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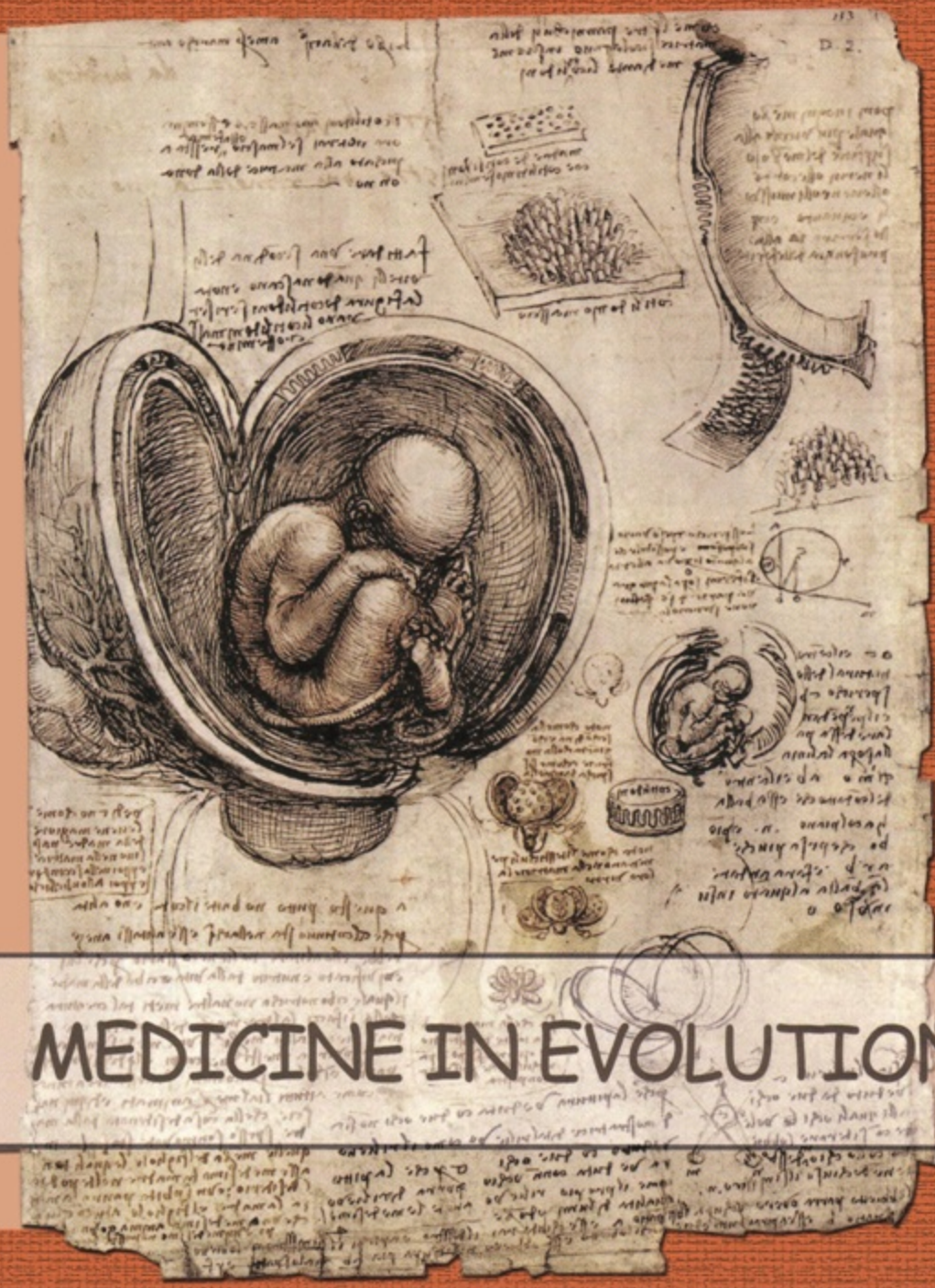

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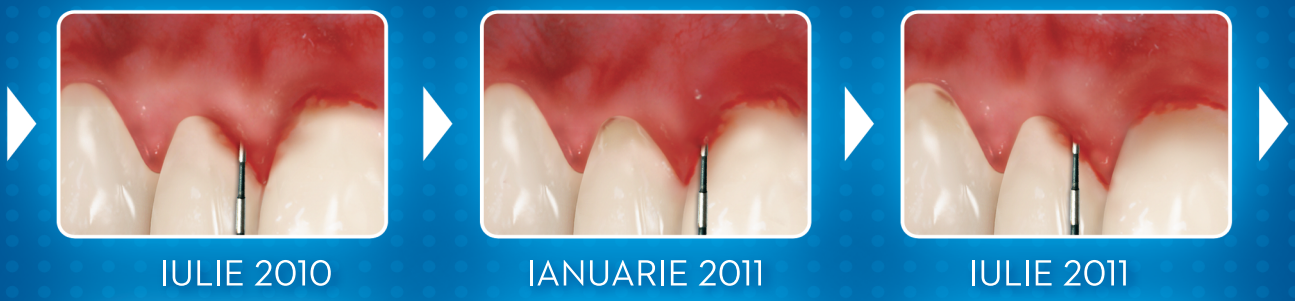

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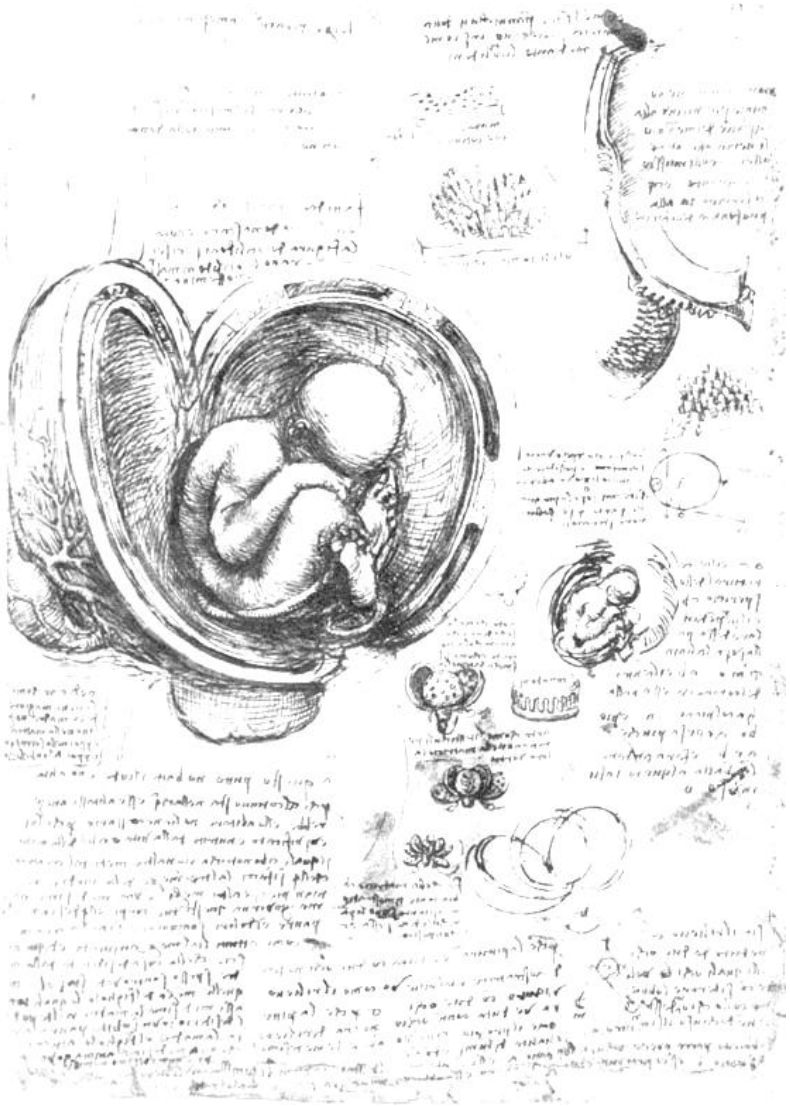

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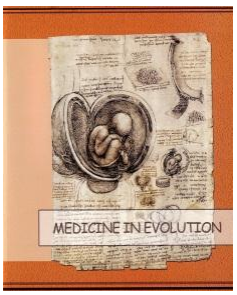

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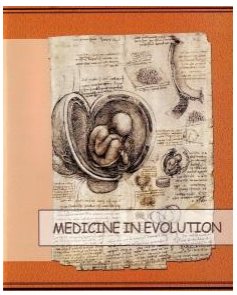
Sleep Quality in Patients with Obstructive Ventilatory Dysfunction and Bronchiectases



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Abstract

Obstructive ventilatory dysfunction is a frequently encountered pathology in current practice. When associated with the presence of bronchiectases, it determines higher mortality rates among patients and affects their quality of life. Sleep disorders in these patients are another important factor with a part in determining patient prognosis.

Methods: The parameters in the Pittsburgh sleep quality questionnaire, the VEMS parameter, as well as the serum levels of CRP and ESR were analysed in two groups of patients with COPD and bronchiectases that associate an obstructive pathology confirmed via spirometry testing.

Results: In patients with bronchiectases, the objective sleep quality as per the Pittsburgh questionnaire is affected and has a higher level of severity than in COPD patients. Chronic systemic inflammatory syndrome is an important factor that influences the quality of life for patients with bronchiectases and associated obstructive ventilatory dysfunctions.

Conclusions: Sleep quality must be investigated in order to determine the need for therapeutic intervention in order to improve long-term outcomes.

Keywords: Pittsburgh questionnaire, bronchiectases, obstruction, sleep

INTRODUCTION

Obstructive pulmonary pathologies cause significant changes in terms of patients' quality of life. The severity of the obstruction leads to self-imposed limitations on various individual activities. The description of sleep efficiency in these patients is important because it is a cumulative factor influencing the quality of life.[1,2] The main objective of the study is to identify the primary characteristics and factors associated to inefficient sleeping so as to enable medical intervention to remedy this problem.

It is a well-known fact that a large share of patients with bronchiectases experience laboured expectoration, particularly during exacerbation periods, as well as in the mornings.[3] The association with an obstructive ventilatory dysfunction causes breathing difficulties which in turn impacts sleep quality.[1,2,4] When these aspects are also connected with hypoxemia, the patient must undergo investigations in view of oxygen-therapy. Note that polygraph testing is recommended when the patient's self-assessment and the clinical examination reveal a sleeping disorder.

MATERIAL AND METHODS

The study included 70 patients with obstructive lung diseases, of which 35 bronchiectases patients and a control group comprising 35 COPD patients included in the registers of the Pneumology Hospital of Iaşi. The clinical and paraclinical assessment of the groups was based on the filling out of the Pittsburgh questionnaire for sleep quality (the Romanian version), performing a spirometry examination (VEMS), and dosing the systemic inflammatory syndrome (ESR, CRP). The filling out of Pittsburgh questionnaires and use of the results was only possible after obtaining the consent for using such data from the appointed persons. The parameters of the pulmonary function and the chronic systemic inflammatory syndrome were also used for publishing other results within other studies conducted on the same two patient groups.

The inclusion criteria comprised: the existence of a computer-tomography scan confirming the bronchiectases diagnosis, the existence of a spirometry test representing a diagnostic criterion for obstructive ventilatory dysfunction, adult age, male gender, and signing of the informed consent. The patients included in the study were unaffected by an exacerbated or coexisting extrapulmonary infection.

The statistical analysis entailed the calculation of mean values, T testing, and the study of correlations.

RESULTS

Sleep latency is a subscale that quantifies the time it takes the patients to fall asleep. 42.86% of the patients in the bronchiectases group require more than 60 minutes to fall asleep, while only 11.43% of the patients in the COPD control group require such a long time to fall asleep. Thus, the bronchiectases patients have a much higher sleep latency level than the control group in the study. As for sleep efficiency, it was noted that both groups reported a level thereof upwards of 85% in equal shares (71.43%). 25.17% of the patients with bronchiectases and only 14.29% of COPD patients report a level below 65% on this subscale. In terms of sleep duration, 32.35% of bronchiectases patients and 54.29% of the patients in the COPD control group reported sleeping 6-7 hours. We noticed that 41.18% of the bronchiectases patients had a low quality of sleep, reporting 5-6 hours of sleep per night.

T testing was applied to check for any significant differences in terms of sleep latency in the two patient groups and it revealed that bronchiectases patients require a longer time to fall asleep (Levene test $F=16.44$ $p=0.99$, $t(68)=-2.5$ $p\leq0.001$), thus highlighting a significant

difference between the two patient groups. (table 1) Large shares of patients in both groups reported severe sleep disorders, yet there was a higher percentage thereof in the COPD patients group (85.71% vs. 77.14%).

Table I. T testing for sleep latency, efficiency and duration factors

Independent Samples Test

		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
Sleep latency	Equal variances assumed	16.449	.000	2.703	68	.009	.34286	.12683	.08977	.59595
	Equal variances not assumed			2.703	63.327	.009	.34286	.12683	.08943	.59629
Sleep efficiency	Equal variances assumed	1.401	.241	-.379	68	.706	-.11429	.30142	-.71575	.48718
	Equal variances not assumed			-.379	66.905	.706	-.11429	.30142	-.71593	.48736
Sleep duration	Equal variances assumed	3.475	.067	1.774	67	.081	.31849	.17951	-.03982	.67680
	Equal variances not assumed			1.769	63.381	.082	.31849	.18007	-.04131	.67828

Both groups denied in significant percentages the use of sleep medication, however 37.47% of the bronchiectases patients reported using such medication. 25.17% of the patients in the COPD group confirmed using such medication, ergo by a much lower number of patients. (fig. 1)

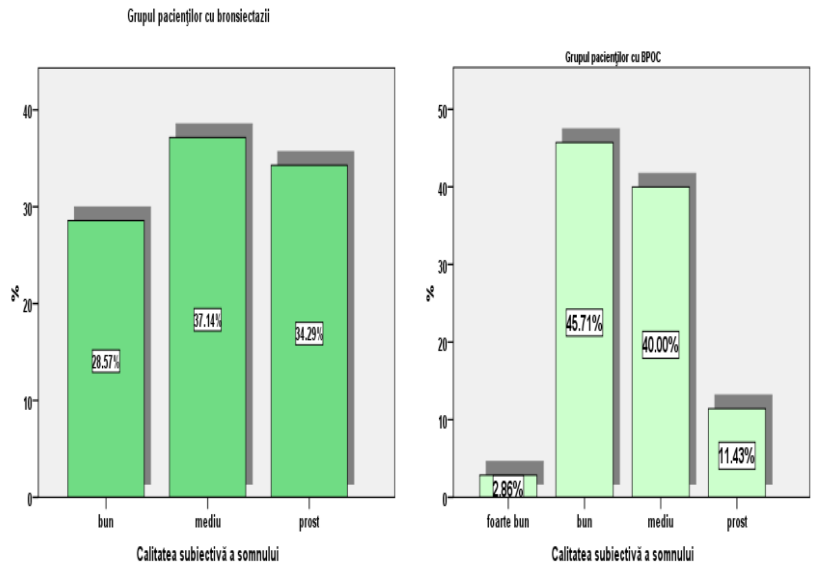

Figure 1. Chart representation of the subjective description of sleep quality as per the Pittsburgh questionnaire for the cu bronchiectases and COPD patient group

The study also analysed the patients' subjective perception on their sleep quality. We have thus noted that a small percentage of COPD patients (2.86%) reported very sound sleeping. Of the bronchiectases group, 34.29% of the patients reported poor sleep quality. As for the patients reporting average levels of sleep duration, the relevant percentages in both groups are relatively similar (namely 37.14% and 40%, respectively). The application of the T test in order to check for any significant differences in the subjective sleep quality levels reported in the two patient groups revealed a significant statistical difference in terms of subjective sleep quality between the two groups (Levene test F=0.094 p=0.94, t(68)=1.9 p=0.015).

Severe sleepiness was identified in 31.43% of the patients in the bronchiectases group and in a significantly lower share in the other group (2.86%). 74.29% of the COPD patients and 37.14% of the bronchiectases patients reported an average level of sleepiness.

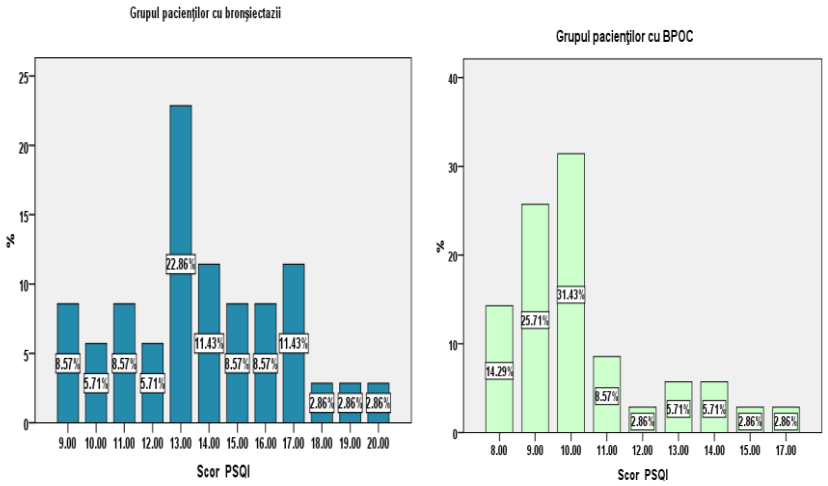

Figure 2. Chart representation of the PSQI score as per the Pittsburgh questionnaire for the bronchiectases and COPD patient group

Bronchiectases patients constantly reported high scores in this questionnaire correlated with the values obtained in each of the subscales calculated previously. 71.44% of the patients reported values ranging between 13-20. Note that values that are closer to 21 indicate a poorer sleep quality. (fig.2) The application of the T test in order to check for any significant differences in the subjective sleep quality levels reported in the two patient groups revealed that bronchiectases patients have constantly reported higher scores in this questionnaire and we can therefore say that they also have a poor level of sleep quality (Levene test F=3.6 p=0.06, t(68)=5.6 p≤0.001).

ESR and CPR values were dosed in order to describe the inflammatory syndrome. 23 of the patients in the bronchiectases group (65.71% of the group) ranged between 20-60mm/hour, with a calculated mean value of 55.29mm/hour. In 25 of the patients in the bronchiectases patients group, the C-reactive protein ranged between 20-60 (71.42% of the group). The mean value of C-reactive protein levels was 32.69.

COPD patients have a calculated mean value of 34.75 mm/hour. In the case of C-reactive protein, the mean value was 11.31.

Table 2 shows two correlations in relation to systemic inflammatory syndrome in bronchiectases patients, namely: a reversed average correlation between ESR and sleep efficiency (r=-0.352, p=0.038) and an average correlation between CRP and sleepiness (r=0.387, p=0.022).

