang Y, Yusuf S, The relationship between glucose and incident cardiovascular events: a metaregression analysis of published data from 20 studies of 95783 individuals followed for 12,4 years. Diabetes Care. 1999;22:233-240.
29. Dietrich WD, Alonso O, Busto R. Moderate hyperglycemia worsens acute blood-brain barrier after forebrain ischemia in rats. Stroke. 1993;24:111-116.
30. DeCourten-Meyers GM, Kleinholz M, Holm P, DeVoe G, Schmitt G, Wagner KR, Myers RE. Hemorrhagic infarct conversion in experimental stroke. Ann Emerg Med. 1992;21:121-126.

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1. Wolff M, Corby P, Klaczany G, et al. *J Clin Dent* . 2013;24(Spec Iss A):A45-A54. 2. Data on file. Colgate-Palmolive Company. 3. Cantore R, Petrou I, Lavender S, et al. *J Clin Dent* . 2013;24(Spec Iss A):A32-A44. 4. Yin W, Hu DY, Fan X, et al. *J Clin Dent* . 2013;24(Spec Iss A):A15-A22. 5. Data on file. Colgate-Palmolive Company. 6. Kraivaphan P, Amornchat C, Triratana T, et al. Caries Res. 2013;47(6):582-590.

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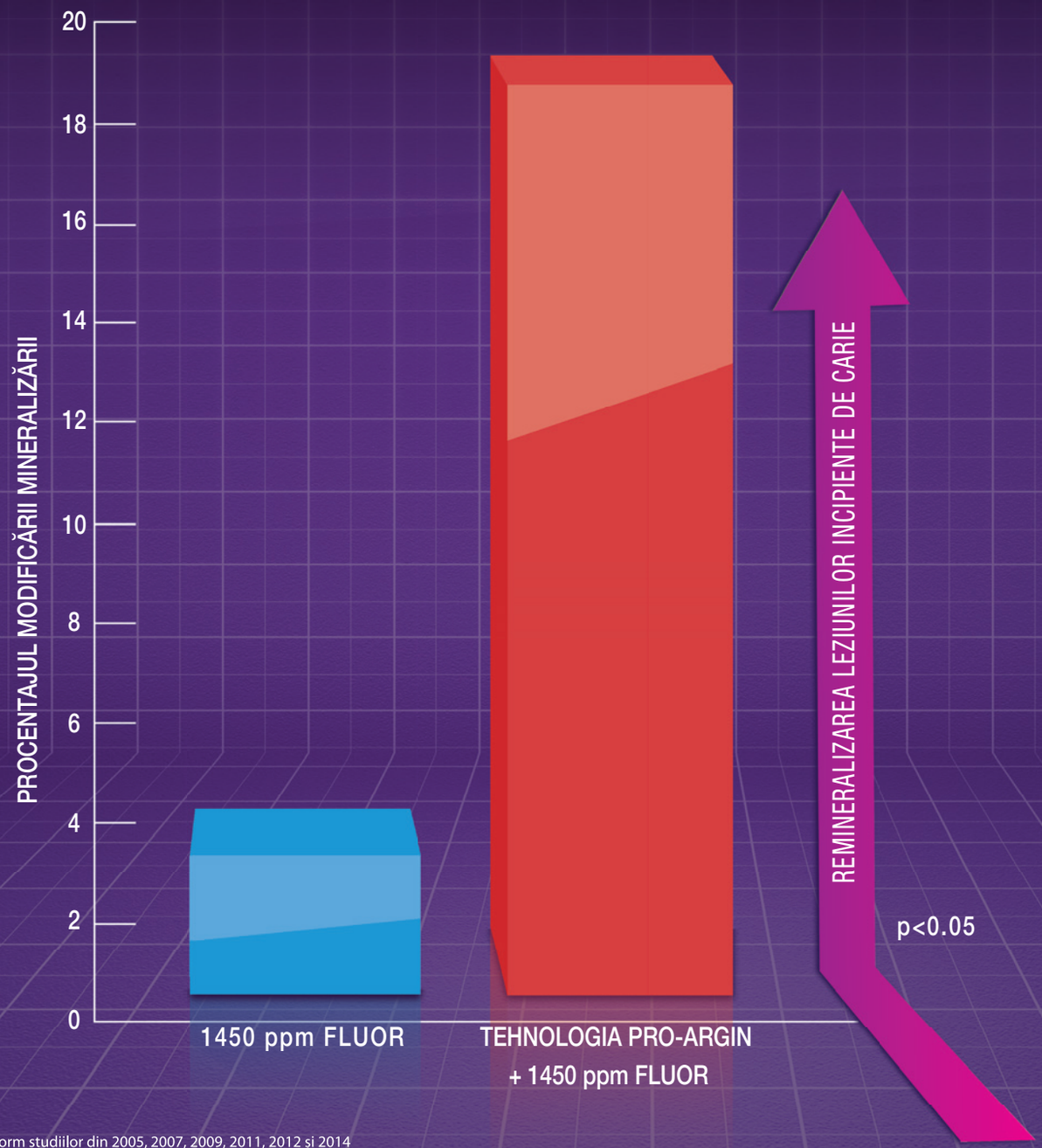
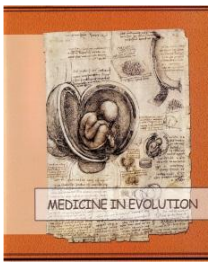


* Conform studiilor din 2005, 2007, 2009, 2011, 2012 și 2014

**Cantore R, Petrou I, Levander S, et al. J Clin Dent. 2013; 24 (Spec Iss AA): A32-A44.

NUTRITION BEHAVIOR OF CHILDREN FROM PRIMARY SCHOOL. CASE STUDY OF THREE SCHOOLS FROM TIMISOARA



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ABSTRACT

Objective of this paper is to present a social research on nutritional behavior among children with age between 7 and 10 years old, in order to establish nutritional behavior and to propose solutions for improving it, because nutrition and oral health can not be taken separately. For achieving our aim we designed our research using quantitative approach and we applied a specialized questionnaire to a sample of 772 children from 3 different schools from the area of Timisoara. Results highlight different nutritional behaviors between the 3 schools and show possibilities to conduct nutritional campaigns in schools.

Key words: *nutritional behavior, children, Timisoara, Romania*

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INTRODUCTION

The purpose of this paper is to study the importance of nutrition in oral health. Nutrition is the sum of dietary quality and physiological and biological activity necessary to maintain life.(Adrianne Bendich, Riva Touger-Decker, Connie Mobley, Joel B.Epstein,2014). Nutrition and diet are the most important for the maintenance of body health thorough the life. A inadequate nutrition can lead to a series of diseases such as cardiovascular diseases, cancers, stroke, pulmonary illnesses, diabetes and oral cavity diseases.

In preventing caries and to keep oral health at it's best is very important what we eat and what we drink, and how often we eat and drink. When starting to eat some aliments, changes in oral cavity are happening: oral bacteria start to transform sugar into acid. So eating frequently and with more sugar or crunching between meals leads to a rapid development of caries. The aliments containing calcium and phosphorus increase minerals on the tooth enamel affected by caries.

The literature shows us that dental erosion is increasing with acids which are found in soft drinks. Evidences give us a relation between sugar consumption and dental caries. In Sweden a experiment has done to establish a correlation between intake of sugars and dental caries. This experiment proved that restriction of sugar intake to four meals daily did not significantly increase the caries incidence, but if larger amount of sugar was given, the development of caries increased significantly. (Dr. Jayaprasad Anekar, 2011)

Lactose from milk has been reported as being low cariogenic, but several observations on babies breast-fed over periods of a year or longer have shown that lactose can be highly cariogenic when drunk frequently. (Stefano Petti, Roberto Simonetti,1997). Studies show that sugars contained in fruits are more cariogenic than sugar from pack or other extrinsic sugars. Apples, which have high content of free acids can rise the formation of caries. Some research in rat feds various fruit indicate that, apples, banana, grapes, can rise to a high level of caries sometimes even more than sucrose itself (Jayaprasad Anekar,2011, p.178). In order to reduce caries risk associated with consumption of sugars, the idea is to eat more food with complex carbohydrates. Starchy food can lead very quickly to acid formation on dental plaque. In 1993 the acidogenity of white bread, cooked spaghetti, cooked long-grain rice and many other starch products with sugar or without sugar. These tests showed that none of the test products was significantly different from 10% sucrose solution, from that it is sure that starches are acidogenic in the mouth.(Pollard et al 1993) Even with sugars, acids in the fruits and vegetables it is not feasible to advice against consuming them, because fruits and vegetables have positive effects on health. The main idea is to advice people to avoid eating the same fruits every day, because not only to avoid teeth erosion because to ensure that people gets all essential nutrients, vitamins and minerals.

We consider nutrition not just a matter"of eating and drinking"', but also a complex process that include instruction, motivation. On this direction, our research was oriented by the next questions: When do you use to brush your teeth? Usually somebody checks if you have brushed your teeth? Who checks you if you have brushed your teeth? How often did you eat the following products last week? Until now did you see the dentist? Why you never see the dentist? How gender, class, school and parents profession affect nutrition? The main purpose of this paper is to lay emphasis on how nutrition influence the oral health.

METHOD AND DATA COLLECTION

This study will explore nutritional behavior of children from primary schools. To achieve our purpose we chose to apply specialized social questionnaire on the children. The research instrument was a questionnaire with 37 questions related to: oral hygiene, nutrition and dental care. The research sample was 772 children divided between 3 different schools: two from the area of Timisoara and one school from a village close to Timisoara. The first school is from a rich village close to Timisoara (n=207). The second one is from center of Timisoara (n=326) and the third one is from a middle class suburb Timisoara (n=239). From the initial sample size of 791 children, 19 cases were dropouts because of the age of 6 or 11 years old. The instrument was firstly tested on a pilot sample of 20 children and after that was optimized and adapted for 7-10 years old children. The University „Victor Babes"ethics committee approved the study and we obtained approval form the schools for our research.

RESULTS

For studying nutritional behavior of the children as a important and complex process, we investigate the parameters such as: oral hygiene, frequency of consumption of certain alimentary products, and dental care.

Children were asked when they use to brush their teeth, and they answered: Morning(69.9%), At noon(14.6%), Evening(58.4%), After each meal(25.5%), When I rememer(5.7%), Never(1.7%). If they are checked when they brush their teeth, they answered: Everytime-38.9%, Sometimes-37.4%, Never-23.1%. The persons who check children when they brush their teeth are:Mother-71.1%,Father-24.5%,Grandmother-6.6%.

In order to investigate nutritional behavior, each child was asked how frequently they eat 19 usual products (aliments). Further we divided these 19 products (aliments) into two main groups. First group is represented by products of high cariogenic risk, which are: Chocolate, Sweets, Biscuits, Juices, Salty products, Chewing gum, Marmelades, Cakes, Caramels, Pizza, Crisps, Croissant, Cheesecake. These products can lead very quickly to acid formation on dental plaque, which evolve fast into caries. Second group is represented by products of low cariogenic risk, which are: Orange, Carrot, Pear, Celery Milk products.These products help to increase mineral amount on dental plaque and to reduce acidity.

How often did you eat these products last week?

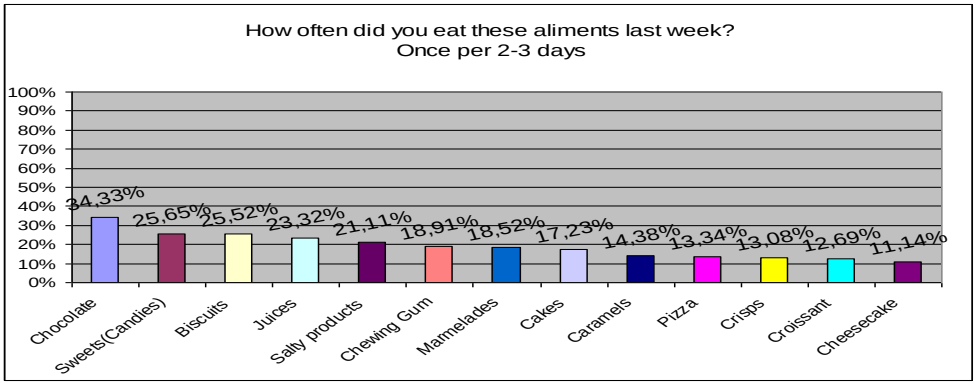

Figure 1. Products of high cariogenic risk (consumed once in 2-3 days)

According to our data the first two products of high cariogenic risk that are consumed once in 2-3 days are: Chocolate eaten by 34,33% of the children, and Sweets(Candies) eaten by 25.65% of the children. So these products are dangerous for the childrens teeth, because chocolate and sweets contain high amounts of acids, which cause rapid development of caries. As a result, these products are consumed relatively often, resulting in a prevalence of caries among 7-10 years children.

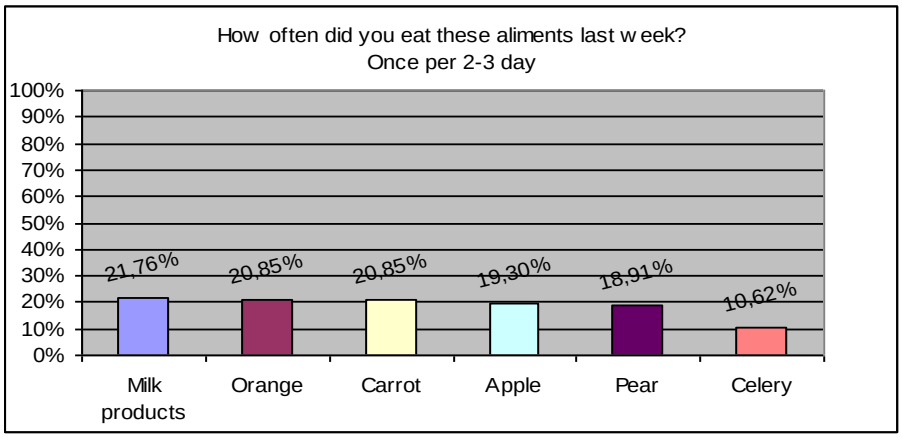

Figure 2. Products of low cariogenic risk (consumed once in 2-3 days)

Regarding products of low cariogenic risk, the first three are: Milk Products(21.76%), Orange and Carrot, both eaten by 20.85% of the children, once in 2-3 days. On the contrast, with products of high cariogenic risk, low cariogenic risk products are not so preferred by the 7-10 years children. From these we can remark a relatively high prevalence of caries among primary school children.

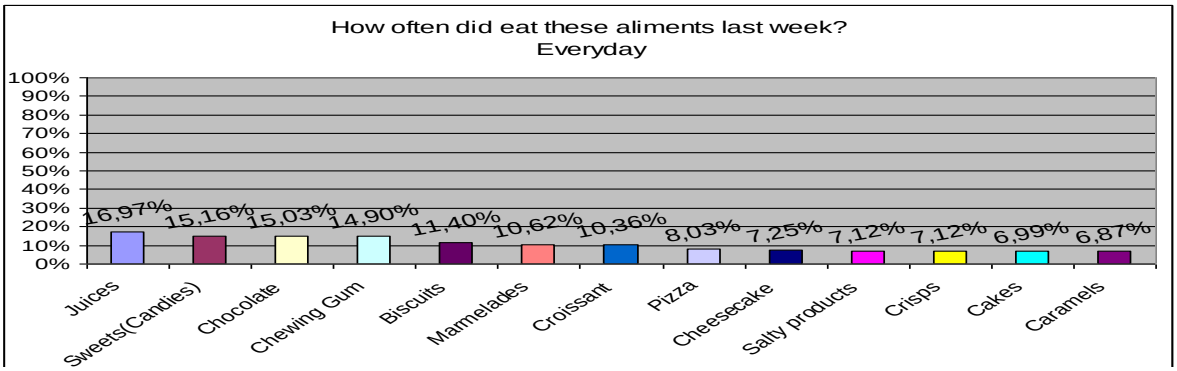

Figure 3. Products of high cariogenic risk (consumed everyday)

Juices(16.97%), sweets(15.16%), chocolate(15,03%) and the other products of high cariogenic risk, are not so consumed everyday by so many children as they are consumed once in 2-3 days.

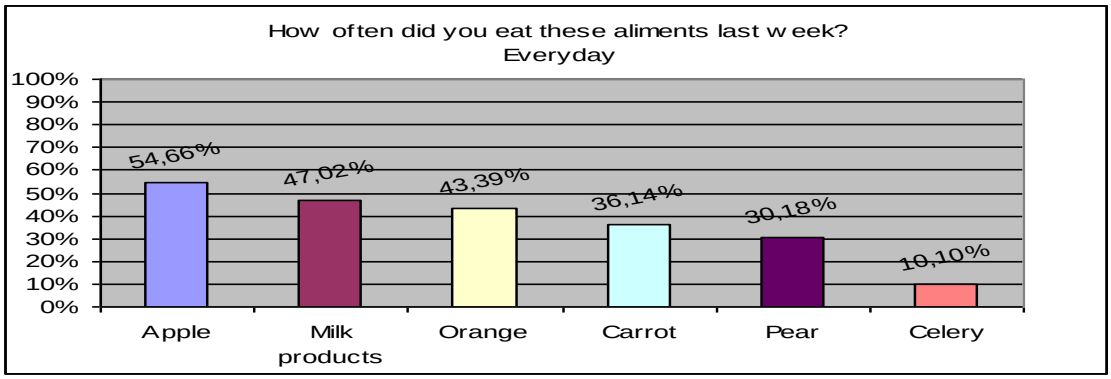

Figure 4. Products of low cariogenic risk (consumed everyday)

In contrast with products of high cariogenic risk, the products of low cariogenic risk are consumed by many children everday: Apple(54,66%), Milk products(47,02%), Orange(43,39%).

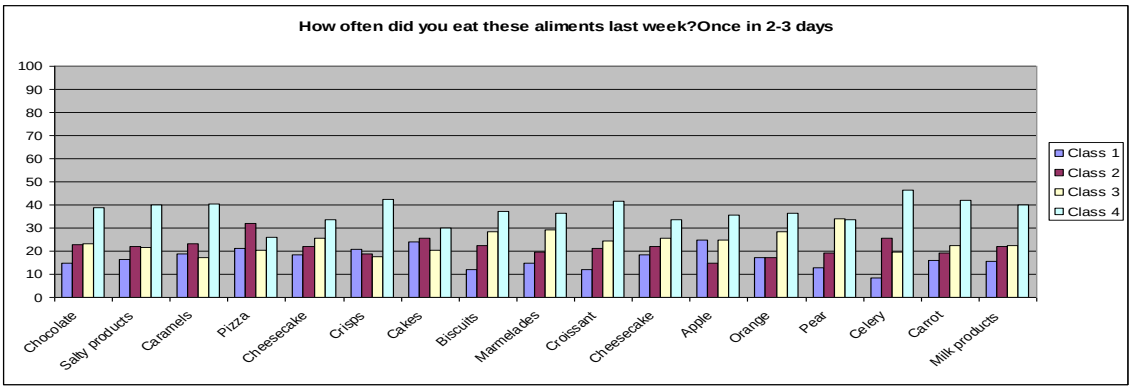

Figure 5. Relation between once 2-3 day frequency of consumption and class level

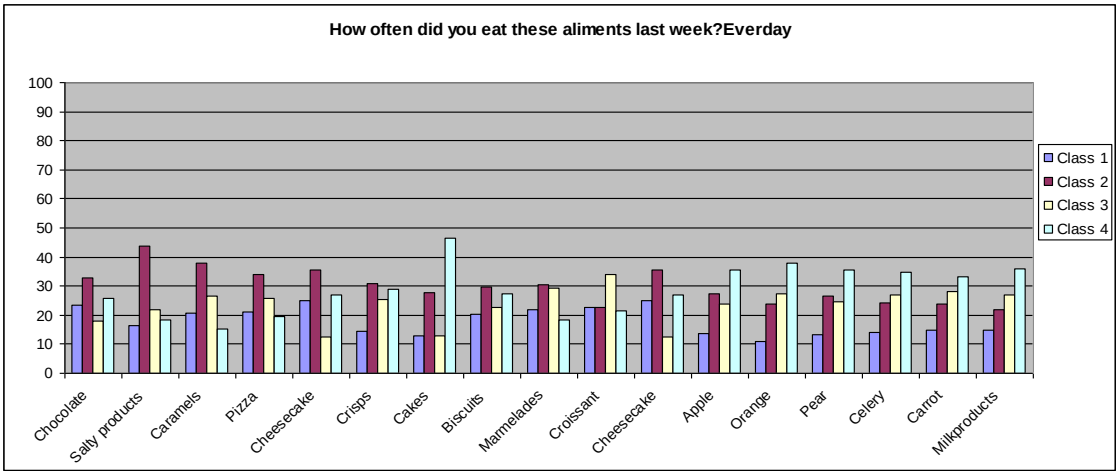

Figure 6. Relation between every day frequency of consumption and class level

Fourth class consume chocolate, once in 2-3 days(38.9%), significantly more than other classes but second class consume chocolate everyday (32.8%) significantly more. In case of salty products: are consumed significantly more, once in 2-3 days, by the children of fourth class(39.9%), but consumed significanly more everday by the second class(43.6%). In case of caramel: are conumed significantly more, once in 2-3 days, by the children of fourth class, but consumed significanly more everday by the second class. Pizza is consumed significantly more, both once in 2-3 days(32%) and everyday(33.9%), by the second class significantly more than other classes. Crisps are consumed once in 2-3 days(42.6%) by the fourth class. Cheesecake is eaten everyday by the second and the fourth class significantly more than by the other classes.

Fourth class consume crisps once in 2-3 days. Cakes(46.3%-everyday) are consumed, both once in 2-3 days and everyday, by the fourth class significantly more than the other classes. In case of biscuits, fourth class consume them once in 2-3 days(37.1%) significantly than other classes, but second class consume them everyday(29.5%). Marmelde is consumed everyday(30.5%) by the second class. Croissants are consumed everyday by the third class, significantly more than by the other classes.

Figure 7. Consumption of high cariogenic risk products related to gender

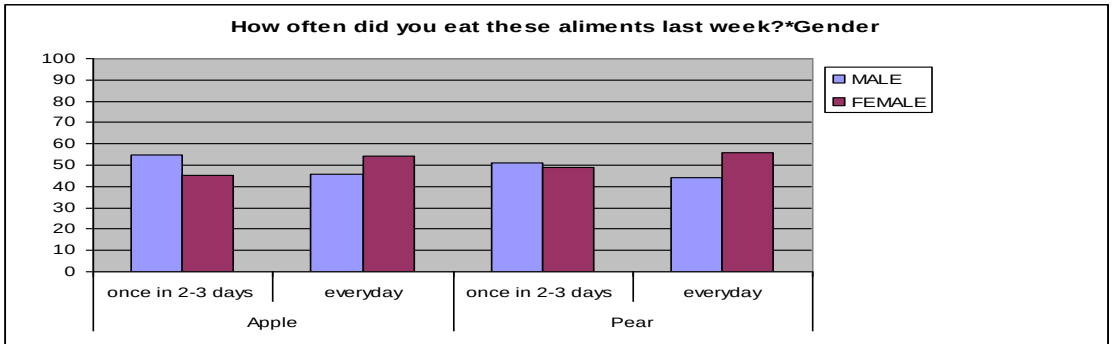

Figure 8. Consumption of low cariogenic risk products related to gender

Apple(35.6% once in 2-3 days, 35.5% everyday), orange(36.6% once in 2-3 days, 37.9% everyday) and pear(33.6% once in 2-3 days, 37.9% everyday) are consumed by the fourth class. Celery(46.3%) and carrot(42.2%) are consumed once in 2-3 days by the fourth class. Milk products(36.1%) are cosumed everyday by the fourth class, more than the other classes.

Boys eat everyday, significantly more of the following products, than girls: sweets(59.3%), juices(64.8), crisps (62.7%), cakes(67.9%), croissant(60.8%). Apples(54%), pears(56%), are eaten everyday significantly more by the girls than by the boys

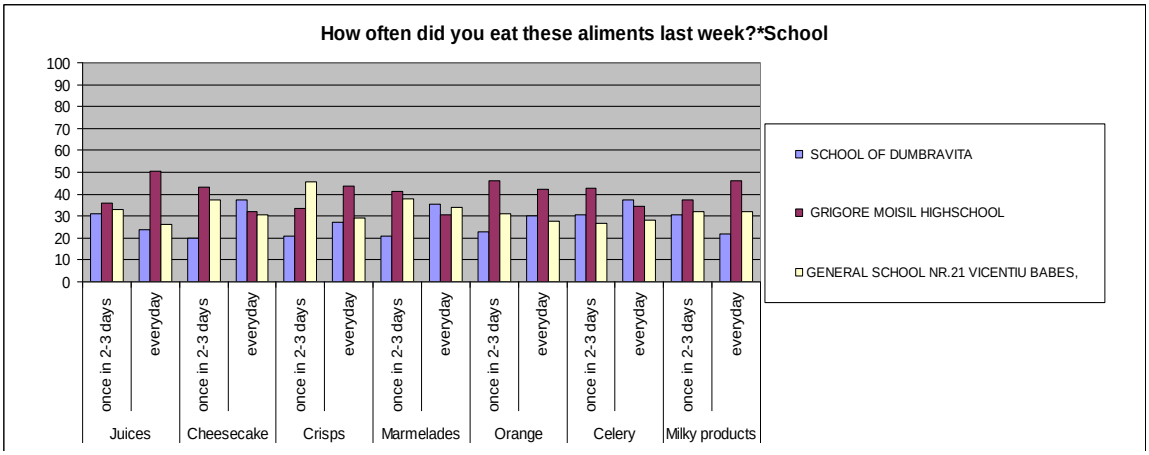

Figure 9. Frequency of consumpton of high cariogenic risk products related to school

Children form GRIGORE MOISIL HIGHSCHOOL drink significantly more juices(36.1%), once in 2-3 days, significantly more than the children from the other 2 schools. Children form GRIGORE MOISIL HIGHSCHOOL drink significantly more milk products(46%) everyday, significantly more than the children from the other 2 schools. Cheesecake is eaten everyday by the children from SCHOOL OF DUMBRĂVIŢA, significantly more than the children from the other 2 schools. Children form GENERAL SCHOOL NR.21 VINCENŢIU BABEŞ eat significantly more crisps(45.5%), once in 2-3 days, significantly more than the children from the other 2 schools. Marmelade(35.4%) is consumed everyday significantly more by the children from SCHOOL OF DUMBRAVITA, than the children from the other 2 schools. Children form GRIGORE MOISIL HIGHSCHOOL consume significantly more orange(42.4%) everyday than the children from the other 2 schools. Children form SCHOOL OF DUMBRĂVIŢA consume significantly more celery(37.2%) everyday, than the children from the other 2 schools.

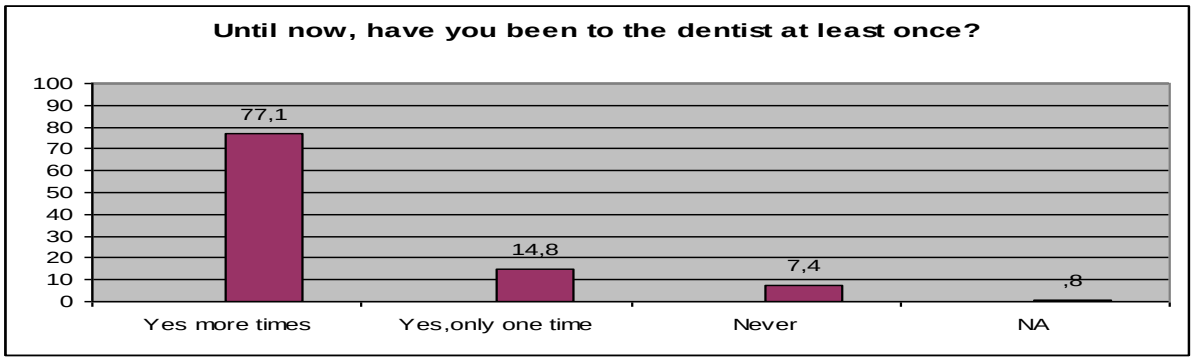

Figure 10. Frequency of visits to the dentist office

According to our data 77.1% percent of the 7-10 years old children were to dentist more times. About 7 percent were never to dentist. From the children that never been to dentist,we can identify following reasons for never being to the dentist: they did not need(59.1%), fear(12,1%), other reasons(28,8%).

CONCLUSIONS

Our research give a complex image regarding nutrition and it's implications on the oral health of children from the 3 schools. Nutrition is a complex process which has more dimensions: class, gender, school. In the Grigore Moisil school children have the less healthier nutrition behavior. In the same time nutrition of girls is healthier than the one of boys because girls eat more products with low cariogenic risk than boys.

Our analyse of nutriton behavior, shows that nutrition of the children is not healthy. The frequency of eating products with high cariogenic risk are very high. A lot of factors could generate this high risk context, but one of the most evident is the lack of information campaigns in Romania and low level implications of school teachers in healthy nutrition. Considering very close relation between children from primary school and their teachers, we can consider schools and teacher an opportunity for implementing an information campaign for a healthy nutrition.

Acknowledgment

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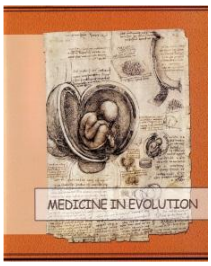
REFERENCES

1. Riva Touger-Decker, David A. Sirois, Connie C. Mobley(2005)-Nutrition and Oral Medicine (Nutrition and Health),Humana Press p.3
2. Tinanoff N, Palmer CA. Dietary determinants of dental caries and dietary recommendations for preschool children. Refuat Hapeh Vehashinayim. 2003 Apr; 20(2):8-23, 78.
3. Marshall TA, Levy SM, Broffitt B, et al. Dental caries and beverage consumption in young children. Pediatrics. 2003 Sep; 112(3 Pt 1):e184-91.
4. Burt BA, Eklund SA, et al. The effects of sugars intake and frequency of ingestion on dental caries increment in a three-year longitudinal study. J Dent Res. 1988 Nov; 67(11):1422-9.
5. Sheiham A. Dietary effects on dental diseases. Public Health Nutr. 2001 Apr; 4(2B):569-91.
6. A.J. Rugg Gunn. Nutrition & Dental Health; 1993 Oxford University Press
7. Dr Jayaprasad Anekar (2011) Diet and Oral Health,Volume 2 Issue 1:175-180

BACTERIAL REPOPULATION OF PERIODONTAL POCKETS IN THE ABSENCE OF SUPPORTIVE MANINTENANCE THERAPY



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ABSTRACT

Aim and objectives: Assessment of periodontal pathogens repopulation of treated periodontal pockets in the absence of maintenance therapy.

Material and method: 20 patients diagnosed with aggressive periodontitis examined. Scaling and root planing (SRP) was performed. Periodontal parameters and levels of 9 periodontal pathogens were registered at baseline, 6 months and 12 months post-treatment.

Results: A significant improvement in clinical parameters was observed. All bacterial species showed a decrease of levels at 6 months post-treatment with a slight increase at the end of the observation period.

Conclusions: Recolonization by periodontal pathogens can occur in the absence of maintenance therapy and it may lead to periodontal disease recurrence.

Key words: *periodontal pathogens, SRP, maintenance*

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INTRODUCTION

Periodontitis is a mixed bacterial infection, and subgingival colonization by the biofilm elicits a systemic antibody response. One of the main goals in the treatment of periodontal disease is to suppress periodontal pathogens or to reverse the subgingivalmicroflora from a 'pathogenic' to a 'non-pathogenic' state. The main bacterial species implicated in the pathogenesis of periodontitis are Aggregatibacteractynomicetemcomitans (Aa), Porphyromonasgingivalis (Pg), Treponemadenticola (Td),Tanerella forsythia (Tf), Prevotella intermedia (Pi), Peptostreptococcus (Micromonas) micros (Pm), Fusobacteriumnucleatum (Fn), Eubacteriumnodatum (En) and Capnocytophagagingivalis (Cg). [1, 2]

Mechanical periodontal therapy (SRP) is the first treatment phase of periodontitis. It is directed primarly towards removing biofilm and dental calculus from the root surfaces, leading to ecological changes in the subgingivalmicroflora. The clinical benefits of scaling and root planing are majorly due to biofilm disorganization, resulting in the decrease of periodontal pathogens. However, proper and comprehensive mechanical debridement of deep pockets is difficult to accomplish. Previous studies have demonstrated that scaling and root planing alone has a limited effect on some pathogens due to the fact that some of these bacterial species can reside in soft tissues, root surfaces irregularities or dentinal tubules, leading to treatment failure. [3, 4, 5] Furthermore, ecological niches, other than periodontal pockets, may act as source or reservoir for recolonization by pathogens, rapidly occurring after mechanical therapy. [6]. Consequently, to prevent rebound of periodontal pathogens in the subgingival area, repeated mechanical removal of biofilm, through regular supportive periodontal therapy, is essential for the maintenance of periodontal health.

One means to decide the optimal recall interval should not be based on changes in clinical parameters, but studying the kinetics of bacterial repopulation of periodontal pockets following therapy. The polymerase chain reaction (PCR) is now one of the most common, sensitive and specific molecular method that permits not only a qualitative, but also a quantitative analysis of the microbiota present in periodontal pockets.[ ]

PURPOSE OF STUDY

The main objective of this study was to asses the rate of bacterial repopulation by Aa, Pg, Td, Tf, Pi, Pm, Fn, En and Cg of periodontal pockets following scaling and root planing with the extensive use of chlorhexidine irrigations during clinical procedure, in patients with aggressive periodontitis, without maintenance therapy, over a period of 1-year observation.