As for VEMS levels in bronchiectases patients, we noticed two incidence peaks at around 30% and 70%. Most of the values are range in the interval between 20-60%. The

calculated mean for VEMS was 55.25%. In COPD patients, data analysis revealed two incidence peaks: the first one at around 25% (28.57% of the patients) and the second one at around 45% (17% of the patients). (fig.3)

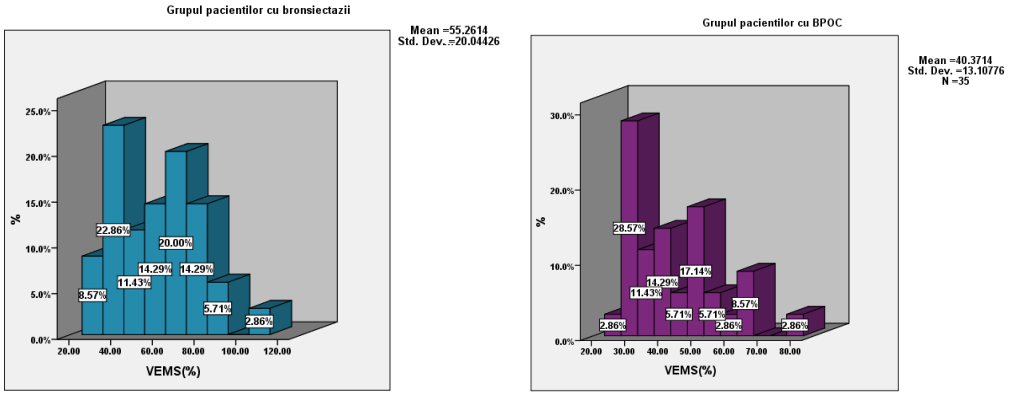

Figure 3. Percentage distribution of patients with bronchiectases and COPD based on VEMS levels

In relation to the pulmonary function as quantified by VEMS levels, we were able to note that there are four correlations between this parameter and the following items in the Pittsburgh questionnaire in the bronchiectases patients group: sleep latency (r=-0.710, p≤0.001), subjective sleep quality (r=-0.788, p≤0.001), sleep medication (r=-0.552, p=0.001), sleepiness (r=-0.834, p≤0.001). (table 2)

The control group did not reveal any significant correlation between the systemic inflammatory syndrome, pulmonary function, and Pittsburgh questionnaire parameters.

Table II. Correlations for C-reactive protein, ESR, VEMS, and the Pittsburgh questionnaire parameters regarding sleep quality in the bronchiectases patients group

		Sleep efficiency	Sleep duration	Sleep latency	Sleep disorders	Subjective sleep quality	Sleep medication	Sleepiness	PSQI score
CRP	Pearson Correlation	-.076	.037	.217	-.098	.284	.302	.387*	-.033
	Sig. (2-tailed)	.665	.834	.210	.577	.099	.078	.022	.853
	N	35	34	35	35	35	35	35	35
ESR	Pearson Correlation	-.352*	.118	-.129	-.228	-.159	.049	-.202	-.248
	Sig. (2-tailed)	.038	.507	.461	.187	.362	.782	.245	.150
	N	35	34	35	35	35	35	35	35
VEMS	Pearson Correlation	-.093	-.230	-.710**	.135	-.788**	-.552**	-.834**	-.291
	Sig. (2-tailed)	.595	.191	.000	.439	.000	.001	.000	.090
	N	35	34	35	35	35	35	35	35

DISCUSSIONS

The evolution of bronchiectases leads to the onset of a chronic systemic inflammatory syndrome and obstructive ventilatory dysfunction, which over time becomes symptomatic. The existence of ventilatory dysfunctions affects these patients' quality of life, which translates into impairment of their effort capacity, the onset of sleep disorders and various forms of depression (86,87,89).

This study focused on revealing the correlations between the Pittsburgh questionnaire parameters, systemic chronic inflammation and the respiratory function in patients diagnosed

with bronchiectases that have an associated obstructive pathology as compared to a control group of patients with COPD. The patients did not present with any acute pathology that could have influenced chronic inflammation. No data was included on any potentially inflammatory chronic disorders.

Our study showed in most of the analysed items a statistically significant difference in terms of symptomatology severity in the case of bronchiectases, which was objectivized via the scores obtained in filling out the Pittsburgh questionnaire.

The specialty literature does not include sufficient data on sleep quality in patients with bronchiectases. Concurrently, there are multiple studies that have confirmed and substantiated the association of COPD with sleep apnea syndrome.[5,6]

Erdem et al applied the Pittsburgh questionnaire in children with non-cystic bronchiectases and analysed the final score, the connection with respiratory functional testing, the symptomatology described and the results of the scores in the computer-tomography scanner. Dyspnea and nocturnal wheezing are directly connected to the self-assessed sleep quality, snoring was associated with sleep affectation, wheezing was more frequent among patients that snored, and children with altered HRCT scores had the most affected quality of sleep.[7]

There is an important connection between ESR values and sleep efficiency: the higher its value, the lower the drop in terms of sleep efficiency ($r=-0.352$, $p=0.038$). The CRP serum level is also connected to the degree of sleepiness. We can state that chronic inflammation plays a major role in altering sleep quality.

The fact that there is a strong reverse correlation between sleepiness and respiratory status can indicate that infectious exacerbations accompanied by respiratory failure phenomena influence the quality of life, and from a paraclinical perspective this can be associated with changes in blood pH, $PaCO_2$, PaO_2, which can present with clinical symptoms and excessive drowsiness.

The correlations between sleep inducing medication and the occurrence of effects related to respiratory problems as self-assessed in the Pittsburgh questionnaire can be explained by the existence of an obstructive ventilatory dysfunction associated with the effects of this medication on the respiratory system, as their effects are cumulative and subsequently determine symptoms that the patients perceive as a decrease in terms of their quality of life.

Coughing, laboured expectoration of secretions and secondary dyspnea are the main factors that determine the quality of life in bronchiectases patients.[8] These elements are significantly correlated with the Pittsburgh questionnaire parameters and is indicative of a chronic sleep affectation. The importance of this assertion is reflected in the morbidity and mortality rates associated with alveolar hypoventilation and intermittent hypoxemia, and the sleep apnea syndrome that can be associated. Pathological modifications potentiated by the confirmed chronic inflammation can lead to the onset of chronic pulmonary heart disease and can also affect other organs or systems (metabolic syndrome, cardiovascular pathology, diabetes mellitus, neurological pathology, etc.).[9,10,11]

We believe that the results we have obtained are relevant, as a poor sleep quality and accentuated symptomatology impact patients' quality of life.

CONCLUSIONS

In patients with bronchiectases, sleep quality as objectivized via the Pittsburgh questionnaire is affected, thus also substantiating an even greater level of severity than in the case of COPD patients. Chronic systemic inflammatory syndrome is a major influencing factor that affects the quality of life for patients with bronchiectases.

Therapeutic intervention is necessary for these patients in order to improve their long-term outcomes.

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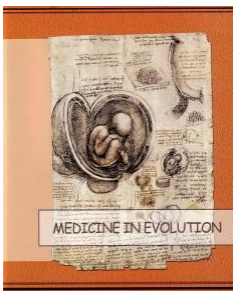
Introduction into the human microbiome universe



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Abstract

Introduction: Knowledge of the live world of microorganisms was difficult to acquire, although its implication was convincingly illustrated ever since human and animal paleopathology research.

Discussions: Of all the microorganisms present in the Universe, the microbe world represents an important segment that cohabits with man from the beginning of his existence. Each bacterial population acts based on existing interrelations between its composing species, but also with the host organism, respectively with the specific of the occupied anatomic territory.

Microbe ubiquity (from species that reproduce on anorganic matter to species that develop only inside of live cells) illustrates the diversity of their physiological properties and the ability to adapt along their multi-millennial existence.. Each bacterial population acts based on existing interrelations between its composing species, but also with the host organism, respectively with the specific of the occupied anatomic territory.

Conclusions: The involvement of the microbe in both disease and health, still contains many unknowns. A better understanding of the microbe will allow for the concept of personalized treatments.

Key words: microbiome, natural niches,specific phenotypic markers, ribotyping

INTRODUCTION

Knowledge of the live world of microorganisms was difficult to acquire, although its implication was convincingly illustrated ever since human and animal paleopathology research.

It was only in 1675 that the microbes' world was discovered by Antony Van Leeuwenhoek with the help of his rudimental microscope with moderate augmenting power of around 200 times. Visualized microbes were described as"animalcules" and the discovery was the subject of many letters sent to the Royal Society in London; the one in 17.09.1683 has the merit of inaugurating the scientific study of microbes.

Two centuries later (1878), microorganisms acquire their true identity when, through Louis Pasteur's and his collaborates' research, the specificity principle of diseases caused by microbes imposed.

At the end of the 19th century, the live world divided by Karl Linné in human and animal reign (1767) is joined by the Procaryotae reign. Prokaryotes are unicellular organisms in which the genetic material (bacterial genome) is free in cytoplasm, with no nuclear membrane. In the large group of microorganisms, besides prokaryotes there are also protozoa and mushrooms, with the equivalent denominations of fungi or micelles. These two groups have, however, eukaryote cell organization, of unicellular organism with nuclear membrane, the transcription of genetic material happens inside the nucleus, the translation in the cytoplasm and, unlike superior eukaryotes, protozoa have no cellular wall and the levs have a vegetal structure cellular wall. In the live world's system, viruses are subcellular structures, on the edge between abiotic and biotic world. Each of the 4 groups of microorganisms (protozoa, levs, prokaryotes, viruses) engulf tens of thousands of species.

DISCUSSION

Of all the microorganisms present in the Universe, the microbe world represents an important segment that cohabits with man from the beginning of his existence. Each bacterial population acts based on existing interrelations between its composing species, but also with the host organism, respectively with the specific of the occupied anatomic territory.

Microbe ubiquity (from species that reproduce on anorganic matter to species that develop only inside of live cells) illustrates the diversity of their physiological properties and the ability to adapt along their multi-millennial existence. Each bacterial population acts based on existing interrelations between its composing species, but also with the host organism, respectively with the specific of the occupied anatomic territory.

Subsequent to this ubiquity, it is known that ever since birth, the human organism is submitted to a continuous contact with the live world of microorganisms, life form that dominates our planet and which numerically out-passes all others taken together, and that in the human organism microbial cells outnumber tens of times the number of the host organism's cells.

Microbial world's trait of living in populations (not as an isolated organism), together with the tendency of occupying certain anatomical areas and especially their obvious implication in triggering various diseases led to the structuring of some completely opposed perceptions; for some, they are friends, for others they are enemies of the man.

Considering them enemies is supported by the large number of severe clinical boards, specific diseases (typhoid fever, disenteria, cholera etc.), severe systemic infections or the important number of human lives lost in the history of great epidemics. Association of friends of the man comes from the fact that bacteria are not found as isolated individuals, but always as complex populations with their own dynamic and intimately connected with the environment in which they develop.

With the limits imposed by the clinical and bacteriological exam's data, the colonization process of the human organism was limited to enclosing 4 anatomical areas: teguments, superior respiratory tract, digestive tract, inferior genital tract. Bacterial population present in these areas were described under the name of *resident and transitory normal bacterial flora* and the relation with the host-organism was interpreted as a symbiotic relationship in some microbial species or commensal relationship in other species (species depending on certain growth factors provided by epithelial cells of the host-organism).

Intestinal flora stepped into attention because it is the owner of the largest taxonomic group – Enterobacteriaceae family. Significantly involved in infectious pathology were: Salmonella group, Shigella, Yersinia and commensal or saprophyte bacteria group, present in man and animals, formed of Escherichia, Proteus, Enterobacter. The last three groups, initially considered as non-pathogenic, proved in time"conditionally pathogenic" and are currently included in the"hospital germs" group, partially or completely resistant to antibiotics.

Microorganisms' particularity to live as complex populations together with the fact that their genetic material (in the absence of a nuclear membrane) becomes more accessible to influences from the intestinal environment explains the frequent emergence of mutations (spontaneous or induced), of modifications at the nucleic acids level (substitution, insertion, deletion) and the transition to a dominant bacterial population with a mutant start point.

Of the intestinal flora's activities beneficial for the human organism outstands maturation of the immunocompetent cellular system, subsequent to the multitude of antigenic stimuli at the level of an ecological niche. This maturation is also supported by the fact that populations of B lymphocytes are well represented at the level of the entire digestive tract. Lymphoid formations begin with the Waldayerring, continue with lymphatic follicles spread in the subepithelial mucosa, in the submucosa, in Payer's plates, between intestinal columnar cells.

Metabolic function: in the synthesis takes part the coliform flora (through vitamin K, folic acid, biotin, vitamin B12 synthesis); catabolic function begins in the area proximal to the colon through the degradation of undigested or unabsorbed carbohydrates, the scission of polysaccharides, anaerobic degradation of monosaccharides into lactic, acetic, butyric, propionic acid. With the help of anaerobic flora undigested proteins are divided, decarboxylation and deamination of resulting amino acids are carried on. Certain commensal species participate in raising the force of intercellular protein junctions at the bowel level through a phosphorylation mechanism. Following this phosphorylation intestinal permeability drops and the absorption of nutritional principles drops, useful effects for overweight persons.

The limits of the bacteriological exam in being able to identify the structure of bacterial populations and their specific interventions led to the ecological approach of the relations between these microbial populations and their host macro organism. In the terminology of this approach, microbial population is the biocenosis (with the synonyms of microbial biocenosis or microbiocenosis), the intestinal environment or other anatomical centers represent the biotope (synonym with habitat) and the whole of existing interrelations between microbial biocenosis and biotope represents an eco-system (synonym with bio-system).

Human pathology genuinely experiences the consequences of a perturbation intervening at the level of an eco-system, in our case of the intestinal eco-system. The change emerged in the structure of the intestinal bacterial population as a result of abusive utilization of antibiotic therapy led to the selection of some hospital germs with total or partial resistance to"usual","backup" or even"exceptional" antibiotics. To the same context we can add the frequent implication of Clostridium difficile in the etiology of diarrhea.

The methodology of classical bacteriology has proved efficient in identifying pathogen agents largely involved in human pathology, but could not as successfully involve in deciphering the structure of bacterial populations that occupy a certain sector of our internal

environment and especially in decoding interrelations between microorganisms and the host organism.

The new direction of research orientation, the biochemistry and molecular biology one, is expected to provide a more targeted answer to questions related to the position of these microbial populations in maintaining a healthy or ill condition.

We remind the following few significant moments that have made possible this new research orientation:

- ✓ deciphering the DNA and RNA structure, the carriers of genetic information both in live prokaryote and eukaryote cell and in viruses (J.D.Watson-Fr.Crick, 1953);
- ✓ discovering and developing modern genetic technology: recombining DNA technology – 1970, sequencing DNA – 1970, hybridization – 1975, cloning DNA – 1977, chained polymerase reaction – 1980, molecular probes – 1986;
- ✓ sequencing the first bacterial genome in HaemophilusInfluenzae – 1995, complete sequencing of the human genome between 1990-2007 (3.2 billion of nucleotides)
- ✓ while talking about structuring the new road in research, we cannot omit the live world of microorganisms, especially bacteria. Through their cellular division rate of only 7-20 minutes, bacteria have represented a valuable experimental environment and have allowed that, in a very short amount of time, eventual cellular modifications emerged on a large number of microbial generations be observed;
- ✓ bacterial cell was preferred because it presents the simplest organization unit, of autonomous activity and replication;
- ✓ the new research orientation imposes the clear definition of the following three terms: *genome* represents the set of hereditary information in the DNA molecule of a cell/organism; *gene*: set of DNA segments necessary for the production of a functional molecule (protein or RNA); *codon* represents the triplet of nucleotide bases owning the genetic information;
- ✓ starting with the last decade of the past century (1996), for identifying bacteria and viruses the technique of spotting genome markers caught interest. Of the genome markers, a priority was knowing the structure of the genes that encode the ribosomal RNA (RNAr16S). Ribotyping patterns can be used to identify and differentiate bacterial strains and also as taxonomical markers: phylogenetic systematic (cladistic) and for putting together a dendrogram (positioning a specie in phylogenetic scale);
- ✓ sequencing the DNA that encodes the RNAr is present in all organisms, therefore it opens up the possibility of evaluation of diversity in nature, diversity passing by more than 1000 times the number of species we can cultivate;
- ✓ the study of RNAr16S subunits gives information on the evolutionary process which determined the grouping of microbes in classes, families, genders, species. The modification that marked these framings were imprinted in the RNAr sequences and received the value of"seals" or"molecular clocks". Low variability sequences belong to ARCHAEBACIERIILOR (ancestral bacteria); to the determinism of the evolutionary process belong modifications of the type of mutations, deletions, insertions, translocations, transpositions, which occur spontaneously or unde the influence of the environment.

Through the new strategy called"metagenomics" we can grasp"in a block" the biodiversity of bacterial populations and of other microorganisms composing a complex eco-system in soil, water, organism etc. Metagenomics, as a researchmethod, allows the evaluation of the genetic content of a sample coming from diverse ecologic niches of the human body or from the external environment. The prefix"meta" refers to actions that are to be taken after this first evaluation; therefore, the studi of that population will follow without going through the laboratory cultures stage.

CONCLUSIONS

The techniques based on the study of nucleic acids begin to become standard methods in clinical practice. They also highlight uncultivable pathogen agents which cannot be identified using classical bacteriology methods. The perspective open by molecular genetic imposes owning a new work terminology. Thus, we need to acknowledge that the term *microbial flora* is improper; microbes do not belong to the vegetal reign (the term of *flora* belongs exclusively to the vegetal reign). The term *microbe* (created in 1880) has a broad cover: bacteria, microorganism, germ, pathogen agent. Microbes, through the equivalent term of *microorganism*, surpass the Prokaryotae reign. The term of *microbial flora* becomes more appropriately expressed through the one of *human microbiota*; *microbiome* refers to the totality of microbiotain an organism; therefore, the term of *human microbiome* covers the totality of microbes that live at the surface or inside the human body; the term of hologenome covers the sum of human genome with its microbiota's genome (holos=whole); the term of biota represents the number of species that compose the live world.

The techniques based on the study of nucleic acids will gradually become standard tools for clinical microbiology labs. They can highlight uncultivable unidentifiable pathogen agents. The new research direction led to identifying with arguments two more ecological niches, respectively placenta and pulmonary microbiota. The subglottic respiratory tree, until recently considered a sterile space in healthy individuals, has proved to be cultivated with various microbes, whose structure differs reported to the prelevation type (spit, suction, wash, tissue) or with health-illness condition.

In the structure of pulmonary microbiota enter: Proteobacteria, Fermicules, Prevotella, Streptococcus, Veillonella, Haemophilus, Neisseria.

In conditions of diminished oxygen concentration (pulmonary emphysema) a growth of anaerobic bacteria concentration is noticed. The hypothesis that associating pulmonary disbiose contributes to the installing of asthma clinical board, BPOC and aggravation of the clinical board of pulmonary fibrosis or mucoviscidosis is outlined. Presentations in medical literature do not meet the elements based on which the structure of pulmonary microbiota or the age at which the population of the airways takes place would be able to define a certain pulmonary pathology (especially asthma, BPOC); they do have the merit of drawing our attention to the areas that deserve close supervision and with the evolution in time of the respective observations.

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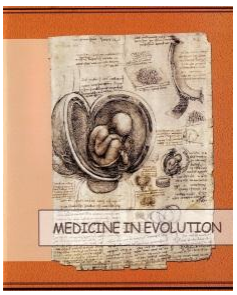
Current clinical-evolutional aspects in convulsive cough



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Abstract

Introduction: The incidence of convulsive cough dropped after the vaccination programs have been introduced, but in the last years, due to multiple reasons, a"trend" unfavorable to vaccines in general has emerged, this being a factor in the growth of the number of measles, convulsive cough, rubeola etc. cases.

Material and method: We have performed a retrospective study regarding 120 convulsive cough cases admitted into the Clinic II Infectious Diseases of the Victor Babes Hospital Timisoara within the last 6 years, analyzed according to various criteria: gender, age group, background, personal antecedents including vaccines, associated diseases, disease form, treatment schemas, laboratory investigations, evolution.

Results and conclusions:

1. The number of convulsive cough cases has gone up within the last years in our country, with differences and depending on the counties, Timis county has been the third one in 2014 case number-wise.
2. The most cases – 25 – have been registered in 2015.
3. The most affected age group is the one under 2, but the disease can occur both in teenagers and in adults.
4. Convulsive cough can be prevented through vaccination, some countries currently vaccinate even the adult population (England, Belgium).

Keywords: convulsive cough, incidence, retrospective study

INTRODUCTION

Pertussis (also known as whooping cough or 100-day cough) is a highly contagious bacterial disease. The time between infection and the onset of symptoms is usually seven to ten days. Disease may occur in those who have been vaccinated, but symptoms are typically milde. Pertussis is caused by the bacterium Bordetella pertussis.It is an airborne disease which spreads easily through the coughs and sneezes of an infected person. People are infectious to others from the start of symptoms until about three weeks into the coughing fits. [1]

Hospitalisation may be required, particularly in infants less than six months of age or in the more severe cases where complications arise such as apnoeas, cyanosis, pneumonia, seizures or encephalopathy. [2]

The incidence of convulsive cough dropped after the vaccination programs have been introduced, but in the last years, due to multiple reasons, a"trend" unfavorable to vaccines in general has emerged, this being a factor in the growth of the number of measles, convulsive cough, rubeola etc. cases.

MATERIAL AND METHODS

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RESULTS

The number of convulsive cough cases has gone up within the last years in our country, with differences and depending on the counties, Timis county has been the third one in 2014 case number-wise.The most affected age group is the one under 2, but the disease can occur both in teenagers and in adults. *Figure 1*

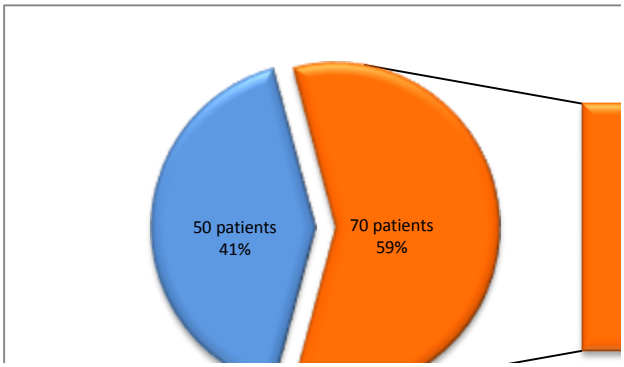

Figure 1. Number of cases of vaccinated/unvaccinated patients with ages between under 2/above 2 years old

The most cases – 25 – have been registered in 2015. *Figure 2*

Notable is the fact that until 2008 confirmation of convulsive cough cases was done especially based on clinical and paraclinical criteria (hemogram and leucocyte formula); afterwards confirmation was done based on the positive result at the serologic and/or culture exam respectively PCR.

On national level there were 3 peaks, the years 2000, 2004, respectively 2008, but there was a constant increase in the number of cases within the last years due to non-vaccination in many cases and accumulation of receptive population.

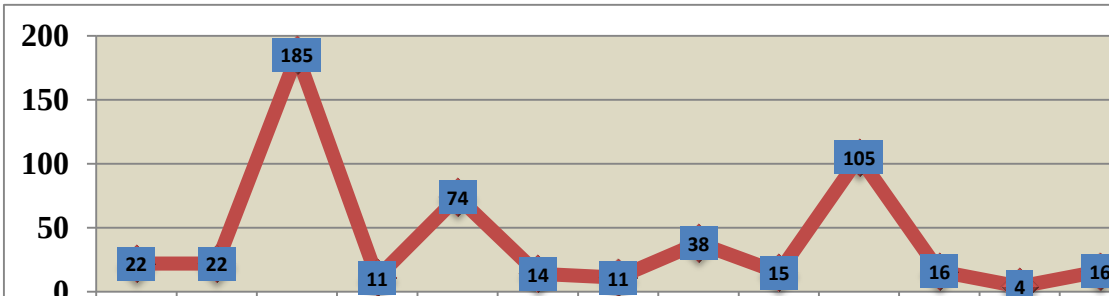

Figure 2. Convulsive cough case situation from previous years

Case 1:

- Female, rural environment, 1 year and 4 months
- Diagnosis: Cardiorespiratory failure, Convulsive cough, Acute Pneumonia, Leukemoid reaction, Arterial hypertension, Mixt anemia, Staturo-ponderal hypotrophy.
- The toddler was not vaccinated, with repreated respiratory infections, 6.6 kg weight. Clinical and paraclinical case data. *Figure 3,4*

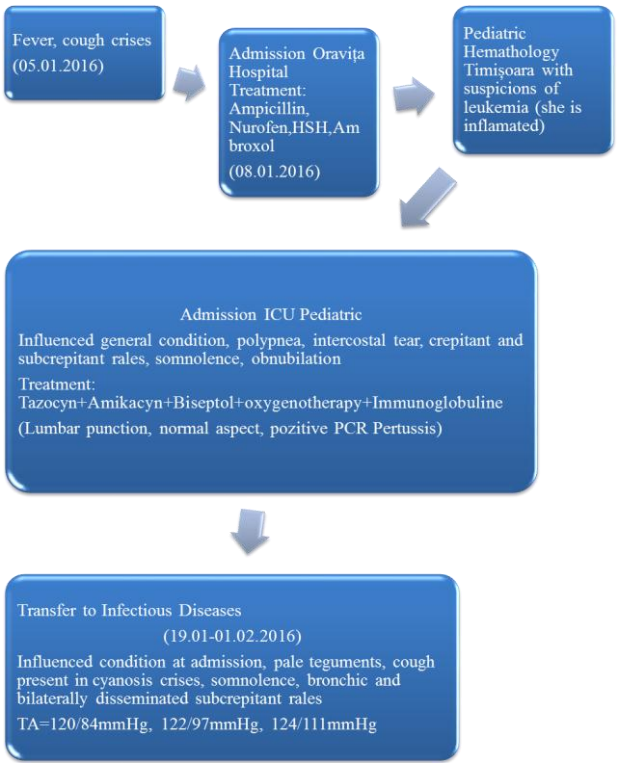

Figure 3. Clinical and Paraclinical data Case 1

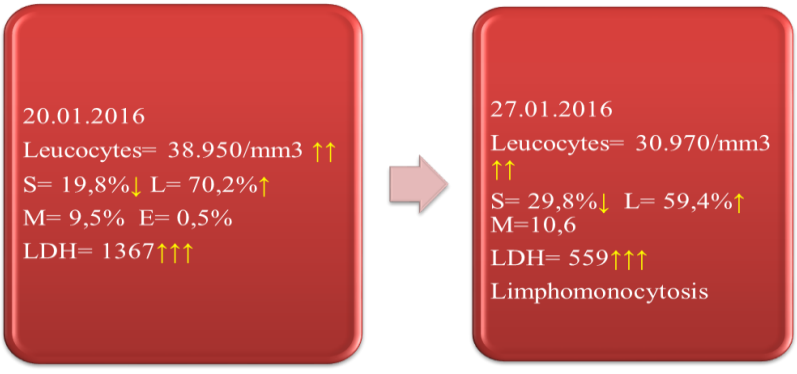

Figure 4. Clinical and Paraclinical data Case 1

Treatment: Antibiotic, hydrocortisone hemisuccinate, Arnetin, Ambroxol, Metoprolol associated with Captopril with TA monitoring. Afterwards she was transferred to Pediatric Cardiology for further investigations and specific treatment for arterial hypertension.

Case 2:

- Infant, 8 months, male, 25 days of admission (10.03-04.04.2016). He was admitted into the ICU of Victor Babes Hospital for 18 days.
- Diagnosis: Acute respiratory failure, Convulsive cough, Pneumonia, Inguinal hernia.
- Born premature, at 27 weeks, mechanically ventilated and admitted into Prematures 3 months.

Clinical and Paraclinical data Case. *Figure 5*

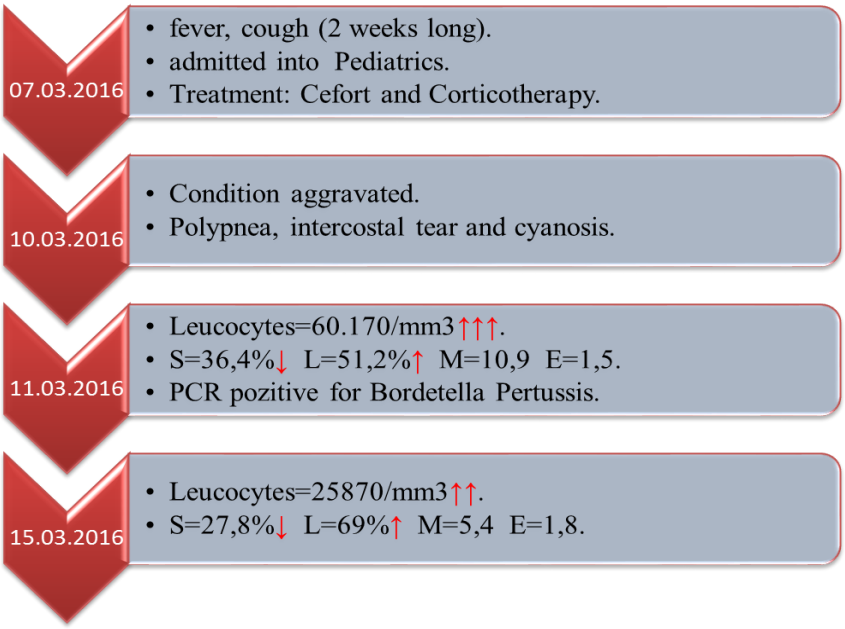

Figure 5. Clinical and Paraclinical data Case 2

Evolution was favourable, but prolonged under complex treatment with antibiotherapy, corticotherapy, oxygenotherapy – 18 days in the ICU.

CONCLUSIONS

1) The number of convulsive cough cases increased within the last years in our country with variations depending on counties.
2) Timis County was third in 2014 in the number of cases.
3) The most cases, respectively 25, happened in 2015. For 2016 there are already 16 cases (partial results up until May).
4) The most affected age group is children under 2, who also present severe forms, respectively complications.
5) Malformations, anemia, distrophy and other associate diseases aggravate the evolution of the illness.
6) The disease can also emerge in young adults who represent the source for infants and children.
7) Convulsive cough is a disease which can be prevented through vaccination, some countries currently vaccinate even the adult population (England, Belgium).
8) Within the last years, in our country the vaccination rate for measles, rubella, mumps, poliomyelitis, diphtheria, tetanus has dropped under 95%, this caused the WHO to send alarm signals.

9) Organizing discussions, round tables with infectious diseases specialists, epidemiologists, family doctors, pediatricians, DSP, pneumologists, mass-media, NGOs, parents for resumption of vaccination is necessary. It is also notable that Spain had diphtheria cases in 2015 and so did Belgium in 2016.

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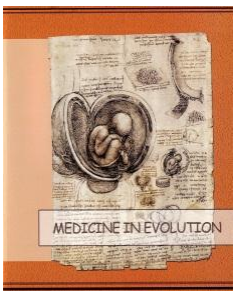
Protocols of communication in medicine: a brief review



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Abstract

This article will help physicians review their knowledge about communicating bad news to their patients. The overall goal of the article is to provide a brief review of different approaches of delivering bad news, helping the physicians in choosing the best for the benefit of their patients and to understand how important it is to learn new skills in their medical practice.

In an attempt to encourage and aid future research regarding this issue, this paper presents some key protocols of communication.

Keywords: communication, bad news, protocols

INTRODUCTION

Historically, medical education has placed more value on technical proficiency than communication skills. This leaves physicians unprepared for the complexity and emotional intensity of breaking bad news [1] but, beginning with the second half of the last century, patients, physicians, and the general public started communicating the diagnostic and prognostic aspects with a more open and clearer approach. [2]

Even though delivering bad news is something that occurs daily in most medical practices, this is one of the most daunting tasks faced by physicians. The majority of them have not received formal training for this essential and important task and would consider this as extremely difficult.

When medical residents were evaluated regarding the skills considered necessary for giving bad news in a caring and informative manner, they showed a general lack of competence in this area. Part of this problem is associated with self-fears, lack of support from supervisors, and time constraint [3].

Another thing to note is that many fail because they do not take into consideration the perspectives and expectations of the patient.[4,5].

DEFINITION

The term 'bad news' refers to any information transmitted to patients or their families that directly or indirectly involves a negative change in their lives,"any news that adversely and seriously affects an individual's view of his or her future". [6]

Bad news encompasses a wide variety of diagnoses and situations ranging, for example, from patients being no longer able to drive a car after a diagnosis of epilepsy, or needing to have an amputation as a complication of diabetes, to a life-threatening disorder such as cancer or ischemic heart disease.

The way the diagnosis of serious diseases, like cancer, is communicated can have a significant impact not only on the perceptions of patients about their disease, but also on the long-term relationship with their physician. [7]

Breaking bad news is a stressful task, many physicians either avoid it or perform it inadequately because it"results in a cognitive, behavioral, or emotional deficit in the person receiving the news that persists for some time after the news is received." [8].

Physicians used to believe that disclosure of bad news would cause anguish, threatening to cripple the preservation of hope for patients, justifying thus the concealment of bad news. [9]

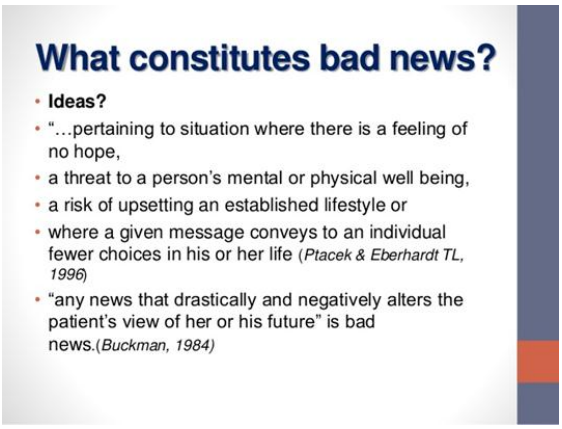

Figure 1. Definitions of bad news

APPROACHES TO COMMUNICATING BAD NEWS

A doctor's communication and interpersonal skills encompasses the ability to gather information in order to facilitate accurate diagnosis, counsel appropriately and give therapeutic instructions in order to improve the patient's health and medical care [11,12].

Unfortunately studies on doctor-patient communication have demonstrated patient discontent even when many doctors considered the communication adequate or even excellent, maybe because physicians tend to overestimate their abilities in communication. [13]

Tongue et al [14] reported that 75% of the orthopedic surgeons surveyed believed that they communicated satisfactorily with their patients, but only 21% of the patients reported satisfactory communication with their doctors.

So, patient surveys have consistently shown that they want better communication with their doctors. [15]

The best training will embrace a patient-centered approach that includes the patient's family. [16]. This type of approach has been shown to yield the highest patient satisfaction and results in the physician being perceived as emotional, available, expressive of hope, and not dominant [17].

The 3 main goals of current physician-patient communication are the following:

- creating a good interpersonal relationship
- facilitating exchange of information
- including patients in decision making [18,19,20,21]

Much more, a good communication has the potential to help regulate patients' emotions, facilitate comprehension of medical information, and allow for better identification of patients' needs, perceptions, and expectations. [18,19,20]

The benefits of good communication

- ❖ identify patient's problems more accurately
- ❖ patients are more satisfied with their care and can understand their problems, investigations and treatment options [1]
- ❖ patients are more likely to adhere to treatment and follow advice [2]
- ❖ patient's anxiety and depression are lessened
  physicians' wellbeing is improved [3,5]

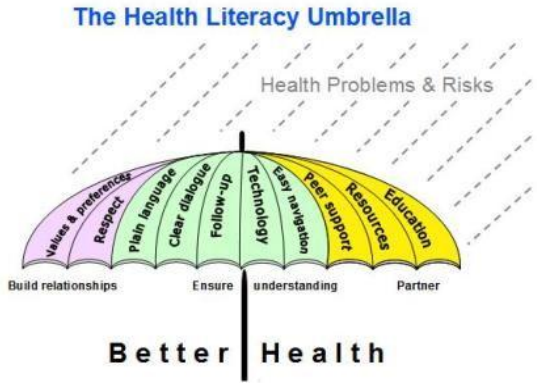

Figure 2. Key tasks in communication with patients

In light of these needs we found out some protocols for communicate bad news. Results revealed that 91% of respondents perceived delivering bad news as a very important skill, but only 40% felt they had the training to effectively deliver such news.

Several protocols have been proposed and tested in the literature. Buckman has written extensively on this subject [22, 23, 24, including his landmark 1992 book, How to Break Bad News: A Guide for Health Care Professionals [25].

One of the most successful approaches in breaking bad news is through client-centered counseling, as proposed by **Carl Rogers**. He put forward three points in order to achieve a better therapeutic relationship between the client (the patient) and the counselor (the physician). They are: (1) be genuine and congruent, (2) offer unconditional positive regard, and (3) feel and communicate a deep, empathetic understanding.[26] A patient-centered communication style has the most positive outcome for recipients of bad news on a cognitive, evaluative, and emotional level.[27]

Baile et al proposed a protocol called **SPIKES** [28]: S - setting up the interview; P - assessing the patient's perception; I - obtaining the patient's invitation; K - giving knowledge and information to the patient; E - addressing the patient's emotions with empathic responses; and S - strategy and summary.

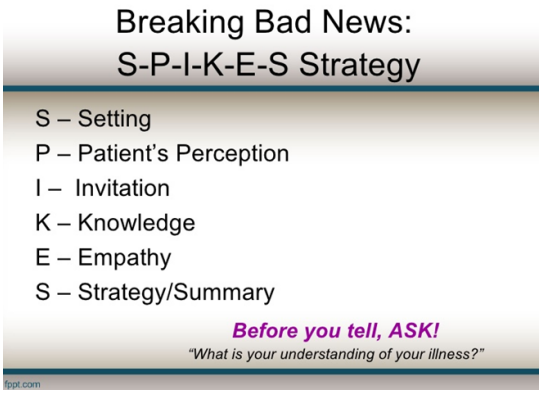

Figure 3. Key tasks in communication with patients

The SPIKES protocol for breaking bad news has four objectives:

- Gathering information from the patient
- Transmitting the medical information
- Providing support to the patient
- Eliciting patient's collaboration in developing a strategy or treatment for the future
- Strategy for breaking bad news

Six Steps of SPIKES:

S – Setting □ Arrange for some privacy □ Involve significant others □ Sit down □ Make connection and establish rapport with the patient □ Manage time constraints and interruptions.