MATERIAL AND METHODS

Subject Population

The study included 20 young adult patients, 13 females and 7 males, age 28 to 40 years, mean age 32.30 ± 3.43 with moderate or severe aggressive periodontitis. The patients were diagnosed according to criteria described by the American Academy of Periodontology. [7,8] All patients were in good general health and none of them had taken antibiotics or used antimicrobial rinses the past 3 months. Only non-smokers were selected for this study, to eliminate the eventual influence of smoking on the microbiota. All patients had signed a written consent form after a thorough explanation of the nature of this study and the risks involved.

Clinical Parameters

The following clinical measurements were determined at baseline, 6 months and 12 months after periodontal therapy: plaque index (PI), bleeding on probing (BOP), probing depth (PD) and clinical attachment level (CAL). The measurements were performed at six sites per tooth with a conventional periodontal probe, excluding third molars.

Site Selection and Bacterial Sampling

Forty inflamed pockets with 6 mm probing depth or greater (mean 6.65 ± 0.77 mm), 4 sites per each patient, were selected for bacterial sampling. Probes of gingival fluid were taken on sterile paper points one week after the removal of supragingival plaque, before scaling and root planing, followed by 6 months and 12 months sampling after performing SRP, in the absence of any other therapeutic procedure. The identification and enumeration of periodontal pathogens (Aa, Pg, Td, Tf, Pi, Pm, Fn, En and Cg) were accomplished through PCR preoperatively, at baseline, and 6 months and 12 months post-treatment, for each site initially selected.

Therapeutic Procedure

Scaling and root planing was performed for each patient, under local anesthesia, using ultrasonic tips and Graceycurets in one stage. One episode of irrigation with a 0.2 % chlorhexidine solution was performed for all periodontal pockets at the end of SRP session. No additional prophylactic or periodontal therapy, except instructions for a correct tooth brush technique, was rendered throughout the one year observation period.

Statistical Analysis

SPSS version 2.0 software program was used for statistical analysis. Descriptive analysis was used to compute the mean age of the subjects. For each patient, plaque index and bleeding on probing were recorded as percentages and expressed as mean ± standard deviation (SD) for the subject population at baseline, 6 months and 12 months post-treatment. PD and CAL were registered for each site of sampling and mean ± SD was calculated for each examination. The level for each periodontal pathogen tested was registered and a mean count ± SD was computed for the three determinations. Kruskal- Wallis test for 3 samples was used to achieve the statistical significant difference in clinical and microbiologic parameters between baseline and the 6 month and 12 month reevaluation.

RESULTS

Clinical Results

The pre- and post-therapy clinical parameters measured are shown in Table 1. The patients presented a significant clinical improvement in time, including a decrease in BOP ($p< 0.05$) and PI ($p< 0.05$) but also in PD and CAL at the sampling site ($p< 0.05$) 6 months post-treatment. Figure 1.and Figure 2.present the evolution of these clinical parameters in time. A slight increase of PI and BOP can be observed between the 6 month and 12 month recall, while no major difference can be noticed regarding PD and CAL.

Table 1. *Mean clinical parameters and statistical significance*

CLINICAL PARAMETERS	BASELINE	6 MONTHS	12 MONTHS	P VALUE*
PI (%; mean±SD)	51.35 ± 12.29	28.73 ± 9.43	39.61 ± 6.44	**0.000**
BOP (%; mean±SD)	66.60 ± 17.54	38.61 ± 10.07	40.08 ± 9.16	**0.000**
PD (mm; mean ±SD)	6.65 ± 0.77	4.28 ± 0.96	4.10 ±1.00	**0.000**
CAL (mm; mean ±SD)	4.08 ± 1.52	3.48 ± 1.30	3.45 ± 1.21	**0.014**

* Kruskal-Wallis test for k samples, statistically significant for $p < 0.05$

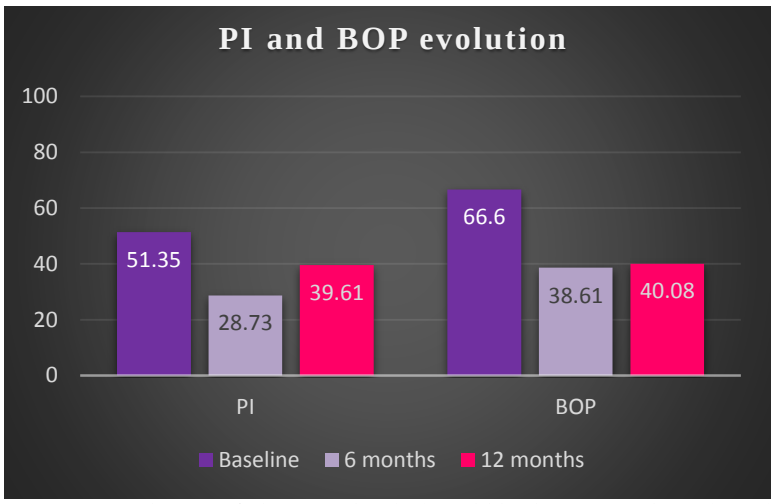

Figure 1. Evolution of plaque index (PI) and bleeding on probing (BOP)

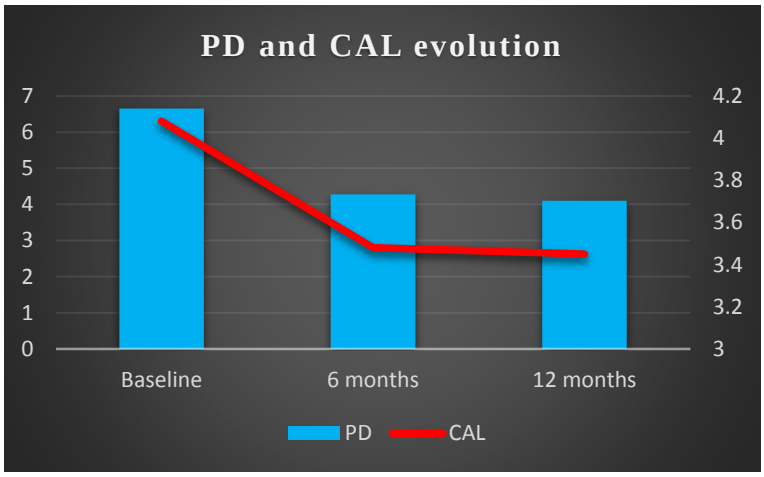

Figure 2. Evolution of probing depth (PD) and clinical attachment level (CAL)

Microbiologic Results

Table 2.presents the mean counts ± SD for Aa, Pg, Td, Tf, Pi, Pm, Fn, En, Cg detected in the sampling sites, in patients with aggressive periodontitis at baseline and 6 and 12 months after SRP and the significant statistical differences.

Table 2. *The mean counts ± SD for Aa, Pg, Td, Tf, Pi, Pm, Fn, En, Cg detected in the sampling sites*

	Mean ± SD			
Pathogens	**Baseline**	**6 months**	**12 months**	**P Value ***
Aa	74924.25 ± 2567.47	17595.25 ±8987.02	43476.5 ±759.25	**0.234**
Pg	218137.5 ± 4250.58	1349.25 ± 674.42	98567.3 ± 835.27	**0.000**
Td	178965.3 ± 1787.63	1989.5 ± 548.71	23589.5 ± 640.27	**0.000**
Tf	42805.5 ± 15461.05	1994.75 ± 511.70	2038.25 ± 509.98	**0.000**
Pi	78978.25 ± 2031.72	8658.5 ± 533.73	8716.5 ± 574.63	**0.000**
Pm	64579.25 ± 721.69	755.5 ± 264.24	13578.5 ± 3608.34	**0.000**
Fn	24673.5 ± 1408.92	55.75 ± 332.14	2348.3 ± 675.28	**0.000**
En	6196.5 ± 171.18	0 ± 0.00	1165.5 ± 121.46	**0.000**
Cg	19517.75 ± 998.94	25.25 ± 112.43	934.6 ± 144.08	**0.000**

* Kruskal-Wallis test for k samples, statistically significant for $p < 0.05$

The microbial changes that followed the clinical outcome pre- and post-therapy are depicted in Figure 3. All of the bacterial species evaluated showed a decrease of levels in time (Figure 3.), particularly at 6 months

after SRP. One year after mechanical treatment, two species, Aggregatibacteractynomicetemcomitans and Porphyromonasgingivalis increased to almost baseline values. A slight increase was also observed in levels of Td, Tf, Pi, Pm, Fn, En and Cg.

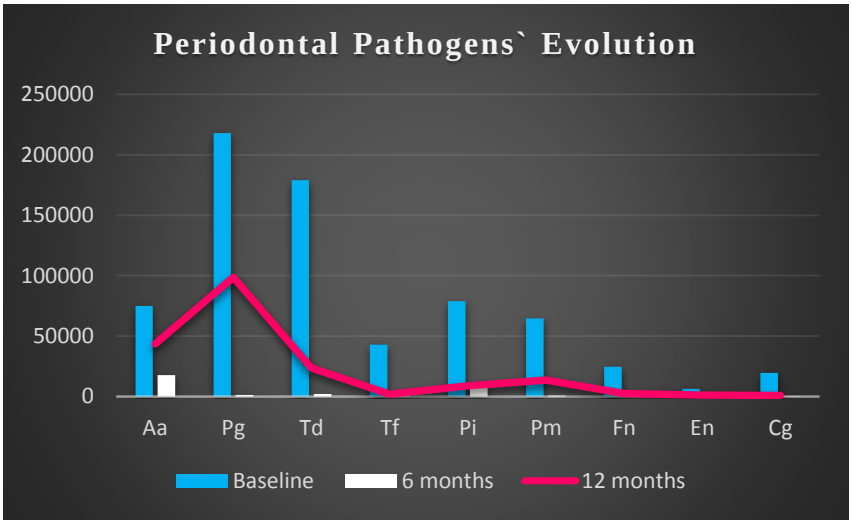

Figure 3. Evolution of levels of periodontal pathogens in time

DISCUSSIONS

To the best of our knowledge, little information is available regarding the presence of periodontal pathogens in patients with aggressive periodontitis previously treated, who do not subsequently receive supportive therapy. The recurrence of periodontitis may be attributed to opportunistic overgrowth by pathogens that have survived periodontal therapy or to reinfection from extracrevicular reservoirs of bacteria. [10]

Clinical parameters such as PI, BOP, PD and CAL are generally used to facilitate diagnosis and detect inflammatory lesions during patients` recall. In the present study, after SRP, a major decrease in these parameters could be observed 6 months post-treatment, in the absence of any supportive therapy. Levels of all periodontal pathogens were also significantly reduced. However, while therapy resulted in prolonged suppression of the tested species, they were detected in a growing level at the end of the observation period. Whereas the level of the targeted bacterial species fluctuated during the experimental period, it was not always accompanied by changes in clinical parameters. A slight increase of PI, 12 months post-therapy, might suggest that supragingival biofilm encourages the repopulation and overgrowth of periodontal pathogens in the subgingival area. Especially higher amounts of Aa and Pg were found at the last evaluation. This can be explained by the ability of these bacteria to invade tissues.[11] These bacteria may have invaded gingival tissues, evaded mechanical debridement, and after SRP recolonized the periodontal pocket, where they may have found an appropriate environment for growth.

In the long run, control of pathogenic species is primarily based on habitat change. Control of subgingivalpathogens can be significantly improved by minimizing supragingival plaque, reducing gingival inflammation that provides the pathogenic species with nutrients, and decreasing PD, which also serves as a reservoir of pathogens. This points

to the significance of periodic maintenance care in the treatment of periodontal diseases, especially aggressive periodontitis.

CONCLUSIONS

Scaling and root planing has a lasting suppressive effect on periodontal pathogens associated with aggressive periodontitis.The reduction in the bacterial load and the concomitant reduction in inflammation and probing depth seen at 6 months were basically maintained at 1 year.

Bacterial repopulation of treated periodontal pockets may be a risk factor that diminishes the effect of non-surgical mechanical therapy in the absence of maintenance care. Changes in levels of Aa and Pg might serve as a predictor of disease recurrence in patients not receiving supportive therapy.

To prevent recolonization and overgrowth of periodontal pathogens, maintenance therapy is absolutely necessary.

ACKNOWLEDGMENT

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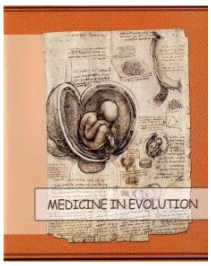
REFERENCES

1. OniseiDoina, Onisei Dan, Parodontologieclinică, EdituraMirton, Timişoara, 2011.
2. Armitage GC. Comparison of the microbiological features of chronic and aggressive periodontitis. Periodontol 2000 2010;53:70-88.
3. Deas DE, Mealey BL. Response of chronic and aggressive periodontitis to treatment. Periodontol 2000 2010;53:154-166.
4. Rosalem W, Rescala B, Teles RP, Fischer RG, Gustaffson A, Figueredo CM, Effect of non-surgical treatment on chronic and agressive periodontitis: clinical, imunologic and microbiologic findings. J Periodontol. 2011 Jul; 82(7):979-89. Epub 2011 Feb 10.
5. Cugini MA, Haffajee AD, Smith C, Kent RL Jr, SocranskySS. The effect of scaling and root planing on the clinicaland microbiological parameters of periodontal diseases:12-month results. J ClinPeriodontol 2000;27:30-36.
6. Boutaga K, van Winkelhoff AJ, Vandenbroucke-Grauls CM, Savelkoul PH. The additional value ofreal-time PCR in the quantitative detection of periodontal pathogens. J Clin Periodontol 2006;33:427-433.
7. Johnson JD, Chen R, Lenton PA, Zhang G, HinrichsJE, Rudney JD. Persistence of extracrevicular bacterial reservoirs after treatment of aggressive periodontitis. J Periodontol 2008;79:2305-2312.
8. Carranza F.A., Takei H.H –Clinical Diagnosis 540,"Carranza's Clinical Periodontology", Saunders Elsevier, 2007
9. Carranza F.A., Takei H.H –Clinical Diagnosis, 626,"Carranza's Clinical Periodontology", Saunders Elsevier, 2007
10. Danser MM, Timmermann M, van Winkelhoff AJ, van der Velden U. The effect of periodontal treatment on periodontal bacteria on the oral mucous membranes. J Periodontol 1996;67:478-485.
11. Socransky SS, Smith C, Haffajee AD. Subgingivalmicrobial profiles in refractory periodontal disease.J ClinPeriodontol 2002;29:260-268

UP TO DATE CONCEPTS IN THE THERAPY OF AGGRESSIVE PERIODONTITIS.A SYSTEMATIC REVIEW



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ABSTRACT

Aim and objectives: *Periodontal therapy usually begins with a non-surgical phase, including scaling and root planing (SRP) and, occasionaly, with the use of systemic antibiotics. The aim of this review is to evaluate the data regarding the effect of adjunct systemic antibiotics on periodontal therapy in patients with aggressive periodontitis.*

Material and methods: *The JOP online data base was searched to identify appropriate studies. Eligibility criteria established led to a selection of full-text articles. Only the latest four studies were analyzed and processed.*

Results: *Changes in clinical parameters and microbiologic data were followed for each of the study and presented regarding the effect of the combination of amoxicillin-metronidazole associated with periodontal therapy.*

Conclusions: *The use of amoxicillin-metronidazole as an adjunct to non-surgical mechanical therapy can enhance the clinical results in the treatment of aggressive periodontitis.*

Key words: *aggresive periodontitis, SRP, amoxicillin, metronidazole*

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INTRODUCTION

Aggresive periodontitis is a complex periodontal disease characterized by a rapid destruction of the periodontium, leading to early tooth loss in young adults, otherwise healthy. As a infectious inflammatory disease, it is associated with the presence of certain microbial species, such as Aggregatibacter actynomicetemcomitans, Porphyromonas gingivalis, Treponema denticola and Tanerella forsythia, although other factors such as neutrophil function abnormalities and a poor antibody serum response to infecting agents are frequently detected in patients with aggressive periodontitis. [1]

The goal of periodontal therapy is to eliminate the microbial etiology, thereby arresting the progression or recurrence of the disease. It is well known that completion of scaling and root planing (SRP) and a good plaque control are essential in the treatment of periodontal disease [2]. However, in cases of aggressive periodontitis, only mechanical non-surgical treatment does not always provide the expected results. Current treatment strategies recommend the adjunctive use of systemic antibiotics. Especially the combination of amoxicillin plus metronidazole is highly documented in several studies. [3,4]

The reason for the use of systemic antibiotics in the therapy of aggressive periodontitis is to rapidly suppress or eliminate multiple bacterial species leading to a better stability of the microbiota and an improved host response.

The aim of the present paper is to compare and evaluate the available literature regarding the efficacy of the combination of amoxicillin and metronidazole as an adjunct to non-surgical mechanical therapy in cases of aggressive periodontitis.

MATERIAL AND METHODS

Focused Question

The focused question of this systematic review was: ` Does the combination of amoxicillin and metronidazole improve the clinical outcome of non-surgical mechanical treatment in patients with aggressive periodontitis?`

Search Strategy

The search aimed to identify randomized, controlled clinical trials that studied the efficacy or clinical outcomes of the use of amoxiciline and metronidazole as an adjunct to periodontal non-surgical therapy in cases of aggressive periodontitis. The JOP database was searched using as key words `aggressive periodontitis/amoxicillin and metronidazole`. The database was searched from its earliest records until march 2015. The most recent articles were selected and analysed.

Eligibility criteria and selection strategy

The following eligibility criteria was imposed for inclusion in this review: 1) randomized controlled clinical trials or controlled clinical trials ; 2) patients diagnosed with aggressive periodontitis in good general health ; 3) treatment consisting of SRP or full-mouth debridement in association with systemic use of the combination of amoxicillin and metronidazole ; 4) clinical parameters as probing depth (PD) and clinical attachement loss (CAL) as well as microbiologic data as outcome parameters ; 5) presenting the data pre- and post-treatment including a follow-upfor ≥ 1 month ; 6) latest studies (within the past five years).

The studies were screened by two reviewers, independently, initially by

title and abstract. Case reports, consenses and history reviews were excluded. If the search key words and the eligibility criteria were present in the title or abstract, the article was selected for full-text reading. Finally,four recent studies were selected and processed for data extraction, in order to have an up to date view. [4,5,6,7]

RESULTS

The search resulted in 88 recent studies and reviews in the JOP data base. The screening of titles and abstracts resulted in 14 full-text articles. After full-text reading,8 articles were excluded after applying the eligibility criteria. 2 reviews were included as major references. Only four recent studies were used for data procession.

Generally, a considerable heterogeneity in the design, duration and regimen of mechanical treatment were present. The number, age and sex of the participants also varied among the studies. All the studies were randomized.

The evaluation period varied among the studies from 45 days to one year.

Clinical parameters` evolution in each of the four studies included plaque index (PI), bleeding on probing (BOP), probing depth (PD), clinical attachment level (CAL). One of the studies [6] also registered values for gingival index (GI) while another study [7] determined also the relative gingival margin position (GMP), gingival crevicular fluid (GCF) concentration of IL-10 and IL-1β. Recession and supuration were also considered in one of the studies [8]. The following bacterial species were assesed: Aggregatibacter actynomicetemcomitans (Aa), Porphyromonas gingivalis (Pg), Treponema denticola (Td), Tanerella forsythia (Tf) and Dialister pneumosintes, at baseline and 45 days after SRP and adjunctive use of amoxicillin and metronidazole [5], Aa, Pg, Td, Tf, Prevotella intermedia (Pi), Prevotella nigrescens, Prevotella pallens among two groups of patients (control group who received only SRP and test group who received the combination of amoxicillin-metronidazole and SRP) at baseline, 3 and 6 months post-therapy [6], Aa, Pg and Tf at baseline, 3 months and 6 months after therapy for study groups (full-mouth ultrasonic debridement (FMUD) group and FMUD plus amoxicillin-metronidazole combination) [7]. Only one of the four studies [8] was a randomized placebo-controlled crossover clinical trial with a 1-year follow-up in which all eighty subjects had Aa present at baseline. The effect of antibiotics (500 mg metronidazole plus 375 mg amoxicillin three times per day for 7 days) was tested on two groups of subjects in different phases: one group received antibiotics during the first, non-surgical phase of periodontal therapy and placebo during the second, surgical phase,while the other group, placebo during periodontal therapy and antibiotics during surgical phase. Clinical parameters (PD and BOP) were monitored.[8]

The results of the four studies are relatively different. In one study [5] all clinical parameters improved significantly after 3 months post-therapy, with the exception of CAL. Furthermore, the combination of antibiotics seemed to result in a significant decrease in level of pathogens. [5]. The two studies which compare two groups of subjects [6,7] report better clinical results in the test group which received the combination of amoxicillin and metronidazole as an adjunct to the clinical procedure. The study which compares the effect of antibiotics in different phases of periodontal therapy [8] shows that antibiotics prescribed in the first non-

surgical phase of periodontal therapy reduce, in most cases, the need of surgical intervention.

DISCUSSIONS

This study evaluates the effects of the systemics use of antibiotics, namely the combination of amoxicillin-metronidazole,in different clinical procedures during the non-surgical phase of periodontal therapy. Limitations of the analyzed studies are evident. This is due to the heterogeneity of the selected studies. Many additional factors are not taken into consideration, such as the influence of risk factors or efficacy of plaque control.

Furthermore, the short follow-up time in three of the four studies [5,6,7] it may not be as relevant as considered for the real evolution of periodontal disease. Therefore, recording clinical and microbiologic data before 12 months has questionable value.

The core of our research is that essentially all studies of the adjunctive effect of antibiotic therapy in the treatment of aggressive periodontitis should be applied taking into consideration the patient`s microbiological status and environmental host-interractions.

CONCLUSIONS

The evidence resulting from this review indicates that the combination of amoxicillin and metronidazole improves clinical and microbiologic results of non-surgical periodontal therapy, in cases of aggressive periodontitis. However, before considering antibiotic treatment as an adjunct to mechanical therapy, one should consider that just as the mechanical therapy may fail to remove all the subgingival biofilm from anatomically difficult sites, so will indeed the antibiotic since microorganisms in a biofilm are not readily affected.

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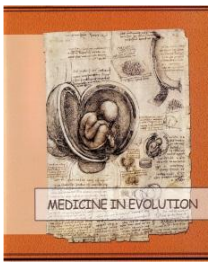
REFERENCES

1. Onisei Doina, Onisei Dan, Parodontologie clinică, Editura Mirton, Timişoara, 2011.
2. American Academy of Periodontology. Comprehensiveperiodontal therapy: A statement by the AmericanAcademy of Periodontology. J Periodontol 2011;82:943-949.
3. Zandbergen D, Slot DE, Cobb CM, Van der WeijdenFA. The clinical effect of scaling and root planingand the concomitant administration of systemicamoxicillin and metronidazole: A systematic review.J Periodontol 2013;84:332-351.
4. Sgolastra F, Petrucci A, Gatto R, Monaco A. Effectivenessof systemic amoxicillin/metronidazole as anadjunctive therapy to full-mouth scaling and rootplaning in the treatment of aggressive periodontitis:A systematic review and meta-analysis. J Periodontol2012;83:731-743.
5. Rodrigues A. S., Lourencxao D. S.,Lidio G. Lima N., Claudio M. P.,Clinical and Microbiologic Evaluation by Real-Time Polymerase

Chain Reaction, of Non-Surgical Treatment of Aggressive Periodontitis Associated With Amoxicillin and Metronidazole, J Periodontol 2012;83:744-752.
6. Emine Cifcibasi Yek, Serdar Cintan, Nursen Topcuoglu, Guven Kulekci, Halim Issever, Alpdogan Kantarci,Efficacy of Amoxicillin and MetronidazoleCombination for the Management of Generalized Aggressive Periodontitis, J Periodontol2010;81:964-974.
7. Renato C.V. Casarin, Erica Del Peloso Ribeiro,Enilson A. Sallum, Francisco H. Nociti Jr.,Reginaldo B. Goncxalves, Marcio Z. Casati, The Combination of Amoxicillin andMetronidazole Improves Clinical andMicrobiologic Results of One-Stage,Full-Mouth, Ultrasonic Debridementin Aggressive Periodontitis Treatment, J Periodontol 2012;83:988-998.
8. Andrea Mombelli, Adnan Almaghlouth, Norbert Cionca, Delphine S. Courvoisier, Catherine Giannopoulou, Differential Benefits of Amoxicillin–Metronidazole in Different Phases ofPeriodontal Therapy in a RandomizedControlled Crossover Clinical Trial, J Periodontol2015;86:367-375.



CORTICAL BONE THICKNESS EFFECTS ON THE SUCCESS RATE OF ORTHODONTIC MINI-IMPLANTS AND OTHER FACTORS ASSESSED BY CONE BEAM COMPUTED TOMOGRAPHY.

POPA ADELINA, SZUHANEK CAMELIA, BRAD SILVIU

Faculty of Dental Medicine, University of Medicine and Pharmacy"Victor Babes"Timișoara

ABSTRACT

***BACKGROUND**:The purpose of this study was to determine the optimal sites for mini-implant placement in the maxilla and the mandible, based on the thickness of the cortical bone and correlate it with other factors that influence the success rate of orthodontic mini-implants.*

***MATERIAL and METHODS:**We summarize the knowledge from published clinical trials regarding the cortical bone thickness at common mini-implant placement sites. We present our clinical cases comparing the results assessed by cone beam computed tomography, with the international published reviews.*

***RESULTS**:The thickness of alveolar cortical bone differs in different parts of the jaws. Buccal cortical bone thickness was greater in the mandible than in the maxilla. The maxillary cortical bone is thicker in the palate compared to the buccal surface. The highest buccal cortical thickness in the maxilla was between the first and second premolars.In the mandible cortical bone thickness increases from anterior to posterior. The highest buccal cortical thickness was between the first and second molars.*

***CONCLUSIONS**: A combination of clinical, animal and artificial bone studies has demonstrated that the most important patient determinants of primary stability are the density and thickness of the cortical plates. It was concluded that the posterior area is the best site for inserting mini-implants. The buccal alveolar bone between the first premolar and first molar in the maxilla and the interradicular spaces from the first premolar and second molar in the mandible were found to be adequate for orthodontic mini-implants.*

***Key words:** orthodontic mini-implants, CBCT, cortical thickness, orthodontics*

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INTRODUCTION

Skeletal anchorage is possibly one of the most important advances in recent times in the field of orthodontics. Mini-implants have become increasingly popular as source of stable anchorage because of their versatility, minimal invasiveness and low cost.

They can be loaded immediately after insertion and they can provide absolute anchorage for many types of orthodontic treatment with no need for special patient compliance.

Many variables that affect the stability of orthodontic mini-implants are still poorly understood.

According to Raed Alrbata: THE SINGLE MOST IMPORTANT FACTOR FOR THE SUCCES OF THE MINI-IMPLANT IS BONE !

Costa et al [3] and Miyawaki et al [4] reported that cortical bone quality and quantity are major factors associated with primary stability of orthodontic mini-implants. Wilmes et al[5] found that cortical bone thickness has a strong effect on the primary stability of mini-implants.

Clinically, mini-implant failures have been reported to result from thin cortical bone.

According to Miyamoto et al [12] cortical bone thickness plays a greater role in determining stability than implant length.

STUDY OBJECTIVES

The purpose of this study was to determine the optimal sites for mini-implant placement in the maxilla and the mandible based on the thickness of the cortical bone and correlate it with other factors that influence the success rate of orthodontic mini-implants.

MATERIAL AND METHODS

Pretreatment cone beam computed tomography scans using Cranex Sordex 3D were taken to evaluate 10 orthodontic patients. The CBCT scans were imported into 3-dimensional software for analysis as digital imaging.(OnDemand3App with the 3D Dentar).(fig 1).

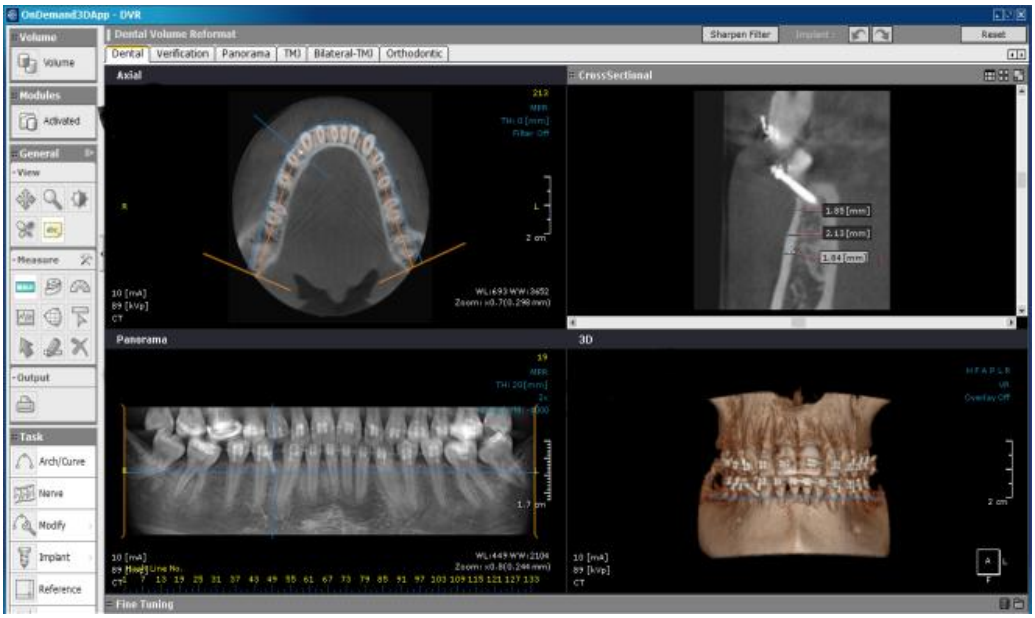


Figure 1. OnDemand3DApp

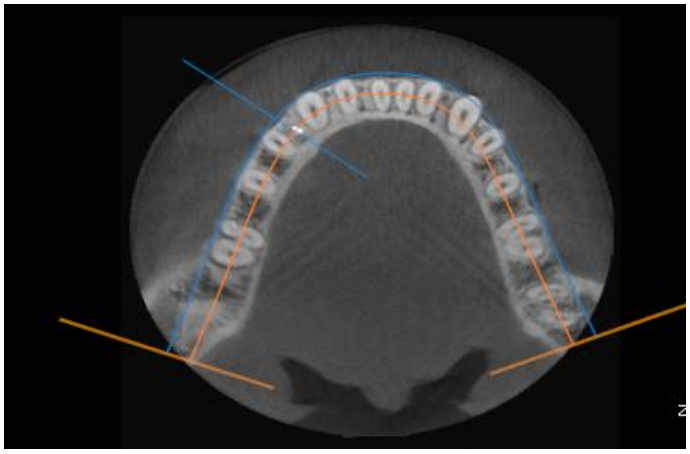


Figure 2. Axial slice orientation,with the reference line perpendicular to the cortical bone

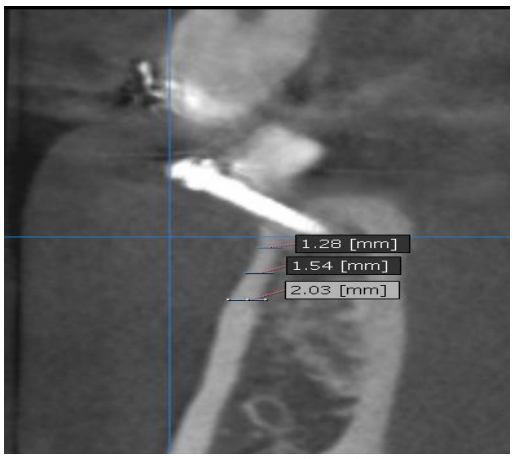


Figure 3. Two-dimensional interdental slice showing cortical and trabecular bone with measurements of buccal cortical bone thickness

Cortical bone thickness was measured in 4 interradicular areas between: lateral incisor and canine, first and second premolars, second premolar and first molar and first and second molars.

The distance between the internal and external aspects of the cortex, in the middle of the interradicular distance between each two adjacent teeth was measured bucally and lingually/palatally

The interradicular measurements were made 4 mm apical to the alveolar crest, which is approximately at the level of the mucogingival junction.

The interradicular sites selected for measurement had been previously used for orthodontic mini implant placement.

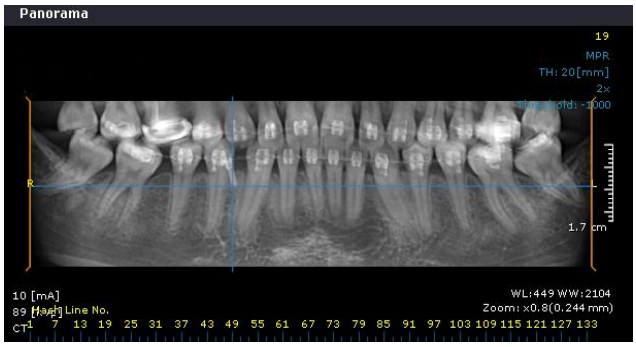


Figure 4. 2D Panorama

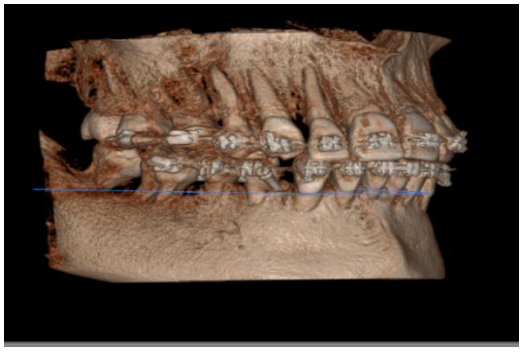


Figure 5. Dental 3D

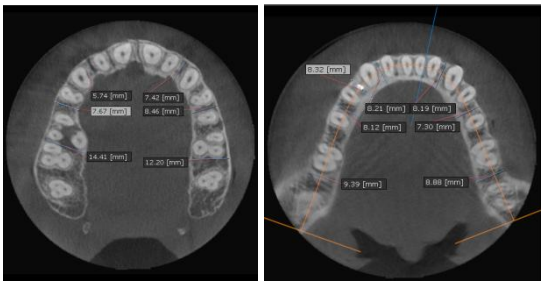


Figure 6. Maxilla and mandibula sagittal slice orientation

RESULTS AND DISCUSSIONS

The mandible provides more buccal cortical bone than the maxilla. Baumgaertel et al [2] and Friberg et al found similar results, they reported more compact cortical bone in the mandible than in the maxilla.

The mandibular buccal region had the thickest cortical bone of all regions evaluated.This has been previously reported by Farnswort et al [1], Peterson et al [7] and Schwartz et al [8].

The cortical bone in the mandibular buccal region was thicker than the cortical cone in the maxillary buccal and lingual regions: [1,9,10]Cortical bone thickness in the mandibular buccal regions increases from anterior to posterior. Cortical thickness has been previously reported to decrease from posterior to anterior [1, 8-11].

The highest buccal cortical thickness in the maxilla was between the first and second premolars. The highest buccal cortical thickness in the mandible was between the first and second molars

Other factors that influence the success rate of orthodontic mini-implants that can be assessed using CBCT are: insertion torque, interradicular space (mesiodistal distance and buccolingual thickness), distance from CEJ, bone density, insertion angle

CONCLUSIONS

It is important to be aware of the differences in cortical bone thickness between and within regions of the jaws.

Thicker cortical bone has been reported for the mandible than the maxilla.

There are differences in each jaw, with the thickest cortical bone in the molar region, followed by the premolar and incisor region respectively [7,8,11]

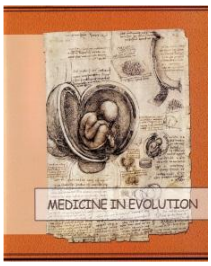
Interdental buccal cortical bone thickness varies in the jaws.

The optimal site for mini-implant placement in the anterior region is between the lateral incisor and the canine in the mandible.In the posterior region of both jaws the optimal sites are between the second premolar and first molar and between the first molar and second molar.

REFERENCES

1. David Farnsworth,a P. Emile Rossouw,b Richard F. Ceen,c and Peter H. Buschangd Gilbert,: Cortical bone thickness at common miniscrew implant placement sites
2. Sebastian Baumgaertela and Mark G. Hans: Buccal cortical bone thickness for mini-implant placement
3. Costa A, Raffainl M, Melsen B. Miniscrews as orthodontic anchorage: a preliminary report. Int J Adult Orthod Orthognath Surg 1998;13:201-9.
4. Miyawaki S, Koyama I, Inoue M, Mishima K, Sugahara T, Takano-Yamamoto T. Factors associated with the stability of titanium screws placed in the posterior region for orthodontic anchorage. Am J Orthod Dentofacial Orthop 2003;124:373-8.
5. Wilmes B, Rademacher C, Olthoff G, Drescher D. Parameters affecting primary stability of orthodontic mini-implants. J Orofac Orthop 2006;67:162-74.
6. Motoyoshi M, Yoshida T, Ono A, Shimizu N. Effect of cortical bone thickness and implant placement torque on stability of orthodontic mini-implants. Int J Oral Maxillofac Implants 2007;22:779-84.
7. Peterson J, Wang Q, Dechow PC. Material properties of the dentate maxilla. Anat Rec A Discov Mol Cell Evol Biol 2006;288:962-72.
8. Schwartz-Dabney CL, Dechow PC. Variations in cortical material properties throughout the human dentate mandible. Am J Phys Anthropol 2003;120:252-77.
9. Ono A, Motoyoshi M, Shimizu N. Cortical bone thickness in the buccal posterior region for orthodontic mini-implants. Int J Oral Maxillofac Surg 2008;37:334-40.
10. Deguchi T, Nasu M, Murakami K, Yabuuchi T, Kamioka H, Takano-Yamamoto T. Quantitative evaluation of cortical bonethickness with

computed tomographic scanning for orthodontic implants. Am J Orthod Dentofacial Orthop 2006;129:721.e7-12.
11. Katranji A, Misch K, Wang HL. Cortical bone thickness in dentate and edentulous human cadavers. J Periodontol 2007;78:874-8
12. Miyamoto I, Tsuboi Y, Wada E, Suwa H, Iizuka T. Influence of cortical bone thickness and implant length on implant stability at the time of surgery—clinical, prospective, biomechanical, and imaging study. Bone 2005;37:776-80.



ROLE OF SALIVARY AND MICROBIOLOGICAL TESTS IN CARIOUS RISK ASSESSMENT OF A GROUP OF 7 YEARS OLD SCHOOLCHILDREN IN BUCHAREST

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ABSTRACT

***Aim and objectives**: The aim of this study was evaluation of carious risk assessment at a group of elementary school children in Bucharest using Cariogram as a multifactorial prediction model. **Materials and method**: The study was realized on December 2014, on a sample of 45 elementary school children (fete, 51.1%). from Bucharest. Dental status and plaque level were assessed thorough clinical examination in the school dental office using ICDAS coding system and OHI-s Index. Also, there were evaluated salivary and microbiologic parameters, qualitative and quantitative. Diet and fluoride intake were evaluated using a questionnaire.*

***Results:** For temporary dentition, caries prevalence was 82.22% and the mean values for def-t and def-s were 3.33 and 5.16. For permanent dentition, the caries prevalence was 26.66% and the mean value for DMF-T and DMF-S was 0.33. Mean value of OHI-s Plaque Index was 0.91,. Streptococcus Mutans were found at a high level at 75.6% of children. Salivary flow had a mean value of 0.72ml/min, pH – 7. The buffer capacity had a normal or high values for almost all children. Most children are at medium risk for developing new caries – 40%; one third have a high risk – 27%.*

***Conclusions:** According to the multifactorial prediction model used, one third of the children evaluated are at high risk to develop new caries and the the risk factors with the highest impact in this group – affecting two thirds of children, are microbiologic – levels of salivary S. Mutans, behavioral, like oral hygiene, and physical, fluoride administration.*

***Key words:** carious risk, salivary and microbiological factors, caries prevalence*

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INTRODUCTION

Dental caries predictability using risk assessment and classification of the population in risk categories is useful in oral health to be applied not only at the community level but also individually, as long as there is a necessity of prioritizing our prevention actions in communities and of influencing our decision-making in the treatment plan for each person. Framing the population in risk groups helps identifying the group that needs our efforts to be focused on.

Among the dental caries risk factors, some are modifiable, others are not and for those that are, specialist can take actions to minimize them. In order for these actions to be efficient, there must be determined which risk factors prevail in each target group.

Carious experience is one of the prediction factors for developing future caries and as a single predictor it gives the most accurate prediction results. In children, the most accurate prediction results are when the temporary caries experience is taken into consideration, instead of the first permanent molar caries experience[4,5].

Saliva is analyzed as part of the risk assessment due to the negative correlation between salivary parameters values and carious risk, but, because of the low sensitivity of the salivary tests, they cannot be used as singular predictors [8].

Microbiologic tests are used to reveal the levels of Streptococcus Mutans and Lactobacilli due to their positive correlation with number of caries. However, tests results for Lactobacilus evaluation has a low accuracy in caries prediction and tests results for S. Mutans have an accuracy not higher that caries experience accuracy in caries prediction, microbiologic tests having the drawback of high costs[8].

Fluoride intake influences carious risk, not only through the higher enamel mineralization level but also through the inhibitory effect on the metabolism of the cariogenic microorganisms in a presence of sugars. Taking this into consideration, fluoride is indicated, irrespective of the way it is delivered – systemic or local (locally delivered showing a greater impact in erupted teeth that systemic during the intra-osseous development)[8].

Dietary assessment is useful for revealing the quantity and frequency of sugars consumption, their impact in caries development being well known. There are limits in the accuracy of data collected about diet in cases of short period recordings and especially if the recordings are based only on patients' statements[8].

Oral hygiene is evaluated for the risk assessment using as objective parameter Plaque Index but it is also helpful to assess self-reported oral hygiene behavior in order to correct it if necessarry[8 9].

Taking into consideration the interference and summing of all these risk factors for cavities development, there have been initiated and applied plenty of multifactorial prediction models. A Cochrane study published in 2013 shows that multifactorial prediction models have a higher accuracy applied on preschool children that on elementary school children and teenagers and that single predictors like socio-economic status and caries experience are more accurate and more efficient than plaque level or diet, and least accurate – salivary tests [4,7.]

Nevertheless, only few prediction models are very precise [3,4]and Cariogram shows its utility when applied at preschool children[3]. This software generates a chart that reveals the interference of risk factors and the chances for developing new cavities in the future, specifically for each person, and not only sums the effect of each risk factor but also gives each factor a weight for the total effect [1.4]. Cariogram

is indicated, thus, in presenting the patient their risk, the prevailing factors and the necessary preventive measures.

Aim and objectives

The aim of this study was evaluation of carious risk assessment at a group of elementary school children in Bucharest. The objectives established were as follows:

- assessment of caries experience and plaque level, through clinical examination
- assessment of exposure levels to behavioral factors – diet and oral hygiene, through questionnaire, microbiological factors – through microbiological tests, and host-related factors: saliva (qualitative and quantitative) – through salivary tests and fluoride intake – through questionnaire.

MATERIAL AND METHODS

The study was realized on December 4th-11th 2014 by the Department of Oral Health and Community Dentistry of the Faculty of Dentistry,"Carol Davila"Medicine and Pharmacy University, Bucharest, both academic staff and 6th year students. In the study, there were included 45 elementary school children from"Mihai Eminescu"School in Bucharest. Ethical consent was given by the University Ethical Commission, Hospital and medical Services Administration of Bucharest, Schools Inspectorat, staff of school and informed consent of parents of the participant children. The dental status and the plaque level were evaluated during the clinical examination that took place in the school dental office. Caries assessment was performed using the ICDAS coding system (International Caries Detection and Assessment System) and the plaque level was assessed using OHI-s Index – (Oral Hygiene Index – simplified).

Also, in the dental office there was analyzed microbiological and salivary parameters. Saliva was evaluated from quantitative point of view – unstimulated salivary flow: saliva was collected in graduated containers for 5 minutes. From the qualitative point of view, there was evaluated salivary pH and buffer capacity using salivary tests produced by GC (Saliva Check Buffer). The levels of Streptococcus Mutans were assessed using microbiological tests produced by GC (Saliva Check Mutans).

Diet and fluoride intake were evaluated using a questionnaire consisting of close-ended questions and applied with investigation operators represented by 6th year dental students. Regarding the diet, questions referred to the frequency of daily meals and their consistency. Regarding the fluoride intake, the questions asked about the products used and the way of delivery. Evaluation sessions were followed by oral health lessons offered to children included in the study. Data were collected and processed using SPSS and the carious risk was established using Cariogram.

RESULTS

The subjects were equally represented by female – 51.1% and males – 48.9%, with a mean age of 7 years, all of them in the first grade.

Regarding the carious experience, the caries prevalence was 82.22% for temporary dentition and 26.66% for permanent dentition. When it comes to caries index, for the temporary teeth, the mean def-t was 3.33 and def-t was 5.16. For permanent teeth, the mean DMF-T and DMF-s was 0.33.

When we analyzed the differences in caries experience

between sexes, the resulted showed that boys have temporary teeth more affected than girls but less permanent teeth affected by caries than girls. These differences, still, are not statistically significant. (t-test for independent samples – $p>0.05$)

When it comes to the diet, the frequency of daily meals was, for the most of the subjects, 5 intakes per day – 60%. One third of children – 38%, have only 3 intakes per day (Graph 1). As for the content of their meals, children report a similar consumption of food that induce caries and protects teeth against them. (Graph 2).

When it comes to plaque levels, results show an avarage value of OHI-s Plaque index of 0.91, thus a satisfactory oral hygiene. Only 17.8% of children had no plaque on the examined teeth, most of them – two thirds, having plaque on the cervical third of teeth (Graph 3)

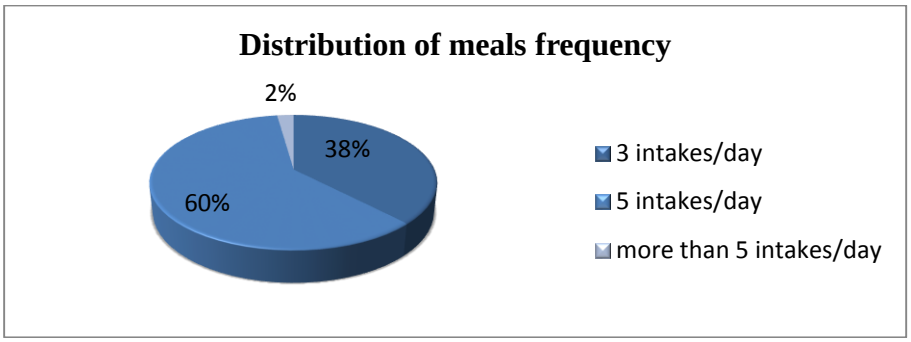

Chart 1. Distribution of meals frequency

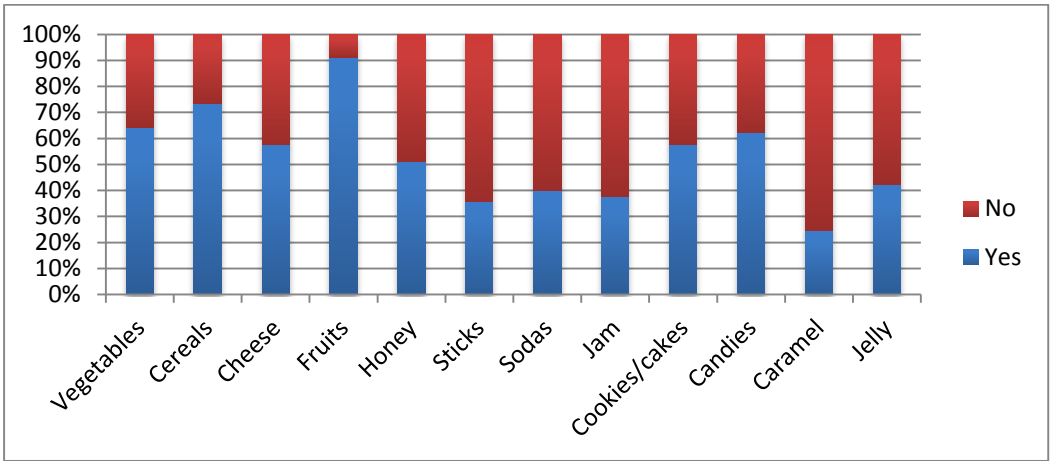

Chart 2. Distribution of food consumed daily

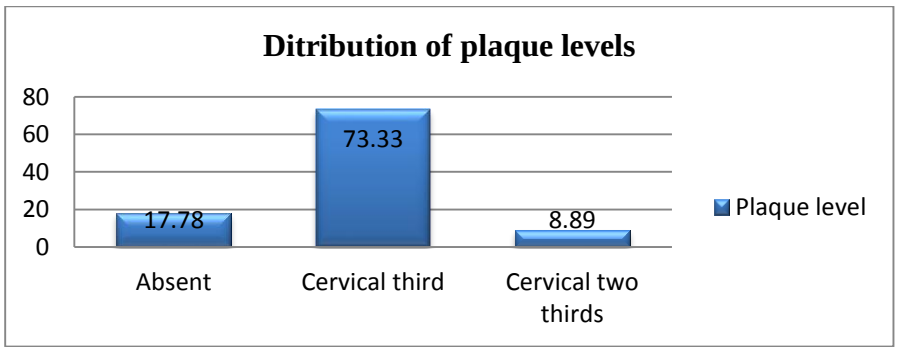

Chart 3. Distribution of plaque levels

About the fluoride intake, two thirds of children are offered fluoride only through toothpaste. 2 out of 10 children use additional fluoride through secondary oral hygiene products. Only 7% of children use fluoride through products mentioned

before and also systemically delivered fluoride (Graph 4).

Salivary analyze revealed a mean salivary flow of 0.72ml/min and a mean pH – 7. The buffer capacity was found normal for more than half of children (55%) and even high for one third (38%).

Regarding the level of salivary Streptococcus Mutans, high levels (greater than 100.000 CFU) were found at 75.6% of children. Comparing boys and girls from risk factors point of view, the results showed that boys have higher S. Mutans levels, pH and a lower salivary flow but they have higher fluoride intake. Plaque index had similar values for both sexes. So statistically significant correlations were found between mean DMF and risk factors like S. Mutans levels, salivary flow / pH / buffer capacity, meals frequency, fluoride intake.

A statistically significant correlation was, however, found between plaque index and def-s mean value (Pearson correlation coefficient r = 0.415, p=0.005). According to this, children with a higher level of plaque had, also,

a greater number of surfaces affected by caries.

For each child, there was established the carious risk, based on the parameters analyzed, using Cariogram. Most of the children had a medium risk of developing new caries – 40%. One third were found with a high risk and 27% with a low risk (Graph 5).

For the entire group, on average, the chances of avoiding new caries in the future were 50.91%, which represents a medium risk.

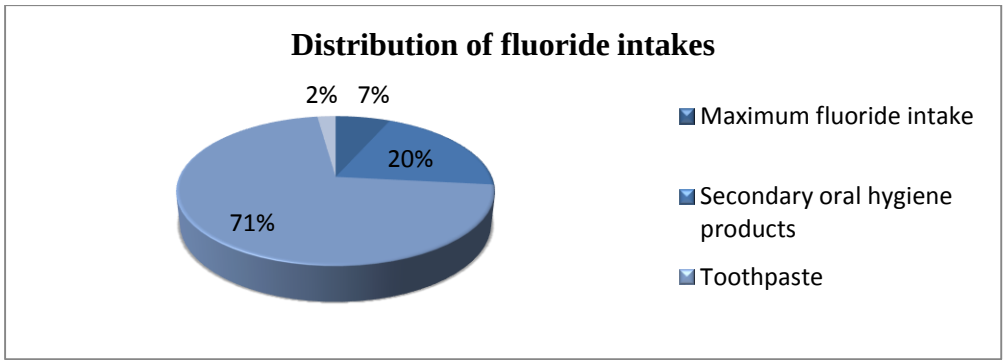

Chart 4. Distribution of fluoride intakes

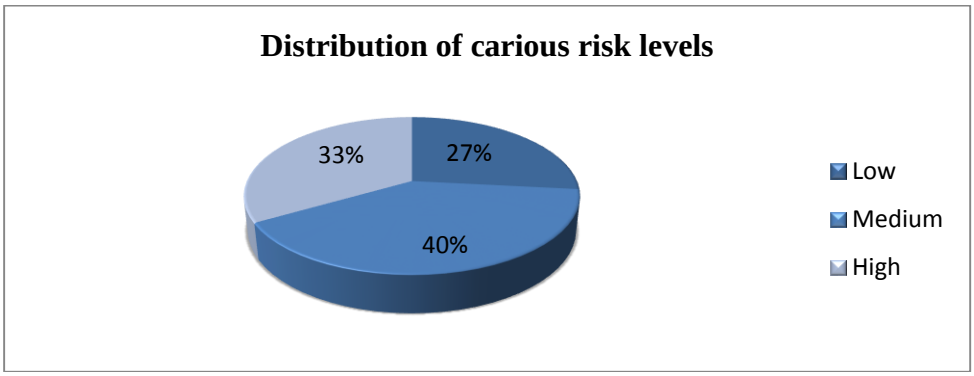

Chart 5. Distribution of carious risk levels

DISCUSSIONS

Among the children evaluated, one third have a high risk for developing new caries and they represent the priority target group.

Among the risk factors with the lowest impact was saliva properties (salivary flow, pH, buffer capacity), which are of normal values. Risk factors with a medium impact was diet, children having a normal meals frequency per day and a similar consumption of protective and dangerous food. The products rich in sugars, that children eat most frequently and are recommended to be avoided are cookies, cakes and candies. The risk factors with the highest impact in this group – affecting two thirds of children, are microbiologic – levels of salivary S. Mutans, behavioral – oral hygiene, and physical - fluoride administration. The recommendations are for children to enhance their oral hygiene practices and also to b administered antiseptic products and fluoride supplements.

When it comes to the most important predictor – caries experience, it is significant for this group, due to the fact that a high number of children are affected by caries and in addition, each children have a high number of teeth affected. Although the prevalence and the mean of caries indices for temporary and permanent teeth at their age (7 years) is lower than mean values reported at national level [2,6], the values are higher than the objectives established by WHO for year 2020 [2].

CONCLUSIONS

According to the multifactorial prediction model used, one third of the children evaluated are at high risk to develop new caries and the risk factors most frequently found were inappropriate oral hygiene, which must be improved, and also high microbiological load and low fluoride intake, thus the necessity of delivery, not only in the dental office, but also home, of antiseptic and fluoride products.

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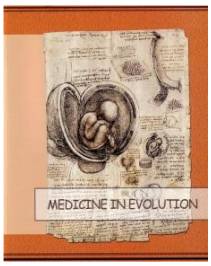
REFERENCES

1. Cabral RN, Hilgert LA, Faber J, Leal SC. Caries risk assessment in schoolchildren - a form based on Cariogram® software. J Appl Oral Sci. 2014;22(5):397-402
2. Dumitrache MA, Sfeatcu IR, Buzea CM, Dumitrascu LC, Lambescu DG. Concepte si tendinte in sanatatea orala. Ed. Universitara"Carol Davila"Bucuresti, 2009
3. Gao XL, Hsu CY, Xu Y, Hwarng HB, Loh T, Koh D. Building caries risk assessment models for children. J Dent Res. 2010;89(6):637-43
4. Kemparaj U, Chavan S, Shetty NL. Caries risk assessment among school children in davangere city using cariogram. Int J Prev Med. 2014;5(5):664-71
5. Mejàre I, Axelsson S, Dahlén G, Espelid I, Norlund A, Tranæus S, Twetman S. Caries risk assessment. A systematic review. Acta Odontol Scand 2014;72(2):81-91
6. Petersen PE, Danila I, Delean A, Grivu O, Ionita G, Pop M, Samolia A. Oral health status among schoolchildren in Romania, 1992. Community Dent Oral Epidemiol. 1994;22(2):90-3
7. Sánchez-Pérez L, Golubov J, Irigoyen-Camacho ME, Moctezuma PA, Acosta-Gio E. Clinical, salivary, and bacterial markers for caries risk assessment in schoolchildren: a 4-year follow-up. Int J Paediatr Dent. 2009;19(3):186-92.
8. Yip K, Smale R. Oral diagnosis and treatment planning: part 2. Dental caries and assessment of risk. Br Dent J. 2012;213(2):59-66.
9. Galuscan A, Jumanca D, Vasile L, Podariu AC, Ardelean L, Rusu LC, Clinical Antibacterials Inhibitors used in Toothpaste, Rev. Chim. (Bucharest): 63: No. 7:2012.



CARIES PREVALENCE AMONG CHILDREN AND ADOLESCENCE WITH TYPE 1 DIABETES ATTENDING ONE DIABETIC CENTER IN ROMANIA

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ABSTRACT

The main objective of this study is to determine the prevalence of dental caries in type I diabetic children and adolescents.

Material and methods: 116 patients (65 girls and 51 boys, mean age 12.81, SD 3.74) with type I diabetic referred to Medical Centre for children and adolescents"Cristian Serban"Buzias were included in this study from May 2014 until April 2015. Controls were 116 healthy students matched for age and sex. According to age diabetic patients and controls were divided in 4 groups: 6 to 8 years, 9 to 11 years, 12 to 14 years and 15 to 18 years. The DMF index (WHO,1987), gingival index (GI) and calculus index (CI) were evaluated. Data obtained from each group were compared statistically using independent sample t-test.

Results showed that the total mean value of caries experience by the diabetic group (DMFT=5.79, SD=2.639) was higher than that of the control group (DMFT=4.74, SD=2.955) with significant differences ($p<0.01$). Also for each age group the mean value of DMFT was higher than in controls. The gingival index (GI) among diabetic patients was higher than the control group. The total mean value of simplified debris index in control group was higher than the diabetic group. calculus index was higher in diabetic group with a significant difference between them at age group 12-14.

Conclusion: Caries experience was significantly higher in children with type 1 diabetes than in non-diabetic controls.

Key words: *caries prevalence, diabetes, children, adolescence*

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INTRODUCTION

Dental caries is an infectious disease resulting in destruction of mineral tooth structure by acid-forming bacteria found in dental plaque, an intra-oral biofilm. Diabetes mellitus is the most common endocrine disorder and this means a condition of impaired carbohydrate utilization (impaired glucose tolerance) caused by an absolute or relative deficiency of insulin from variety of causes. In Diabetus mellitus (DM) the balance and metabolism of energy is disturbed for lack of secretory insulin or functional disorders, which would lead to an abnormal metabolism of carbohydrates, protein, and fat [1].

Diabetes Mellitus has an effect on the oral cavity as patients with uncontrolled diabetes have been observed to be more prone to inflammation of highly vulnerable mucosa, due to a decreased systemic immunity and disturbed function of polymorph nuclear lymphocytes, which represent first-line defense of the oral cavity and the whole body against bacterial toxins [2].

The relationship between type 1 diabetes mellitus (DM) and caries experience is controversial. For example, it has been reported that inadequate control of DM resulted in higher caries experience in Lithuania, Turkey, Sweden and Italy. This has been said to be due to excess sugar secreted into saliva of hyperglycemia patients [3-6].

On the other hand, some studies have failed to demonstrate any association between metabolic control and caries experience, as reported from studies in Sweden, the United States,Finland and Yugoslavia [7,8]. In fact, other study reported that caries experience was lower among children with well-controlled DM in Italy, and this was thought to be due to restriction in sugar consumption among controlled diabetics [9].

Many cross-sectional studies have reported low caries prevalence in diabetes mellitus and this has mainly been explained by the sucrose-restricted diet that is a part of the life-long treatment. Other investigators have related caries development to the level of metabolic control, indicating a higher caries incidence in cases with poor control compared to those with a well-balanced disease [10, 11].

MATERIAL AND METHODS

All 116 patients 6 to 18-year-old patients with DM, attending the Medical Centre for children and adolescents Buzias, over an 12-month period from 2014-2015 were recruited for the study. The nature of the research was explained to the subjects' parents, who then indicated their consent.

The selected children for the control group (using cluster random sampling technique) were not on any medication, had not been treated by a doctor within the previous 3 months, and had not been diagnosed with diabetes. 116 clinically healthy children were randomly selected, approximately 2 month after data collection from the experimental group. In the process of control selection, we made sure that age and gender distribution remained similar to that of the diabetic group (ie, the same number of boys and girls who were 12, 13, 14, and 15 years old, respectively, were in the experimental and control groups).

Examinations and oral health assessments were performed according to the basic method of the WHO for the year (1997); subjects were seated in an dental chair and examined under direct illumination.

Dentition was the first thing we looked for on the dental examination. Teeth which manifest caries (DMFT) were scored according to the examination protocol that has been advocated by World Health Organization (WHO) [12] for the year (1987).

The level of oral hygiene was estimated with the Simplified Oral Hygiene Index (debris index and calculus index)to evaluate the oral cleanliness[13,14]. Each of these indices, in turn, is based on numerical determinations representing the amount the debris or calculus found on the selected tooth surface [15].

Gingival index described by Loe and Silness was used for diagnosis and assessment of gingival health conditions and the Ramfjord teeth was examined which is the following: (16,21,24,36,41,44) for permanent and (55,61,64,75,81,84) for deciduous, the missing tooth was not substituted [16].

Statistical analysis

Descriptive statistics include percentages, means and standard deviation, with statistical analysis data by using independent sample t-test for significant differences between two populations.

RESULTS

The study group consisted of 116 subjects with type I diabetes mellitus (65 girls and 51 boys) age 6-18 years (mean age 12.81, SD 3.74). In the second group (control group) there were 116 healthy subjects who did not suffer from any systemic disease (67 girls, 49 boys), age 6-18 (mean age 12.79, SD 3.62).

Results showed that the mean value of DMFT in the diabetic groups was higher than the controls with significant and highly significant differences for age groups (6-8) and (9-11) respectively, as shown in Table 2 and 4 (p<0.01).

Table 1 and 3 demonstrate that the mean value of DMFT in the diabetic groups was higher than that of control groups for both age groups (6-8) and (9-11), while for age group (12-15) and (15-18) the mean value of DMFT in the diabetic group was higher than that of control groups (Table 5 and 7), however the differences was statistically not significant (p>0.1) (Table 6 and 8).

The result showed that the total mean of DMFT in the diabetic group was higher than the total mean of DMFT in control with significant differences between the two groups, as shown in Table 9 and 10 (P<0.01). The gingival index (GI) according to the age groups for both diabetic and control group is seen in Table 11. Results showed that the gingival index among the diabetic group was higher than that in control group, with no statistical difference between them. The total mean value of Simplified Calculus Index in the diabetic group was higher than that of the control group with significant difference for the age group (12-14) years old as in Table 12

Table 1. *Mean value of DMFT for diabetics and controls in age group 6 to 8*

	Age 6-8	N	Mean	Std. Deviation	Std. Error Mean
DMFT	Diabetics	20	2,55	,999	,223
	Controls	20	,80	,768	,172

Table 2. *Independent Samples Test for comparing the mean values of DMFT for diabetics and controls in age group 6 to 8*

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
DMFT	Equal variances assumed	2,232	,143	6,213	38	,000	1,750	,282	1,180	2,320
	Equal variances not assumed			6,213	35,645	,000	1,750	,282	1,179	2,321

Table 3. *Mean value of DMFT for diabetics and controls in age group 9 to 11*

	AGE 9-11	N	Mean	Std. Deviation	Std. Error Mean
DMFT	DIABETICS	24	4,2917	1,36666	,27897
	CONTROLS	24	2,4167	1,21285	,24757

Table 4. *Independent Samples Test for comparing the mean values of DMFT for diabetics and controls in age group 9 to 11*

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
DMFT	Equal variances assumed	,134	,716	5,027	46	,000	1,87500	,37298	1,12423	2,62577
	Equal variances not assumed			5,027	45,360	,000	1,87500	,37298	1,12394	2,62606

Table 5. *Mean value of DMFT for diabetics and controls in age group 12 to 14*

	AGE 12-14	N	Mean	Std. Deviation	Std. Error Mean
DMFT	DIABETICS	22	7,55	2,064	,440
	CONTROLS	22	6,32	1,961	,418

Table 6. *Independent Samples Test for comparing the mean values of DMFT for diabetics and control in age group 12 to 14*

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
DMFT	Equal variances assumed	,010	,919	2,022	42	,050	1,227	,607	,002	2,452
	Equal variances not assumed			2,022	41,891	,050	1,227	,607	,002	2,452

Table 7. *Mean value of DMFT for diabetics and controls in age group 15 to 18*

	AGE 15-18	N	Mean	Std. Deviation	Std. Error Mean
DMFT	DIABETICS	50	7,06	2,280	,323
	CONTROLS	50	6,74	1,936	,274

Table 8. *Independent Samples Test for comparing the mean values of DMFT for diabetics and control in age group 15 to 18*

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
DMFT	Equal variances assumed	,865	,355	,756	98	,451	,320	,423	-,519	1,159
	Equal variances not assumed			,756	95,482	,451	,320	,423	-,520	1,160

Table 9. *Total mean of DMFT for diabetics and controls in the total group 6 to 18 years*

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
DMFT	DIABETICS	116	5,79	2,639	,245
	CONTROLS	116	4,74	2,955	,274

Table 10. *Independent Samples Test for comparing the total mean values of DMFT for diabetics and control in the total group 6 to 18*

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
DMFT	Equal variances assumed	3,530	,062	2,859	230	,005	1,052	,368	,327	1,777
	Equal variances not assumed			2,859	227,122	,005	1,052	,368	,327	1,777

Table 11. *Gingival Index (GI) of permanent teeth in the diabetic and control groups by age groups*

Diabetic group				Control group			
Age	No.	Mean	SD	NO	Mean	SD	pvalue
6-8	20	1.2	0.32	20	1.1	0.4	0.27
9-11	24	1.4	0.35	24	1.3	0.3	0.21
12-14	22	1.5	0.3	22	1.4	0.5	0.57
15-18	50	1.7	0.4	50	1.6	0.7	0.12

Table 12. *Calculus Index Simplified (CI-S) of the diabetic and control groups by age groups*

Diabetic group				Control group			
Age	No.	Mean	SD	No.	Mean	SD	P value
6-8	20	1.1	0.8	20	0.5	0.8	0.172
9-11	24	2.0	1.8	24	1.6	1.4	0.534
12-14	22	5.0	1.2	22	2.4	2.9	0.01
15-18	50	5.7	1.3	50	3.4	1.5	0.512

DISCUSSIONS

Children with diabetes have many problems during the course of their life. Dentition and oral health problems are among these.