P – Perception of condition/seriousness □ Determine what the patient knows about the medical condition or what he suspects. □ Listen to the patient's level of comprehension □ Accept denial but do not confront at this stage.

I – Invitation from the patient to give information □ Ask patient if s/he wishes to know the details of the medical condition and/or treatment □ Accept patient's right not to know □ Offer to answer questions later if s/he wishes.

K – Knowledge: giving medical facts □ Use language intelligible to patient □ Consider educational level, socio-cultural background, current emotional state □ Give information in small chunks □ Check whether the patient understood what you said □ Respond to the patient's reactions as they occur □ Give any positive aspects first e.g.: Cancer has not spread to lymph nodes, highly responsive to therapy, treatment available locally etc. □ Give facts accurately about treatment options, prognosis, costs etc.

E - Explore emotions and sympathize □ Prepare to give an empathetic response: 1. Identify emotion expressed by the patient (sadness, silence, shock etc.) 2. Identify cause/source of emotion 3. Give the patient time express his or her feelings, then respond in a way that demonstrates you have recognized connection between 1 and 2.

S – Strategy and summary □ Close the interview □ Ask whether they want to clarify something else □ Offer agenda for the next meeting

Another protocol for delivering bad news is **CLASS**. There are five Key Steps for Clinical Interviews:

C – CONTEXT: the physical set up of the area you choose for the interview

L - LISTENING SKILLS: how to be an effective listener

A - ACKNOWLEDGE: how to validate, explore and address emotions and concerns

S - STRATEGY: how to provide a management plan that the patient can understand

S - SUMMARY: how to summarize and clarify the conversation

C - Context (setting)

The C-O-N-E-S Protocol

C - Context

O - Opening Shot

N - Narrative

E - Emotions

S - Strategy & Summary

We can use the C-O-N-E-S Protocol when: • Disclosing that a medical error has occurred • There is a sudden deterioration in the patient's medical condition • Talking to the family about a sudden death

The E-V-E Protocol

E - Explore the Emotion (identify the emotion and ind out more about the emotion and what is causing it

V - Validate the Emotion (let the person know you understand the emotion was appropriate)

E - Empathic Response (respond in a way that shows you have seen the emotion and that you can understand it)

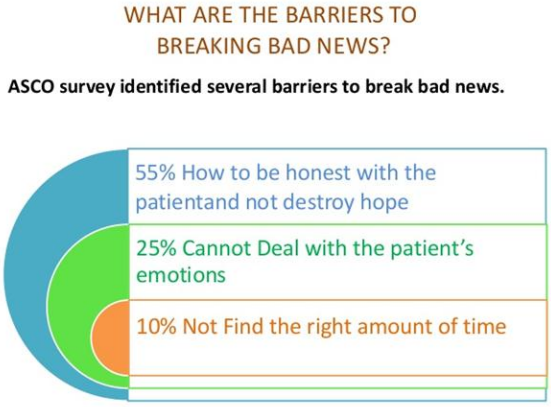

Figure 4. Spikes Protocols

CONCLUSIONS

This review shows that there is concern about the quality of communicating bad news to the patient, we can state that breaking bad news is indeed a part of the art of medicine and that the best training for medical students should include a protocol for delivering bad news.

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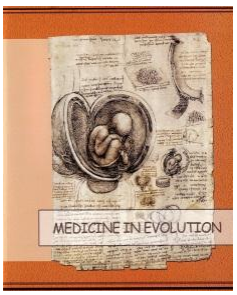
Pericardial effusion as the initial presentation of systemic lupus erythematosus –a case report



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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease that can involve nearly any organ system resulting in a great diversity in presentation. Pericardial effusion as the initial form of presentation in SLE is rare. We present the case of a 19-year-old -female who presented with complaints of shortness of breath, non-productive cough, visual disturbances, asthenia, arthralgia and fever over the past 2 months. On admission, the patient was febrile, had a heart rate of 145 beats/min, a respiratory rate of 42 breaths/min and the physical examination revealed muffled heart sounds, decreased breath sounds at the left lung base, mouth sores and conjunctival hyperemia. Investigations suggested large cardiac and minimal pleural effusion. After a thorough investigation, the diagnosis of SLE was confirmed using the Systemic Lupus International Collaborating Clinics (SLICC) criteria and the therapy with methylprednisolone was initiated. Our case report aims to emphasize the importance of SLE as a differential diagnosis when presented with pericarditis.

Key words: *systemic lupus erythematosus, pericardial effusion, autoimmune disease*

INTRODUCTION

Systemic lupus erythematosus (SLE) is a complex, heterogeneous disease characterized in 95% by autoantibody production that can involve nearly any organ system resulting in a great diversity of clinical presentation which can be difficult to diagnose in the emergency department.[1] Pericardial involvement can be the initial form of presentation of systemic lupus erythematosus; however, clinically significant pericarditis occurs in less than 30%. [2]. Cardiac tamponade is a medical emergency that develops when a pericardial effusion reaches a critical amount, limiting cardiac inflow and leading to hemodynamic compromise. We present the case of a pericardial effusion as a first manifestation of systemic lupus erythematosus to a 19-year-old female patient for emphasize the importance of systemic lupus erythematosus as a differential diagnosis when presented with pericarditis in the presence or absence of cardiac tamponade.

CASE PRESENTATION

A 19-year-old female patient presented to the emergency department with complaints of shortness of breath aggravated by supine position, non- productive cough, visual disturbances (diplopia), asthenia, arthralgia (especially of the interphalangeal joints) and fever over the past 2 months. She had no past medical history.

On admission, the patient had a heart rate of 145 bpm, a respiratory rate of 42 breaths/min, blood pressure of 105/70 mmHg and a temperature of 38.4˚C. On physical examination, cardiac auscultation revealed muffled heart sounds and the apex beat diffuse and displaced inferiorly. Respiratory auscultation revealed decreased breath sounds at the left lung base, with no other pathological findings. The rest of the examination only proved mouth sores (Figure 1) and conjunctival hyperemia.

Electrocardiography showed sinus tachycardia at a rate of 142 beats/min with diffuse but non-specific repolarization abnormalities. (Figure 2) The chest radiography displayed a diffuse enlargement of the cardiac silhouette and bilateral pleural effusion. Echocardiographic examination revealed the presence of large amount of pericardial fluid (20 mm – maximal diameter at end-diastole), without signs of cardiac tamponade. (Figure 3). We started to administrate Anti-inflammatory therapy (1600 mg Ibuprofen daily- according to the pericarditis guideline) and empiric antibiotics (Ciprofloxacin 400 mg iv plus Ceftriaxone 2g iv) and we continued with the other investigations to find out the cause of the pericardial effusion.

Laboratory investigations showed a normocytic moderate anaemia (Hgb 7, 6 g/dl) with a normal white and platelet cell count. Erythrocyte sedimentation rate was 83mm/h, C-reactive protein was › 30 mg/L. Cardiac biomarkers (cTnI 0,038 ng/mL, CK-MB 0,372 ng/mL, NTproBNP 310 pg/mL), renal, liver and thyroid function testing were normal and blood cultures were negative. Urinalysis was within normal range and showed no proteinuria. The immunologic panel testing showed that C3, C4, rheumatoid factor, RPR, SSA, SSB, Sm were within the normal range. However, we found that serum antinuclear antibodies (ANA) was positive and antiDs-DNA by ELISA were 67 (normal values ‹ 40U/mL).

Pleural fluid cytology revealed cells of an inflammatory response, with no microorganisms detected on Gram stain or Ziehl-Neelsen stain. On the other hand, there was no evidence of malignancy.

Despite the double antibiotherapy, the patients condition was stationary, with persistent fever. We suspended the antibiotherapy and we started methylprednisolone, initially with an intravenous load, and subsequently per *os* at a dosage of 32 mg. The fever, dyspnea responded. Repeated echocardiographic examination and chest radiography showed

a decrease in the amount of pericardial and pleural fluid. The diagnosis of SLE was established based on the positive clinical and immunologic findings. The patient satisfied 5 of the 17 Systemic Lupus International Collaborating Clinics (SLICC) for classifying SLE, namely serositis, mouth sores, anaemia, positive serum ANA and positive anti- dsDNA antibodies. The patient was discharged by the 20th hospital day, on a therapeutic regimen of 32 mg/day of methylprednisolone.

Figure 1. Clinical examination- mouth sores

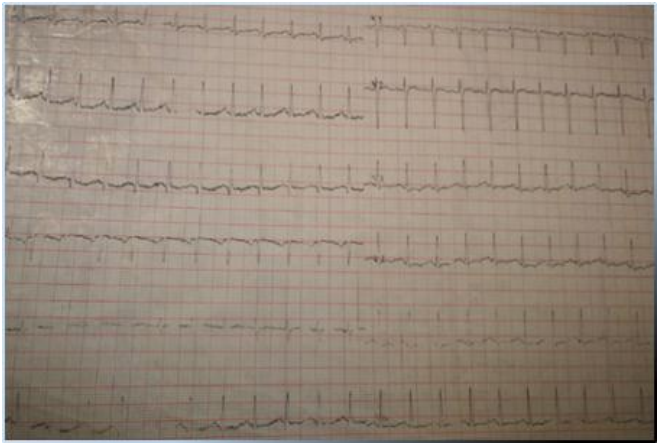

Figure 2. Sinus tachycardia, HR 142 bpm, with diffuse but non-specific repolarization abnormalities

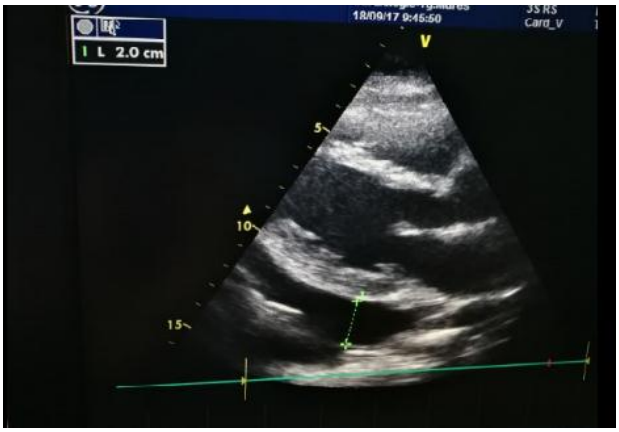

Figure 3. Echocardiographic parasternal long-axis view, showing moderate pericardial effusion, which appears more prominent in the posterior pericardial space

DISCUSSIONS

Even though pericarditis in systemic lupus erythematosus has already been described in regard to its clinical and echocardiographic features, occurrence of cardiac tamponade as a first manifestation in systemic lupus erythematosus remains a rare onset of this disease. [3]

Studies showed that the most common initial presentations of systemic lupus erythematosus included constitutional complaints- such as malaise, fatigue, fever as well as renal disease, musculoskeletal and cutaneous involvement. [4, 5]

Fever in systemic lupus erythematosus remains a challenging clinical problem. About 42% of patients with systemic lupus erythematosus accuse fever as a manifestation of active lupus.[4] In our case, we tried to make all investigations necessary to exclude other causes of fever such as infections, medications or malignancies. Studies showed that lupus is a cause of fever of unknown origin in less than 5% of patients. [5]

In conclusion, this is an interesting case of an atypical presentation in systemic lupus erythematosus that can often lead to major diagnostic delay. By allowing for greater weighting of immunologic criteria the use of Systemic Lupus International Collaborating

Clinics (SLICC) criteria may be more sensitive for diagnosis, potentially leading earlier diagnostic and treatment.

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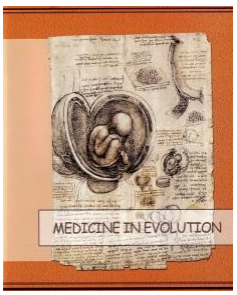
Empathy and emotional stress in forensic medicine



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Abstract

This paper aims at the issue of empathy and emotional distress in Forensic Medicine. The study was conducted on a group of 30 people aged between 36 and 60, with a work experience between 10 and 40 years, forensic experts. For data collection, the Profile of Affective Distress (PDA) and Emotional Intelligence (SEI) questionnaires were used.

The results show that there are significant differences between the groups regarding the length of service, for the emotional distress scale as well as for the empathy scale.

Keywords: empathy, emotional stress, dysfunctional emotion

INTRODUCTION

Doctor-patient relationship is one of the basic issues that medical psychology deals with. Unlike other professions, physicians have to develop particular skills, namely the ability to communicate, understanding, empathy, observation, patience, and compassion [1].

The implications of empathy and emotional distress in forensic practice become even more important because more and more research shows their negative impact on the profession and everyday life, leading to various mental and emotional disturbances and imbalances.

MATERIAL AND METHODS

The study was conducted on a group of 30 people aged between 36 and 60, having a work seniority between 10 and 40 years, forensic experts working on the territory of Romania, namely in Bucharest, Craiova, Cluj and Târgu Mureş. The average age of the group is 48 years, of which 12 subjects are female, with the remaining 18 subjects being male. Subjects participating in this study were asked to complete two questionnaires: Profile of Affective Distress (PDA) and Emotional Intelligence (SEI), previously signing a consent to be included in the study.

The scale of affective distress is a tool developed for the purpose of assessing the subjective dimension of functional negative emotions, dysfunctional negative emotions, and positive emotions [2]. The emotional intelligence scale includes 4 subscales: emotion assessment (EvE); personal emotion adjustment (REP); the emotions regulation of others (REC) and the emotions utilisation (EU) [3, 4].

RESULTS

For the working seniority range of 10 to 20 years, a correlation coefficient equal to 0.229 was obtained, which suggests that there is a direct correlation between variables, moderately to poor [Table 1].

The Sig. corresponding value is equal to 0.499> 0.05, which indicates that an insignificant correlation coefficient was obtained; there is an insignificant correlation between the two, that is to say, between 10-20 years of work and the total PDA score is a direct, moderate to poor correlation.

Table 1. The relationship between the seniority of the subjects and the overall PDA score

Group seniority = 10-20 years

Correlations[a]

		SCOR TOTAL PDA	Seniority
SCOR TOTAL PDA	Pearson Correlation	1	.229
	Sig. (2-tailed)		.499
	N	11	11
Seniority	Pearson Correlation	.229	1
	Sig. (2-tailed)	.499	
	N	11	11

For the range of 20-30 years of working seniority, a correlation coefficient of -0.429 was obtained, indicating that there is a inverted correlation between variables, moderate to poor [Table 2].

The value of Sig. is equal to 0.097 <0.05, which shows that an insignificant correlation coefficient was obtained, there is an insignificant correlation between the two. In conclusion,

there is a moderate to moderate backward correlation between the range of 20-30 years of work and the total PDA score.

Table 2 The relationship between the seniority of the subjects and the overall PDA score

Group seniority = 20-30 vears

Correlations[a]

		SCOR TOTAL PDA	Seniority
SCOR TOTAL PDA	Pearson Correlation	1	-.429
	Sig. (2-tailed)		.097
	N	16	16
Seniority	Pearson Correlation	-.429	1
	Sig. (2-tailed)	.097	
	N	16	16

For the group of subjects with the range of 30-40 year working experience, a correlation coefficient of 0.749 resulted, suggesting that there is a direct, moderate to strong correlation between the variables [Table 3].

The value of Sig. is 0.461> 0.05, which signifies an insignificant correlation coefficient, there is an insignificant correlation between the two. In other words, there is a direct, moderate to strong correlation between the working experience of the 30-40 years range and the total PDA score.

Table 3. The relationship between the seniority of the subjects and the overall PDA score

Group seniority = 30-40 vears

Correlations[a]

		SCOR TOTAL PDA	Seniority
SCOR TOTAL PDA	Pearson Correlation	1	.749
	Sig. (2-tailed)		.461
	N	3	3
Seniority	Pearson Correlation	.749	1
	Sig. (2-tailed)	.461	
	N	3	3

Following the statistical results, taking into account the three working time intervals and the total PDA score, we can say that there is no correlation between the two.

The obtained correlation coefficient is equal to 0.080 and the value of Sig. is equal to 0.815> 0.05, which indicates that an insignificant correlation coefficient was obtained; between the working experience of 10-20 years and the IE score there is a direct but very poor correlation [Table 4].

Table 4. The relationship between the seniority of the subjects and the total IE score

Group seniority = 10-20 vears

Correlations[a]

		Seniority	Scor_Total_QE
Seniority	Pearson Correlation	1	.080
	Sig. (2-tailed)		.815
	N	11	11
Scor_Total_QE	Pearson Correlation	.080	1
	Sig. (2-tailed)	.815	
	N	11	11

In the present case, a correlation coefficient equal to 0.687 was obtained, Sig value is 0.003 <0.05, which shows a significant relation between the two; between the working experience of 20-30 years and the total IE score there is a direct and moderate correlation [Table 5].

Table 5. The relationship between the seniority of the subjects and the total IE score

Group seniority = 20-30 vears

Correlations[a]

		Seniority	Scor_Total_QE
Seniority	Pearson Correlation	1	.687**
	Sig. (2-tailed)		.003
	N	16	16
Scor_Total_QE	Pearson Correlation	.687**	1
	Sig. (2-tailed)	.003	
	N	16	16

**. Correlation is significant at the 0.01 level (2-tailed).

The correlation coefficient is 0.984, the value of Sig. being 0.114> 0.05, showing an insignificant relation; between the group with a working experience of 30-40 years and the total IE score there is a direct, strong correlation [Table 6].

Table 6. The relationship between the seniority of the subjects and the total IE score

Group seniority = 30-40 vears

Correlations[a]

		Seniority	Scor_Total_QE
Seniority	Pearson Correlation	1	.984
	Sig. (2-tailed)		.114
	N	3	3
Scor_Total_QE	Pearson Correlation	.984	1
	Sig. (2-tailed)	.114	
	N	3	3

Following the statistical results, taking into account the three intervals of work and the total IE score, we may affirm that the result is inconclusive, because a significant correlation coefficient was obtained only in the range of 20-30 years of working experience.

Following the Levene test, we notice that there are no significant differences regarding other's emotion regulation for the two genres: masculine and feminine.

Table 7. The difference in gender in terms of regulating the emotions of others

Independent Samples Test

		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
REC	Equal variances assumed	1.253	.273	.897	28	.377	2.889	3.219	-3.705	9.483
	Equal variances not assumed			.867	20.877	.396	2.889	3.333	-4.046	9.824

Table 8. The difference in gender from the point of view of emotion assessment

Independent Samples Test

		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
Eve	Equal variances assumed	.506	.483	1.632	28	.114	3.111	1.906	-.794	7.016
	Equal variances not assumed			1.683	26.042	.104	3.111	1.849	-.689	6.911

In conclusion, we may state that both genres have the same coefficient of empathy, with no differences between them.