Twetman et al. studied the risk assessment of 64 young type I Diabetes Mellitus (DM) patients (8–16 years) and suggested that a dental caries risk assessment at the diagnosis of Diabetes Mellitus mellitus in children may be a good indicator of overall health care [17]. Piatelli et al. conducted an epidemiological study on 26 type I diabetics and 24 healthy subjects with similar age and sex, and observed a higher incidence of dental caries in

diabetic patients than in the healthy subjects, probably due to the rich carbohydrate diet. Also the low addressability and the inconstancy in follow up controls could explain the high incidence of caries to diabetic patients.

The result of present study showed that the total mean value of (CI-S) in the diabetic group was higher than that of the control group, this comes in agreement with Siudikiene and Orbak in which they found that the difference between the diabetic and control groups in the amount of calculus [18,19]. Increased calculus formation reported in patients with diabetes, may be due to an increased concentration of salivary calcium in parotid and submandibular saliva of subjects with type I diabetes in addition to elevated salivary proteins and urea which lead to heavy calculus formation.

The prevention of periodontal problems in diabetic patients is mostly based on the education of the individual. Thus, patients should be informed about the importance of oral health for diabetics, and they should be taught that the main symptom of periodontal disease is gingival bleeding. Plaque and calculus deposits, which are the most important pathogenic factors of periodontal disease in the oral cavity, should be removed through careful selfcare and regular professional care to reduce the risk of periodontitis for diabetics.

Patients should also learn how to brush their teeth correctly, which should be done at least twice a day, and how to use dental floss and sometimes chlorhexidine digluconate 0.2%.The pediatrician's concern is to maintain good metabolic control and to make diabetic patients aware of a diet that suits their unique nutritional needs. The obligation of the dentist to the patient is to evaluate and help maintain good oral hygiene.

Previous studies have indicated that there was no significant correlation between dental caries and blood glucose values, as well as the duration of Diabetes Mellitus. In agreement with this finding, two other studies showed no relation of the DMFT index with the disease [3, 17], while in another study reported a negative correlation between Diabetes Mellitus onset and DMFT [20].

Some investigators have reported a significant association, [3-5] others observed no associa- tion [7,8]. It should be remembered that dental caries is a multi- factorial disease, with interplay between the effect of the primary etiologic factors (e.g. sugar consumption and bacteria) and the secondary factors such as fluoride exposure and dietary constituents. This interplay may vary in different communities. Hence, DM may not always have the same effect on caries experience in all communities. Besides, glycated hemoglobin level fluctuates in diabetics, and this complicates cross-sectional studies on the association between DM and caries experience.

Similarly, caries activity is a dynamic process, and its measurement at a point in time for lesions at different stages of lesion progression might not reveal a statistically significant difference between non-diabetics and DM children. There is a need for longitudinal studies to further clarify this association among caries experience and caries activity in diabetics and non DM children. Nevertheless, the higher caries experience among DM children observed in the present study agrees with the report from a longitudinal study on Swedish children by Twetman et al.[5].

CONCLUSIONS

Caries experience was significantly higher among children with type 1 diabetes mellitus than the non diabetic controls. The obligation of the dentist to the patient is to evaluate and help maintain good oral hygiene. Diabetic patients appear to lack of important knowledge about oral health and complications associated with their disease. However, the number of patients analyzed was limited, and a study with bigger sample size is needed to confirm this result.

Acknowledgement

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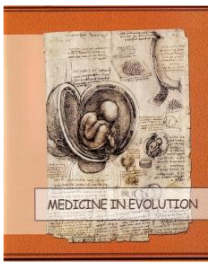
REFERENCES

1. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its com-plications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO con-sultation. Diabetic Med 1998; 15: 539-53.
2. Levin JA, Muzyka BC, Glick M. Dental management of patients with diabetes mellitus. Compen-dium 1996;1:82-90
3. Siudikiene J, Machiulskiene V, Nyvad B, Tenovuo J, Nedzel- skiene I. Dental caries and salivary status in children with type 1 diabetes mellitus, related to metabolic control of the disease. Eur J Oral Sci 2006;114:8-14.
4. Bolgül BS, Celenk S, Ayna BE, Atakul F, Uysal E. Evaluation of caries risk factors and effects of a fluoride-releasing adhesive material in children with insulin dependent diabetes mellitus (IDDM): Initial first-year results. Acta Odontol Scand 2004;62:289-92.
5. Twetman S, Johansson I, Birkhed D, Nederfors T. Caries incidence in young type 1 diabetes mellitus patients in relation to metabolic control and caries-associated risk factors. Caries Res 2002;36:31-5.
6. Canepari P, Zerman N, Cavalleri G. Lack of correlation between salivary Streptococcus mutans and lactobacilli counts and caries in IDDM children. Minerva Stomatol 1994;43:501-5.
7. Edblad E, Lundin SA, Sjodin B, Aman J. Caries and salivary status in young adults with type 1 diabetes. Swed Dent J 2001;25:53-60.
8. Moore PA, Guggenheimer J, Etzel KR, Weyant RJ, Orchard T. Type 1 diabetes mellitus, xerosto-mia, and salivary flow rates. Oral Oral Med Oral Pathol 2001;92:281-91.
9. Siudikiene J, Machiuskiene V, Nyvaad B, Tenovuo J, Nedzelskiene I. Dental caries increments and related factors in children with type 1 diabetes mellitus. Caries Res 2008; 42:354-62.
10. Moreira AR, Passos IA, Sampaio FC, Soares MSM, Oliviera RJ. Flow rate, pH, and calcium concentration of saliva of children and adolescents with type 1 diabetes mellitus. Brazilian J Med Biol Res 2009;42:707-11.
11. Karjalainen KM, Knuutila ML, Kaar ML. Relationship between caries and level of metabolic control in children and adolescents with insulin-dependent diabetes melli- tus. Caries Res 1997; 31: 13-18.
12. World Health Organization. Oral health survey, basic methods, 3rd ed. Geneva, Switzerland 1987; 31-7.
13. Green JC, Vermillion JR.the simplified oral hygiene index. J Am Dent Asso 1964; 68: 7-13.
14. Oredugba FA, Akindayomi Y. Oral health status and treatment needs of children and young adults attending a day center foe individuals with special health care needs. Biomed Chromatogr Oral Health 2008; 8: 30.

15. World Health Organization. Oral health survey, basic methods, 4th ed. Geneva, Switzerland 1997.
16. Ramfjord SP. Indices for prevalence and incidence of periodontal disease. J Periodontol 1959; 30: 51-59.
17. Twetman S, Petersson GH, Bratthall D. Caries risk assessment as a predictor of metabolic con-trol in young Type 1 diabetics. Diabet Med. 2005;22(3):312–5.
18. Siudikiene J, Maciulskiene V, Nadzelskiene I, Dobrovolskiene R. Oral hygiene in children with type 1 diabetes mellitus. Stomatologija 2005; 7 (1): 24-7
19. Orbak R, Simsek S, Zerrin O, Kavrut F, Colak M. The influence of type 1 diabetes mellitus on dentition and oral health in children and adolescents. Yonsei Med J 2008; 49(3): 357-65.
20. Samimi P, Zoratipour A, Fathpour K. A comparative study on den- tal caries prevalence in dia-betic children in Isfahan in the summer of 2000. J Res Med Sci. 2004;9(2):97–98

PILOT STUDY ON TOOTH MORPHOLOGY IN PATIENTS WITH SUPERNUMERARY TEETH



MIRCEA DRAGNE GARDEF, ANGELICA BENCZE, ELINA TEODORESCU, ŞTEFAN MILICESCU JR., ECATERINA IONESCU

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ABSTRACT

Based on previous reported correlations between tooth number anomalies and the size of the remainder of the dentition, the study is aimed to investigate possible interrelations between the occurrence of supernumerary teeth and coronal morphology of permanent teeth.

The study is retrospective, cross-sectional, case-control. The study group consisted of 25 patients with supernumerary teeth (9 females and 16 males); the control group included an equal number of matched patients with normal dental formula.

The research collected the mesiodistal (MD) and buccolingual (BL) dimensions of the permanent teeth (excluding 3rd molars), as recorded on study models.

The results suggest that the occurrence of supernumerary teeth is linked to generalized effects on tooth size to the whole dentition. Tooth parameters of patients with supernumerary teeth had, on average, higher values than those measured on patients without dental surplus, the extent of difference in tooth size being greater in female patients.

Key words: *supernumerary teeth, permanent teeth morphology, effect on dentition*

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INTRODUCTION

Clinical observations related to morphological alterations of the other teeth in the dentition (the"normal"ones) in patients with supernumerary teeth (or hypodontia) suggest a correlation between the causes of these dental anomalies and genetic determinants of coronal tooth dimensions and shape, but it is still unclear whether the effect is manifested consistently throughout the dentition, or localized in certain dental units, or influences some crown-root morphological characteristics (Miles 1954, *11*; Rajab and Hamdan 2002, *14*; Ionescu 2006, *7*; Brook et al. 2009, *3*; Neville et al. 2009, *12).*

Some studies published to date have found that in patients with supernumerary teeth exists a tendency to shift the incisive sum to values above the upper limit of normodontia (Boboc 1971, *1*; Brook 1984, *2*; Khalaf et al. 2005, *9)* and that the presence of supernumerary teeth is not associated to absolute microdontia (Grivu and Mecher 1973, cited by Ionescu 2000, *6*; Schalk-van der Weide and Bosman 1996, *15).*

Brook (1984, *2)* proposed a theoretical model that brings together different genetic and environmental etiological factors as variables in supernumerary teeth and hypodontia occurrence and teeth sizes. The model postulates a normal distribution of tooth size and number, the dental anomaly installing when the genetic and environmental influences amount on an individual exceeds the permissible threshold for that particular type of anomaly.

The studies published by Townsend et al. (2005, *16*), Kondo and Townsend (2006, *10)* converge on the hypothesis that dental morphology variation is mainly due to genetic and environmental factors that interfere with the formation and development stages of tooth.

Thus, based on data from the literature and from clinical observations, we considered of interest to compile a study aimed to investigate possible correlations between the presence of supernumerary teeth and coronal morphology of the remainder of the permanent dentition, in order to improve the scientific knowledge of the etiology of these two conditions.

MATERIAL AND METHODS

In order to analyze these correlations, a retrospective, cross-sectional, case-control study was conducted. The study group consisted of 25 patients *with supernumerary teeth* (9 females and 16 males), selected from the patients referred for treatment between 2009 and 2014 to the Department of Orthodontics and Dento-Facial Orthopedics,"Carol Davila"University form Bucharest. The control group included an equal number of subjects without teeth number anomalies.

Patients with supernumerary teeth were selected for the study based on criteria regarding the absence of a genetic syndrome, and hypodontia.

The control group was composed on an equal number of patients *with normal dental formula,* chosen to match the supernumerary group in terms of sex, dental age, pattern of the cranial development, and incisive sum (as defined by Pont 1909, *13*).

The study measured on study models the mesiodistal (MD) and buccolingual (BL) dimensions of the permanent teeth of patients with supernumerary teeth and of patients with normal dentitions (excluding 3rd molars).

Measurements were performed by a single operator, in one day, using a spacer and a ruler. The spacer was applied parallel to the incisal edges or occlusal surfaces, perpendicular to buccal or lingual ones, to detect the maximum coronal diameters (Ionescu et al. 2001, *8*). Teeth with carious lesions or restorations, teeth with defects on the study models, and teeth which were not completely erupted were excluded from the study. Each tooth was measured twice, and the mean value of the two measurements was used.

To check the accuracy of the data recorded, 15 randomly selected study models were measured again after two weeks form the first measurements. The values obtained were compared with those of the initial measurement using the Student t-test for pair. The differences obtained were not statistically significant ($p > 0.05$), conducting to the conclusion that there is no study error due to measurement method.

After evaluating the type of distribution of the obtained data, the differences between the dental dimensions of patients in the two groups were analyzed with ANOVA test, t-student test (for variables with normal distribution) and the"U"Mann-Whitney test (for variables with non-normal distribution). The level of significance was set at $p=0.05$. The statistical analyses were performed by computer, using the statistic package offered by IBM SPSS_Statistics_Trial_17.

RESULTS

The study group included a variety of supernumerary clinical forms, 68% of patients presented one supernumerary tooth, and the other 32% had 2 or more supernumerary teeth. Totally, 39 clinical forms of hyperdontia were diagnosed. 25.64% of supernumerary teeth were maxillary mesiodentes, an equal number were geminated maxillary incisors, 17.94% supernumerary lateral incisors (10.26% located in the maxilla, and 7.69% in the mandible), 10.26% mandible supernumerary premolars, maxillary and mandible supernumerary molars (7.69% each), maxillary"dense in dente"and mandible supernumerary incisors (2.56% each).

The dental ages ranged between 6 and 18 years; 56% of patients had dental ages below eight years. The distribution by sex (M: F) was 1.7:1 (64% male subjects, 36% female).

The study data were obtained from measurements made on the 50 study models; a total number of 1685 teeth were assessed. Considering dental ages of patients included in the study and the criteria required for precise diameters measurements, most often were registered the coronary dimensions of permanent molars (recorded on average 94% of cases), incisors, especially lower ones (85%), followed by premolars (recorded on average 34.25% of cases), canines (19.37% of patients) and 2nd molars (recorded on 16.87% of the models). The only tooth parameter measured on all study participants was the mesiodistal diameter of the lower right central incisor.

Both in study and control group, the majority of dental dimensions were larger in males, some differences being statistically significant. The MD and BL dimensions of first molars, the MD diameter of frontals first premolars and first molars were frequently larger in males, both in maxilla and mandible.

Comparing the tooth dimensions of patients in the study group and the control group, regardless of gender, results showed that:

- tooth parameters of patients with supernumerary teeth had, on average, higher values than those measured on patients without

dental surplus, except BL dimensions of 21 and 25, and MD dimensions of 33 and 35; statistically significant differences were obtained in the MD dimension of first upper right premolar;

- the percentage average differences were positive in most cases, ranged between 0 and 10.54% (three quarters of the values being below 3.75%); the four negative registered differences were in the range of (-2.85%, -0.30%).

The box-plot graphics for MD and BL average percentage differences between supernumerary patients and control group show that differences in the MD distances are in absolute terms larger than the differences in the BL distances (figure 1). This observation implies the idea that the mesiodistal dimensions are more affected in patients with supernumerary teeth, than the bucolingual ones.

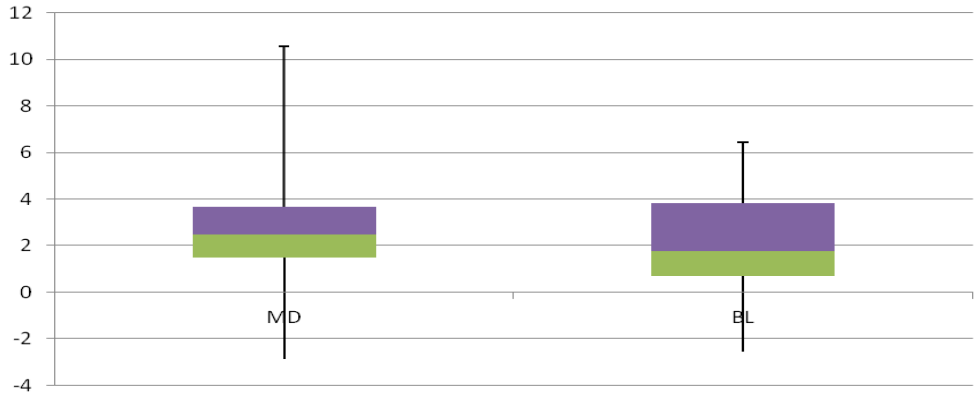


Figure 1. Box plot graph of average percentage differences in MD and BL dimensions between supernumerary patients and controls

Noting the significant differences related to patient's gender, the data were further analyzed separately for males and females, seeking relevant differences between dental dimensions of patients in the study group and control.

Comparing the MD and BL dimensions in supernumerary patients and controls, separately for males and females, most statistically significant differences are in favor of surplus dental cases:

- both dental dimensions, regardless of gender, were more frequent increased in patients with supernumerary teeth, MD diameter more than the BL dimension;
- MD dimension of the upper first right premolar (the only parameter that showed positive, statistically significant variation, in subjects with supernumerary teeth, regardless of patient's gender) was, on average, 0.88 mm larger in females, and 0.65 mm higher in males;
- BL dimension of the left lower 2nd premolar was the only parameter which recorded negative statistically significant differences (mean, 0.80 mm), in male patients with supernumerary teeth;
- BL diameters of lower lateral and right central incisors were on average 0.33-0.65 mm larger in male patients with supernumerary teeth (statistically significant results). On female patients, the parameter values were similar in the study and control groups;
- MD diameter of the lower right lateral incisor was on average 0.45 mm greater in male supernumerary patients (statistically significant difference).

Analyzing the graphs of parameter variations between study patients and the controls separately for gender (figures 2 and 3), it seems that the occurrence of supernumerary teeth

is linked to generalized effects on tooth size to the whole dentition; the dental dimensions were more frequent increased in patients with supernumerary teeth.

21, 23, 32 lower BL dimensions in females with supernumerary teeth, than in control females. For males, the teeth 15, 25, 37, 35, 34, 33, 44 had lower MD diameter values and teeth 17, 15, 13, 21, 24, 25, 27, 35(statistically significant difference), 44, 45 had lower BL dimensions in patients with supernumerary teeth than in controls (figure 3).

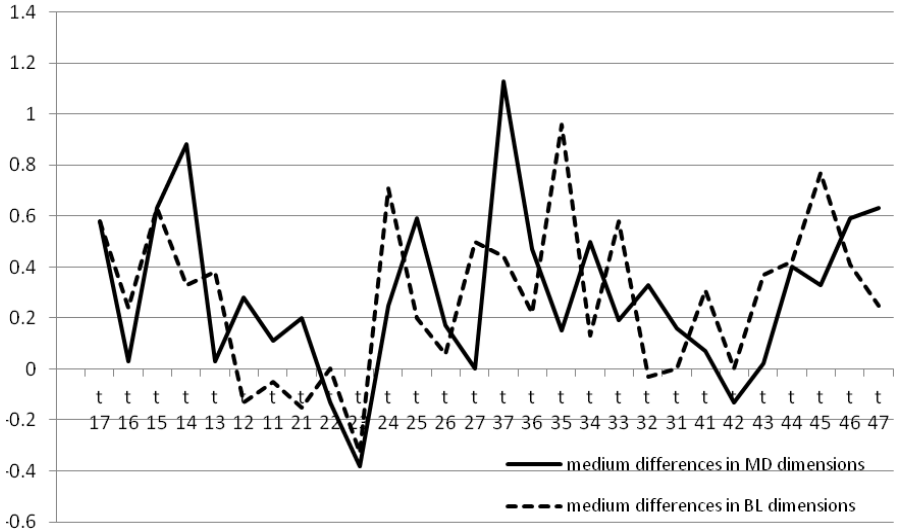


*Figure 2. Medium differences between MD and BL dimensions (mm) between study group and controls, for females; * - statistically significant difference*

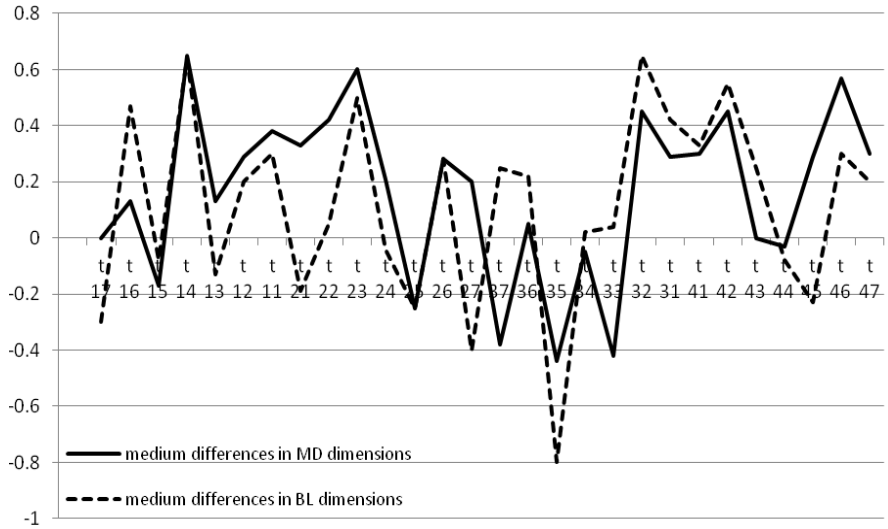


*Figure 3. Medium differences between MD and BL dimensions (mm) between study group and controls, for males; * - statistically significant difference*

Generally, the differences were greater for MD diameter, than for the BL dimensions, in both sexes. Exceptions were found regarding teeth 16, 13, 22, 23, 24, 27, 35, 33, 41, 42, 43, 44, 45 for females and teeth 16, 15, 37, 36, 34, 33, 32, 31, 41, 42, 43 for males, where differences were in favor of BL diameter.

The results didn't reveal a predictable pattern of changes in coronary dental dimensions, related to the type or location of supernumerary tooth, due to the relatively small sample size.

Female patients with supernumerary teeth showed a greater extent of difference in tooth size than males (reaching 1.13 mm versus males,

0.64 mm), confirming the prediction model Brook (*3*), which states that the dental volume of females with supernumerary teeth exceeds the average population parameters with higher values than men with supernumerary teeth.

The results showed different values of variations in MD and BL dimensions, respectively in males vs. females, between study group and controls, supporting the hypothesis of specific influences over tooth morphology in patients with supernumerary teeth. The study published by Khalaf et al. (2005, *9*) argues that the MD diameter of the tooth is more frequently increased than the BL one in patients with supernumerary teeth, compared to the average population values.

The largest increases in tooth size in patient with supernumerary teeth were recorded on MD diameter of 14 regardless the gender (statistically significant), MD and BL dimensions of 37 and 35 for females, respectively MD diameter of 23 and BL dimension of 32 (statistically significant) for males. The maximum negative difference was recorded for males in the BL diameter of 35 (statistically significant).

DISCUSSIONS

The largest increases in sizes of second premolars, second molars and canines in patients with supernumerary teeth can be explained by the longer period of time over which these teeth develop (canine and second molar present some of the longest periods of development in the dentition).

Regarding the variations in coronary dimensions within the arches, the results suggest that the female front teeth, especially maxillary, presented reduced BL dimensions in patients with supernumerary teeth than in controls, the remaining teeth being wider in female patients with supernumerary teeth, than in the study group patients. In male patients with supernumerary teeth, the reduction in coronal dimensions is encountered especially in posterior teeth (most commonly affected is the BL diameter), whereas the frontals crowns are often larger than in male control patients.

Extrapolating the results of the study conducted by Garn and Lewis (1969, *5*), the literature suggests the existence of localized influences on coronary morphology of the teeth adjacent to a supernumerary tooth formation. The relatively reduced number of subjects in our research, and variety of clinical forms of dental surplus didn't enable such an analysis. The mentioned authors have shown that the presence of mesiodens correlates with increased coronal diameters in upper incisors and lower lateral incisors. We appreciate that our data showing significant positive differences in the lower incisors in favor of male patients with supernumerary teeth, most of them being mesiodentes, partly confirms the findings of authors Garn and Lewis *(1969, 5).*

At the same time, the results of our study, suggesting a generalized influence on the dentition morphology in case of supernumerary teeth occurrence, are in agreement with the theory expounded by Brook (1984, *2),* which considers the dental system, in terms of training and development stages, as an unitary system.

CONCLUSIONS

The majority of tooth parameters of patients with supernumerary teeth had, on average, higher values than those measured on patients without dental surplus. Generally, the differences were greater for MD

diameter, than for the BL dimensions, in both sexes. Female patients with supernumerary teeth showed a greater extent of difference in tooth size than males.

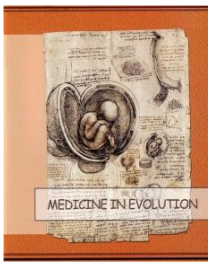
The results of this study support the importance of the dental measurements on study models as complementary exam in investigating the etiology of dental anomalies. Among potential coronary parameters, we choose the MD and BL diameters, which are most often used by practitioners. However, clinical observations have shown us that patients with supernumerary teeth not only show changes in tooth crown sizes, but also in tooth shapes.

Hence the need to conduct further investigations of coronary morphology, using 2D and 3D imaging methodologies, such as the method proposed by Brook et al. (1998, *4*) for the investigation of developmental defects of the dentition. Such data could help clarify the interrelation between the occurrence of number dental anomalies, such as supernumerary teeth, and shape dental anomalies.

REFERENCES

1. Boboc Ghe.: Anomaliile dento-maxilare. Ed. Medicalã, Bucureşti, 1971.
2. Brook A.: A unifying aetiological explanation for anomalies of human tooth number and size. Arch Oral Biol, 1984, 29, (5), 373-378.
3. Brook A. H., Griffin R. C., Smith R. N., Townsend G. C., Kaur G., Davis G. R., Fearne J.: Tooth Size patterns in Patients with Hypodontia and Supernumerary teeth. Arch Oral Biol, 2009, 54, S63-S70.
4. Brook A., Smith R., Elcock C., Al-Sharood M., Shah A., Karmo M.: The measurement of tooth morphology: Development and validation of a new image analysis system. In Mayhall J., Heikkinen T., editors: Proceedings of the 11th International Symposium on Dental Morphology. Oulu University Press, Oulu, 1998, 380-387.
5. Garn S., Lewis A.: Effect of agenesis on the crown-size profile pattern. J Dent Res, 1969, 48, (6), 1314.
6. Ionescu Ecaterina: Anomaliile de numãr. Ed. Cerma, Bucureşti, 2000.
7. Ionescu Ecaterina: Anomaliile dentare. Ed. Cartea Universitarã, Bucureşti, 2006.
8. Ionescu Ecaterina, Duduca Milicescu Ioana, Popescu Manuela, Popoviciu Olivia, Milicescu Viorica: Ortodonție şi Ortopedie Dento-Facială. Ghid Clinic şi Terapeutic. Ed. Cerma, Bucureşti, 2001.
9. Khalaf K., Robinson D., Elcock C., Smith R., Brook A.: Tooth size in patients with supernumerary teeth and a control group measured by an image analysis system. Arch Oral Biol, 2005, 50, 243-248.
10. 1Kondo S., Townsend, G. C.: Associations between Carabelli trait and cusp areas in human permanent maxillary first molars. Am J Phys Anthropol, 2006, 129, 196-203.
11. Miles A.: Malformations of the teeth. Proc Royal Soc Med, 1954, 47, 817-826.
12. Neville B. W., Damm D. D., Allen C. M., Bouquot J. E.: Oral and maxillofacial pathology. Saunders, St Louis, 2009, 60-95.
13. Pont A.: Der Zahn-Index in der Orthodontie. Zeitschrift für Zahnfirtzliche Orthopaedie, 1909, 3, 306-321.
14. Rajab L. D., Hamdan M. A.: Supernumerary teeth: review of the literature and a survey of 152 cases. Int J Paed Dent, 2002, 12, 244-254.
15. Schalk-van der Weide Y., Bosman, F.: Tooth size in relatives of individuals with oligodontia. Arch Oral Biol, 1996, 41, 469-472.
16. Townsend G., Richards L., Hughes T., Pinkerton S., Schwerdt W.: Epigenetic influences may explain dental differences in monozygotic twin pairs. Aust Dent J, 2005, 50, (2), 95-100.

THE STATUS ASSESSMENT OF THE ORAL HEALTH DURING MIXED DENTITION (PART 2)



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ABSTRACT

Abstract:

The aim of the study *was to establish some aspects of the current situation in our country regarding the oral health status of children, by assessing the orodental status during mixed dentition.*

Material and methods*: The study was conducted in children aged 6-8 years old, from Galati and Iasi, having clinical examinations performed in school offices, using the consultation kit. The assessment of the dental status was achieved by using the ICDAS assessment system (International Caries Detection and Assessment System), and orthodontic status through the IOTN index (Index of Treatment Need).*

The results *show that under the conditions of this study, the average value of CAO.S is very high, 9.47 surfaces affected by caries and their complications, predominantly the decay component - cs (decayed surfaces) with an average value of 8.13 compared to filling component of only 0.62. In these teeth, the caries prevalence reported on surfaces was of 83.19%. For permanent dentition, the caries prevalence compared to the total examined area was of 81.4%, which is high for this age group (6- 8 years old).*

Conclusions: *From the assessment of the orthodontic status, it results that most children with abnormalities are from 1st grade (78.8%), only a small percentage of abnormalities in the 2nd (15.4%) and in the 3rd grade (2.2%).*

Key words: *dental status; mixed dentition; oral health; maxillary dental anomalies*

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INTRODUCTION

Caries in dentin without direct access cavity (code 04) were recorded with a greater frequency in the case of temporary teeth. Of the 149 dentine caries (code 04), 134 were of temporary teeth (Table 1), the lesions were located on the proximal surfaces: 63 surfaces and occlusal: 48 surfaces (Table 2).

Table 1. Distribution of the study group in relation to the ICDAS assessment system: dentin caries without direct access cavity (code 04)

		S.Total.04	S.perm.04	S.temp.04
Total	Validated	137	137	137
	Excluded	0	0	0
Average value			0,11	0,98
Standard deviation			0,465	1,468
- Minimum			0	0
- Maximum			4	8
Total		149	15	134
%		9,00	4,00	8,00

Table 2. Distribution of the study group in relation to the ICDAS assessment system: caries in dentin surfaces without direct access cavity (code 04) in deciduous teeth

		S.temp .04	S.temp.MD .04	S.temp.Ocl. 04	S.temp.VO. 04
Total no	Validated	137	137	137	137
	Excluded	0	0	0	0
Average value			0,46	0,35	0,17
Standard deviation			0,805	0,744	0,703
- Minimum			0	0	0
- Maximum			3	4	6
Total		134	63	48	23
%		8,00	3,00	4,00	6,00

Hollow cavities in dentin (code 05) without affecting the pulp were recorded only for temporary teeth (Table 3), most lesions were located in the proximal surfaces: 148 surfaces and occlusal: 123 surfaces (Table 4).

Table 3. Distribution of the study group in relation to the ICDAS assessment system: hollow cavities in dentin (code 05)

		S.Total.05	S.perm.05	S.temp.05
Total no	Validated	137	137	137
	Excluded	0	0	0
Average value			0,00	0,56
Standard deviation			0,000	1,070
- Minimum			0	0
- Maximum			0	6
Total			0	77
%		6,00	0,00	6,00

Table 4. Distribution of the study group in relation to the ICDAS assessment system: hollow cavities in dentin surfaces (code 05) in deciduous teeth

		S.temp.05	S.temp.MD.05	S.temp.Ocl.05	S.temp.VO.05
Total no	Validated	137	137	137	137
	Excluded	0	0	0	0
Average value			0,35	0,17	0,04
Standard deviation			0,753	0,589	0,205
- Minimum			0	0	0
- Maximum			4	5	1
Total			148	123	16
%		6,00	4,00	5,00	1,00

What is important to note is the high frequency of deep dentine caries with pulp involvement: Code 06 (Table 5). Most decayed surfaces, code 06, were recorded for temporary teeth: 733 surfaces, 354 being proximal surfaces, 202 occlusal and 177 vestibular or oral (Table 6).

The presence of root residues was recorded with a higher frequency in deciduous teeth, although for this age group there were root residues also for the permanent teeth (Table 7).

Table 5. Distribution of the study group in relation to the ICDAS assessment system: hollow caries deep in the dentine (code 06)

		S.Total.06	S.perm.06	S.temp.06
Total no	Validated	137	137	137
	Excluded	0	0	0
Average value		5,36	0,01	5,35
Standard deviation		7,267	0,120	7,147
- Minimum		0	0	0
- Maximum		33	1	32
Total		736	3	733
%		34,00	1,00	33,00

Table 6. Distribution of the study group in relation to the ICDAS assessment system: surfaces with hollow caries deep in the dentine (code 06) in deciduous teeth

		S.temp.06	S.temp.MD.06	S.temp.Ocl.06	S.temp.VO.06
Total no	Validated	137	137	137	137
	Excluded	0	0	0	0
Average value			2,58	1,47	1,29
Standard deviation			3,131	1,959	2,441
- Minimum			0	0	0
- Maximum			14	8	12
Total		733	354	202	177
%		32,00	14,00	8,00	12,00

Table 7. Distribution of the study group compared with the presence of root residues

		Rest. rad. d. perm	Rest. rad. d. temp
Total no	Validated	137	137
	Excluded	0	0
Average value			0,53
Standard deviation			1,058
- Minimum			0
- Maximum			6
Total			72
%		2,00	6,00

The assessment of orthodontic status in the age group 6-8 years shows that about half of the subjects (51.8%) are with IOTN 1, 16.9% with IOTN 2 and 19.7% with IOTN 3; these categories have not expressly required the achievement of orthodontic treatments. The assessment results indicated an increased need of orthodontic treatment in 11 cases (8%) with IOTN 4 and 5 cases (3.6%) with IOTN 5 (Table 8).

From the aesthetic point of view, 69.3% of subjects were classified in group 1-4 (without need of orthodontic treatment), 23.4% in group 5-7 and 7.3% in group 8-10 of IOTN aesthetic (Table 9).

Regarding the dental maxillary anomaly class, where the subjects fit, the results showed that 78.8% presented abnormalities of class I, 15.4% of class II and only 2.2% of class III (Table 10).

In the case of recorded dental alveolar inconsistencies most affected subjects presented aspects of incongruity between mild and moderate, and most (75.9%) were unaffected of this condition (Table 11).

The assessment of the orthodontic status shows that only 1.5% of the subjects undergo orthodontic treatment, that being with mobile devices.

Table 8. Distribution of the study group compared with IOTN

IOTN		No. cases	%	% valid	% cumulative
Valid	1	71	51,8	51,8	51,8
	2	23	16,9	16,9	68,7
	3	27	19,7	19,7	88,4
	4	11	8,0	8,0	96,4
	5	5	3,6	3,6	100,0
	Total	137	100,0	100,0	100,0

Table 9. Distribution of the study group compared with aesthetic IOTN

IOTN **aesthetic**		No. cases	%	% valid	% cumulative
Valid	1-4	95	69,3	69,3	69,3
	5-7	32	23,4	23,4	92,7
	8-10	10	7,3	7,3	100,0
	Total	137	100,0	100,0	100.0

Table 10. Distribution of the study group compared with dental maxillary anomaly class

Anomaly class		**No. cases**	**%**	**% valid**	**% cumulative**
Valid	I	108	78,8	78,8	78,8
	I › III	5	3,6	3,6	82,4
	II/1	12	8,8	8,8	91,2
	II/2	9	6,6	6,6	97,8
	III	3	2,2	2,2	100,0
	Total	137	100,0	100,0	100,0

Table 11. Distribution of the study group compared with the presence of dental alveolar inconsistencies

Incongruence		No. cases	%	% valid	% cumulative
Valid	absent	104	75,9	75,9	75,9
	mild	17	12,4	12,4	88,3
	moderate	14	10,2	10,2	98,5
	severe	2	1,5	1,5	100,0
	Total	137	100,0	100,0	100,0

Table 12. Distribution of the study group compared with the presence of orthodontic treatment

Orthodontic treatment		**No. cases**	**%**	**% valid**	**% cumulative**
Valid	absent	135	98,5	98,5	98,5
	Ortho mobile device (max./mand.)	2	1,5	1,5	100,0
	Total	137	100,0	100,0	100,0

INTERPRETATION OF RESULTS AND DISCUSSIONS

For Romania, the existing WHO studies show that children of 6 years, in 1995, the percentage of those without caries was very low - 17%, the prevalence is very high, 83%, and the index value of caries in the temporary teeth is: cao-d = 4.4 in 2003 [1,5].

In a study conducted in Bucharest in 2008, the prevalence of dental caries in the study group (6-8 years) was found still high: only 28.4% of the total examined lot were unaffected by the cavities and experience index of cavity on surfaces in the temporary dentition had had high values ranging between 0 and 57, with an average value for the whole group of 8.06 (± 8.67). In the temporary teeth it is noticed the existence of a 5/1 ratio in the favor of the number of untreated caries compared to that of fillings [2].

In this study, the medium value of cao.s is very high, 9.47 surfaces affected by caries and its complications, predominantly the decay component - cs (decayed surfaces) with a value of 8.13 versus restorative component, only 0.62, which shows that treatment needs for the temporary teeth are very high.

The medium value for teeth caries index, cao.d, for the two studied groups, is 4.55; it is considered high compared to other developed European countries: Norway (1.4), Finland (1.5), Belgium (1.7), France (1.7), Austria (2.1), Spain (2.1), Sweden (2.4), Germany (2.6) [1, 5].

The ration of teeth caries index components is operating throughout in the favor of decayed teeth (cd component with an average value of 4.09) and net detriment of the component *ad* (absent teeth) and OD (restrict teeth) report their average in the index cao.d as being 11/4/5. Of the total 7129 dental surfaces examined, 1198 were free from caries, the rest of 5931 being affected by caries, which it shows a prevalence of caries reported on surfaces of 83.19%.

In what concerns the distribution of caries depending on the affected degree in ICDAS system, most superficial enamel caries (code 03) for deciduous teeth were located on the occlusal surface (69%) and only 21% on proximal surfaces.

Dentin caries without cavity (code 04) were recorded with a higher frequency in the case of temporary teeth compared to the permanent dentition (ratio 9/1), the lesions were located predominantly on proximal surfaces (47%), followed by occlusal surfaces (35.8%) and only 17.2% on buccal / oral surfaces.

Hollow cavities in dentin (code 05) without affecting the pulp were recorded only for the temporary teeth, most lesions were located in the proximal (51%) and occlusion (42%) surfaces. It should be emphasized the very high average index for deep dentin caries with pulpal involvement (code 06), with an average value for the entire group of 5.35, 48% of them being proximal, 27.5% occlusion and the remaining vestibular or oral. The presence of root residues was recorded with a high frequency for the temporary teeth, their average being 0.53 to the entire group. These results are explained by the presence in a considerable proportion of temporary teeth in the arch, submitted for a longer period of time to the attacks of caries risk factors than for the permanent teeth, which barely erupt at this age.

For permanent dentition, the percentage of unaffected surfaces was of 18.6%, so the prevalence of the caries compared to the total examined area was of 81.4%, which is high for this age group, 6-8 years.

Average caries index CAO.S has a value of 0.94 and CAO.D has averaged 0.85, what demonstrates that at the age of 6-8 year old, the children

already have at least one surface dental caries in permanent teeth (less likely obscuration, the ratio for caries / filling surfaces being of 14.6/1).

The assessment for dental status for permanent teeth indicates a CAO.D value of 0.85, where the CD component (decayed teeth) has the highest value: 0.80. In what concerns the permanent teeth affected surfaces, CAO.S, has the value of 0.94, of which 0.88 is the CS component - decayed surfaces, comparable to the index value of CAO.S for children of 12 years old in the Nordic countries (Finland, Norway, Denmark Sweden) which have the national average of CAO.D below 1)

Most of the superficial enamel caries (code 03) for permanent teeth were located on the occlusal surface (79%) and only 20% on the proximal surfaces. This distribution can indicate the type of optimal preventive strategy for this age group, i.e. after professional cleaning, sealing grooves and fissures, followed by fluoride, thus avoiding these superficial injuries to reach the stage of hollow cavities, consequently irreversible.

According to the IOTN index for the entire study group, the largest proportion, approximately half of the subjects (51.8%) are found in the group without the need of orthodontic treatment. It follows in almost equal proportions the group with reduced need for orthodontic treatment (class 2) (16.9%) and the group of students who have a need to limit the orthodontic treatment (class 3) (19.7%). The small proportion (8%) is found to those with high need (class 4) and only 3.6% for those with very high need of treatment (class 5).

In terms of impact of dental maxillary anomalies on the aesthetic, the majority (69.3%) of the subjects were classified in group 1-4 of the aesthetic component of IOTN (without the need of orthodontic treatment), almost a quarter of them (23.4%) with moderate needs (group 5-7) and 7.3% in the group with high impact on the physical appearance (group 8-10). Most children present abnormalities of class I (78.8%), only a small percentage present abnormalities of class II (15.4%) and only 2.2% of class III, being considered the most severe and hardly treatable.

CONCLUSIONS

In comparison with the results of this study, the entire group of examined pupils of 6-8 years (in Iasi and Galati), for the temporary teeth, the caries index average reported on surfaces (cao.s) and reported on teeth (cao.d) have high values, much higher than in European countries with a tradition in preserving the oral health [4]. These results indicate that treatment needs at the level of temporary teeth are very high, given the prevalence of caries reported on surfaces of 83.19% in these teeth.

The distribution of caries lesions depending on the injury degree in ICDAS system shows high number of carious lesions in dentin for the deciduous teeth. It should be emphasized the very high average index for deep dentin caries with pulpal involvement (code 06), of which 48% are with proximal location.

The presence of root residues was recorded with a high frequency to the temporary teeth, their average being 0.53 for the entire lot.

The prevalence of dental caries in the case of permanent teeth reported to total number of examined surfaces was of 81.4%, which is high for this age group, i.e. 6-8 years.

From the assessment of orthodontic status it results that most children have abnormalities of class I (78.8%), only a small percentage have abnormalities class II (15.4%) and only

2.2% of Class III, being considered more severe and hardly treatable.

The assessment of IOTN index for the entire study group shows that about half of the subjects (51.8%) are found in the group without the need of orthodontic treatment. The small proportion (8%) is found in those with high need (class 4) and only 3.6% of those with very high need for treatment (class 5).

The assessment of IOTN aesthetic component shows that the majority (69.3%) of the subjects were classified in group 1-4 of the aesthetic component of IOTN (without the need for orthodontic treatment in terms of impact on the physical appearance).

The extremely low percentage, only 1.5% of the examined children, which are currently under orthodontic treatment (this is only with mobile devices), shows a lack of awareness of dental maxillary presence at this age, the lack of supervision or lack of information from parents and a low frequency of dental health checks.

Acknowledgment

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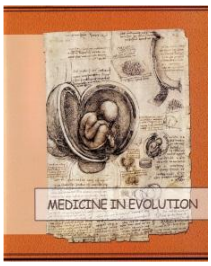
REFERENCES

1. Dumitrache, M.A., Sfeatcu, I.R., Buzea, C.M., Dumitraşcu, L.C. & Lambescu, D.G. Concepte şi tendinţe în sănătatea orală/Concepts and Trends in oral health. Bucharest: Editura Universitară"Carol Davila"; 2009.
2. Dumitrache, M.A., Ranga, R., Sfeatcu, I.R., Ionescu, E. & Dănilă, I. Modelul regresiei lineare de predicţie al riscului carios la elevii din Bucureşti/Prediction Linear regression model of caries risk in students from Bucharest. Medical-Surgical Review, 2009, Vol. 113, no. 2, Suppl. no. 2 (1-4 April).
3. Petersen, P.E. & Rusu, M. Oral health status of Romanian schoolchildren - national survey 2000. Copenhagen, WHO Regional Office for Europe, 2002.
4. Petersen, P.E., Christensen, L.B., Möller, I.J., Staehr-Johansen, K. Continuous improvement of oral health in Europe - The approach of the WHO Regional Office for Europe. European Dent J, 1994; 4: 21-23.
5. ***World Health Organization. European health for all data base. WHO, Geneva, 2005; www.euro.who.int/eprise/main/WHO/InformationSources/Data.



ODONTOMAS: 3 METHODS OF RADIOLOGICAL PREOPERATORY DIAGNOSIS – CASES PRESENTATION AND REVIEW OF THE LITERATURE

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ABSTRACT

Odontomas are odontogenic benign tumors composed of dental tissue. Odontoma is stated to be a hamartomatous lesion rather than a true odontogenic tumour. It has an unknown etiology and is often suspected when there are retained deciduous teeth in children. Early detection and surgical enucleation of the tumour is recommended to prevent impaction of unerupted teeth. The goal of this article is to present the main advantages and disadvantages of the radiological and imagistic methods used preoperatively for an accurate diagnosis.

Key words: *Odontoma, radiological diagnosis*

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INTRODUCTION

In 1867, Paul Braco was the first who described tumors formed by enamel, dentine and pulpal tissue, arranged in a disorderly manner and called them odontomas [1].

Histologically, there are 2 types of odontomas: compound odontoma (calcified structures arranged in many teeth-like structures, but without morphological resemblance to normal teeth), and complex odontoma (nondescript masses of dental tissue) [2].

Various causes like local trauma, infection, hereditary anomalies (Gardner's syndrome, Hermann's syndrome), odontoblastic hyperactivity are also considered in the etiology of odontomas [3]. Experimental studies in rats and studies by Glasstone (1952) and Rushton (1957) suggested the role of trauma in odontoma formation [4,5]. Levy's studies concluded that the moment of the trauma can determine various anomalies: hypoplastic teeth, supernumerary teeth, or odontomas [5].

Odontomas were discovered at any age, but the most prevalent age of detection was between 10-20 years old, more frequently in males [6]. Compound odontomas were more common in the incisive-canine region of the jaws (61%), and complex odontomas were more common in the premolar-molar region of mandible (59%) [4,7].

Most odontomas were intraosseous, when seen totally embedded in the bone. These intraosseous odontomas were sometimes clinically asymptomatic, although frequently there may have been some signs and symptoms: impacted deciduous or permanent teeth, pain, tooth displacement, cortical bone expansion, and swelling [8]. Damage to neighboring teeth (malpositioning, devitalisation, malformation, aplasia and retained teeth) were observed in 70% of the cases [9]. The extraosseous odontomas were prominent and visible in soft tissues, either intraoral or determined extraoral asymmetries [10].

The diagnosis and classification of odontoma is usually by radiographic interpretation. In a radiography, a compound odontoma shows well-organized malformed tooth or tooth-like structures in a radiolucent space, whereas the complex type shows irregularly shaped radiopacity surrounded by a radiolucent rim. In cases where there are numerous tooth-like structures in a compound odontoma, differentiation becomes difficult [3]. If both clinical and radiographic images fail to give a final diagnosis, the histologic examination (mandatory postoperative) is used [11].

CLINICAL CASES

Case 1

A 48 years old female patient reported to maxillo-facial clinic with a complaint of pain in the right posterior mandibular region for about half a year. The pain was intermittent and was aggravated upon chewing.

There were no pathological signs in extraoral examination. During intraoral examination, a partially erupted tooth-like structure was seen in an edentoulous right mandibular zone. As a first impression, it was diagnosed to be a molar with advanced carious destruction. Radiographic retroalveolar investigation revealed the presence of a near-ovalar opaque mass resembling calcified tissue, measuring about 2/1 cm in diameter (with the large axis horizontal). The radiopaque mass with a density greater than bone, and equal or greater than that of the tooth, was surrounded by a radiolucent rim in all areas except the erupted

portion. Unfortunately, the radiography did not fully cover the entire mass, and could not reveal relationships with surrounding anatomic structures.

Removal of the mass was planned under local anaesthesia. The calcified mass was removed directly, like a tooth extraction, without adittional flaps or mucous surgery. The ovalar mass was about 2/1 cm in diameter with small irregular areas of indentations. The inferior side of the mass showed a hollow invagination giving the appearance of a small cup. The specimen was sent for histopathological examination. A diagnosis of complex odontoma was made clinically, histologically and radiologically. The intervention was succesful, but the radiological investigation was inadequate.

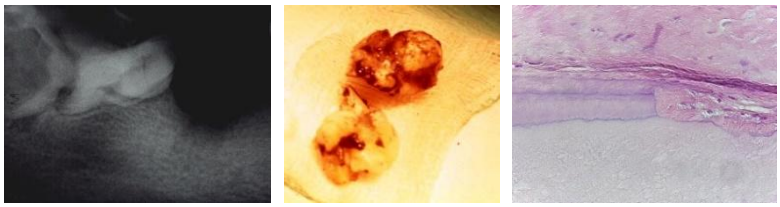


Figure 1. Case 1, radiographic, clinical and histological aspects

Case 2

A 16 year old male patient presented in the dentistry service with upper incisors heavy destructive processes. The panoramic radiography revealed the presence of the destroyed teeth with periapical inflammatory lesions and an unclear left maxillary radiopaque image. The patient was sent to the maxillofacial clinic.

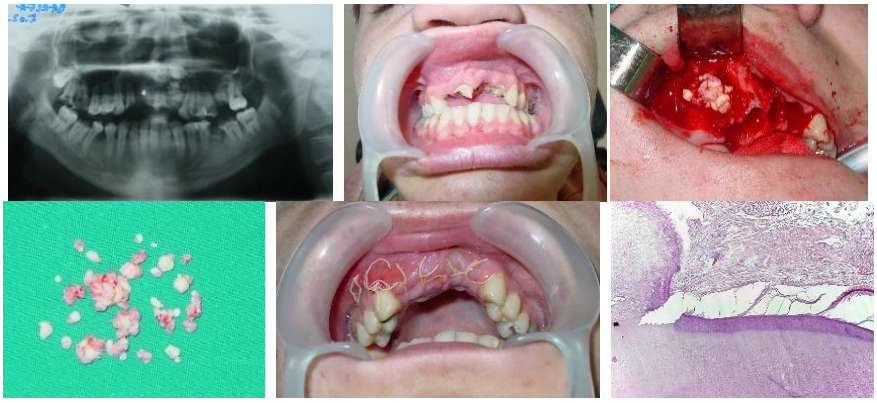


Figure 2. Case 2, radiographic, clinical and histological aspects

The patient did not describe previous maxillary or dental trauma. No clinical pathological signs were found in the extraoral examination. In the intraoral examination, the right and left central and lateral incisors occurred with severe coronary destruction. No other vestibular or palatal clinical pathological signs were present.

The analysis of the panoramic radiography revealed a number of structures that look like deformed teeth, placed up from the apex of 11 tooth and in the left anterior maxillary zone, between the 21 and 22 teeth apex and the nasal cavity.

The surgical procedure was performed in intravenous anesthesia, potentiated with local anesthesia. All the four maxillary incisors were extracted, and we removed the mineralized structures showing a tooth-like appearance. After complete detachment of the odontoma's small masses, we counted a total number of 68 pieces. The main disadvantage of the panoramic radiography was the lack of the image clarity. We could only

distinguish the many small opacities, without a complete 3D analysis.

Case 3

A 32 year old man presented in the maxillo-facial clinic, sent by a dentist to clarify the clinical and radiographic aspects of an edentolous area corresponding to the 23 and 24 teeth. The patient reported at one year old he fell, hitting his mouth on the floor.

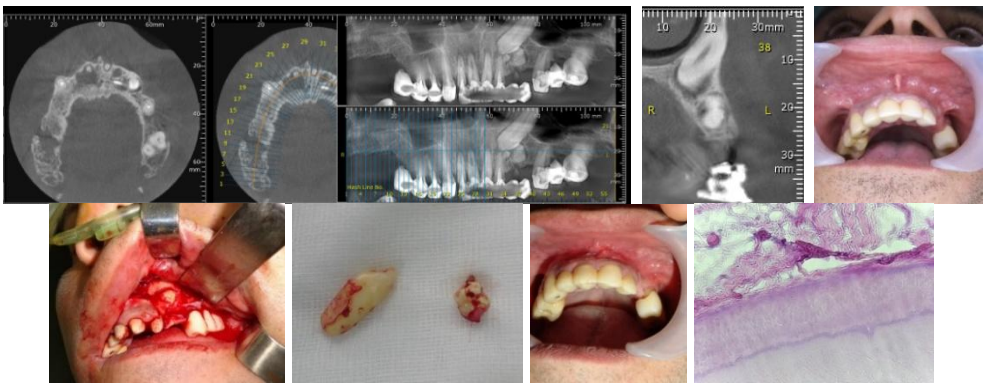


Figure 3. Case 3, imagistic, clinical and histological aspects

No clinical pathological signs were found in the extraoral examination. In the left maxillary zone, no clinical pathological signs were present, except the missing 23 and 24 teeth.

Panoramic radiography showed in the edentulous space an opaque inhomogeneous zone and the existence of the impacted 23 tooth, without further clarifying the situation. After clinical and radiographic examination, we suspected an odontoma placed lower from the 23 impacted tooth. Only after the patient performed the CBCT, could we clarify the situation: in the edentolous space it was confirmed that there were radioopaque masses (two soldered fragments), without contact with surrounding teeth. The lesion caused an impacted position of the 23 tooth, placed higher.

Surgical removal of the odontoma was performed in intravenous and local anesthesia, and two calcified small structures looking like teeth were found in it, as was anticipated from the CBCT. We made the odontectomy of the 23 impacted tooth (modified in shape and volume) too. The histological diagnosis of the radioopaque mass was compound odontoma.

DISCUSSIONS

We analyzed the odontoma radiological investigation methods from several points of view: price, irradiation, efficiency.

From the price point of view, the costs of the dental panoramic radiography is 3 times higher than the retroalveolar radiography, and the costs of the CBCT is 7-10 times higher than the retroalveolar radiography (depending on the segment analyzed).

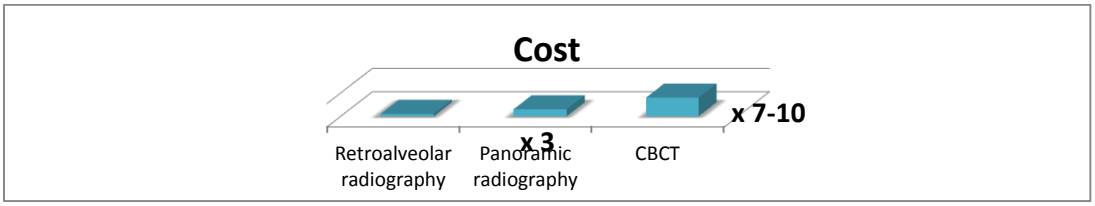


Figure 4. Cost comparison between retroalveolar radiography, panoramic radiography and CBCT

From the irradiation point of view, the lowest dose of radiation is recorded in retroalveolar radiography (less than 8 microsievert). The irradiation of the dental panoramic radiography vary between 9-26 microsievert (1 to 3 times greater). In comparison, the irradiation of cone beam CT (full mouth series) varies between 35 and 388 microsievert (4 to 48 times greater than retroalveolar radiography) [12].

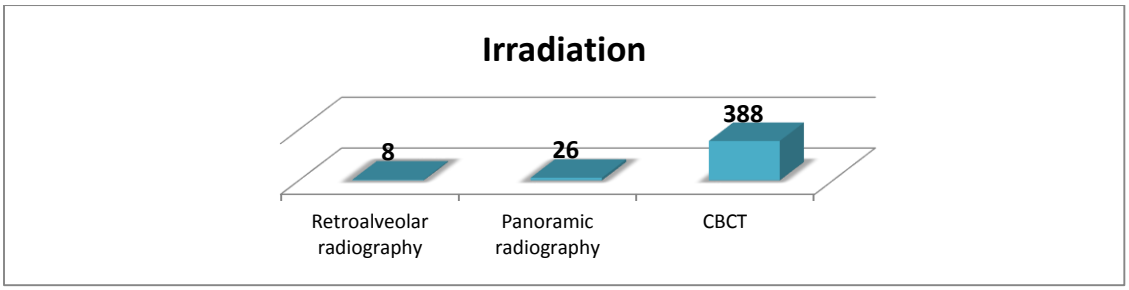


Figure 5. Irradiation comparison between retroalveolar radiography, panoramic radiography and CBCT

From the efficiency point of view:

- Retroalveolar radiography is cheap, with a massive radiation reduction, reduced exposure time, and short execution time (2-3 minutes). The main disadvantages that remain are that it is segmental, and sometimes only partially captures the pathological lesions.

- The main advantages for the panoramic radiography are: high visibility of the bones and teeth, low patient radiation dose, short execution time (3-4 minutes), and it is usable in patients with limited mouth opening. The main disadvantages that remain are the occasional lack of clarity of the image and the limitation to a bidimensional analysis.

- The disadvantages of the CBCT are the relative high irradiation level, the image noise and the poor soft tissue contrast, while its main advantages are the high speed scaning (less than 30 seconds), submilimetric resolution, and interactive 3D analisys.

CONCLUSIONS

Odontomas are common odontogenic tumors, which are usually asymptomatic and are diagnosed by routine radiographs. Any method of odontomas radiological investigation can not be considered ideal in several aspects [13,14].

The retroalveolar radiography can be considered optimal for the quality of the image, price, low irradiation and cost, but inacceptable in many cases to appreciate the real extension of the odontomas and the relation with the surrounding anatomic elements (teeth, sinuses, bone canals).

The panoramic radiography remains a good solution for the patient with a moderate budget, and patients who don't want radiate excessively. The predictive value of the investigation is intermediate, and the lack of clarity sometimes makes interpretation difficult. The main disadvantage is the lack of a 3D analysis.

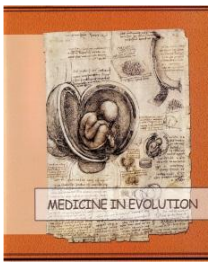
The advantages to the CBCT are: the 3D images intake, the possibility to establish a true relation of the odontomas with the surrounding teeth preoperatively, and it enables a better preparation of the operation, but is expensive and the radiation level is high in comparison with the other 2 methods.

The surgeon, sometimes after consultation with the radiologist, will decide what type of radiography (imagistic) is needed for his patient, taking into account all the above considerations.

REFERENCES

1. G. W. Shafer, M. K. Hine, and B. M. Levy, Eds., A Text Book of Oral Pathology, WB Saunders, Philadelphia, Pa, USA, 4th edition, 1983.
2. I. R. H. Kramer, J. J. Pindborg, and M. Shear, Histological Typing of Odontogenic Tumors, WHO International Histological Classification of Tumors, Springer, Berlin, Germany, 2nd edition, 1992.
3. V. Satish, M. C. Prabhudevi, and R. Sharma,"Odontoma: a brief overview,"International Journal of Clinical Pediatric Dentistry, vol. 4, pp. 177–185, 2011.
4. A. D. Hitchin,"The etiology of the calcified composite odontomas,"British Dental Journal, vol. 130, pp. 475–482, 1971.
5. B. A. Levy,"Effects of experimental trauma on developing first molar teeth in rats,"Journal of Dental Research, vol. 47, no. 2, pp. 323–327, 1968.
6. M. Vengal, H. Arora, S. Ghosh, and K. M. Pai,"Large erupting complex odontoma: a case report,"Journal of the Canadian Dental Association, vol. 73, no. 2, pp. 169–172, 2007.
7. O. P. Kharbanda, C. S. Sambi, and K. Renu,"Odontoma: a case report,"Journal of the Indian Dental Association, vol. 58, pp. 269–271, 1986.
8. M. S. Tuzum,"Orofacial pain associated with an infected complex odontoma—case report,"Australian Dental Journal, vol. 3, pp. 352–354, 1990.
9. M. Kaneko, M. Fukuda, T. Sano, T. Ohnishi, and Y. Hosokawa,"Microradiographic and microscopic investigation of a rare case of complex odontoma,"Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, vol. 86, no. 1, pp. 131–134, 1998.
10. L. Junquera, J. C. de Vicente, P. Roig, S. Olay, and O. Rodrıguez Recio,"Intraosseus odontoma erupted into the oral cavity: an unusual pathology,"Medicina Oral, Patologia Oral y Cirugia Bucal, vol. 10, no. 3, pp. 248–251, 2005.
11. Sujatha Govindrajan, J. Muruganandhan, Shaik Shamsudeen, Nalin Kumar, M. Ramasamy, Srinivasa Prasad. Complex Composite Odontoma with Characteristic Histology. Dentistry, volume 2013 (2013), ID 157614.
12. White SC, Pharoah MJ. Oral radiology, principles and interpretation, Mosby, 2009
13. Owens BM, Schuman NJ, Mincer HH, Turner JE, Oliver FM. Dental odontomas: a retrospective study of 104 cases. J Clin Pediatr Dent 21:261-64, 1997.
14. Philipsen HP, Reichart PA, Praetorius F: Mixed odontogenic tumours and odontomas. Considerations on interrelashionship. Review of the literature and presentation of 134 new cases of odontomas. Oral Oncology 33:86-99, 1997.

MICROSCOPIC ESTHETICS OF COMPOSITE-ENAMEL INTERFACE



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ABSTRACT

The disappearance of the harmonic balance of dental-maxillary elements acts negatively on two components: mechanical and aesthetic. To resolve that is a challenge both from macroscopic point of view (the proper dental clinic restoration), but also from microscopic point of view (the resistance of this restoration, the adhesion between materials).

We intended to answer the following question: are the composite restoration clinical performance influenced by the type of adhesive clinical technology, in order to obtain a homogeneous structure?

Were used 16 upper bicuspids, extracted for orthodontic reasons, and a"2 steps"adhesive system. The adhesive was applied onto the enamel surface in two manners: brushing (classical) and mechanical rotation (innovative). The composite paste was placed by layering and with transparent acetate crowns.

The dental composite constructions resistance in time depends on adhesion quality between enamel substrate and composite material. From optic microscopic point of view this means an interface with a homogenous aspect.

The mechanical innovative adhesive system application (rotation), the use of acetate crowns to configure the dental crown, and the increased enamel retention (enamel preparation with burs) can lead to a composite system with improved qualities.

Key words: *enamel, dental composites, crown restorations, aesthetics*

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INTRODUCTION

The introduction of composite resins and adhesive techniques led to more natural-looking restorations and with physical, chemical and biological properties closer to those of dental hard tissues. With the arrival of these techniques was possible to apply a fundamental biological concept - the tissue economy (preparation of conservative cavities, or strictly lesion treatment) [1, 2, 5, 8, 11].

Since these crown restorations retention is ensured in most cases by adhesion form/shape, results an aesthetic, functional and very fast treatment for dental pathology [7, 9, 12, 14, 15]. Still the longevity of such restorations in the oral cavity is subject to a number of factors involving the status of the patient, physician performance and quality of restoration [10, 11, 13, 15].

AIM AND OBJECTIVES

We intended to inquire that the composite restoration clinical performance is influenced by the type of adhesive clinical technology, in order to obtain a homogeneous structure, and thus a microscopic aesthetic structure.

MATERIAL AND METHODS

Our in vitro study was performed on the enamel of 16 upper bicuspids, extracted for orthodontic reasons. We used a 2 steps adhesive system (Gluma®, Heraeus-Kulzer, Germany), and a micro hybrid composite (Charisma®, Heraeus-Kulzer, Germany).

The teeth were kept in a solution of chloramine T 2% before ultrasonic cleaning for organic residues. Then the teeth were stored in saline solution at room temperature (25°C) up to the execution of the examination samples.

The adhesive was applied in two manners:

- in the classical way with a brush/applicator tip, and
- in a new original way – *mechanical rotation*.

The composite paste was also placed in two manners:

- in layers, and
- with transparent acetate crowns.

Its application was carried out according to the manufacturer's instructions, with the curing time of 20 seconds using a LED curing light (Dentmate®, Korea).

Then the teeth were sectioned using a diamond disc with active edge at conventional speed and running water, along to the vertical axis of the tooth, from buccal to oral direction. The buccal faces were sectioned into two halves to expose the stratification of the investigated area. The root portion has also been removed.

The samples were stored in a container in sterile saline solution at 4-5°C, until the surface examination. The samples were prepared in a specialized rotary facility using P800, P1200 and P2200 SiC sandpaper. Grinding was carried out under running water. To avoid prolonged contact of the sample with the air, between the three rounds of abrasive paper, the samples were washed thoroughly and were stored in a glass vessel with water at 25°C. After the polishing with P2200 SiC paper the samples were washed with running water and were stored for microscopic examination in a container with distilled water at 25°C for 24 hours.

Surface examination was qualitative, being achieved by high power light microscopy (100x) with a microscope type Neophot 21 (Microstructures Investigations Lab, Research Centre, INTEC SA, Bucharest), aiming uniformity and

continuity of the hybrid layer and mass characteristics of the composite.

The enamel was merely acid etched, or previously prepared with burs to increase surface retentivity.

RESULTS AND DISCUSSIONS

1. Dental composite in layers

Simple enamel acid etching provides a slight smear layer. After brushing application of adhesive are observed smear layer agglomerations in some areas, and denudation of other areas. This fact is marked with red colour, and this is the space between composite/adhesive and enamel surface. This limit is not unique, and has variable thickness. The composite mass (C) is almost homogenous.

From the width point of view, the interface between enamel and composite is similar with the one in fig. 1, but appears more as one line. The smear layer and adhesive rotated mechanical distribution is almost uniform. Although the composite mass has an aesthetic structure, due to layering and polymerization contraction, there are splits into the composite. These splits are going from the interface and getting into the composite building. They are parallel to each other and have a linearly direction (arrows).

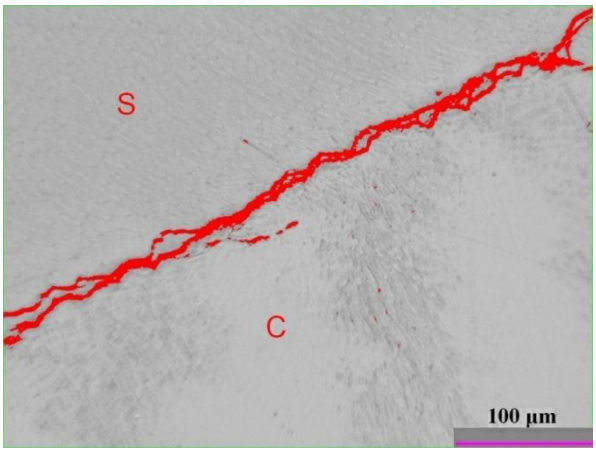


Figure 1. Acid etched enamel (S) and composite (C) interface, adhesive applied by brushing (100x)

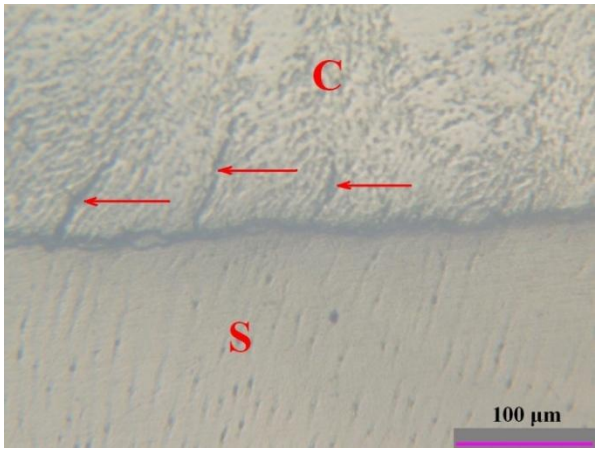


Figure 2. Acid etched enamel (S) and composite (C) interface, adhesive applied by mechanical rotation (100x)

2. Dental composite in acetate crowns

In this case we used a bulky composite mass. This presents short parallel splits (like in fig. 2), even the adhesive rotated application provides an aesthetic homogenous interface (quite linear).