DISCUSSION

Some studies on this subject show a continuous increase in both empathy and distress among pathologists.

Based on these experimentally validated data, the formulation of the objectives and conclusions of this study was attempted.

The long-term objective of the study was to analyze the implications of empathy and emotional distress in forensic practice [5-7].

Shuman concluded that the empathy of the pathologists makes them believe in a therapeutic relation; he argues that they should use empathy moderately, not to regard it as a component of subjectivity and pseudo-therapy, but rather as a useful tool for an effective assessment [8-11].

A study made in Chile, on the distress theme, showed that one in three pathologists reported depressive symptoms, distress, and psychotropic drug use; experts have testified that work related problems contribute to these symptoms or consumption; at the same time, it was observed that subjects exposed to psychosocial risk have had a greater chance of experiencing mental health problems than those who were not exposed [12-15].

Some specialists say that from the distress point of view, females are more affected, leaving far behind the males. This may also be dued to the fact that women are more susceptible to harassment (for personal aspects of emotional and relational factors) than men. Knowing the phenomenon is an essential requirement to counteract physical or psychological aggression. Preventing this from happening can be done by both informing and instructing doctors in this regard [16-18].

CONCLUSION

Analyzing the scientific literature as well as the results of the current study, it was concluded that the work experience has no influence on the total PDA score, namely distress:

- the range of 10-20 years of work experience has a direct, but insignificant, influence on distress;
- the range of 20-30 years of work experience has an indirect, but insignificant influence on distress;
- the range of 30-40 years of work experience has a direct but insignificant influence on distress.

The same results for the first and the last age range were also reported in the case of the influence on IE, namely empathy, except for the range of 20-30 years of working experience where the correlation coefficient is significant, direct.

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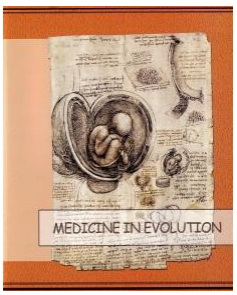
Psiho-socio diagnostic aspects in Alzheimer maladia



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Abstract

Alzheimer's disease continues to be a topical issue because, firstly, the incidence of this disease among the elderly is maintained at a high level and, secondly, research has brought a series of extremely valuable data for therapy, prognostic and the prediction of the evolution in the social and family environment.

The purpose of this paper is to determine as to what extent the quality of life of patients with Alzheimer's neurodegenerative disease is affected, regardless of the stage of the disease and to what extent the familial and social interpersonal relationships of these patients are affected.

Keywords: Alzheimer, quality of life, mental condition

INTRODUCTION

Worldwide Alzheimer's disease is the most common form of neurodegenerative disease of the elderly persons and represents half of all cases of dementia. When we discuss about Alzheimer's disease, we mostly have in mind only the most characteristic manifestation of the disease, namely progressive dementia, but the other features, such as cognitive symptoms (memory disorders, speech disorders, inability to perform various coordinated motor activities, problems related to abstract thinking, computational disorders, temporal and spatial disorientation) and non-cognitive symptoms (physical or verbal agitation and aggression, psychotic disorders, affective disposition disorders, eating behavior disorders, sexual disinhibition, urinary and faeces incontinence, the satisfying of physiological needs in inappropriate places, or in the presence of others) are just as important in assessing the patients quality of life [1, 2].

Few international studies relate to the social developments of patients with Alzheimer's disease, which is not to be neglected given the multitude of cognitive and non-cognitive symptoms encountered in patients with dementia.

MATERIAL AND METHODS

The present paper represents a study of correlation between the clinical aspects and the social evolutions of patients with Alzheimer's disease, regardless of the evolutionary stage of the disease, diagnosed at the Department of Neurology of the County Hospital for Emergencies”Pius Brinzeu" Timisoara. Patients diagnosed with Alzheimer's dementia have been identified and selected. Patients were between 56 and 88 years old, the average age being 72 years.

For the collection of the data required for the study, patients' anamnestic data were used as well as two questionnaires: the SF-36 questionnaire (Short Form 36) - a generic instrument for the measuring of the health status and the MMSE (Mini Mental State Examination).

The processing of the obtained data was done using the IBM SPSS Statistics 2015 program, so the coefficient r was calculated. The coefficient r can take values between -1 and +1, where 0 signifies the absence of the relation between the two variables analyzed.

RESULTS

By correlating the percentages of the test with the MMSE values, a correlation index value of 0.788132 was obtained. The value obtained shows that there is a statistically significant correlation between the MMSE variable and the interpersonal relationships variable. Therefore, a higher MMSE value implies an increase in the quality of life and a better relationship with others [Figure 1].

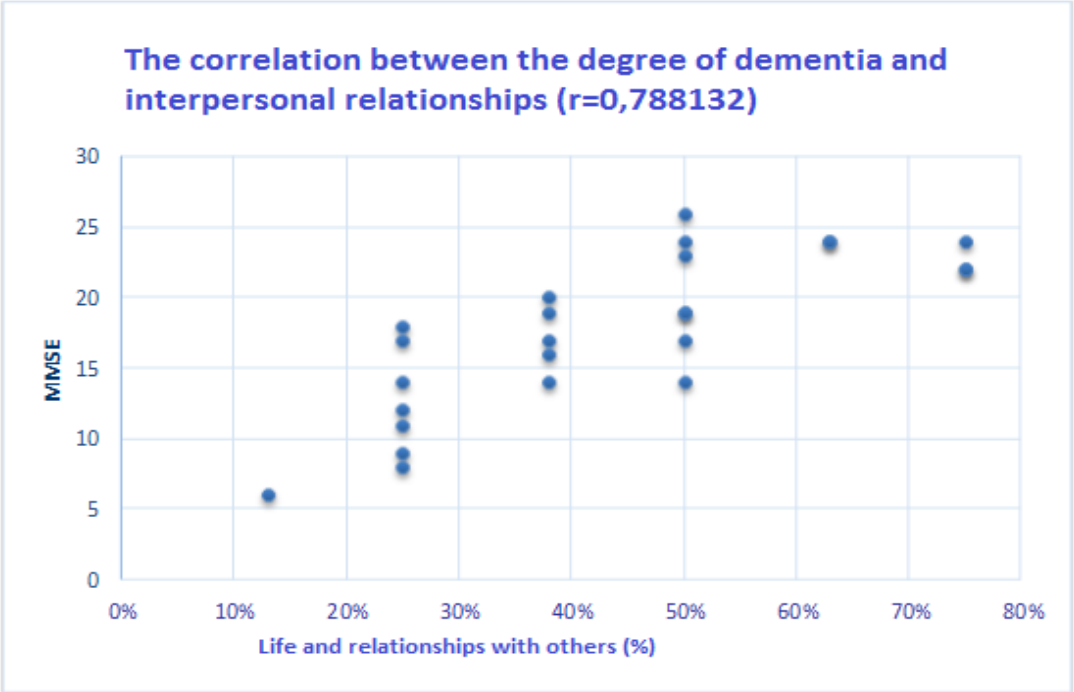

Figure 1. The correlation between the degree of dementia and interpersonal relationships (n=25)

Following the correlation between the perception of health and the degree of dementia, a coefficient equal to 0.268128 was obtained. The value of the coefficient indicates an acceptable degree of correlation. The existence of the correlation shows that a significant decrease in the value of MMSE changes in a negative sense the patient's perception of his own health [Figure 2].

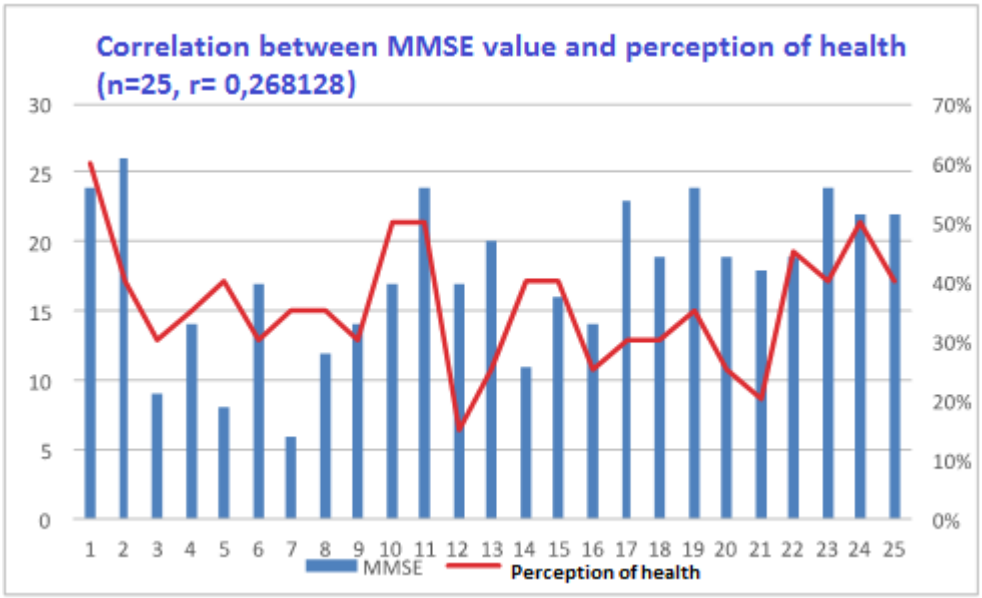

Figure 2. Correlation between the degree of dementia and the perception of health (n=25)

The correlation index between the MMSE value and the mental health variable is 0.099613. This value of the index represents a poor or null correlation. [Figure 3].

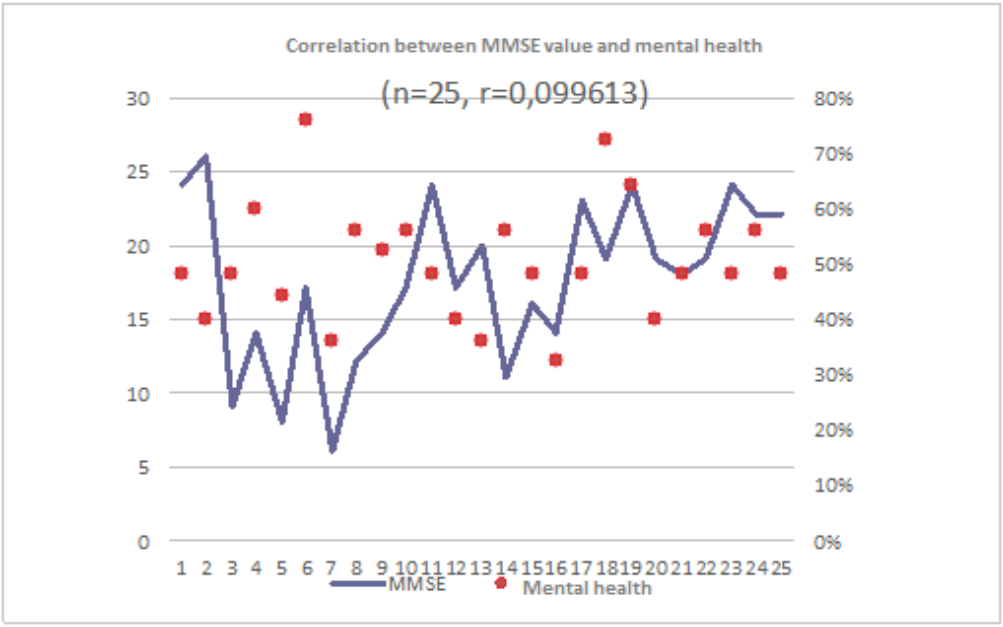

Figure 3. Correlation between the degree of dementia and mental health (n=25)

By correlating the percentages of the test with the MMSE values, a correlation index value of 0.807948 was obtained. The value obtained shows that there is a very good statistical correlation coefficient between the MMSE variable and the physical activity variable [Figure 4].

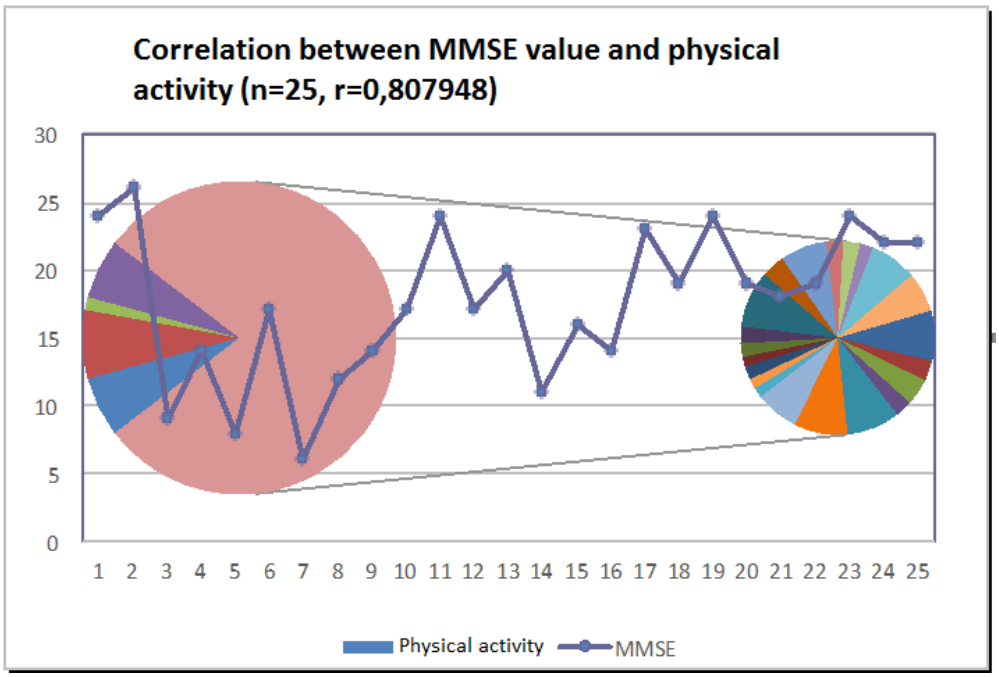

Figure 4. Correlation between the degree of dementia and physical activity (n=25)

Therefore, the correlation between dementia and physical activity is positive: a higher MMSE value implies an increase in physical activity.

The limitations of the patient's mental state were assessed by the 5th dimension of the SF-36 test. The correlation coefficient was 0.057407, which means a weak or null correlation. Within the group of patients to whom the questionnaire was applied no direct relation was observed between the two variables, as demonstrated by the correlation coefficient [Figure 5].

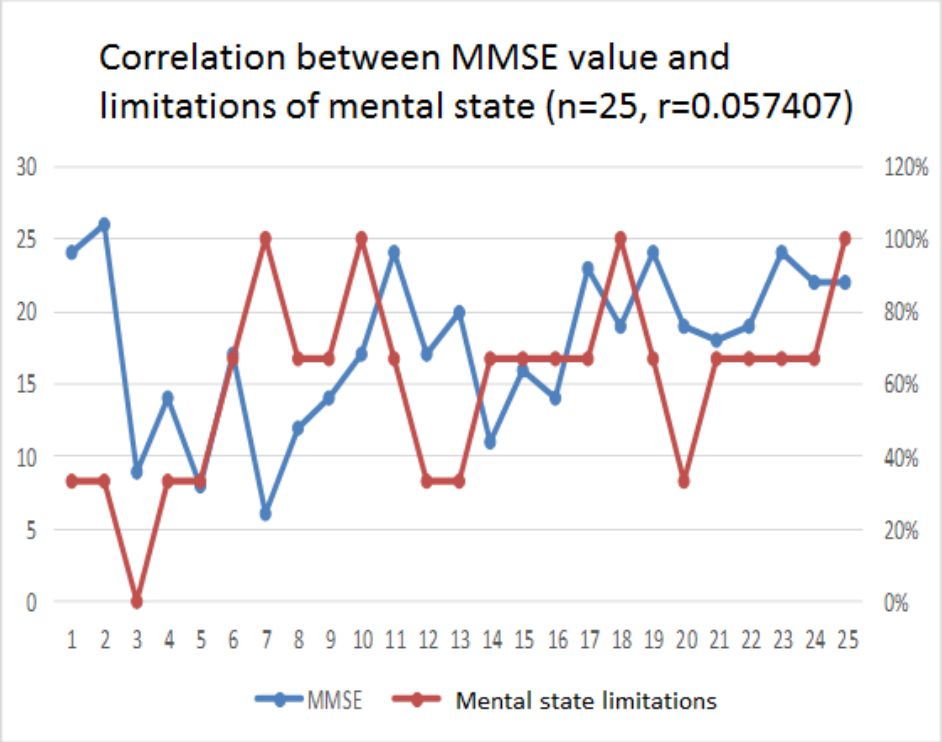

Figure 5. Correlation between the degree of dementia and the limitations of the mental state (n=25)

Physical pain represents the sixth dimension of the SF-36 questionnaire. The correlation coefficient between this dimension and the MMSE value had a value of 0.743458, a value indicating a moderate to good correlation. The existence of the correlation highlights that there is a positive relation between the two variables [Figure 6].

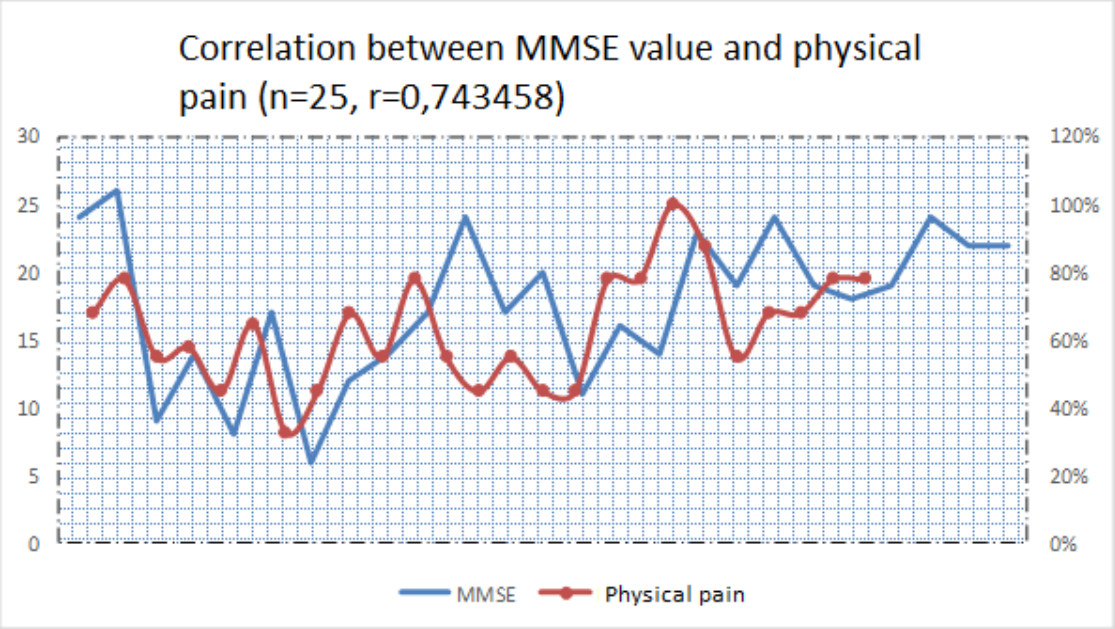

Figure 6. Correlation between the degree of dementia and physical pain (n=25)

The vitality of patients with Alzheimer's dementia was also evaluated by the SF-36 test. Using Pearson's correlation coefficient, where the first variable was the MMSE value and the second variable the percentages obtained from the questionnaire we obtained a coefficient value of 0.54065, which shows a moderate to good statistical correlation. The existence of the

correlation highlights that there is a positive relationship between the two variables [Figure 7].