This image shows a very close contact between enamel and composite structure (red square). This is the result of increased dental substrate retentivity (mechanical enamel preparation and acid etching) and of an innovative adhesive uniform distribution (mechanical rotation).

The acetate crowns allow a quasi-isostatic pressure during dental operations, and a successful composite modelling with small composite amounts (thin layers). There are no splits into the composite mass, and this has microscopic aesthetic homogenous aspect.

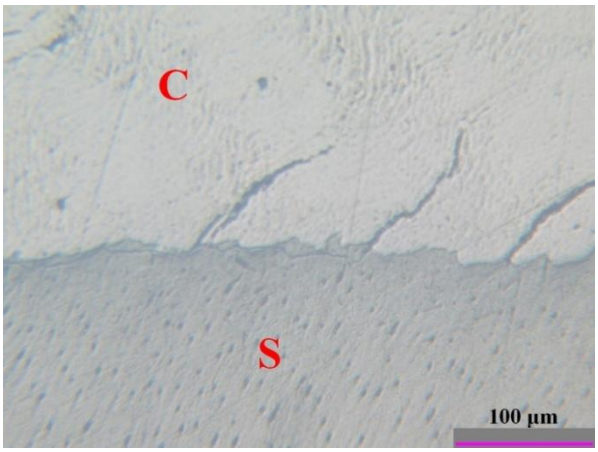


Figure 3. Acid etched enamel (S) and composite (C) interface, adhesive applied by mechanical rotation (100 xs)

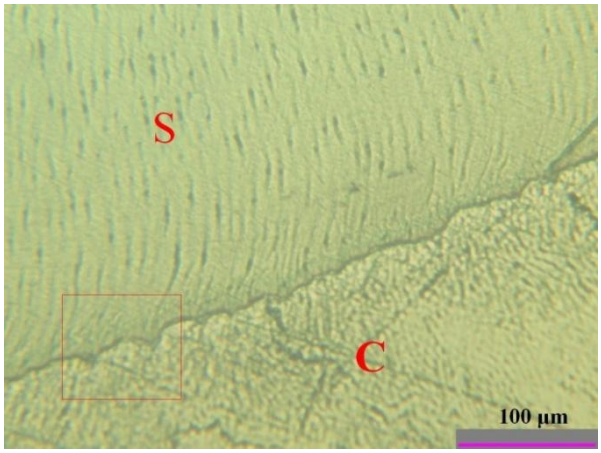


Figure 4. Mechanical prepared acid etched enamel (S) and composite (C), adhesive applied by mechanical rotation (100x)

CONCLUSIONS

The resistance in time of dental composite constructions depends on adhesion quality between enamel substrate and composite material.

From optic microscopic point of view this means an interface with a homogenous aspect together with the homogenous aspect of composite building.

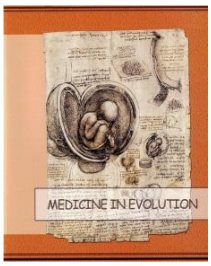
The mechanical innovative adhesive system application (rotation), the use of acetate crowns to configure the dental crown, and the increased enamel retention (enamel preparation with burs) can lead to a composite system with improved qualities.

REFERENCES

1. Abate, PF, Betacchini, SM, Polack, MA, Macchi, RL, Adhesion of a compomer to dental structures, Quintesence int., 1997, 28, 509-512,
2. Anusavice, KJ, Marker, VA, Preservative dentistry: A longitudinal approach, Dent Abstr, 1995, 270-272,
3. Beloica, M, Carvalho, CAR, Radovic, Ivana, Margvelashvili, Mariam, Goracci, Cecilia, Vulicevic, ZR, Ferrari, M, Efficacy of all-in-one adhesive systems on unground enamel, Int Dent SA, 2008, 10, 5, 12-17,
4. Bratu, D, Mikulik, L, Munteanu, D, Tehnici adezive în stomatologie, Ed. Facla, Timişoara, 1982,
5. Bunea, D, Nocivin, Anna, Materiale biocompatibile, Ed. Bren, Bucureşti, 1998,
6. Cox, CF, Hafez, AA, Akimoto, N, Otsuki, M, Biocompatibility of primer adhesive and resin composite systems on non-exposed and exposed pulps of non-human primate teeth, Am Dent J, 1998, 10, 55-63,
7. Desay, M, Tyas, MJ, Adhesion to enamel of light-cured polyacid dental materials, Aus Dent J, 1994, 41, 393-397,
8. Elbaum, R, Remusat, M, Brouillet, JL, Biocompatibility of enamel dentin adhesive, Quint Int, 1992,23, 773-782,
9. Gordan, VV, Vargas, MA, Denehy, GE, Interfacial ultrastructure of the resin-enamel region of three adesive systems, Am J Dent, 1998, 11, 13-16,
10. Kaeble, DH, Physical chemistry of adhesion, John Wiley, New York, 1971,
11. Krejci, I, New perspectives on dentin adhesion-differing methods of bonding, Pract Period Aesthet Dent, 2000, 12, 8, 727-732,
12. Murdoch-Kinch, C, McLean, M, Minimale invasive dentistry, J Am Dent Assoc, 2003, 134, 87-95,
13. Öztürk, B, Malkoç, Sıddık, Koyutürk, AE, Çatalbaş, B, Özer, Füsun, Influence of different tooth types on the bond

strength of two orthodontic systems, Eur J Orthod, 2008, 30 (4), 407-412,
14. Shapira, J, Eidelman, E, The influence of mechanical preparation of enamel prior to etching on the retention of sealants. Three year follow-up, J Pedont, 1984, 8, 272-274,
15. Van Meerbeek, B, Kanumilli, P, De Munck, J, Van Landuyt, K, Lambrechts, P, Peumans, M, A randomized, controlled trial evaluating the three-year clinical effectiveness of two etch & rinse adhesives in cervical lesions, Oper Dent, 2004, 29, 376-385,
16. Yazici, A, Ozgunaltay, G, Dayangac, B, A scanning electron microscopic study of different caries removal techniques on human dentin, Oper Dent, 2002, 27, 360-366

IMAGISTIC ASPECTS CONCERNING THE INCLUSION OF THE MAXILLARY THIRD MOLAR



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ABSTRACT

The most cases of tooth inclusion are those implying the third molars. Depending on its place, the inclusion can be intra-osseous or total, when fully developed tooth is fully retention in bone structure and osteomucous or partially, when the tooth is partially retained in bone and partly submucosal.

From the topographic point of view, it can be unilateral or bilateral, alveolar, ectopic and aberrant or heterotopic (remote socket).(1,2)

Key words: *maxillary third molar, inclusion, anodontia, radiography*

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INTRODUCTION

Valuable aid, might say indispensable in obtaining precious data on bone quality, condition reports with tooth and nearby structures has proven and continues to be radiological examination.

MATERIAL AND METHODS

To study included upper wisdom teeth we used retroalveolar and panoramic radiographs. Thus, in a first step, we establish whether it is an inclusion or an anodontia of the upper third molar. Once we establish that is inclusion, we determine the angle between its axis and tangent line passing the cusps of premolars and molars, thus establishing dental impaction type = angle α. If, on retroalveolare radiographs, we can not draw the occlusal plane, we determine the angle between wisdom tooth axis and second molar axis = angle β. So α = 90 - β (figure 1). (3,4,5)

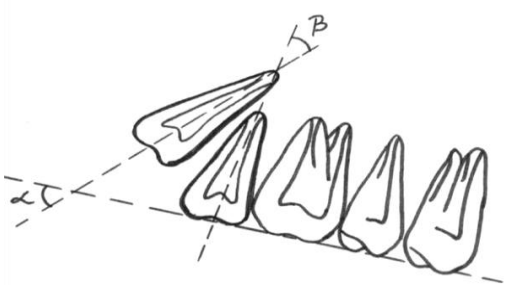


Figure 1. Determining the type of dental inclusion

We studied radiographic in order to examine 171 patients included in this study, who do not have in their oral cavity one or both maxillary third molars. Since only panoramic radiography simultaneously provide the two upper wisdom teeth, and because not all patients have x-rays on both three upper molars, we could not determine how many patients have anodontia, unilateral or bilateral inclusion respectively.(7,8,9)

RESULTS

Out of 205 maxillary third molars missing from the oral cavity, 42 of them missed on account of anodontia (20.49%), 163 on account of inclusion (79.51%): between they, 70 were in an osteomucous inclusion, 93 in a osseous inclusion; 81 at the level of the right quadrant and 82 at the level of the left quadrant.

A number of 115 maxillary third molars were found in a vertical inclusion, 3 were in a horizontal inclusion and 45 in an inclined inclusion: 37 were in distoinclination and 8 were in mesioinclination (table I).

Table I. *Percentage distribution by types of inclusions of upper wisdom teeth*

VERTICAL	HORIZONTAL	INCLINED	
		DISTAL-INCLINED	MESIAL-INCLINED
70,55%	1,84 %	22,70%	4,91%

We have not met vertically inversions, molars included axes ranging between 80°-100°. Also we have not met aberrations.

In terms of complications and accidents caused by superior wisdom teeth included (table II) we have:

- impacted third molars with no symptoms
- maxillofacial conditions of pain with radiation into the ear canal and orbit
- follicular cysts
- odontogenic maxillary sinusitis
- odontom.

Table II. *Complications and accidents caused by upper wisdom teeth*

ASYMPTOMATIC INCLUSION	86,65%
MAXILLOFACIAL PAIN	8.06%
FOLLICULAR CYST	3,68%
ODONTOGENIC MAXILLARY SINUSITIS	1,23%
ODONTOM	0,61%

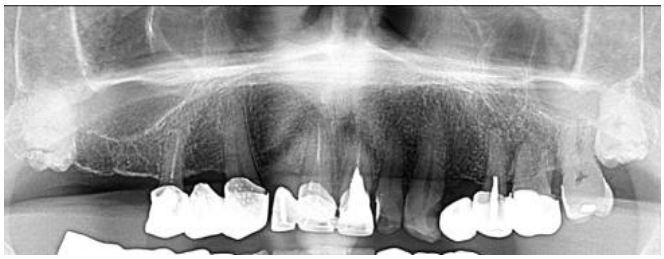


Figure 2. Molars 18, 28 - osteomucous vertical inclusions

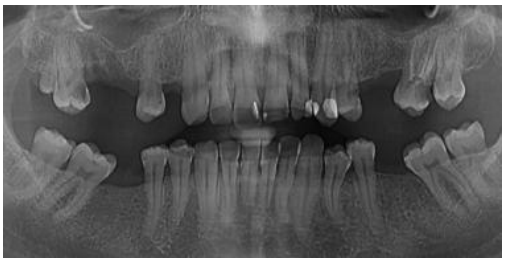


Figure 3. Molar 18 microdont, osteomucous vertical inclusion

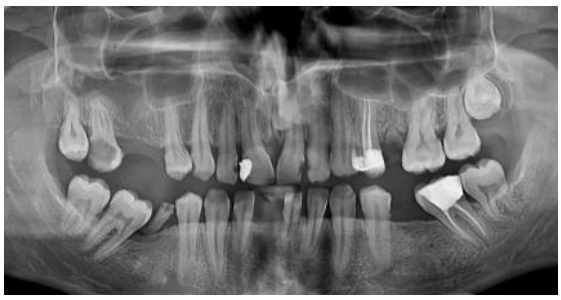


Figure 4. Molar 28 - vertical bone impaction

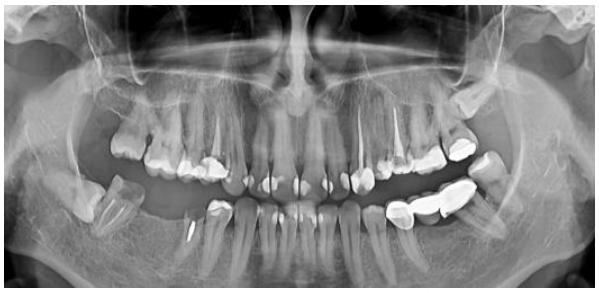


Figure 5. Molar 28 - horizontal bone impaction

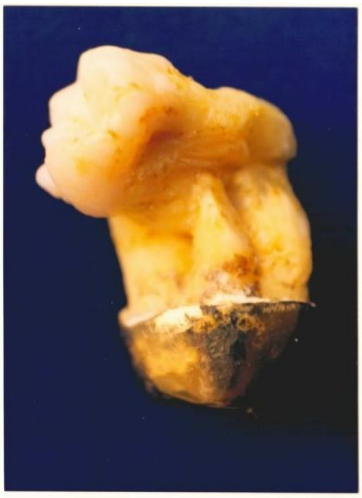


Figure 6. Molar18 - horizontal bone impaction

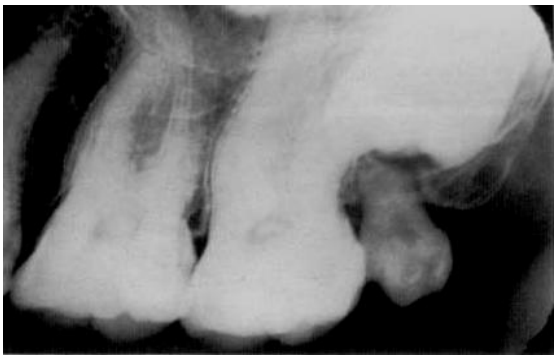


Figure 7. Supernumerary microdont, molar 28 - bone mesioinclined impaction

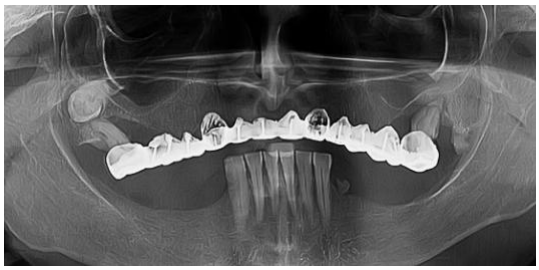


Figure 8. Molar 18 - bone distoinclined impaction

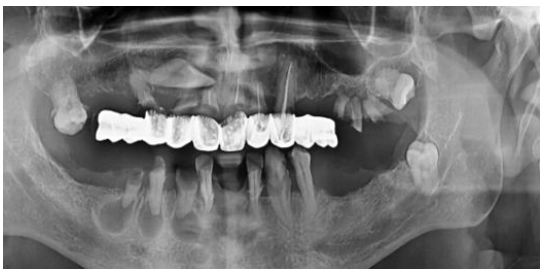


Figure 9. Molar 28 - osteomucous distoinclined impaction

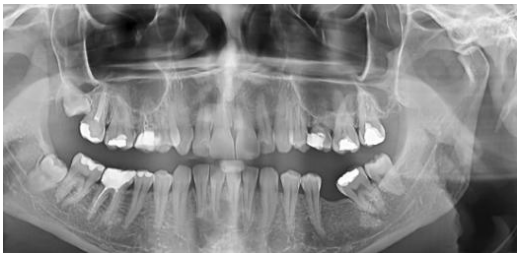


Figure 10. Molar 18 - osteomucous mesioinclined impaction

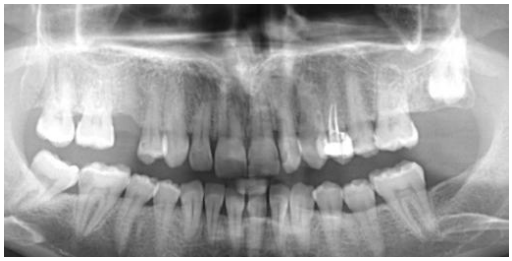
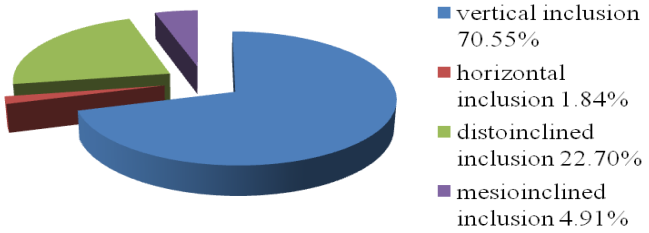


Figure 11. Molar 28 - bone mesioinclined impaction

DISCUSSIONS

Regarding the type of inclusion of upper wisdom tooth, data obtained are similar to those in the literature. The order of the frequency of superior wisdom tooth impaction is: vertical inclusion (two-thirds), distoinclined inclusion (a quarter) and with very small share mesioinclined and horizontal inclusion (one twelfth) (graphic 1).

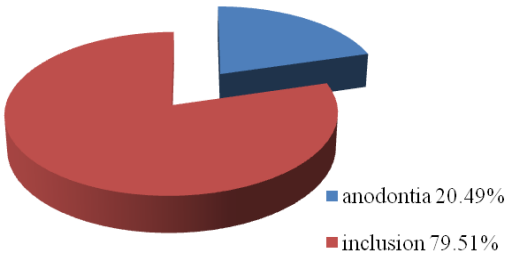


Graphic 1. Percentage ratio on the types of inclusions

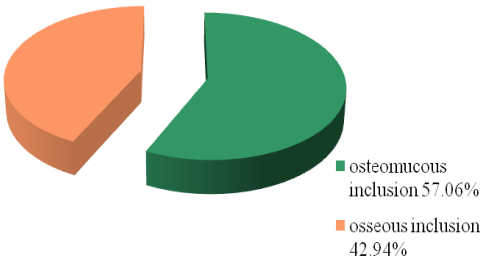
About a fifth between maxillary wisdom teeth are missing (anodontia) (graphic 2).

From the point of view of the depth, the osseous inclusion has 57.06%, while the osteomucous inclusion is 42.94% (graphic 3).

Radiographic methods used were not given the opportunity to determine whether inclined inclusions are in the sagittal or transverse plane.



Graphic 2. Percentage of anodontia



Graphic 3. Depth of impaction

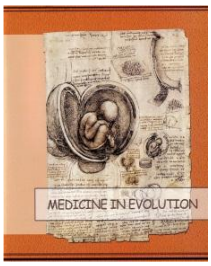
CONCLUSIONS

Included teeth can remain long time without clinically symptoms (86,65%), being discovered by chance during a radiographic exam, or other causes a series of accidents and complications, causing the patient to come to the dentist (13,35%). The clinical diagnosis, in cases where evolve with no disorders, is the finding of absence from the arch of the maxillary third molar, which the patient does not remember to be extracted, by mesial tooth movements, through the presence of a distal or vestibular swelling near the second molar. Correct diagnosis of dental impaction is given by radiological examination. (6, 7)

REFERENCES

1. Bratu E., Grivu O., Voinea C. - Normal and Pathologic Tooth Eruption, Helicon Publishing House, Timisoara, 1996.
2. Bratu E. - Glinical and Experimental Aspects of Dental Eruption (PhD Thesis), IM Timisoara, 1982.
3. Cindres Blaj S. - Wisdom Tooth Pathology, thesis, 1973.
4. Poyton A.G. – Radiographictehnique for Third Molars, Brit. Dent. J., 1958.
5. Rădulescu M. – Curs de radiologie stomatologică, Lito I.M.F., Bucureşti, 1980
6. Rădulescu M., Popescu V. – Radiologie stomatologică, Ed. Medicală, Bucureşti, 1985
7. Regezi J.A., Sciuba J. - Oral Pathology: Chemical - Pathologic Correlations, WB Saunders Company, Philadelphia, 1993.
8. Ricketts R.M. - Prognostische Untersuchungen zur Entferung dritter Unterkiefermolaren, Medica-Stuttgart, 1980.
9. Tetsch P., Wilfried W. - Operational Wisdom Extraction of Teeth, Wolfe Medical Publications Ltd, 1990.

PATIENTS MONITORING AND MOTIVATION FOR REDUCING THE INCIDENCE OF DENTAL CARIES



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ABSTRACT

Aim and objectives: correlating the degree of medical education of patients, the ability to address the dentist, dental health, motivation for adopting an individualized therapeutic hygienic-dietary behaviour to reduce the extent of damage to teeth due to caries. Material and methods: completing periodic evaluation questionnaires (every 6 months) relating the patient to the dentist using a type of Caries Risk Assessment Form; quantifying salivary pH levels, buffer capacity and stimulated saliva volume using a commercial kit (GC Saliva-Check Buffer); determination of oral hygiene index(GC Tri Plaque ID Gel); identifying the pathogenesis of bacterial dental plaque (GC Saliva-Check Mutans). Results: caries incidence decreased by 21,66% by motivating patients to comply to the hygienic and dietary rules that are noncariogenic, and by being present at standard evaluation and prophylaxis meetings and treating caries discovered. Conclusions: periodic dental eaminations, interceptive treatment and educating patients have significantly decreased the number of incipient caries detected during the monitoring period (2 years).

Key words: *caries incidence, dental health, motivating patients, salivary tests, oral hygiene, monitoring*

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INTRODUCTION

In Northern and Western Europe and the US, the incidence of dental caries experienced a significant decline in recent decades, in both primary and secondary caries[1]. The explanation of this phenomenon is found in numerous studies in medical literature and is due to the high level of health education, the constant rise in the concern for maintaining optimal orodental health and an aesthetic facial aspect, through accessing detailed information provided by specialized personnel and by using continuously improving oral care products (toothpastes, mouthwashes, interdental brushes, water flossers etc.)[2,3].

Regarding the oral health of the Eastern Europe population and from countries with low living standards, existing studies [4,5] reveal no significant improvement. This implies the need to implement educational strategies, motivation and orodental hygiene control for all ages, but with more concern twoards children and youth. [6,7].

Early diagnostics of preliminary caries using modern identification methods have played a major role in the education, awareness and accountabilitly of patients, as well as tracking the progression of caries for the same subjects examined periodically. Whether these devices use a fluorescent light laser (DIAGNODent), fiber-optic transillumination (FOTI), quantitative light-induced fluorescence (QLF) or digital radiography [8], they all have proved to better evaluate any demineralization of the enamel, type"white spot"than conventional radiography [9,10,11].

Linking classical diagnostic methods through visual inspection and palpation with dental probes and modern methods, which offer an immediate quantification via numeric codes or colours identification may form the optimal diagnostic method. Patients can also visualize the data registered on the devices display. The audible and visual impact of the diagnosis devices provides a good means of educating and keeping the subjects examined accountable. At the same time, using two or more methods, dentists can significantly reduce the risk of getting incorrect results. Any device can provide unreliable data, either due to environmental or any of the infinite variables for each individual's particular tooth structure.

MATERIAL AND METHODS

The present study aims to evaluate dental health improvement through regular monitoring and interceptive treatment, which was conducted between February 2013-May 2015 in Bucharest, on a group of 214 patients between the ages of 19-46. The study diverged in many different directions:

- Determining the patients level of medical education;
- Evaluation of patients access to information concerning methods and means of oral hygiene at home;
- Identifying patients ability to address the dentist outside of emergencies;
- Recording the dental health status through complex screening;
- Providing the rationale and motivation in adopting an individualized therapeutic hygienic-dietary behaviour, that will reduce the degree of impairment of teeth by dental caries;
- Evaluating over time the complications and deterioration of the coronal filling material used.

The following are criteria included in the study: satisfactory oral

hygiene (oral hygiene score OHS≤3), patients reporting regularly to their treatment sessions programmed and their agreement to follow their individualized prevention plan, patients with minimum 24 teeth in the mouth to the evaluation moment. Criteria excluded from the study: patients with diabetes with daily blood glucose values >160 mg/dl, patients taking antihypertensive medication or have xerostomia due to Sjogren's syndrome, with malignant tumors, with radiotherapy in the cephalic extremity or who have missed their scheduled sessions or presented themselves to emergency to calm the pain.

Choosing a lot of young patients is justified by the hypothesis that subjects participating in the study must be able to work well with examiners. Each patient was initially required to complete a form following the modified CRA Form model [12], by adding additional queestionnaires. At the same time, during the first examination, they were registered in patient data records by their degree of hygiene (OHS), dental health, accurate identification of incipent carious lesions (CI), active/cavitated (CA), secondary/marginal caries (CS) and non-cariogenic lesions (NC). Also during the first examination, the salivary tests were performed identifying the pathogenesis of bacterial dental plaque (GC Saliva-Check Mutans), quantifying salivary pH levels, buffer capacity and stimulated saliva secretion volume (GC Saliva-Check Buffer) and determining oral hygiene score (OHS) (GC Tri Plaque ID Gel).

Dental inspection was performed by 2 alternating examiners, by inspection and palpation with a dental probe and using a diagnostic device based on laser-induced fluorescence (DIAGNODent Pen 2190), in order to examine the occlusal, proximal, vestibular and oral dental surfaces. For accurate diagnosis of secondary marginal caries, the same device was used to assess the durability of light-curing composite fillings. All caries diagnosed, at whatever stage they were found, were treated by non-invasive methods (early tooth remineralization), minimally invasive (sealing widened cavities was done by sacrificing minimal dental tissue and adhesive crown restorations materials) or extensive restorations if the lesion passed the enamel-dentine junction.

Incipient caries identified with DIAGNODent Pen≤30 were treated by local fluoridation, in trays, using a 1,23% sodium fluoride and hydrogen phosphate fluoride gel (Densell Fluoride Gel), completed at home by the patient for one month by applying a product based on Recaldent (CPP-ACP=casein phosphopeptides-amorphous calcium phosphate), for example GC Tooth Mousse.

Carious lesions shown by DIAGNODent Pen having values between 30-60, were treated by local fluoridation, appyling a varnish containing 5% sodum fluoride (Profluorid Varnish, Voco GmbH) and by using a home-based Recaldent product and by rinsing 2 times/day with a 0.12% chlorhexidine mouthwash. If within three months, the values indicated were not dimished below 30, they were considered to be active enamel caries and were treated using a minimally invasive cavity preparation method, and the obturation was done with a glass ionomer or giomer/compomer dental material, for the extended-fluoride release effect.

In cases with active caries showing an indicative>60, cavities were prepared no supplementary extention and the restorations were made using a light-curing composite material (GrandioSO, Voco GmbH Germany or Gradia, G-aenial, GC Japan). If vital pulp extirpation was required as treatment, the decision was made to remove these teeth from the

study due to changing dental physiology.

RESULTS

Of the 214 patients, between ages 19-46, the percentage of female patients was almost double in this study, and those excluded represented 7,47% (Tabel 1). We can conclude that women followed their dental treatments and addressed the doctor without having medical emergencies more often than men.

Table I. *Distributing patient lots by age and sex*

Patients Lot	Total = 214							
Age	19-25 years		26-35 years		36-46 years		Excluded	
Female 138	49	22,89%	41	19,15%	39	18,22%	9	4,20%
Male 76	22	10,28%	34	15,88%	13	6,07%	7	3,27%

Oral hygiene index was determined by calculating the index of tartar and dental plaque. As expected, the variations were extremely high and did not meet any affiliation model to a particular group (age, occupation, environment). In general, urban population, raging from thoes with a higher education and ages of 25-35 years showed an OHS≤1 but 58,24% of the examined patients showed a OHS=3-6, which shows an insufficient level of oral hygiene, according to some authors (Arabaci T., Demir T.)[13].

The test for determining Streptococcus mutans present in the oral cavity showed to be positive in over 63,13% of cases, which is a determining factor in producing dental caries. If these results are correlated with thoes of a plaque index over 80% for more than half of the patients examined, with a tartar index up to 64% and with pH or salivary buffer capacity levels that in most cases are normal values, we can deduce that saliva plays an extremely important role in the remineralization of tooth surfaces, as long as acidogenic plaque and genetic structure of the tooth does not disturb the demineralization-remineralization balance.

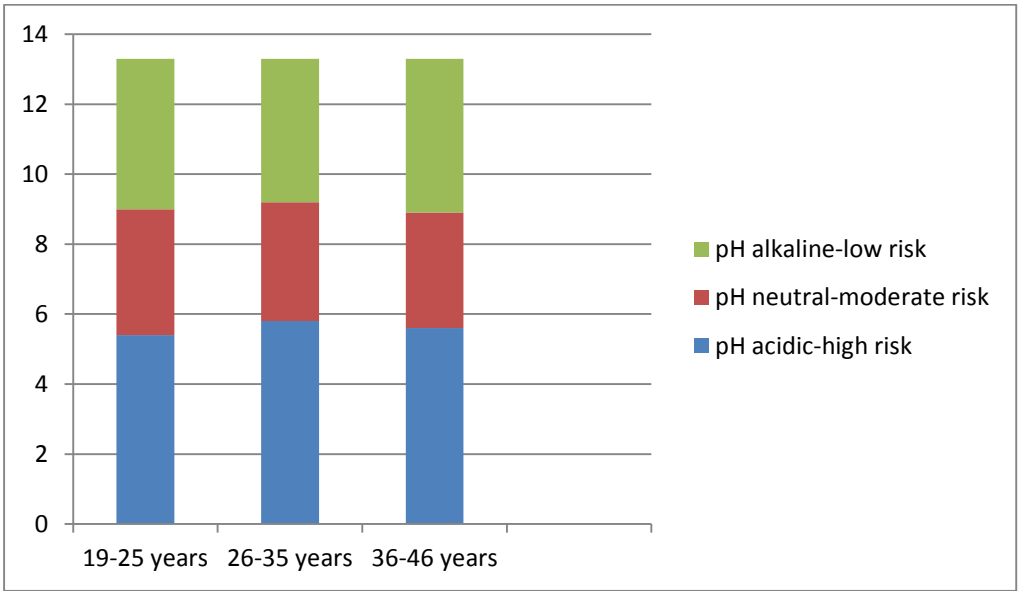


Figure 1. The average pH level by age and compliant risk groups

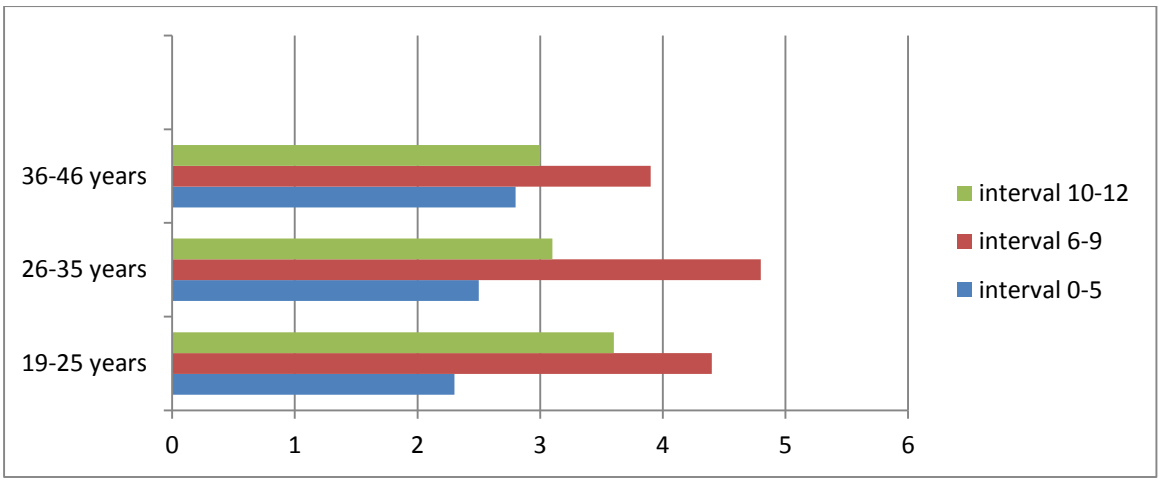


Figure 2. Salivary buffer capacity by age groups

Initially, each patient was examined on all visible tooth surfaces, excluding teeth incompletly erupted, with veneers, partial crowns, or those with metal fillings (amalgam, gold inlays etc.). Of the 21.708 dental surfaces examined, 41,67% had esthetic fillings or partial/complete dental sealings, 7,56% were classified as incipient caries, 4,87% non cavitary lesions, 19,29% were considered active caries and 10,34% were identified as secondary/marginal caries; fillings age range is between 0,3 to 12,4 years. The percent of healthy surfaces was 16,27% (figure 3). The distribution by age groups is represented in tabels II, III, IV.

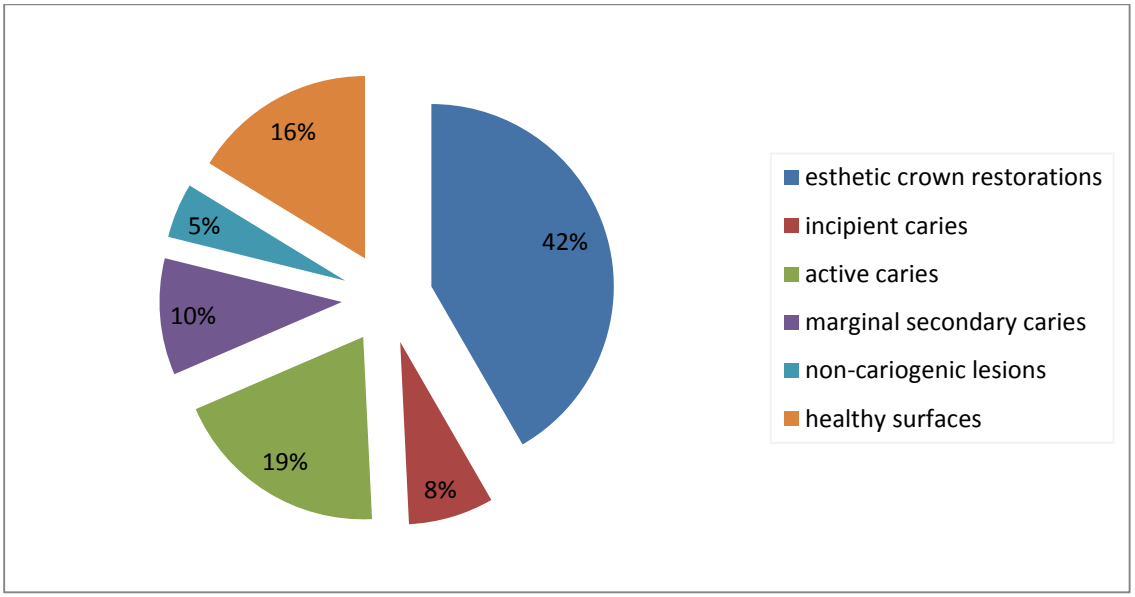


Figure 3. The distribution of carious lesions after the initial examination

Table II. *Distribution of dental defects in group ages 19-25 years*

№ of months	SI	LN	CI	CA	CS	OF
0	28,74	2,39	16,23	31,12	7,15	14,37
6	28,25	2,39	16,01	22,58	3,69	27,08
12	28,09	2,64	17,38	20,37	1,98	29,54
18	27,91	2,62	17,03	13,84	1,43	37,17
24	27,23	2,68	14,33	9,97	1,66	44,13
Group	19-25 years					

SI=healthy surfaces, LN=non carious lesions, CI=incipient caries, CA=active caries, CS= secondary caries, OF=physiognomic dental restorations

Table III. *Distribution of dental defects in group ages 26-35 years*

№ of months	SI	LN	CI	CA	CS	OF
0	26,42	2,64	18,44	37,25	9,23	6,02
6	26, 26	2,72	17,98	29,42	4,12	19,50
12	26,04	2,79	16,32	24,33	1,05	29,47
18	25,76	2,86	16,24	18,35	0,98	35,81
24	25,76	2,34	15,53	7,31	0,78	48,28
Group	26-35 years					

Table IV. *Distribution of dental defects in group ages 36-46 years*

№ of months	SI	LN	CI	CA	CS	OF
0	11,34	5,24	8,49	18,38	17,19	39,36
6	11,22	5,33	8,34	9,78	5,44	59,89
12	11,12	5,36	8,54	4,21	1,32	69,45
18	11,08	6,21	7,79	4,39	0,14	70,39
24	11,02	7,33	7,56	4,11	0,68	69,30
Group	36-46 years					

Correlations between incipient lesions detection and caries risk group assesment study determined an initial decrease of dental surfaces affected by dental caries and can lead to, in the following years, an overall decrease of this type of dental affection.

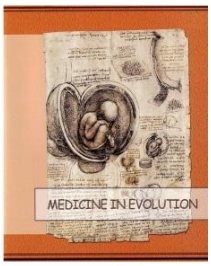
CONCLUSIONS

Given the limitations of the study carried out, the effect of patient monitoring after finishing a correct and complete treatment and placeing everyone in a caries risk group can provide long-term reduction of dental caries. It is important that salivas anti-caries role should not be overlooked and can be used as an individual benefiting factor. A series of usual recommendations, motivating patients to maintain a proper hygienic-dietary regime, selecting correct dental materials and using a minimally invasive preparation technique, can significantly increase the number of teeth preserved for longer periods of time.

REFERENCES

1. Nokhbatolfoghahaie H, Ali Khasi M, Chiniforush N, Khoei F, Safavi N, Yaghoub Zadeh B. Evaluation of Accuracy of DIAGNOdent in Diagnosis of Primary and Secondary Caries in Comparison to Conventional Methods. J Lasers Med Sci 2013; 4(4):159-67
2. Silva BB, Severo NB, Maltz M. Validity of diode laser to monitor carious lesions in pits and fissures. J Dent. 2007;35(8):679-82.
3. Lussi A, Hellwig E. Performance of a new laser fluorescence device for the detection of occlusal caries in vitro. J Dent. 2006;34(7):467-71.
4. Petersen PE. The World Oral Health Report 2003. Continuous improvement of oral health in the 21st century – the approach of the WHO Global Oral Health Programme. Community Dentistry and Oral Epidemiology 2003;31 Suppl 1:3-24.
5. Smedley B, Syme L. Promoting health. Intervention strategies from social and behavioural research. Washington DC: Institute of Medicine; 2000.
6. Marinho VC, Higgins JP, Sheiham A, Logan S. One topical fluoride (toothpastes, or mouthrinses, or gels, or varnishes) versus another for preventing dental caries in children and adolescents. Cochrane Database of Systemic Reviews 2004;(1):CD002780.
7. Batchelor P, Sheiham A. The limitations of a"high-risk"approach for the prevention of dental caries.

Community Dentistry and Oral Epidemiology 2002;30:302-12.
8. Sacuianu AE, Bondari A, Florescu AM, Biclesanu CF, Manu R. „Detectarea si tratamentul minim invaziv al cariei incipiente", Medicine in evolution, Volume XX, 2:277-282, 2014, Timişoara.
9. Shi XQ, Welander U, Angmar-Mansson B. Occlusal caries detection with KaVo DIAGNOdent and radiography: an in vitro comparison. Caries Res. 2000;34(2):151-8.
10. Pourhashemi SJ, Jafari A, Motahhari P, Panjnoosh M, Kharrazi Fard MJ, Sanati I, et al. An in-vitro comparison of visual inspection, bite-wing radiography, and laser fluorescence methods for the diagnosis of occlusal caries. J Indian Soc Pedod Prev Dent. 2009;27(2):90-3.
11. Sridhar N, Tandon S, Rao N. A comparative evaluation of DIAGNOdent with visual and radiography for detection of occlusal caries: an in vitro study. Indian J Dent Res. 2009;20(3):326-31.
12. Courtesy of Kutsch VK: Dental caries: An updated medical model of risk assessment. J Prosthet Dent. 2014;111:280-285.
13. Arabaci T, Demir T. An index developed for the determination of oral hygiene motivation success. Dent Hypotheses 2013;4:9-12.



STATISTIC STUDY OF THERAPEUTIC FAILURES IN THE CASE OF PATIENTS WEARING DENTURES ASSOCIATED WITH PSYCHOSOMATIC ILLNESS

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ABSTRACT

Objective

This here paper wants to show dentists the possibility of therapeutic failure in the case of patients wearing dentures if the case of them suffering from a psychosomatic illness is not taken into consideration.

Materials and methods:

This study was realised on 150 patients wearing dentures. They were given questionnaires that cover the 5 areas of diagnosing psychosomatic illness. The results were put into tables and graphics. We fallowed the next criterions:

-discrepancy subjective symptoms – objective exam
- time alternation of the symptoms
- associated health problems
- errors of the treatment committed by the dentist

Results:

Notice that, associated health problems exists over 78% in women and over 80% in men. Close to that, from the point of view of the frequency it is the related criteria to the coincidence events significant in the patients life.

Conclusions

By analyzing the results we can conclude the fact that there are patients who's psychosomatic pathology can confuse the dentist. A lot of the cases considered therapeutic failures were actually because of psychosomatic illness (a fact that was also confirmed by the psychologist) and were errors of treatment committed by the dentist.

Key words: *psychosomatic illness, dentures, questionnaire, dentist*

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INTRODUCTION

The majority patients who are wearing mobile prostheses are old. From this point of view, when we are applying a mobile prostheses to an old patient we need to considerate the pathology associated with the age (1).

Aging is a physiological process, being the last period of the biomorphosis. Aging is characterized by changes in physiological and psychological and social, changes of the behavior, thinking, attitude and interpersonal relationships (2).

Quality of the old patients life depends of his oral health, aspect which relates both physical and mental life (3).

Because of the involution process, the old patient it is in a state of instability both physical (diseases associated with the age) and psychological. So, extended partial edentation or total edentation on the aged patient has an physical impact (insufficient food mastication cause digestive problems, malabsorption syndromes) and psychological (aged physiognomy, avoiding social life, depression) (4).

Between somatic disorders appeared once with the age and psychological it is a strong connection. So physical disorders may increase or even trigger somatic disorders so as vice versa, diseases of internal organs, physical pain, hormonal changes appeared once with the age may trigger or increase physical disorders, which anyway comes with the age (5,6).

An important part of this process has: patient personality, his life experience that is an active person both physical and social, problems appeared in patient's life and the way how he handles problems. We conclude there is some general features the therapeutic meaning to an old patient, but each patient is the sum of general features given by patient's genetic and the environment he lives (7).

In elderly patients it is hard to figure out if we are dealing with a real problem of the denture or a mental disease. Sometimes discomfort feeling, sting, facial pain states can be caused by a dental prosthesis defect so the patient doesn't need to be treated as a mentally person from the start (8).

There are 5 diagnostic criterions and if are properly interpreted can make the difference between a psychosomatic patient and a patient with a real problem with the denture prosthesis:

1. First criteria – discrepancy between the subjective symptoms and objective one. For example, when the patient describes a facial pain states who doesn't comply the face midline, doesn't comply anatomically with the trigeminal nerve or appears and disappears depending on certain emotional mood swings of the patient, we can consider a psychosomatic condition.
2. The second criteria – significant alternations of clinical symptoms. A patient who describes a total atypical pain as intensity, occurrence, improving conditions, may be suspected by a psychosomatic affection.
3. The third criteria – ex non juvantibus diagnostic. When the therapeutic actions are demonstrated on a patient in terms of efficiency has no effect it can be considered a psychosomatic diagnosis. For example, if the pain doesn't yield after territory's anesthesia, although the patient recognizes onset of the anesthesia.
4. The fourth criteria – patient's personality. A patient with a choleric personality or conversely an introvert with depressive tendencies may be suspected with an psychosomatic affection. Personality peculiarities person's biopsychotipe, and it's

autobiography can suggest a psychosomatic affection.

5. Fifth criteria – coincidence, correlation appearance or symptoms changes with special meaning events for the patient. These events can be ordinary situations for most of the people, but on an individual level, the patient can give it another meaning. For example: moving into another house, children's marriage, retirement, may trigger psychosomatic

Beside these may be other criterions that can lead to this kind of diseases; the existence of family or in the entourage of a patient who is wearing dentures and doesn't tolerate it, developing an idea with negative connotation connected to this, the idea of dental prosthesis associated with age, fear of social rejection (9, 10).

For making a differentia diagnostic, sometimes you need the support of a psychologist or psychiatrist. There are cases where, with skill and tact, with minimal knowledge about the patient's psychology, in easy cases we can make the patient overcome difficult moments. In other cases, tactfully and with family support, guide the patient to a psychologist or psychiatrist (11,12).

OBJECTIVE

This study wants to show some certain specific aspects related to the acceptance of mobile dentures by total edentulous patients, given the fact that most of the patients were older and involves a specific pathology.

MATERIAL AND METHODS

This study was realized on 150 patients wearing dentures in dental offices and in the clinic of the Faculty of Medicine and Pharmacy Oradea, Department of Dentistry, 2012-2014.

The patients have the same area of origin (urban), no significant differences in terms of socio-economic situation and fall in the same age category.

They were given questionnaires, asking them to respond to 11 questions. The questionnaires were made to confirm the hypothesis of the research. The questions were made to ask these 5 criterions, to determine psychosomatic pathology. Also the patients underwent an endooral physical examination.

So, the hypothesis where we started from is:

Hypothesis: Psychosomatic pathology may be the cause of therapeutic failure in the case of patients wearing mobile prosthesis.

The answers were summarized in tables, on which were calculated the percentages. The data was processed by statistical mathematic methods.

Also, on these results were made graphics.

RESULTS

This study was realized on 150 patients, 100 women and 50 men. (img. 1).

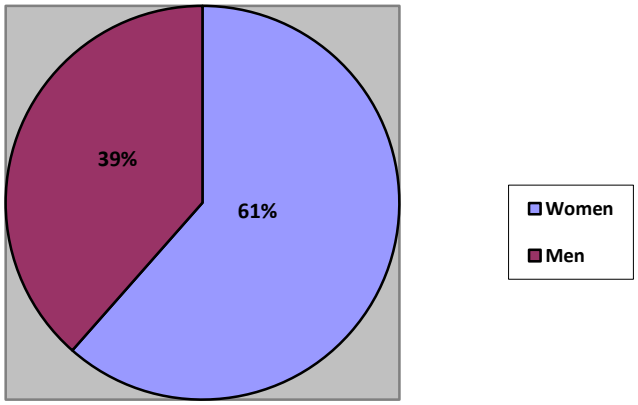


Figure 1. Gender distribution

Table I. *Research results number and percentage)*

CRITERIAS	GENDER		TOTAL
	Women	Men	
Subjective symptoms – objective exam	21 (32.85 %)	12 (30 %)	34 (32.69 %)
Time alteration of symptoms	10 (15.63 %)	7 (17.5 %)	17 (16.34 %)
Coincident events significant to the patient	48 (75 %)	25 (62.5%)	73 (70 %)
Associated health problems	50 (78.12%)	32 (80 %)	82 (78.84 %)
Multiple problems with previous dentures	20 (31.25 %)	7 (17.5 %)	27 (25.96 %)

These percentages relates to the total number of patients in that category. So, we have a clearer image of each criterion – associated health problems in over 78 % (women) and 80% (men). Shortly, from the point of view of the frequency, criterion is linked to significant events in the patient's life. We consider not the event itself but its significance for the patient. A particular event can affect a patient while the other may have a neutral connotation. Overall it is noticed that the group maintains the tendency percentages, criteria 3 and 4, respectively, Associated *health problems* and *Significant events in patient's life* having the highest weight.

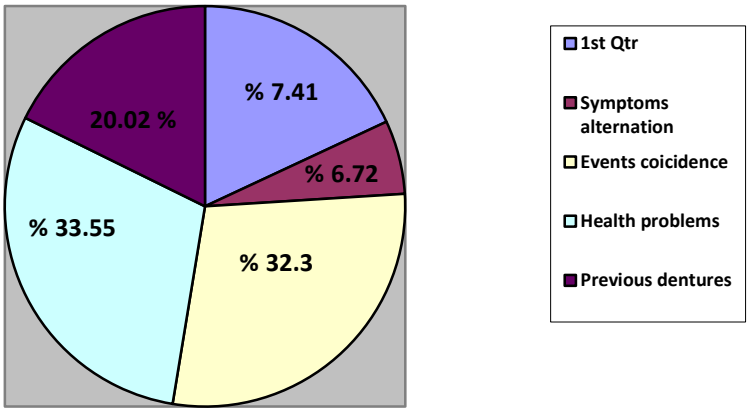


Figure 2. Diagnosis criteria presence for psychosomatic diseases in women

The percentages were calculated related to the patients – women who have been identified with one of those 5 criterions. So, the criteria 'Associated health problems', is not relevant in the absence of another criteria, but we can see from the graphic that this correlates with the 'Coincidence of significant events for the patient'.

We notice that, a significant percentage, caused problems with mobile prosthesis, some patients have a 'collection', we could say, of dentures which they didn't support it, and they changed lots of dentists, with the same result.

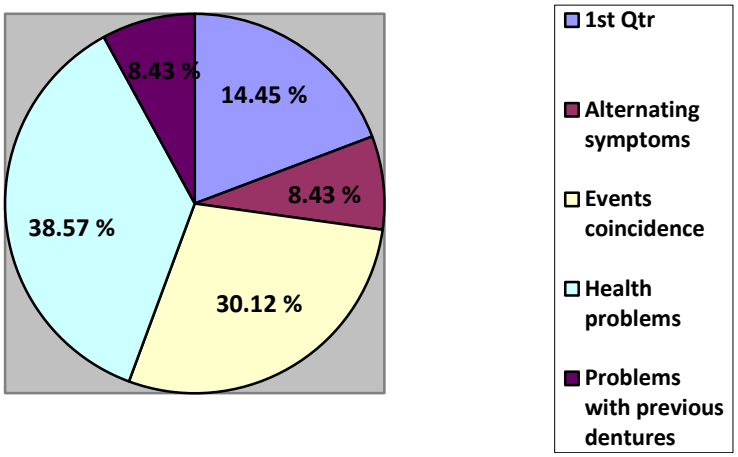


Figure 3. Diagnosis criteria presence for psychosomatic diseases in men

It is clearly observed that in the case of male patients we have similar percentages regarding these 2 criterions: 'Health problems' and 'Coincidence of the events'. Significant differences in male patients, is that there isn't a large number of patients, most of them said that although they had problems with previous dentures they preferred not to wear them and didn't insist so much as female patients in changing the dentist, where from the lower percentage of previous dentures.

Also, the first criteria, 'The alternation of subjective symptoms – objective exam', presents significant differences men-women and because male patients preferred not to wear dentures and they weren't so careful to the subjective symptoms only when it was a real problem.

CONCLUSIONS

From the results we can say that our hypothesis is confirmed, so there are patients that qualify for one or more diagnostic criterions of psychosomatic diseases. The percentage of peoples who are suspected with this disease is higher in women.

Notice that, the criteria with the higher frequency is the existence of associated medical problems (and because of the age), followed by the appearance of an important event in patient's life.

In order to have a suspicion of psychosomatic disease, we must have at least 2 criterions. At this age, the majority of patients experience health problems, but not all of them having psychosomatic disorders. Everything depends on the person and on many other factors, from patient's personality to the environment he lives.

No matter what, the patient must go to the dentist, but if there is a suspicion of a psychosomatic disorder, the treatment should be directed by a

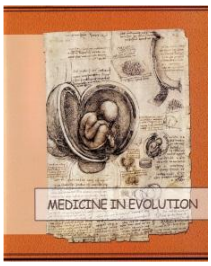
dentist in collaboration with the psychologist.

If this condition it is not recognized and appropriate measure are not taken, the patient returns repeatedly accusing various prosthetic issues, the dentist is trying solve the problems, often, by listening the patient's indications.

REFERENCES

1. Dalai C., Ignat-Romanul I., - Afecţiuni psihice şi psihosomatice în medicina dentară, Ed. Universitatii Oradea, Oradea, 2010
2. Despa E., Bîcleşanu C., Moise G., - Reabilitarea orală a pacienţilor, Revista Română de Stomatologie, Vol. IV, Nr.2, 2009
3. Holdevici I.-Psihoterapia cognitiv - comportamentală pentru cazurile dificile, Bucureşti, Ed. Dual Tech
4. Ionescu G.- Tratat de psihilogie medicală şi psihoterapie,Bucureşti, Ed. Asklepios, 1995
5. Lelord F., Andre C. – Cum sa ne purtăm cu peronalităţile dificile.Bucureşti, Ed. Trei, 2003
6. Radu I. –Metodologie Psihologie si Analiza Datelor.Bucureşti, Ed. sincron, 1993
7. http://www.sistempsi.ro/index.php?page=tulburari-psihosomatice
8. http://articole.famouswhy.ro/bolile_psihosomatice_cauzate_de__stres/
9. Ramona Amina Povovici, Virgil Ciobanu, Angela Codruţa Podariu, Mariana Păcurar, Ruxandra Sava Roşianu – „Sanatate Publică Orală. Management, epidemiologie şi biostatistică medicală", Editura Mirton, Timisoara 2014, ISBN: 978-973-52-1414-2.
10. Atena Găluşcan, Ramona Popovici, Angela Podariu, Daniela Jumanca, Roxana Oancea, Ruxandra Sava Roşianu, Anita Roşu, Carmen Iftimie - Sănătatea orală a pacientului cu dizabilităţi- Accesibilitate şi abordare în cabinetul de medicină dentară, Editura Eurobit, Timişoara 2009; ISBN: 978-973-620-561-3;
11. Ramona Popovici, Angela Podariu, Daniela Jumanca, Atena Găluşcan, Roxana Oancea, Ruxandra Sava Roşianu – Educaţia pentru sănătate oro-dentară, Managementul proiectelor educaţionale, Editura Mirton, Timişoara 2007, ISBN 978-973-52-0180-7;
12. Ramona Amina Popovici - Conexiunea Educaţie- Comunicare în managementul activităţilor de promovare a sănătăţii orale, Editura Nagard, Lugoj, 2009, ISBN 978-973-1900-52-0

THE ASSESSMENT OF IMAGISTIC EXPLORATIONS IN ORTODONTICS



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ABSTRACT

The aim of this study was to identify which are the most common methods for imagistic explorations in Orthodontics. We used 450 cases from the own casuistic of the authors. From the files of orthodontic treatment, we used: retrolaveolar dental radiographies on film, digital retrolaveolar dental radiographies, occlusive radiographies, orthopantomographies (OPT), lateral cephalometrics and CBCT. From the 450 files of treatment used, we observed that the indications of radiography for the retrolaveolar dental radiographies are reduced in number because in the moment of the initial examination of an orthodontic patient is preferred an OPT in the beginning, which offers a panoramic view. The occlusive x-rays of 5/8 cm are used in orthodontics after disjunction therapy with RPE (rapid palatinal expander), to visualize the breaking of the inter-maxillary suture. OPT is the most common used radiological investigations in orthodontics.The lateral cephalometric radiographies are, immediately after OPT, the most common used radiological investigations in orthodontics. The CBCTs are indicated in orthodontics for the cases of impacted maxillary canine.

The radiological investigation in orthodontics is, beside the study of the model, the most important complementary examination. Dental retroalveolar radiography and occlusive radiography are rarely used. The most common methods for imagistic evaluation in orthodontics are: OPT, lateral cephalometric radiographies and CBCT.

Key words: *orthodontics, dental digital radiography, irradiation*

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INTRODUCTION

Pediatric dentistry became in the last years a wellknown discipline, in order to improve the medical services for children and young adults.

But, both concepts and techniques used in pediatric dentistry are different from those used to adult patients.

No other innovation did contribuite so much in dentistry development as X radiation, discovered by Wilhelm Konrad Rontgen, in november 1895.

Since then, the X-ray methods suffered huge changes up to our days

MATERIAL AND METHODS

The aim of this study was to identify which are the most common methods for imagistic explorations in orthodontics because, as an orthodontist in my daily practice, I use many kinds of radiographies.

I will present some of them:

- Retroalveolar radiography
- Ortopantomography
- Occlusive radiography
- Lateral cephalometry
- CBCT

RESULTS

We used 450 cases from the own casuistic of the authors. From the files of orthodontic treatment, we used: retrolaveolar dental radigraphies on film, digital retrolaveolar dental radiographies, occlusive radiographies, orthopantomographies (OPT), lateral cephalometries and CBCT.

Dental retroalveolar radiography is rarely used in orthodontics, because we use more often the panoramic investigations methods of the entire maxilar. I still use it when I want to observe risa-lisa level to a tooth which I intend to extract in orthodontic purpose.

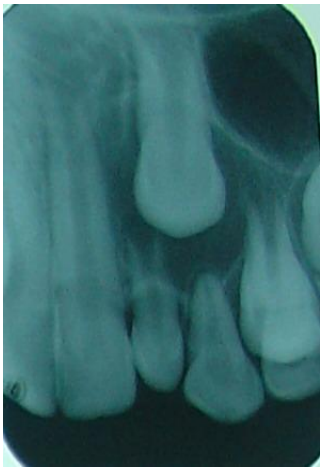


Figure 1. Dental retroalveolar radiography with permanent and temporary teeth

Another indication of dental retroalveolar radiography is in cases with diastema, when I want to observe the maxilar bone between the upper central incisors, in cases with combinated treatment: orthodontic and surgical, too.

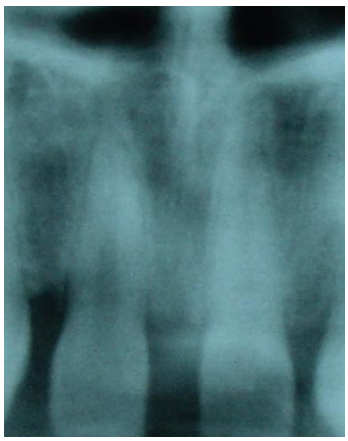


Figure 2. Dental retroalveolar radiography with diastema

The main progress in nuclear Phisics, Informatics, Electronics, computer sciences determinated the appearance of new radiological techniques or they improved the old one. **(1).**

In dentistry radiology an important stage was represented by panoramic technique progresses. In our days we frequently use orthopantomography (OPT). This technique allow us to have the image of upper maxillar and also lower maxillar, on the same X-ray. The technique was developed by Paatero.

Ortopantomography (OPT) offer us informations about:

- Temporary teeth
- Permanent teeth; the presence or absence of dental germs.
- The evolution of erruption
- The presence or absence of the space
- The form of the roots
- Supranumerary teeth

Difficulties of interpret appears in cases with disorders. Ortopantomography is sometimes difficult to make, technically, at small children, because of the long time of exposure. Although, the orthopantomographies are often indicate at children and OPT have a great assessment in orthodontic diagnosis!

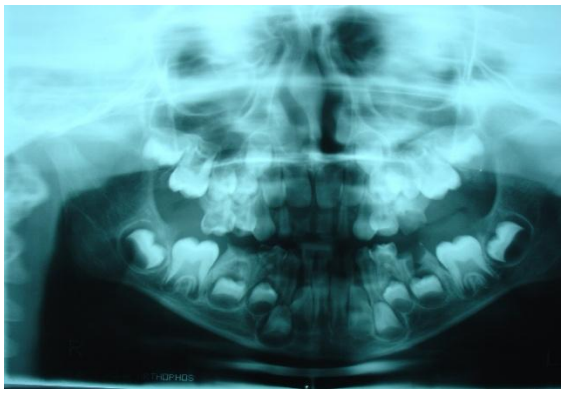


Figure 3. Ortopantomography in mixed dentation

It is also very important in cases with agenesia or supranumerary teeth, unique or multiple. **(2).**

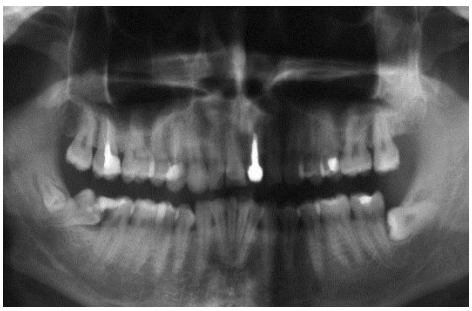


Figure 4. Supranumerary of 4.9

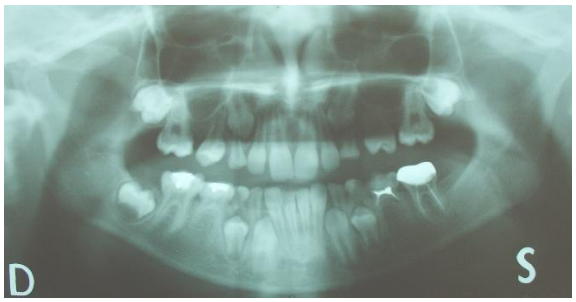


Figure 5. Agenesia of 1.5, 2.5, 3.5 and 4.5.

The occlusive x-rays of 5/8 cm are used in orthodontics after disjunction therapy with RPE (rapid palatinal expander), to visualize the breaking of the inter-maxillary suture **(3).**

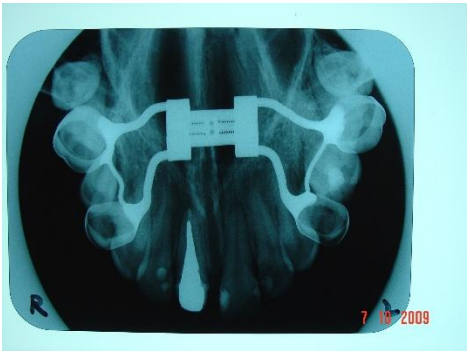


Figure 6. Occlusive radiography in a patient with RPE

The lateral cephalometric radiographies are, immediately after OPT, the most common used radiological investigations in orthodontics **(4).**

The CBCTs are indicated in orthodontics for the cases of impacted maxillary canine **(5,6).**

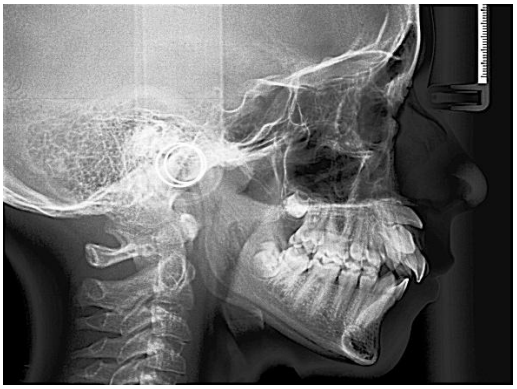


Figure 7. Lateral cephalometry in a patient with two supranumerary incisors

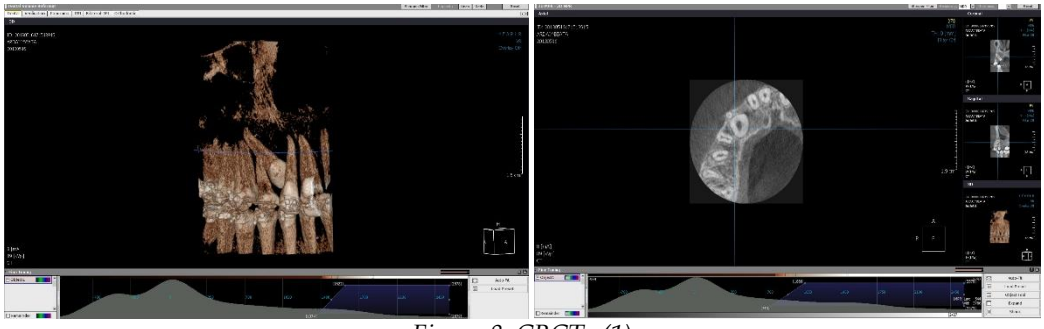


Figure 8. CBCTs (1)

Figure 8. CBCTs (2)

CONCLUSIONS

The radiological investigation in orthodontics is, beside the study of the model, the most important complementary examination.

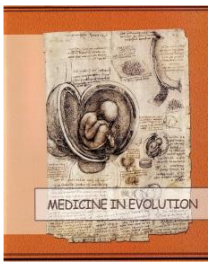
Dental retroalveolar radiography and occlusive radiography are rarely used.

The most common methods for imagistic evaluation in orthodontics are: OPT, lateral cephalometric radiographies and CBCT.

REFERENCES

1. Berkhout, Erwin, NM Kik, VMGG Derks: Quality control and patient exposure in intraoral radiography. The 14-th Congress of the European Academy of Dento-Maxillofacial Radiology, 25-28 iunie 2014.
2. Bornstein Michael M, Dimitrios Kloukos, Nicolas Pandis, Christos Katsaros, Jessica Mossaz: Evaluation of maxillary and mandibular supranumerary teeth using cone beam computer tomography. The 14-th Congress of the European Academy of Dento-Maxillofacial Radiology, 25-28 iunie 2014.
3. Bayrakdar Ibrahim Sevki, Ismail Gumussoy, Ozkan Miloglu, Yasin Yasa: Comparative evaluation of the rapid palatal expansion zone using ultrasonography and conventional radiography. The 14-th Congress of the European Academy of Dento-Maxillofacial Radiology, 25-28 iunie 2014.
4. Durao Ana: The influence of using 2D cephalometry on orthodontic treatment outcome. The 14-th Congress of the European Academy of Dento-Maxillofacial Radiology, 25-28 iunie 2014.
5. Ivanauskaite Deimante, Akvile Bernotiene, Migle Baneviciute, Assistant Gaulute Grigaite: Visual diagnostic template for prediction of treatment difficulty of impacted maxillary canine. The 14-th Congress of the European Academy of Dento-Maxillofacial Radiology, 25-28 iunie 2014.
6. Muntean Alexandrina, Michaela Mesaros, Anca Stefania Mesaros, Dana Gabriela Festila: Radiographic assessment of mesiodistal axial canine angulation in orthodontic patients. The 14-th Congress of the European Academy of Dento-Maxillofacial Radiology, 25-28 iunie 2014.

DOCTOR-PATIENT RELATIONSHIP JUDGING BY ETHICS



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ABSTRACT

The relashionship between medic and patient is very debated as of late, each medic having their own experience on the subject.The perspectives from which we want to analize this relationship are: the psychological, juridical and social perpectives.

From the psichological perspective we analize the communication side of this relationship, the medic's ability to make himself understood by the patient and the common acceptance in building a reltionship based on trust between the two. From the juridical perspective we will analize the patient's consent to the medical act. From the social perspective we will discuss the social factors that influence the medic-patient relationship and basicallu the reform of the health system. In conclusion we will note the principal steps that we consider important for creating a coresponding medic-patient relationship under all the mentioned aspects.

Key words: *ethics, medic-patient relationship, ability*

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INTRODUCTION

The doctor-patient relationship is a topical issue very publicized both by the scientific world and across media or even. Now developments and treatment options increased for patients.These claim being better informed and having access to more doctors and seek more treatment options not only professionaly but also to be compatible psychologically (1).

Some choose their doctor for the following reason: while communicating with patients he is optimistic, provides a reliable state. There are also patients who refuse becouse the doctor did not dispute the professional point of view just because they can not establish a relationship corresponding to it (1).