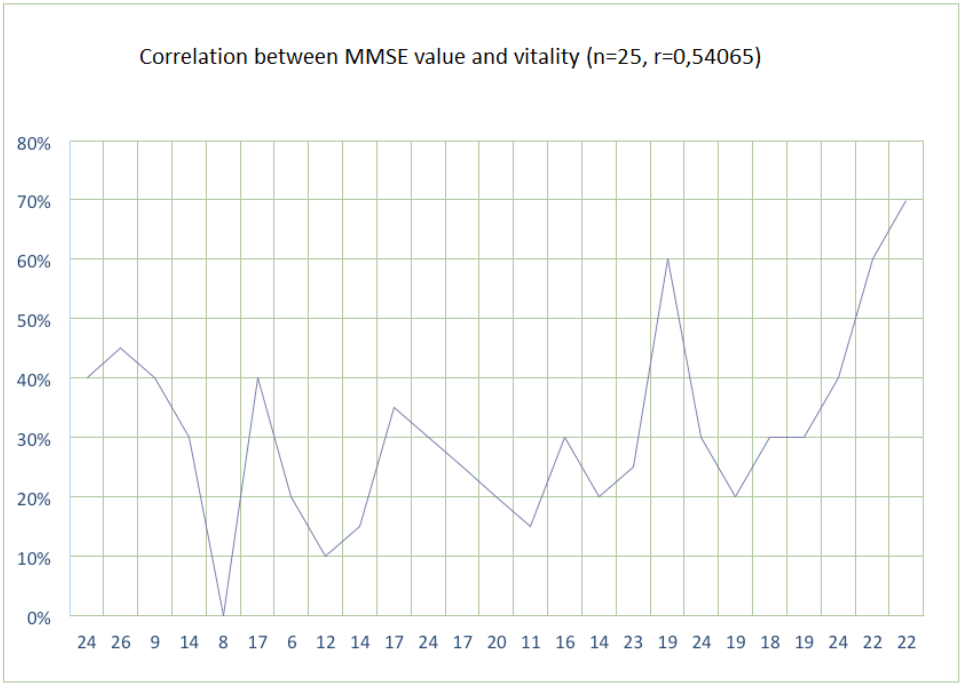

Figure 7. Correlation between the degree of dementia and vitality (n=25)

The correlation coefficient between the limitations imposed by the physical state and the MMSE value had a value of 0.59099, which indicates a moderate to good statistical correlation. The existence of correlation highlights that there is a positive relation between the two variables [Figure 8].

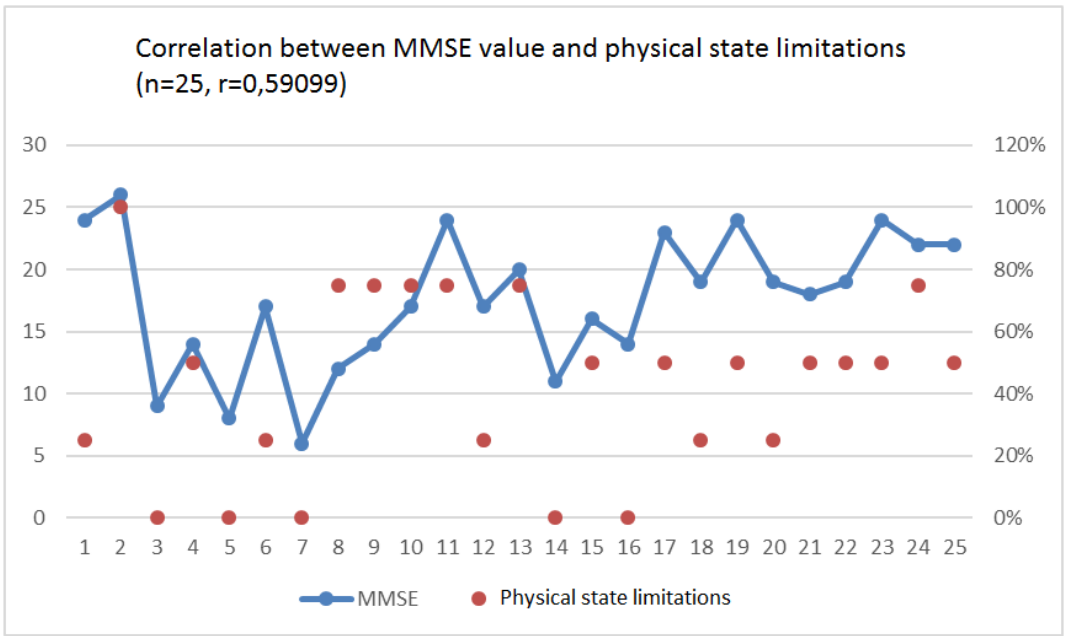

Figure 8. Correlation between the degree of dementia and the limitations of physical condition (n=25)

DISCUSSION

A study conducted in 2012 (May-June) by Borghi AC and Marcon SS informs us that in the case of patients with primary carers represented by the family, their emotional state was

considerably influenced compared to those with secondary carers, such as medical and auxiliary staff. This outlines the need to plan the care action and monitor the patient considering each type of caregiver [3].

A study made on 79 patients diagnosed with Alzheimer's in 2005, conducted by Juanita Hoe, Cornelius Katona, Brigitte Roch, Gill Livingston, produced similar results to this present study. The methods used in the study were MMSE and QOL-AD [4-6].

In the year 2016, Maria I. Andreakon et all, conducted a study on 155 patients diagnosed with Alzheimer's disease and obtained results similar to this present study. Methods used in the named study were SF-36 and HRQol. From the point of view of the quality of life, it has been observed that the long time spent by the caregivers along with the sick becomes a problem for them, the QoL score being low [7-11]

Another study was conducted on a group of 47 people with dementia located in a long-term care unit. The life quality of the subjects was assessed both at baseline and two years later using the Alzheimer's disease-related quality of life (ADRQL). The results of the study revealed a slight improvement in the quality of life for the patients enrolled in the study with the disease duration being less than two years. However, there were subjects with a disease age greater than two years whose quality of life was slightly damaged. The results of the studies do not make it possible to identify with certainty the factors for improving the quality of life of Alzheimer patients, resulting in the necessity of further research on this topic [12-16].

CONCLUSION

The results show that patients diagnosed with Alzheimer's disease have the quality of life affected and while the degree of severity increases, the overall health of patients decreases.

Regarding the medical care of an Alzheimer's patient, it is important to maintain the safety and health of the patient through appropriate nutrition, a proper resting program, proper hygiene, and avoiding acute medical conditions that can degrade the patient's condition.

The results obtained may be useful for clinicians, carers and anyone who has direct contact with patients who suffer from this disease, in order to improve their quality of life and their integration into social life.

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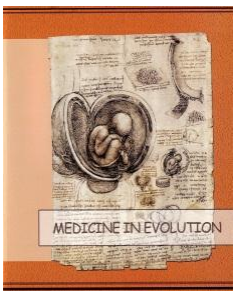
Epidemiology of human trichinellosis in the European Union, 2007-2015



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Abstract

Introduction: Trichinellosis is a foodborne zoonotic disease with worldwide distribution. In the present paper we review the epidemiology of trichinellosis in the European Union between 2007 and 2015.

Materials and methods: We assessed the number of reported and confirmed trichinellosis cases, number of hospitalized cases, hospitalised cases proportion, distribution by gender, age, Trichinella species, clinical signs and meat sources of infection.

Results: The number of trichinellosis cases tended to decrease from 2007 to 2015. Romania ranked first among EU member states, with most trichinellosis cases followed by Bulgaria, Poland and Lithuania. Wild boar and pork were the major source of infection.

Conclusion: Cultural and traditional habits of eating raw or undercooked meat play a key role in the spread of the disease and were responsible for past outbreaks. Therefore, intensive public education, especially for small pig breeders and hunters, is needed in order to prevent human trichinellosis.

Keywords: trichinellosis; outbreak; Europe; review

INTRODUCTION

Trichinellosis is a foodborne zoonotic disease with worldwide distribution, caused by the larval stage nematodes of the genus Trichinella [1]. In addition to *Trichinella spiralis*, found worldwide in many carnivorous and omnivorous animals, several other species of *Trichinella* are now recognized, including: *T. pseudospiralis*, in mammals and birds worldwide; *T. native*, in Arctic bears; *T. nelson*, in African predators and scavengers; *T. britovi*, in carnivores of Europe and western Asia and *T. papuae* in wild and domestic pigs, Papua New Guinea and Thailand. *T. zimbabwensis* is found in crocodiles in Africa but to date there are no known associations of this species with human disease [2].

Transmission of Trichinella spp. in various hosts occurs through the ingestion of infected meat, through predation or scavenging of meat from an infected animal [1]. Human infection results from consumption of raw or improperly cooked meat containing infective larvae and it has historically been associated with pork [3]. However, in Europe, meats of horses and wild boars have played a significant role during outbreaks within the past 3 decades [4]. Human infection is classically characterized by gastroenteritis; myalgia; fatigue; facial edema; headache and increased eosinophils values, leukocytes, and muscle enzymes [5].

The World Health Organization European Region accounted for 87% of trichinellosis cases worldwide; 50% of those occurred in Romania, mainly during 1990–1999 [5]. Current European regulations aim at ensuring that only meat that has been certified *Trichinella*-free after systematic control may be marketed [6]. However, epidemiological data suggests that in spite of these regulations, consumption of uninspected meat still occurs [7] and cases due to the consumption of pork were mostly reported [8].

In the 1990's, an increased prevalence of *Trichinella spp* infections was reported. This has been primarily related to a breakdown of government veterinary services and state farms (e.g., in countries of the former USSR, Bulgaria, Romania), economic problems and war (e.g., in countries of the former Yugoslavia), resulting in a sharp increase in the occurrence of this infection with a prevalence of up to 50% in villages in Byelorussia, Croatia, Latvia, Lithuania, Romania, Russia, Serbia, and the Ukraine, among other countries [9]. In Romania, for instance, the breakdown of large-scale abattoirs post-Communism led to an increase in the incidence of trichinellosis as pig slaughtering moved to small farms in poor rural communities [10].

In the present paper, we reviewed the epidemiology of human trichinellosis in the European Union (EU), during the period of 2007-2015. We undertook this study to assess trichinellosis in the EU, after new member's states joined the organization.

MATERIALS AND METHODS

To collect recent and valuable information regarding human trichinellosis in the EU**, w**e searched Pub Med database for epidemiological studies or outbreak investigations and reviewed data reported by ECDC between 2007-2015. The search terms were trichinellosis and *Trichinella*. These were combined with the terms outbreak, review, and Europe. A search for „trichinellosis, outbreak, Europe" with the application of filters for the date of publication and Trichinella species, resulted in 53 articles in PubMed (Accessed 03 Aug 2017). For the purpose of this study, full length articles and/ or abstracts published in English only, were selected. Papers published in languages other than English and reports from countries outside EU were excluded from the study.

We assessed the number of reported and confirmed cases, number of hospitalized cases, hospitalised cases proportion, distribution by gender, age, Trichinella species, clinical signs and meat sources of infection.

RESULTS

Number of cases

During the period of 2007-2015, the total number of reported and confirmed cases in the EU was 4609 and 3696, respectively. The number of trichinellosis cases tended to decrease from 2007 to 2015 (Table 1). Romania ranked first among EU member states, with 1930 (52.2%) confirmed cases of trichinellosis, followed by Bulgaria, Poland and Lithuania (Figure 1). These 4 countries reported 3155 (85.3%) of the total number of confirmed cases in the EU.

Table 1. Cases of trichinellosis documented in the European Union, 2007-2015

Year	Reported cases*	Confirmed cases**	No. hospitalised cases	Hospitalised cases proportion %***
2007	875	787	0	0 %
2008	680	670	4	0,59 %
2009	1075	750	189	25,2 %
2010	394	223	70	31,4 %
2011	363	268	153	57,1 %
2012	378	301	177	58,8 %
2013	256	217	106	48,8 %
2014	384	324	150	46,8 %
2015	204	156	30	25,6 %
Total	4609	3696	879	23,8 %

* Reported cases represent persons meeting the clinical criteria and with an epidemiological link
** Confirmed cases represent persons meeting the clinical criteria and positive serology for *Trichinella*
*** Hospitalised cases proportion was calculated from reference 11. Hospitalised cases proportion represent the ratio of hospitalised and confirmed cases.

Table adapted according to ECDC's" Surveillance Atlas of Infectious Diseases" [11].

Age, gender and species

The analysis made on age groups indicated that the number of reported and confirmed cases was significantly higher in those aged 25-44 years and 45-64 years (Table 2). Trichinellosis occurred mainly in persons over 15 years of age, representing 89.84% of the total number of cases. The majority of trichinellosis cases occurred in males, except in 2010 and 2011 (Table 2).

T. spirallis, *T. pseudospiralis* and *T. britovi* were the most frequent reported species to cause trichinellosis in humans (data not shown) [11].

Table 2. Distribution of trichinellosis cases in the European Union by age groups and gender, 2007-2015

Year/Age group and gender	0-4	5-14	15-24	25-44	45-64	65+	Male	Female
2007	0	2,1	7,8	37,9	43,3	8,9	55,7	44,3
2008	0	4,7	23,4	29,7	37,5	4,7	56,2	43,7
2009	2,5	8,7	15,9	38,7	28,7	5,3	54,8	45,2
2010	4,4	10,2	16	35	24,3	10,2	48,1	51,9
2011	1,7	7,9	14,5	40,7	29,5	5,8	47,7	52,3
2012	2,5	12,6	14,7	39,1	23,9	7,1	50,9	49,1
2013	2,2	7,2	13,3	38,3	27,8	11,1	52,2	47,8
2014	3,4	12,3	14,8	38,3	25,3	5,9	55,6	44,4
2015	1,9	7,1	7,1	41	30,8	12,2	54,5	45,5

Table adapted according to ECDC's" Surveillance Atlas of Infectious Diseases" [11].

Clinical signs

The most frequent clinical signs, in patients who requested medical care, were myalgia, periorbital edema or eyelid edema, fever, diarrhea, nausea, vomiting, rash, and headache [6-8, 13, 17, 25, 27, 28, 30]. In addition, symptoms like abdominal pain, fatigue,

abdominal distension, low appetite, joint pain and asthenia were also reported [6, 7, 8, 17, 27, 28, 30].

Sources of infection

Wild boar and domestic pig and were the major sources of *Trichinella* spp. infection in humans. Wild board was reported as a source of infection in 8 (47,05%) of the 17 outbreaks, and pork in 7 (41,17%). Both wild boar and pork were reported in 2 (11.76%) outbreaks (Table 3). The most common foods, identified as a source of infection, were ham and smoked sausage from pork or wild boar (Table 3). Exotic foods like"teewurst" (German sausage) [12] and figatelli [13] have also been consumed and detected.

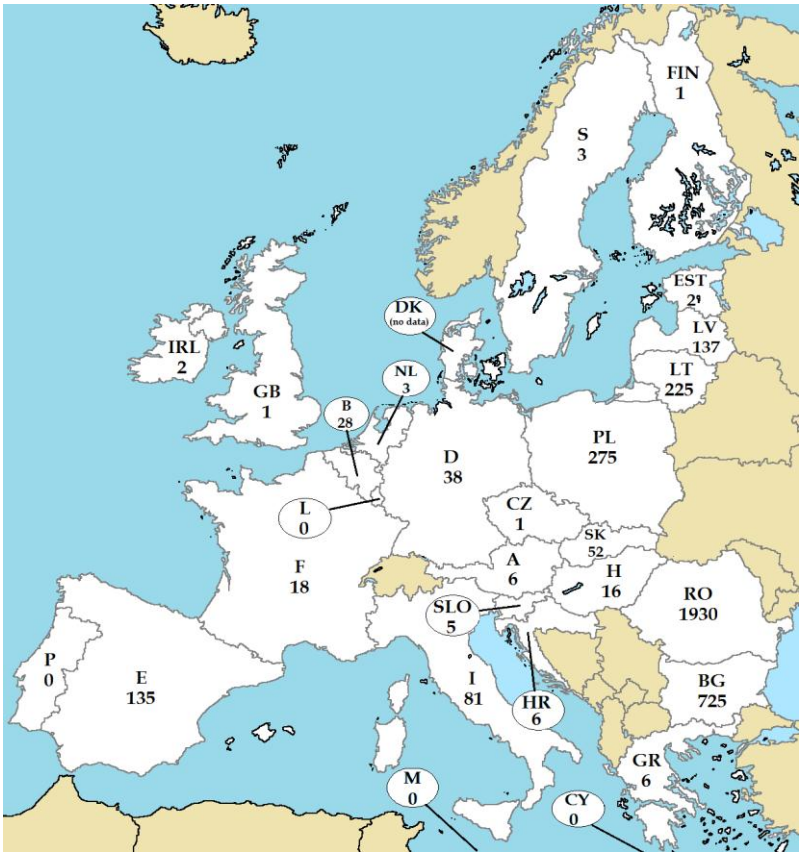

Figure 1. Member States of EU with confirmed cases of trichinellosis by European Centre for Disease Prevention and Control, 2007-2015

Figure adapted according to ECDC's"Surveillance Atlas of Infectious Diseases" [11].

Table 3. Outbreaks of trichinellosis associated with consumption of infected meat in European Union countries, 2007-2015*

Country	Year of publication	Source	*Trichinella* species	References
Spain	2009	wild boar meat	T. spiralis T. britovi	[14]
Germany	2007	pig, minced meat, cured sausage and bacon	T. spiralis	[15]
Ireland	2007	slightly-smoked pork sausages	Not determined	[16]
Slovak Republik	2007	pork smoked sausages and ham	Not determined	[17]
Italy	2009	domestic pigs	T. britovi	[18]
Italy	2008	ham produced from a pig	Not determined	[6]
Poland	2007	wild boar meat raw pork sausage	Not determined	[19]
Lithuania	2009	wild boar sausages	Not determined	[7]
France	2009	warthog ham	Not determined	[20]
Poland	2011	wild boar meat and pork	Not determined	[21]

Poland	2012	wild boar meat raw sausages	Not determined	[22]
Poland	2013	wild boar meat raw sausage	Not determined	[23]
Hungary	2012	pig raw meat	Not determined	[24]
Germany	2013	wild boar meat raw sausages	T. spiralis	[25]
Belgium	2014	wild boar meat	T. spiralis	[8]
Italy	2015	wild boar vacuum-packed sausages	T. britovi	[26]
France	2016	raw pork sausages	T. britovi	[13]

*Outbreak information was obtained through searches of the Pub Med database using the terms trichinellosis, outbreak and Europe.

DISCUSSIONS

During the period of 2007-2015, the number of trichinellosis cases, among EU member states tended to decrease. Romania ranked first among EU member states with 52,2% of the confirmed cases. Four Eastern European countries, Romania, Bulgaria, Poland and Lithuania reported 85,3% of the total number of confirmed cases.

The majority of cases was reported in males and in those aged 25-44 years and 45-64 years. Male predominance among people affected by the disease may be explained by the major role played by men in the slaughtering process and in preparing the traditional products [27].

Our assessment revealed that wild boars and domestic pigs were the major sources of *Trichinella* spp. infection in humans. Game and meat from free-ranging household animals continue to pose a risk to consumers, especially in areas where there is a preference for consumption of raw meat. Recent outbreaks due to the consumption of such foods occurred in Poland, Romania, Lithuania, Italy [25]. However, recently new infection sources, from different hosts (horse, dog), have emerged. In France, for instance, most of trichinellosis cases, in the past 2 decades, have resulted from consumption of raw horse meat, a strong food preference in French culture. In Italy, human infections from consumption of horse meat have also been documented in 2 areas (Emilia Romagna and Lombardy regions in northern Italy and the Apulia region in southern Italy), where the French fondness for raw horse meat was introduced centuries ago [5].

The diagnosis is difficult mainly in the"flu" season and treatment is not satisfactory if it is started in the late stage of the infection [17]. It is important to note, that in trichinellosis, the severity of extraintestinal disease is proportional to the number of larvae produced by adult worms in the small intestine [25]. Therefore, it is essential to rid the gut of adult parasites even if the patient presents late and with mild gastrointestinal symptoms [25]. It has been shown that an early application of anthelmintics may kill larvae and adult forms in the gut before new larvae are produced and migrate to other parts of the body [25]. Post-exposure prophylaxis (PEP) is recommended to all individuals with exposure to infected meat in a similar outbreak setting. Due to the unspecific nature of early symptoms, the decision to recommend or withhold PEP should not be based on symptoms only but on potential exposure [25]. Moreover, recent evidence suggests that PEP within one week after infection should be strongly encouraged because the development of symptoms might be completely prevented [8]. It is therefore important to obtain a detailed food consumption history as quickly as possible when a cluster of infections with a similar clinical pattern like consumed home-made pork products from a backyard pig is observed [8].

This infection should be considered as an epidemiological and clinical emergency because an infected meat could be extensively consumed in a community and this parasitosis may be sometimes fatal to humans, particularly in elderly individuals, in whom severe complications such as myocarditis or encephalitis may lead to death [13].

Trichinella spp infections have also been documented among people of non-endemic countries who consumed infected meat (pork from domestic pigs and wild boars, horse meat, bear meat) clandestinely imported from endemic countries. In addition, persons who acquire trichinellosis abroad may return with the disease in their home countries. Therefore, travel history is important especially in non-endemic countries where physicians are not familiar with the clinical picture of trichinellosis [28]. The disease should be suspected in every patient coming from a highly endemic region and/or with a history of raw meat (or raw meat products) consumption and presenting the unusual association of fever, myalgia and eosinophilia. It is also recommended to consider as potentially infected all homemade uncontrolled meat products coming from countries endemic for trichinellosis [6].

Human behavior is apparently the biggest determinant in the persistence of trichinellosis in the face of increasing regulations directed at ensuring the safety of meat and the enhancement of good management practices in farming, especially in areas where trichinellosis is highly endemic [5]. The majority of outbreaks attributed to domestic pork have been traced to pigs raised in small farms or backyards, often outdoors, where poor husbandry conditions place pigs at high risk [29].

In the past decades, the prevalence of human trichinellosis in the EU had a downward trajectory and this trend is confirmed in our study. There is a need for guidance directed specifically to farm operators on actions that could be taken to minimize exposure of pastured pigs to *Trichinella*. Such guidance should provide information on the biology and epidemiology of *Trichinella spp*. [29]. In addition, the weakness of the economy and lack of veterinary control may have an important role in the maintenance of the favorable conditions for disease development. Consequently, new and efficient public health strategies should be designed and implemented in the nearest future in order to limit the occurrence of this disease [27]. Although *Trichinella* larvae can be destroyed by heating, preparation of boar meat remains problematic given the culinary habit of serving and eating meat that is not always fully cooked [8]. A single infected wild boar carcass can contaminate a large batch of meat products and thus put hundreds of people at risk if it is not heated before consumption [25]. The recommendations of the United States Centers for Disease Control and Prevention (CDC) regarding prevention of trichinellosis stress the use of a food thermometer to evaluate the internal meat temperature [2].

CONCLUSIONS

In conclusion, human trichinellosis, persists as an epidemiological and public health issue in some countries of the EU. This parasitosis was reported especially in areas where the habit of consuming raw or partially cooked meat products was practiced. Cultural traditional habits of eating raw or undercooked meat continue to be the primary risk factor for acquiring trichinellosis and played an essential role in the spread of the disease being responsible for past outbreaks. The key measures to prevent human trichinellosis, remain the prevention of *Trichinella* infection in livestock and the systematic sampling and examination of potentially infected meat intended for human consumption [25].

The apparently increased frequency of outbreaks from eating wild boar meat may be related to the great increase in wild boar populations [5]. Hunters and wild game meat consumers need to be educated about the risk for trichinellosis and the importance of proper handling and cooking game meat. In addition, it is necessary continuously raising the awareness on the epidemiological and clinical features of this zoonosis among healthcare personnel for an immediately suspicion of the disease [30]. An intensive public education, especially for small pig breeders and hunters, is needed in order to prevent trichinellosis [7]. The lack of awareness may increase the risk of infection in the human population.

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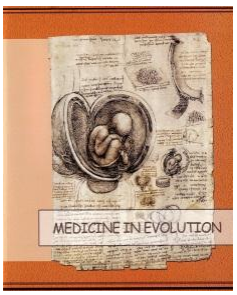
Acute Renal Failure Caused by Leptospirosis



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Abstract

Leptospirosis is the most important zoonosis worldwide. Patients are usually young. There are multiple factors involved in the renal lesions caused by leptospirosis, including the direct nephrotoxic action of leptospirae, hyperbilirubinaemia, rhabdomyolysis and hypovolemia. The most important lesions are acute interstitial nephritis and acute tubular necrosis. Leptospirosis-induced ARF is usually non-oliguric and hypokalemic. Functional abnormalities are preceded by decreased glomerular filtration rate (GFR) which might explain the high frequency of hypokalemia. Antibiotic treatment is effective during early as well as during late and/or severe stages of the disease. For critical leptospirosis patients the following measures are recommended: early daily hemodialysis; reducing the perfusate volume (due to the risk of pulmonary haemorrhage), and applying lung protective therapeutic strategies. The mortality in leptospirosis associated ARF varies between 1 and 22%.

Keywords: leptospirosis, zoonosis, acute renal failure

INTRODUCTION

Leptospirosis is an infectious disease caused by pathogenic leptospirae and characterised by a wide spectrum of clinical manifestations, from inapparent to fatal, fulminant cases. In mild forms, leptospirosis may appear as a flu-like disease, with headache and myalgia. Severe leptospirosis, characterised by jaundice, renal dysfunction and haemorrhages, is known as the Weil syndrome.

Leptospirae are spirochetes belonging to the order Spirochaetales, family Leptospiraceae. Traditionally, genus Leptospira includes two species: L. interrogans pathogen and L. biflexa saprophyte. Even though based on DNA structure, there are seven species of pathogenic leptospirae, clinically and epidemiologically it is more practical to use a classification based on serological differences. Pathogenic leptospirae are classified into various serovars, depending on their antigenic structure. More that 210 serovars from the present 23 known serotypes. [1-4]

The same serovar may induce various clinical forms.[5, 64]

Leptospirosis is a widely spread zoonosis affecting at least 160 species of mammals. Rodents, and especially rats, represent the most important reservoir, particularly in urban areas, even though dogs, other wild mammals, fish and birds may also host these microorganisms. Leptospirae establish a symbiotic relation with the host and may persist in renal tubules for years. Several serovars are associated with certain animals: icterohaemorrhagiae/ copenhageni with rats, grippotyphosa with field mice, hardjo with cattle, canicola with dogs and pomona with pigs.[6]

The transmission of leptospirae may occur after a direct contact with urine, blood or tissues from infected animals or by indirect contact, when damaged mucous membranes of skin are exposed to a contaminated environment (usually contaminated water)[1,2,6,7] Human to human transmission is rare. As leptospirae are eliminated in urine and may survive in water for months, water represents an important vehicle for transmission.

Leptospirosis most frequently occurs in tropical areas, being an endemic disease, with clusters during the rainy season which coincides with flooded areas. The incidence of leptospirosis in certain endemic countries is increasing.

In Thailand, for instance, the incidence increased 30 times between 1995 and 2000.[8]

In Brasil, data from the Ministery of Health showed that between 1996 and 2005, 33.174 cases of leptospirosis were notified, and in 2007, 1547 new cases were detected, most in the Southern region (45.7%) (după http: //www.data- sus.gov.br).

In the USA, 40-120 cases are reported every year to the Centers for Disease Control and Prevention. These cases probably represent a significant underestimation of the total number.

Certain professional groups are at particular risks, such as workers in agriculture, sewage systems, slaughterhouses and fishing industry. These individuals may become infected by direct exposure or by contact with contaminated water/soil.

In developed touristic countries, the exposure or contact with domestic animals also represents an important leptospirosis source. Contact with water, such as rowing, surfing, swimming and water skiing increase the risk of leptospirosis. Sometimes leptospirosis is acquired during voyages abroad. In a recent study conducted in Belgium and Holland, 15% of confirmed leptospirosis patients acquired the infection while travelling in tropical countries, especially in South-East Asia.

Transmission through laboratory accidents is rare, and, occasionally, leptospirosis occurs after immersion in contaminated water.

The average incubation is 15 days, with variations between 2 and 26 days. Typically, the acute leptospiraemia phase is followed by an immune leptospiruria phase. The distinction

between the first and the second phase is not always clear, and mild cases do not always include the second phase.

The clinical manifestations of leptospirosis may be grouped as follows:

- self-limiting anicteric febrile disease (85% -90% of cases);
- the Weil syndrome characterised by jaundice, renal hemorrhagic lesions and myocarditis associated with arrhythmia (5 -10% of cases);
- Meningitis/meningoencephalitis;
- (IV), lung haemorrhage associated with respiratory failure.[1,9]

The clinical evolution of leptospirosis may be divided into two phases:

The initial phase lasts 3-7 days, symptoms being represented by high fever, chills, severe headache, followed by anorexia, diarrhoea, nausea, vomiting, malaise and myalgia, more pronounced in calf muscles. The fever is 38-39 ° C and it remits after 4-7 days from the onset of symptoms. In this phase, leptospirae may be detected in blood. In certain cases (around 20%), the symptoms reappear after 1-3 days, followed by the initiation of the immune phase which lasts from 4 up to 30 days.

During the second phase, the symptoms are more severe and meningitis and uveitis may occur. The IgM antibodies are frequently detected during this phase and the severity of leptospirosis is associated with the intensity of the humoral immune response of the host.[2,10]

Leptospirosis is an infectious vasculitis. The lesions of the capillary endothelium induced by leptospirae causes vasculitis which is responsible for most of the important manifestations of the disease. [10]

Even though leptospirae mainly infect the kidneys and the liver, any organ may be affected as a part of systemic vasculitis.

In the kidneys, leptospirae enter the interstitium, renal tubules and the tubular lumen, causing interstitial nephritis and tubular necrosis. (fig.1,2,3,4,) The glomerules, as well as the vessels, are spared.

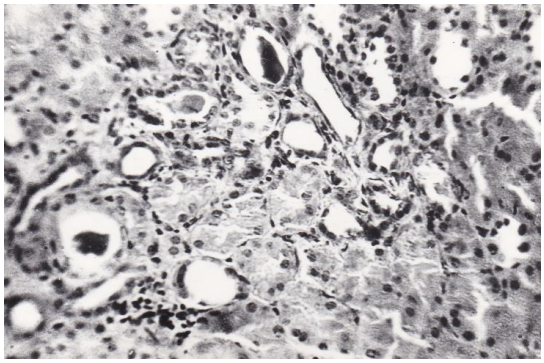


Figure 1. Interstitial nephritis and tubular necrosis

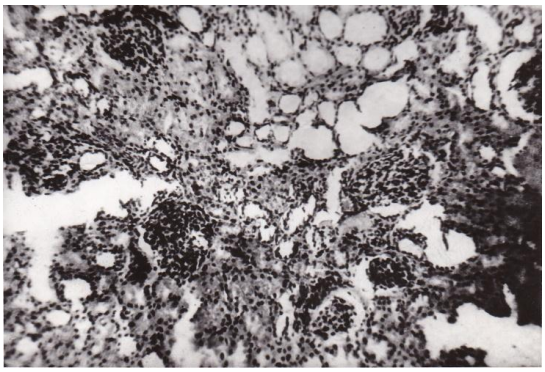


Figure 2. Interstitial nephritis and tubular necrosis

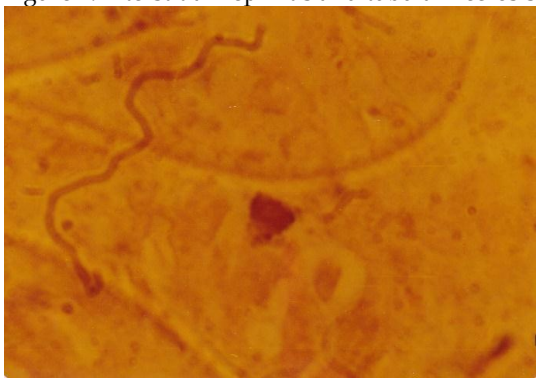


Figure 3. Interstitial nephritis and tubular necrosis

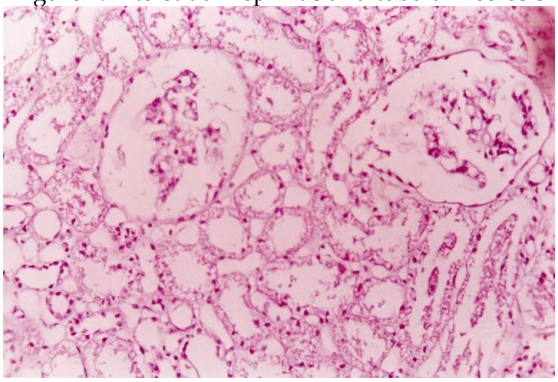


Figure 4. Interstitial nephritis and tubular necrosis

In the liver, centrilobular necrosis may be present, with the proliferation of the Kuppfer cells. Nevertheless, hepatocellular necrosis is not characteristic for leptospirosis.

Lung impairment is the result of haemorrhage and not of inflammatory lesions.

The invasion of skeletal muscles causes oedema, vacuolization of myofibrils and focal necrosis. In leptospirosis vera, vasculitis may affect the microcirculation and may lead to increased capillary permeability, causing fluid loss and hypovolemia.

When antibodies are secreted, leptospira microorganisms are eliminated of the host tissues, except the eye, proximal renal tubules and, probably, the brain, where they may persist for weeks or even months. The persistence of leptospirae in aqueous humour may, occasionally, cause chronic or recurrent uveitis. The systemic immune response is efficient in eliminating the microorganism but may, also, produce symptomatic inflammatory reactions. The increase in antibody titres coincides with the development of meningitis, and this association suggests that an immune mechanism is involved in the pathology of the disease.

After initiation of the antimicrobial treatment, a Jarisch-Herxheimer reaction may develop, similar with that observed in other diseases caused by spirochetes (syphilis). Even frequently described in medical literature, this reaction seems to be a rare event in leptospirosis and is, certainly, less frequent in this infection than in other spirochetal diseases.

The diagnosis is set based on clinical and epidemiological data and confirmed by laboratory tests.

The clinical diagnosis may be difficult and confusing as the symptoms may also occur in dengue fever, hemorrhagic fever (Hantavirus), viral or bacterial meningitis, malaria and acute viral hepatitis. The presence of hypokalemia, an early and characteristic finding in leptospirosis, may often be indicative of the diagnosis.

The precision diagnosis of leptospirosis is based either on the isolation of the microorganism from the patient but a difficult technique is involved, requiring long cultivation period and often only allowing a retrospective diagnosis, or on seroconversion or the detection of an increase in the titre of antibodies by the microscopic agglutination test (MAT). For a presumptive diagnosis of leptospirosis an antibody MAT titre of > 1:100 or a positive macroscopic agglutination test in the presence of clinically compatible symptoms are required. The antibodies do not, generally, reach detectable levels until the second week of disease. The antibody response may be changed by early treatment. The most frequently used laboratory method for the diagnosis of leptospirosis is the microscopical agglutination test (MAT), performed in two blood samples collected at two weeks interval. The results are considered positive when the titers increase four times the reference value. Its efficacy has been recently checked by the International Society for Leptospirosis (ISL), and the rate of false negative results was 13%.[2] The macroscopic agglutination test using inactive antigen is useful for screening, but it is not specific.

The standard serologic procedures are represented by MAT, which uses a set of live leptospirae and by ELISA which uses a widely reactive antigen. These are available only in specialised laboratories and are used to detect antibody titres and to a lesser degree to identify the serovar involved (this is why it is important to use antigens which are representative for the serovars which prevail in specific geographic areas). As frequently cross-reactivity occurs, it is sometimes impossible to identify the infecting serovar. Serology cannot be used in making the decision on the optimal moment to initiate treatment. Other diagnostic tests have been developed along MAT and ELISA such as the indirect hemagglutination, a microcapsular agglutination test and an ELISA – IgM. The detection of IgM antibodies by immune- enzymatic tests (ELISA) have high sensitivity and specificity (around 90%). Recently, dot-ELISA, immunohistochemistry tests and polymerase chain reaction have been introduced but these are not used for routine diagnosis.

Leptospira may be isolated in blood /or CSF during the first 10 days of disease and also in urine for several weeks, starting with the first week. Sometimes, urine cultures stay

positive for months or years from the onset of the disease. To isolate leptospirae in bodily fluids or tissues, the EMJH (Ellinghausen-McCullough-Johnson-Harris) medium, as well as the Fletcher and Korthoff media can be used. Samples may be referred for culture to a reference laboratory, as leptospirae stay alive in blood collected on an anticoagulant for over 11 days. It is important to isolate Leptospira as this is the only method by which the infecting serovar is correctly identified. Darkfield microscopic examination of blood or urine samples frequently leads to erroneous results and should be avoided.

PCR is early applicable and sensitive but its high costs represent a major disadvantage.