In ancient times, the company has proven the need to define a code of conduct own doctors to frame their activities and to give confidence to patients.The most famous, and oldest, is the School of Cos lead by Hippocrates (460-377 BC). The famous Hippocratic oath shall be filed after the entry into medical school and the physician agrees to submit to the rules in the future (2).

In general, doctors have conveyed this message and have complied with these principles contained in the Hippocratic oath over time.

Since 1990, ethics has earned an increasingly important place both in teaching and in medical practice.

In order to discuss ethics in the medical act we must first define the relationship established between doctor and patient.

The factors are not only psihologic.The patient interacts with several factors contributing to the achievement of this relationship. The prospects from which we analyze the doctor-patient relationship are psychological, legal and social (3,4).

1.The doctor-patient relationship from the psychological perspective

From the psychological point of view we can say that there is a defining factor for the doctor-pacient relationship. This relationship brings, in our opinion,efficient communication

Communication in the doctor-patient relationship

Communication is a fundamental element of human existence, since ancient sages were occupied with the art of rhetoric.

The dental office communication starts before the beginning of the treatment itself, sometimes with the first phone conversation,it continues with the consultation when doctor-patient relationship's foundation is set, and it is maintained during dental treatment and if it strengthens the relationship continues in the future.

This communication and the doctor patient relationship will also depend on the doctor's professional success in the future (5,6).

For this to be possible the performance communication are needed:

- Active listening;
- Understanding the message sent;
- Interpreting nonverbal language;
-sustainig the conversation.

Also,for it to be assertive communication, both partners involved have to be open to dialogue and willing positive purposeful communication. Assertiveness is a style of communication.

It requires the ability to express feelings, thoughts, beliefs and opinions openly, without violating the rights of other people. Assertive behavior is the balance between passive and aggressive behavior. It doesn' mean total obedience and submission to patient needs but skillful negotiation and efficiently exchange of medical information. There are three components of communication through which pass on information to

others: verbal, non-verbal and paraverbal.

The doctor has to be not only a good professional but also a good psihologist.Many problems come from failures and deficiencies unpleasant discussion between physician and patient.

In the relationship with the patient, the doctor must know the possibilities or professional boundaries. We must know that we are all conditioned by heredity, socio-cultural environment we come from, the discipline, ideology and religion in which we were raised, which is why we must"practice"the long critical sense to know to grasp differences of opinion or behavior and get closer to the soul and the personality of the patient and to have as good relations with him, we respect and respecting him.

Apart from communication psychologically important are:

• Factors relating to the patient: patient stress and coping resources, previous experience with dental treatment, his personality, socio-cultural background, age

• Factors relating to physician: the physician stress, personality, and psychological training thereof,

• Factors related to the environment: cabinet, auxiliary staff, tutors

• unpredictable factors: events occurring before or during the treatment which may influence its usual working conditions

Ethics in terms of the patient is mutual respect between the two partners doctor-patient relationship.

2.The doctor-patient relationship from a legal perspective

The legal Perspective also has significant repercussions on the doctor-patient relationship in practice. Increased autonomy principle in some advanced countries favored the concept focused on respect for the patient. This made the officials but on doctor-patient relationship to define a particular form of contract.

It is a physician-pacient agreement. The Agreement shall determine the terms and limits of the doctor-patient relationship and the responsibility they have each medical act. Legally, the doctor is an"expert"in the field of medicine, in a certain specialty."Citizen"is not seen in this perspective as a patient but as a payer (CAS), an individual who decides in his advantage (7,8).

In this case the medical profession does not agree, because it overshadows medical ethics and"cool" patient / physician relationship, increasing discontent with. This view is opposed by the Code of Ethics, College of Physicians and that the work which emphasizes the character of the patient / physician relationship practices autonomy, the relationship of trust, the confidentiality of the information and possible damage that it may suffer a patient. Here, as from within its contractual rights, obligations,ethical standards in medicine awarded in compliance with physicians particular patient – doctor relationship.

3.The doctor-patient relationship from the social perspective

Several social factors influence the doctor-patient relationship now:

- health care reform;
- Informing the patient by erroneous media means
- start a culture of individual rights, namely switching to a model of care in which the patient knows and wants to be heard and respected his opinions.

The existence of an austere budget for health, dysfunctions of the National Health Insurance, rising unemployment and the large number of underprivileged social problems it is now facing the doctor-patient relationship.

The patient can not afford certain health services and therefore requires its rights sometimes erroneous or incomplete publicized mass media.We

have numerous examples of patients who know from the media that also qualify some facilities but not the fact that these facilities are granted within his buget. This question can start discussions and accusations against the doctor who would be guilty of impossibility to provide those facilities.

Also the culture and education of the patient will have its say in establishing effective doctor-patient relationship (9,10).

Ethics in the medical and patient doctor relationship

Ethics belongs to the world of ideas, great guidance, trying to bring a theoretical justification principles of action. The profession doctor must undergo a strict code of ethics more than professionals in other fields.

This code is the Code of Ethics, regularly"brought up to date"by order (College) Physicians. In other words it is tailored evolution of medical practice.

Ethics secure medical debts, duties and limits their action. The Code serves as the basis of professional courts, being a precious and indispensable tool, but at the same time, it can not dispense with a personal reflection on medical ethics issues.

Jurisdiction ethics proposes secondly the ability to deliberate, to understand the meaning of different legal rules, medical and institutional question and evaluate them. This assessment, which is performed in a constant dialogue with the patient, claims to know the different rules should be prioritized.

Finally, medical ethics competence involves the ability of the physician to critically analyze its decisions in the light of a number of external elements, both cultural and social. A good example would be the new role of the physician and assumes it as"guardian"of the system, forcing the government to take into account the interests, house insurance, etc., the ultimate goal being the good of the patient.

CONCLUSIONS

The relationship with the patient, the doctor must know the possibilities or professional boundaries. We must know that we are all conditioned by heredity, socio-cultural environment we come from, the discipline, ideology and religion in which I was raised, which is why we must"practice the"long critical sense to know to grasp differences of opinion or behavior and get closer to the soul and the personality of the patient and to have as good relations with him, we respect and respecting him.

In conclusion, to talk about ethics is to speak competently ability to dialogue, to deliberate and make critical analysis of social practices and its own practices. In this regard, ethical competence is not simply applying what you learned or a set of skills that might reduce the technical quality.

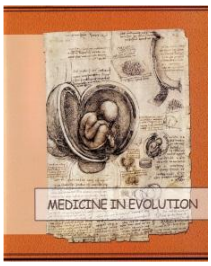
Jurisdiction ethics"comes"from above you college graduation,"grows"along with experience in the relationship with the patient and use critical reflection.

REFERENCES

1. Heifetz D. Milton. Ethics in Medicine.Prometeus Books, 1996
2. Sugarman J, Sulmasy D.Methods in Medical Ethics.Georgetown University Press, 2001
3. Breen K, Plueckhahn V, Cordoner S.Ethics, Law and Medical Practice,Allen & Unwin Press, 1997
4. Radest H.From Clinc to Classroom: Medical Ethics and Moral Education, Praeger Press, 2000

5. Clinical Ethics and Law.https://depts.washington.edu/bioethx/topics/law.html
6. https://depts.washington.edu/bioethx/
7. https://www.ethicsandmedicine.com/
8. Ramona Amina Povovici, Virgil Ciobanu, Angela Codruța Podariu, Mariana Păcurar, Ruxandra Sava Roşianu – „Sanatate Publică Orală. Management, epidemiologie și biostatistică medicală", Editura Mirton, Timisoara 2014, ISBN: 978-973-52-1414-2.
9. Ramona Popovici, Angela Podariu, Daniela Jumanca, Atena Găluşcan, Roxana Oancea, Ruxandra Sava Roşianu – Educația pentru sănătate oro-dentară, Managementul proiectelor educaționale, Editura Mirton, Timişoara 2007, ISBN 978-973-52-0180-7;
10. Ramona Amina Popovici- Conexiunea Educație- Comunicare în managementul activităților de promovare a sănătății orale, Editura Nagard, Lugoj, 2009, ISBN 978-973-1900-52-0

LEGISLATION AND MANAGEMENT IN THE DENTAL OFFICE



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ABSTRACT

Introduction: *The medical office is defined as an unit"providing public services, by state or private, of preventive human health, curative and emergency recovery."According to legal provisions, health services are managed in dental medical offices performed by doctors (dentists, specialists, primary doctors) and other authorized medical staff (nurses, prophylaxis nurses, dental technicians).*

Methodology: *Evaluation of accessibility to dental health services on organizational form (individual, grouped, associated medical office, medical civil company)*

Results: *The mission of a medical office is getting a positive result that is intended to be achieved in future by the structure health, aiming: conclusive results on patients (quality of service, satisfaction degree), substantial internal performance registered by the medical team (professional, financial and material).*

Conclusions: *The mission of a medical office expresses the purpose for which it was created, its reasoning in relation to the health care market and implicitly to the committed or potential patients. By defining the mission, the intentional elements, specific groups of patients, basic needs of existing and own performances of the medical office are set.*

Key words: *medical dental office, dental medicine services, accessibility, quality, performance*

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INTRODUCTION

The medical unit is defined as a"public service providers, public or private, human health preventive, curative and emergency recovery."According to legal provisions, health services management in dental and medical offices is performed by physicians (dentists, specialists, primary) and other authorized medical staff (nurses, prevention, dental technicians). [1]

A dentist, also known as a dental surgeon, is a doctor who specializes in the diagnosis, prevention, and treatment of diseases and conditions of the oral cavity. The dentist's supporting team aids in providing oral health services. [2] The dental team includes dental assistants, dental hygienists, dental technicians, and in some states, dental therapists.

In a dental office business just because something isn't broke, it could still need fixing. For example: if you have been running your practice the same way for decades, without investing in new equipment, staff, skills and management training, marketing and outsourcing, then you are ignoring your business's untapped potential. By spending money on the dental office practice, you can increase the patient-base and the business's profitability and success, while decreasing the stress levels and the pressures that come with running the own business.[3-6]

To be a good dental office manager you have to take care from the begging about:

1. **The dental office space to be in a good condition.** If the dental office space is rented you have to install drywall and plumbing in order to design the examination rooms and sterilization areas your practice requires, for this the doctor had to make improvements to the building. The doctor has to ask the agent about adding"tenant improvements and betterments"coverage in the property insurance so repair or replacement costs for these items don't come out of the doctor pocket in the event of a covered property claim.

2. **The medical equipment to be very well maintained.** Medical equipment isn't just expensive to repair. Broken or malfunctioning equipment can also injure patients, and that's a prelude to a malpractice claim. Luckily this risk can be prevent by:

- Make sure new equipment is checked and calibrated before it's used.
- Remove malfunctioning equipment immediately.
- Test all repaired equipment before use.
- Perform regular preventive maintenance.
- Train all staff on the proper use and care of equipment.
- Keeping a maintenance log, too.
- Record the date and type of service performed, and document who tested the equipment before it was used on patients.

3. **The patient data to be safe and record about the rules.** The doctors have to take care about data protection and for this you have to respect the IT security standards and heavy fines for violations. If patient records are lost or stolen because the doctor must do more than respond to the breach and notify affected parties, he has to may also have to pay fines. Complying with security rules can minimize the risk of exposing patient records in the first place. The doctor might also want to document the efforts, audit your security practices, and train the staff on cyber security. To address the financial side of data breaches, consider carrying cyber liability insurance. Many cyber liability policies can provide coverage for data breach response expenses, such as patient notification and security repairs. Some policies may even offer

coverage for regulatory fines. Good managers have to talk to the insurance agent to learn what the policy can and can't do.

4. **To have a disaster plan.** Good dental office manager have a plan for the heavy-hitting events that could shut down the business, but a disaster doesn't have to be Super storm Sandy-sized to knock the doctor practice off track. Sometimes, someone else's trouble (e.g., a supplier's interruption or a neighbor's fire) may be enough to shut down the dental office for a while. Whether the dental practice can survive these hiccups depends on the manager planning. Even though the doctor/ manager operations may be suspended, the doctor lenders, landlord, and employees still expect to be paid. Without money coming in, covering the dental office expenses can get tricky. A thorough business continuity plan can help you handle adversity. To get the doctor wheels turning on what the manager plan should address, answer the following questions:

- How can we secure our patient records and other documents?
- Do we have a backup energy source?
- How can we secure our computers, servers, and backup data?
- Can we access our insurance documents?
- How many days can our dental supplies last?
- Who is in charge of securing our dental equipment?

To boost the dental office plan, you have to consider purchasing business interruption insurance. This policy can provide coverage for the dental office lost income and fixed costs when certain events (e.g., windstorms or fires) temporarily shut down the medical practice. Some policies even help out when a supplier's interruption keeps the dental practice from operating.

5. **To take care about the finances.** While it may be tempting to hire a bookkeeper and let that person handle all the money issues, that decision could come back to haunt you. Even if embezzlement isn't on the dental office manager radar (read the report before you make that call), the manager don't want other financial mishaps to take you by surprise. The asks which any dental office manager has to have a always an answer are:

- How is our money being spent?
- What's our average production per patient?
- What percentages of accounts pay within 30 days? Within 60 days?
- How often are accounts sent to collections?

The answers to these questions can give to a dental office manager a better picture of their practice's profitability and prompt you to make changes if necessary. As a dentist, the savvy about the risks that lurk in the mouths of the patients is necessary. Treat the business with the same care that use filling a cavity and that will be set for long-term health.[7].

METHODOLOGY

For this study we make an evaluation of accessibility to dental health services on organizational form like: individual, grouped, associated medical office and medical civil company in Timis County in 2014. We wanted to see what facilities are in dental medical practice in this county. We analyzed the management of the dental offices, the accessibility to these services and also the quality of the medical services pretense. This was made by questionnaire applied to 56 doctors, 23 nurses and 14 dental technicians, who ware analyzed in most of the situation together, and a

questionnaire with 15 questions to 103 patients.(see table 1) The statistical analyzes were made with SPSS 19.0 vs.

RESULTS AND DISCUSSIONS

The mission of a medical office is getting a positive result that is intended to be achieved in future by the structure health, aiming: conclusive results on patients (quality of service, satisfaction degree), substantial internal performance registered by the medical team (professional, financial and material).

Table 1. *Sample studied (absolute frequency=n, percentages frequency= %)*

	medical personal		patients	
	n	%	n	%
urban	62	66,66%	68	66,67%
rural	31	33,33%	35	33,93%
20- 35 years	22	23,66%	33	32,04%
35- 50 years	56	60.22%	25	24.27%
50- 60 years	13	13.98%	20	19.42%
> 60 years	2	2.15%	25	24.27%

The dental office management was not very good in rural area, and we observed that the management is better in dental clinics than medical civil company. (See figure 1). In the rural area are problems with the planning of the improvement the quality of work in the dental office 19.35%, they don't have a security mode to record the data patients 64,52%. The same problems were observed also in the urban area. If we analyze this management points we observe also that the best management is made in the dental clinics with 2 or more dental offices, and were are working more than 2 or 3 doctors, and if they have a nurse.

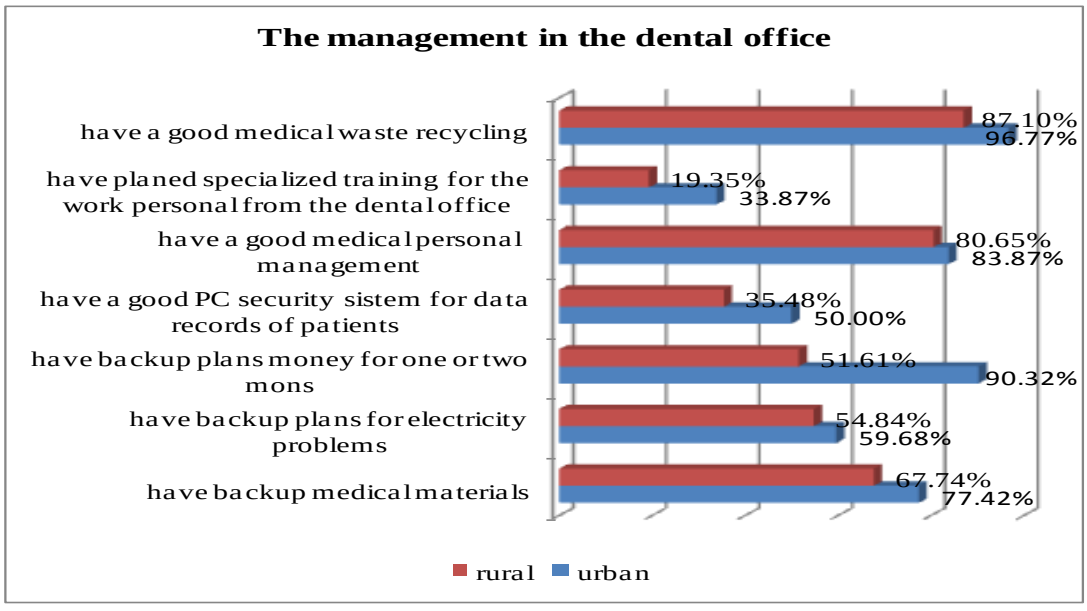


Figure 1. The management in the dental offices

Table 2. *Indicators for a good management plan for running the Dental Office saw by the medical personal*

indicators for a good management plan for the dental office	dental clinics with > 2 doctors and nurse	dental clinics with > 2 doctors without nurse	civile office with nurse	civile offcie without nurse
have backup medical materials	19 100%	15 88,24%	18 69,23%	17 54,84%
have backup plans for electricity problems	16 84,21%	13 76,47%	15 57,69%	10 32,26%
have backup plans money for one or two mons	18 94,76%	16 94,12%	21 80,77%	17 54,84%
have a good PC security sistem for data records of patients	17 89,47%	11 64,71%	10 38,46%	4 12,90%
have a good medical personal management	19 100%	16 94,12%	24 92,31%	18 58,06%
have planed specialized training for the work personal from the dental office	16 84,21%	6 35,21%	4 15,38%	1 3,23%
have a good medical waste recycling	19 100%	16 94,12%	24 92,31%	18 58,06%
Total	19 100%	17 100%	26 100%	31 100%

The accessibility to the dental medical services in Timis County is better in urban area, the best is saw by the patients the easy programming, the time waited in the waiting room less than 20 minute is 72, 06% in urban area and 25, 71% in rural area. The transparency with costs is 75% in urban area, and just 31, 43% in rural area, p= 0, 05. The accessibility at dental medical care is seeing better in the urban area, and also the management of the dental office by the patients. Improving dentists' participation in CJASTimis programme, to have contract with CJASTimis may increase the likelihood of children receiving restorative and preventive dental care. The number of contract with CJASTimis dentists, however, only had a modest effect on children's likelihood of receiving restorative and particularly preventive dental care. Clearly, factors other than the availability of participating dentists influence children's dental care use in public insurance programs.

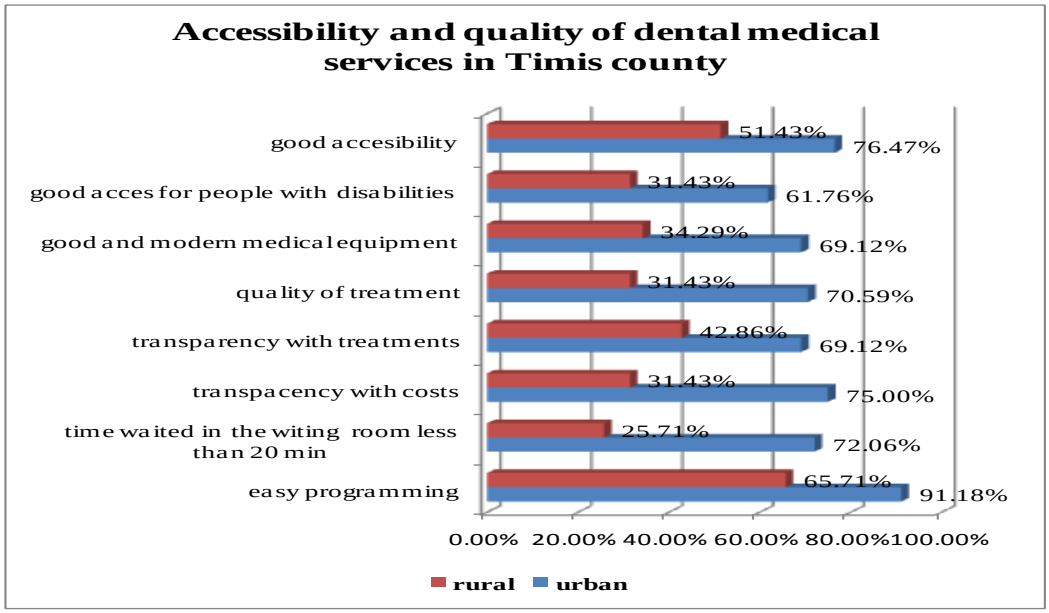


Figure 2. Accessibility and quality of dental medical services in Timis County

Rome and sometimes Hebrew or Hungarians were less likely to report difficulties in accessing medical care, dental care, and prescriptions as compared to whites. These disparities occurred primarily among the uninsured and Medicaid insured. More objective measures of utilization (ie, no doctor visit or dental visit during the past year) showed that minorities experienced less access than Romanians. Racial/ethnic disparities in access to care persist, and cannot be entirely explained by socioeconomic differences. In addition, the nature of these disparities depends on the socioeconomic position of racial/ethnic groups as well as the access measure used.

For the good management in the dental office we have to have a very food medical emergencies management. The medical emergencies were most likely to occur during and after local anesthesia, primarily during tooth extraction and endodontic. Over 60% of the emergencies were syncope, with hyperventilation the next most frequent at 7%. The extent of treatment by the dentist requires preparation, prevention and then management, as necessary. Prevention is accomplished by conducting a thorough medical history with appropriate alterations to dental treatment as required. The most important aspect of nearly all medical emergencies in the dental office is to prevent, or correct, insufficient oxygenation of the brain and heart. Therefore, the management of all medical emergencies should include ensuring that oxygenated blood is being delivered to these critical organs. This is consistent with basic cardiopulmonary resuscitation, with which the dentist must be competent. This provides the skills to manage most medical emergencies, which begin with the assessment, and if necessary the treatment of airway, breathing and circulation.

CONCLUSIONS

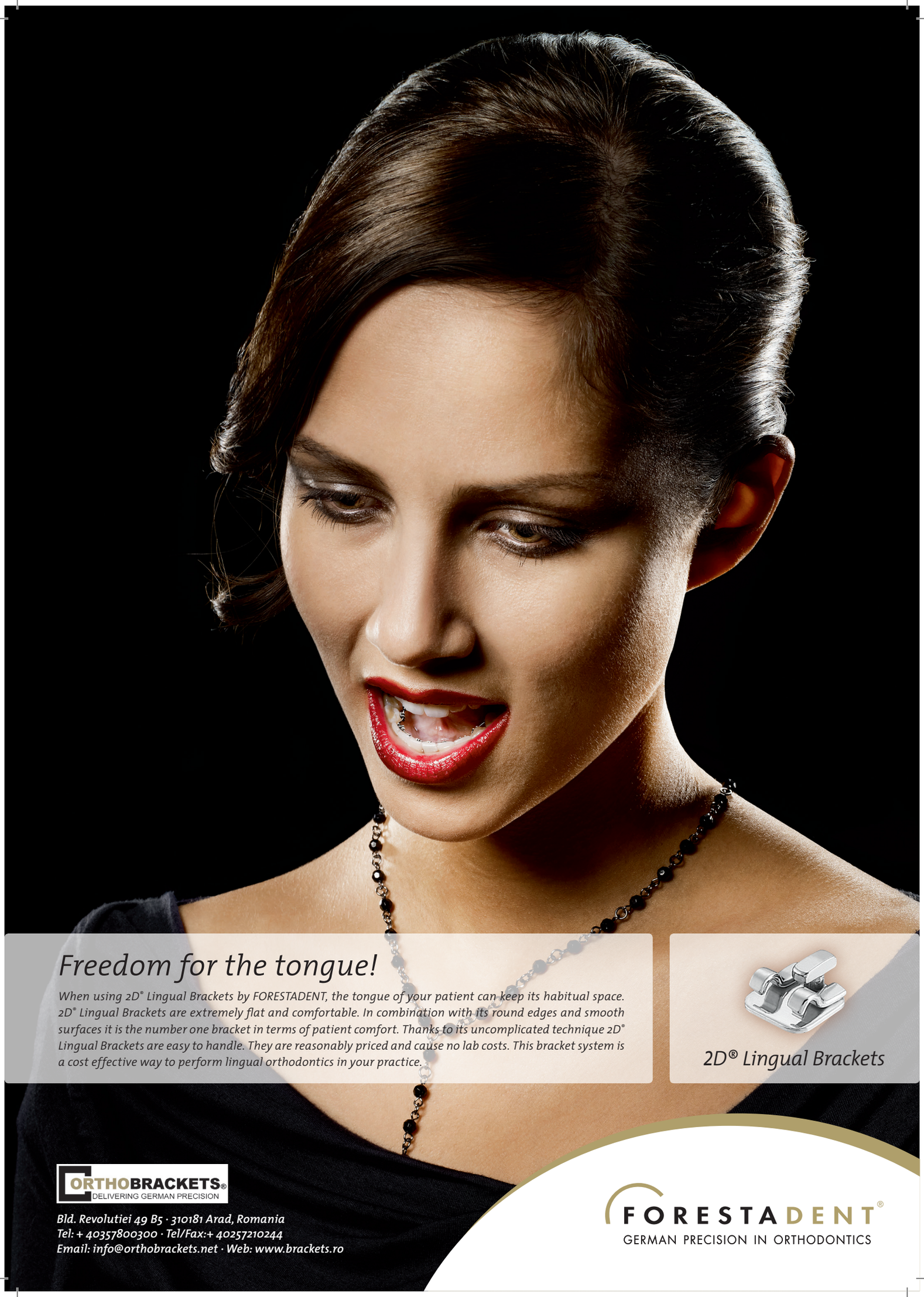
The mission of a medical office expresses the purpose for which it was created, its reasoning in relation to the health care market and implicitly to the committed or potential patients. By defining the mission, the intentional elements, specific groups of patients, basic needs of existing and own performances of the medical office are set.

Nursing home and other long-term care institutions have limited capacity to deliver needed oral health services to their residents. State assistance programs for selected oral health services don't exist; or are very limited and their reimbursement level for oral health services is low. The dentist workforce is declining in relation to the Timis County population, and there is general resistance to exploring new models of dental care delivery to vulnerable populations.

REFERENCES

1. Popovici RA, Ciobanu V, Sanatate Publica Orala. Epidemiologie si Biostatistica, Editura Mirton, Timisoara, 2015;
2. www.wikipedia.com
3. Stuart J. Oberman, Cyber Security for Dental Practices, Dentistry Today, 2013;
4. Bill Blatchford, How to prosper in the New Economy, Dentistry Today, 2014;
5. Dayna Johnson, Three best practice management tips for the new dental patient, Dentistry IQ, 2011;
6. Fast TB, Martin MD, Ellis TM. Emergency preparedness: a survey of dental practitioners, J Am Dent Assoc., 1986; 112:499–501[PubMed]

7. Steven C. Raynolds, Management, Leadership and Teamwork, Journal of Dental Practice Management, may 2015
8. Malamed SF.,Medical Emergencies in the Dental Office.5th ed. St Louis: Mosby; 2000. pp. 58–91. Haas DA. Emergency drugs. Dent Clin North America., 2002;46:815–830.[PubMed]
9. Daniel A Haas, Management of Medical Emergencies in the Dental Office: Conditions in Each Country, the Extent of Treatment by the Dentist, Anesth Prog. 2006; 53(1): 20–24.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- case presentations: 2-4 pages
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The paper will be edited according to international editing rules for manuscripts. The title will be written in capital characters 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 elaborated). Studies and researches will be followed by a brief abstract, followed by 3-4 key-words.

The body of the paper will be structured on the following chapters: introduction, aim, objectives, material and method, results and 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, Harward style (author, year) or Vancouver style (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 inconography, 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:

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- 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. ABSTARCT 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.

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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.

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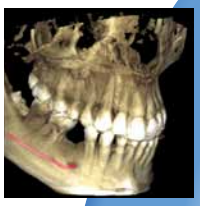

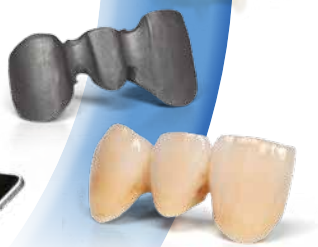

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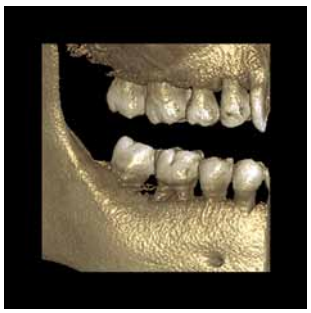

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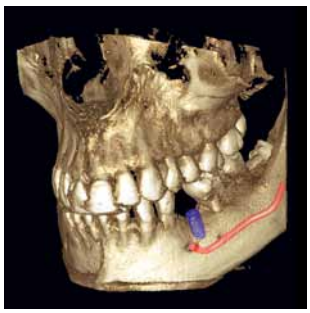

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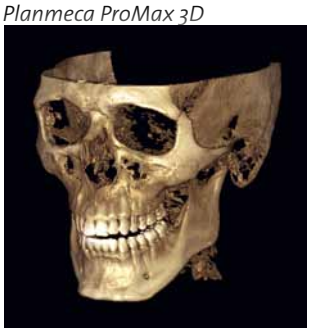

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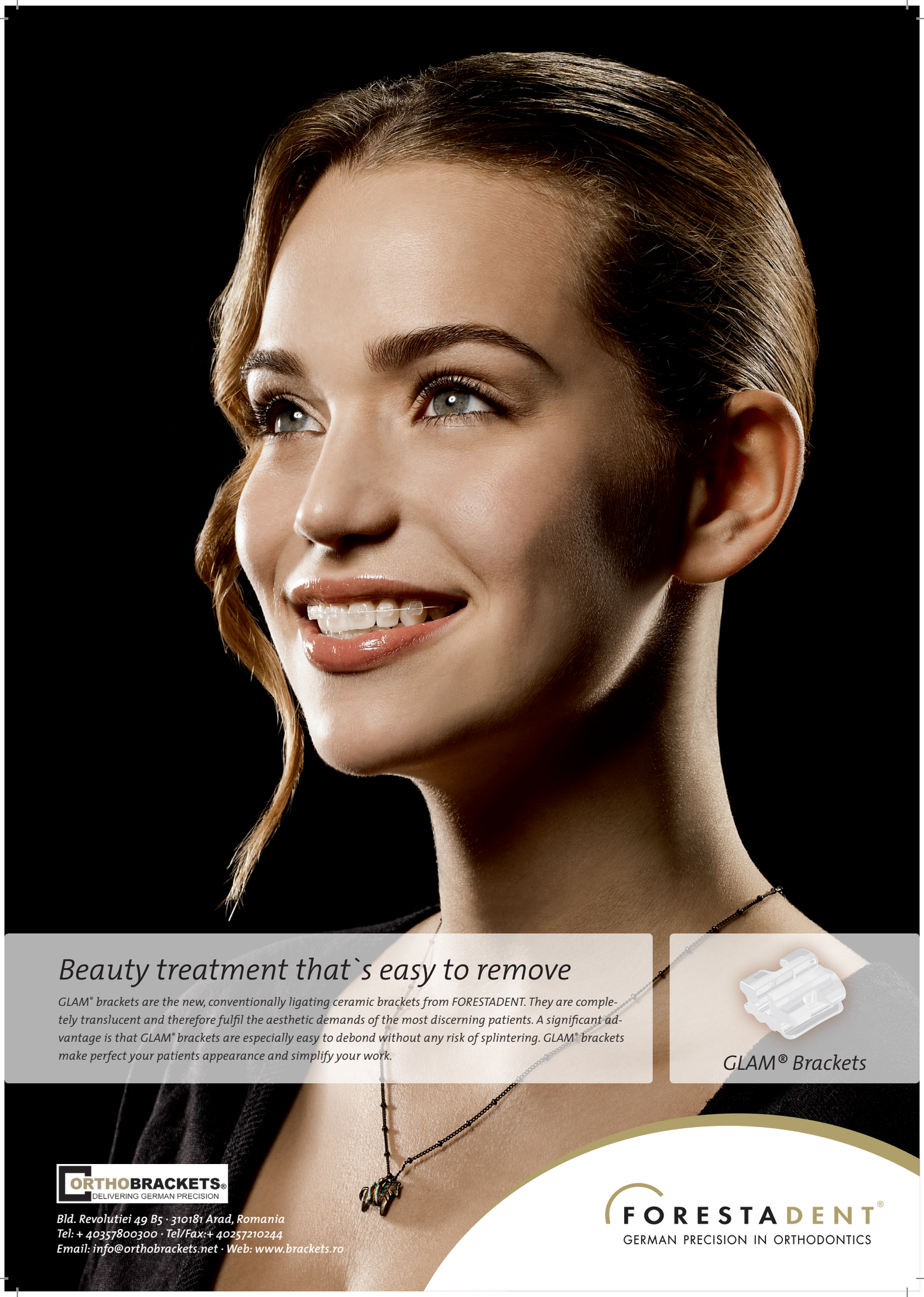
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