EPIDEMIOLOGY OF RENAL IMPAIRMENT

In developed regions, leptospirosis is a rare cause of ARF.[11] Nevertheless, in tropical countries, if the disease is endemic, leptospirosis is an important cause of ARF. The incidence of ARF varies from 10% to 60% depending on the severity of the disease, age or ARF syndrome classification.[12]

RENAL CLINICAL MANIFESTATIONS

Renal manifestations in leptospirosis may vary from subclinical form,s with slight proteinuria and abnormal urine sediment to severe ARF. The examination of the urine sediment may reveal the presence of leukocytes and red blood cells. When present, proteinuria is usually lower than 1 g / 24h. Bile pigments and granular cylinders may be present in the urine sediment.[12,64]

The ARF usually involves a rapid increase in serum urea and creatinine and may be associated with jaundice. Renal lesions in patients with hyperbilirubinemia indicate a severe form of the disease, frequently accompanied by oligo- or anuria.[12]

Leptospirosis-induced ARF is usually non-oliguric with hypokalemia (41% - 45%).[14]

In a recent study, 58 patients with leptospirosis and ARF had a hemorrhagic syndrome (80%), liver failure (72%), respiratory failure (38%), circulatory failure (33%), pancreatitis (25%) and rhabdomyolysis (5%). [15] Low blood pressure is common in all cases.[16,17]

An altered hemodynamic status is present in most patients with severe leptospirosis and it is similar to that observed in patients with severe sepsis. Due to systemic vasodilatation, plasmatic concentrations of aldosterone and hypophyseal antidiuretic hormone are increased, which leads to renal vasoconstriction and decreased diuresis.[18]

Tubular dysfunctions, mainly of the proximal tube are very frequent, even in the absence of ARF. The observed alterations are bicarbonaturia, glycosuria, decreased sodium and uric acid proximal reabsorption, phosphate excretion and a deficit of urine concentration which may persist for long periods of time.[19]

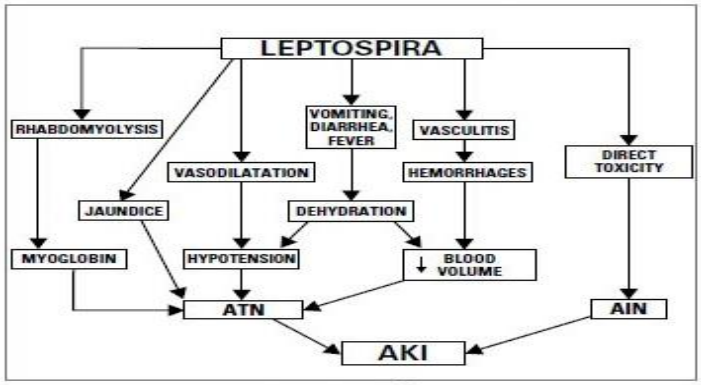
Hypokalemia is frequent in ARF caused by leptospirosis and may be observed in 45 - 75% of patients, upon hospital admission, requiring intravenous potassium supplementation in 80% of cases. In leptospirosis-induced ARF, even oliguric patients do not present hyperkaliemia. Hypokalemia is the most characteristic laboratory finding in ARF caused by leptospirosis. Seguro et al [14] showed that leptospirosis-induced ARF is usually non-oliguric and revealed hypokalemia in 45% of cases. Thus, regardless of the severity of the ARF in leptospirosis, as well as of the hypercatabolism, rhabdomyolysis, acidosis and oliguria, there is normal- or hypokalemia. This is a relevant finding for the ARF in leptospirosis as early as diagnostic stages.[58,64]

Another early characteristic of the ARF is the ultrasound aspect of renal hypertrophy, with a normal echogenic aspect of the parenchyma, indicative for tubulointerstitial nephritis.[20] The kidney return to their normal dimension after the treatment for leptospirosis is completed. (Romoşan 1997-2007)

PATHOPHYSIOLOGY

Acute renal failure is a frequent complication in patients with severe leptospirosis characterised by an association of tubulointerstitial lesions.[22]

The major factors involved in the pathogenesis of ARF in leptospirosis are the direct nephrotoxic action of leptospira and the immune response induced by toxins. Also, hemodynamic alteration, jaundice and rhabdomyolysis are determinant factors of ARF in leptospirosis (figure 5).



Adapted from Abdulkader & Silva.[56]

Figure 5. Psysiopathology of AKI in leptospirosis

ACUTE INTERSTITIAL NEPHRITIS

Experimental studies showed that ARF is associated with the presence of leptospira in renal tissues which triggers a process of acute interstitial nephritis (AIN), which is the main mechanism causing ARF.[22] Some studies suggested that acute interstitial nephritis occurs after tubular lesions. Patients who died during the first week of the disease had acute tubular necrosis (ATN) and cellular oedema, while those who died within two to three weeks had severe and diffuse interstitial nephritis.[22] Both lesions are associated with the presence of leptospira antigens in the renal tissue. The presence of bacteria in the renal mesangium and interstitium was observed in experimental studies, after three to six hours after inoculation of L. icterohaemorrhagiae. The passage of leptospira microorganisms through glomerular capillaries causes a slight and transient mesangial proliferation and very discrete glomerular alterations, consisting in slight mesangial proliferation.[22,56,64]

DIRECT EFFECT OF LEPTOSPIRA

Studies of rat kidneys after inoculation of leptospira showed the microorganism enters by penetration of the capillary lumen as early as the second day from infection, while the entry in the interstitial tissue causing oedema and cellular infiltration occurs between the fourth and the eighth day after the contact with leptospirae. Leptospira may be identified on the surface of the epithelium of the renal tubes starting with the first week of disease and inside the tubular lumen in the second week.[23,24,25]

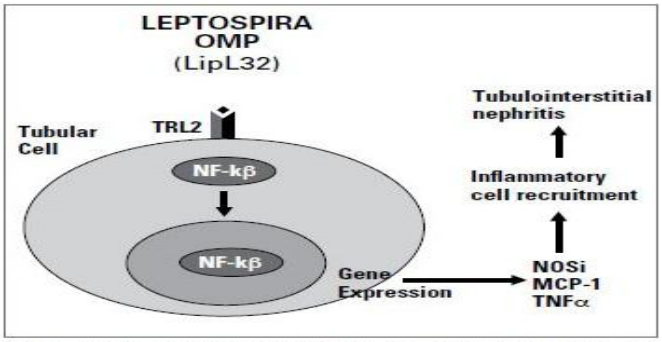
Leptospira antigens are found in the cells of the proximal tubes and interstitially.[24] Acute tubular necrosis foci may also be present.[24]

The external membrane of the leptospira contains antigenic components, including lipoproteins, lipopolysaccharides and peptidoglycans, endotoxins, which have a toxic effect on the kidney, which leads to tubular dysfunction and inflammatory lesions. Within proximal tubes and interstitially, several types of outer membrane proteins (OMPs) of various pathogenic species have been identified in infected animals.[25]

The most important outer membrane protein (OMP) detected during infection is LipL32, which directly affects proximal tubular cells, considerably increasing the expression

of pro-inflammatory genes and proteins, such as the inducible nitric oxide synthetase (iNOS), monocyte chemotactic protein – 1 (CCL2 / MCP-1), T cells (RANTES) and tumour necrosis factor (TNF-a). The CCL2 / MCP-1 chemokine is one of the most important factors at the beginning of monocyte infiltration in interstitial nephritis, while TNF-a, an inflammatory cytokine, is a mediator of endotoxemia. The iNOS and CCL2 / MCP-1 stimulation by the OMP, LipL32 in particular, depends on the presence, in the cells of proximal tubes, of toll-like receptors (TLR) of a specific protein which recognises molecular patterns of pathogenic agents and acts as first defense line of innate immunity, generating the initial inflammatory response, which in this case is TLR2.[26]

Briefly, OMP binds to TLR2 in proximal tubes cells, which leads to the activation of the nuclear factor NF-kp, which stimulates the production of CCL2 / MCP-1 and CXCL2 / MIP-2 for the recruitment of inflammatory cells. NF-kp is also associated with the increase of iNOS and TNF-a in the cells of proximal tubes (Figure 6). [27]



OMP = outer membrane protein; LipL32 = leptospira lipoprotein antigen; TRL2 = toll-like receptor; NF-kβ = transcription nuclear factor kβ. Adapted from Yang et al.20

Figure 6. Sketch of the induction and signaling of NF-kβ in tubulointerstitial nephritis caused by leptospirosis

PRERENAL ARF AND HEMODYNAMIC CHANGES

The ARF in leptospirosis may also have a prerenal component. Hypotension may be observed, due to reduced systemic vascular resistance and dehydration.[18] Dehydration is frequent and secondary to fever, vomiting and diarrhoea.[14,28,29] Low blood pressure may be aggravated by the decrease of sodium reabsorption in the proximal tubes characteristic for leptospirosis. After a blood transfusion, clinical findings improve. Studies show that over 50% of patients with ARF and leptospirosis respond to intravenous rehydration, with a consecutive decrease of uremia and oliguria. Hypovolemia may increase the secretion of aldosterone and cortisol, despite hypokalemia.[30] Haemorrhagic phenomena are mainly attributed to endothelial lesions which also contribute to hypovolemia. Thrombocytopenia may exacerbate the tendency to bleeding.[31] A study conducted in Thailand on patients with severe forms of leptospirosis identified three models of haemodynamic alteration.[18] The first model, observed in 60% of cases, was characterised by an increase of the heart rate and a reduction of the systemic vascular resistance, with consecutive arterial hypotension (a model similar to that occurring in sepsis and malaria). The hemodynamic changes in this model start with peripheral vasodilatation, induced by cytokines and other mediators, mainly nitrous oxide (NO).[18] The second model, observed in 20% of cases, characterised by normal heart rate, increased systemic vascular resistance and hypertension was associated with increased pulmonary vascular resistance. The increase of vascular resistance in the pulmonary vessels may be caused by many factors, including perivascular oedema and humoral factors, such as leukotrienes and thromboxane A2.[18] The third model was characterised by increased systemic vascular resistance, normal pulmonary vascular resistance and relative decrease in the heart rate. The relatively decreased heart rate may be caused by hypovolemia or myocarditis, described in severe forms of leptospirosis.[18]

HYPERBILIRUBINEMIA

Jaundice is present in almost all severe cases of leptospirosis and is associated to ARF. High levels of bilirubin lead to the alteration of the renal function. Sitprija et al[32], analysing patients with obstructive jaundice caused by cholangiocarcinoma reported that those with total serum bilirubin over 26 mg% had a reduction of glomerular filtration and urine concentration capacity. High bilirubin levels are common in severe forms of leptospirosis and are associated with the presence and severity of ARF.

RHABDOMYOLYSIS

Myalgia was observed in almost all cases of leptospirosis, but rhabdomyolysis, detected by the increase of creatine kinase (CK), was reported in 45 to 62% of cases.[10,19,33] The association between rhabdomyolysis and ARF is well established at present.[34,35] The major mechanisms of renal failure secondary to rhabdomyolysis are of renal origin: vasoconstriction, tubular obstruction, and direct myoglobin toxicity.[34] The role played by rhabdomyolysis in the pathogenesis of the ARF in leptospirosis is not so obvious. High CK levels are more frequently found in patients with severe ARF than in those with mild forms of ARF, suggesting that rhabdomyolysis may contribute to the severity of the ARF.[19]

TUBULAR ALTERATIONS

The ARF in leptospirosis is characterised by the absence of oliguria and normal or low serum levels of kalium, in contrast to other infectious causes of ARF such as malaria, diphtheria and meningococcemia.[36,37,38] Experimental and clinical studies showed that these changes result from lesions of proximal tubes and resistance to vasopressin of medular collector tubes.[14,30,39] The lesions of proximal tubes leads to a defect of urine concentration, causing polyuria. The increase of kalium levels in distal tubes seems to be caused by an increase of the urinary flow and an increase of the sodium offer in the distal tube, and this seems to be enhanced by high levels of aldosterone and cortisol.[30] These findings show a predominance of proximal tubular dysfunction and a relative integrity of the distal segments of the nephron regarding sodium and kalium tubular transmembrane translocation. The OMP of leptospira, as well as LipL32, activate the cascades dependent on Toll-like receptors which lead to the activation of NF-kp, kinases and cytokines, with further tubular lesions which cause dysfunction of sodium transporters in kidneys of patients infected with leptospirae.[40,41] The alteration of tubes precedes the decrease in the glomerular filtration rate in leptospirosis.[40,41,42]

Experimental studies proved that, even in the absence of renal lesions, tubular disfunction may occur in leptospirosis. A study on Guinea pigs infected with leptospirae showed increased kalium excretion and low urine osmolarity. The collector tubes of these animals proved to be resistant to the action of vasopressin.[39] Recently, a clinical study on 20 leptospira infected patients proved the presence of proteinuria in all cases, hypermagnesiuria in 75%, reduced tubular reabsorption in 50%, and reduced phosphate reabsorption in 45% of the patients.[43]

TREATMENT

ANTIBIOTHERAPY

The early diagnosis and adequate therapy are the most important objectives in the treatment of leptospirosis. Consensus on the use of antibiotics in the treatment of leptospirosis has not yet been reached.[44-48]

A recent meta-analysis did not find enough proof to indicate the use of antibiotics in leptospirosis. Anyway, the conclusion was that antibiotic therapy seems to bring more

benefits than disadvantages. [44] A recent experimental study evaluated the NHE3 and NKCC2 expression in hamsters with leptospirosis, with or without ampicillin. Leptospira antigens and the expression of renal transporters were evaluated by immunohistochemistry and quantitative detection of thiobarbituric acid (TBARS). Antibiotic therapy was associated with a significant reduction of leptospira antigens, normal expression of the transporters NHE3 and NKCC2, and reduced levels of TBARS.[42]

Nevertheless, clinical studies showed that antibiotic therapy is effective in early and late phases of the disease.[49] Based on the recommendation of the World Health Organisation in 2003, patients with severe leptospirosis must receive intravenous treatment with penicillin (1,500,000 U every 6h), ceftriaxone (1g once a day), or cefotaxime (1 g every 6 hours). All therapeutic schemes are equally efficient.[50,51] Antibiotherapy should be continued for seven days. Oral antibiotics, such as doxycycline, amoxicillin, ampicillin, erythromycin or azithromycin are effective in less severe cases of leptospirosis, as an alternative for patients in whom there is no involvement of vital organs, and outpatient treatment is applicable.[51,52] Doxycycline was mainly used for disease prophylaxis.[51,52]

The Jarisch-Herxheimer reaction (JHR) = fever and arterial hypotension, may occur after the use of penicillins. The toxins released during the lysis of leptospirae by antibiotics may induce the production and release of cytokines. The JHR aspect does not represent a counterindication for the use of antibiotics.[53,54]

INTENSIVE CARE

Severe forms of leptospirosis (Weil disease) require intensive care, mainly for the renal function, including dialysis sessions. (Nicolicioiu, Romoşan et al.1982) Hypotension and hypovolemia are important factors leading to ARF and are found in most patients. These conditions must be immediately reduced, oral hydration being the first choice. In more severe cases, intravenous saline solutions must be given with caution, in order to avoid hypervolemia and pulmonary oedema. Patients in whom a pulmonary haemorrhage is suspected must be admitted into the intensive care unit (ICU) and may benefit from mechanical ventilation.

RENAL DIALYSIS

Recent studies demonstrated the benefit of early dialysis in leptospirosis, with a significant reduction of mortality.[55] In a study conducted in Sao Paulo (Brazil), on 33 leptospirosis patients admitted in an ICU, a significant reduction in mortality was found in the group early subjected to dialysis (upon admission), as compared to the group with late dialysis, i.e. after two days from admission (16.7% as compared to 66.7%).[55]

There is no consensus regarding the best dialysis modality for ARF in leptospirosis, and all modalities for renal epuration have been used, hemodialysis, peritoneal dialysis and hemofiltration included.[56] A recent analysis of leptospirosis associated with ARF in Thailand showed that hemodialysis and hemofiltration are associated with lower mortality, shorter recovery time, as well as a more rapid reduction of the serum levels of bilirubin, urea and creatinine as compared to peritoneal dialysis.[57]

RECOVERY OF THE RENAL FUNCTION

In the anicteric form, the renal function returns to normal spontaneously, within several days to one week. Normalisation of urea and creatinine serum levels usually occurs during the second week of disease together with the increase in the number of thrombocytes and decrease of bilirubin levels.[2] A prospective study for the long-term assessment of the renal function in 35 patients with leptospirosis-induced ARF showed that the creatinine clearance, sodium proximal reabsorption, urine acidification and proteinuria returned to normal during the third month after the disease, but urine concentration remained low to the end of the follow-up period, in the sixth month.[19,Nicolicioiu,Romoşan – Recuperarea funcţiei renale după IRA,Timişoara Medicală, 1986

The prognosis of ARF in leptospirosis is usually favourable, except complicated cases with multiple organ impairments: pulmonary complications, hyperbilirubinemia, oligo-anuria, diarrhoea, hyperkalemia, old age and associated infections or subjacent diseases which may aggravate the prognosis, with mortality varying between 12% and 36%.[10,58-60]

PROPHYLAXIS

Persons who may be or are exposed to contact with leptospirae, due to profession or occupation, must be informed of the risks to contract the disease. The measures for leptospirosis control include avoiding the exposure to infected animal urine or tissues, vaccination of animals and rodent control. The animal vaccine used in a certain area must contain the serovars known for that area. Unfortunately, some vaccinated animals continue to eliminate leptospirae in their urine. Human vaccination against a specific serovar prevalent in a certain area has been tried in certain European countries and proved to be effective. Chemoprophylaxis with doxycycline (200 mg once a week) seemed to be effective in army personnel but is only indicated in rare cases of short-term exposure.[60]

MORTALITY

A review of studies in various countries (Brazil, Thailand, Turkey, and the French Antilles), using logistic regression to identify prognostic factors for death in leptospirosis, demonstrated a mortality between 15% and 18%.[61-63] Death rarely occurs in leptospirosis without ARF. The main aggravating factors were pulmonary and renal complications. Other factors, such as mental alteration, leukocytosis, thrombocytopenia and myocarditis associated with various arrhythmias were associated with a higher mortality.[61-63] Age is not an aggravating factor of prognosis. In Brazil, an analysis of 42 patients with pulmonary haemorrhage, of whom 66% had ARF, revealed a 55% mortality. Another retrospective study conducted on 110 patients with leptospirosis reported the following death risk factors: oliguria, cardiac arrhythmia, dyspnea, and respiratory failure.[10]

The direct effect of Leptospira – The table compares Leptospira with the first seven tropical neglected diseases (from Hotez et al., 2014).

DISEASES	Number of cases	Deaths	DALYs (millions) = Millions of Disability-adjusted Life Year
Intestinal nematodes	1,723 million	2,700	5.19
Leishmaniosis	10 million	51,600	3.32
Schistosomiasis	252 million	11,700	3.31
Leptospirosis*	**1 million**	**58,900**	**2.90**
Lymphatic filariosis	36 million	-	2.78
Trematode food poisoning	16 million	-	1.88
RABIES	1,100	26,400	1.46
Dengue fever	179,000**	14,700	0.83

* Not a neglected tropical disease (Torgerson et al., 2015).

** Only acute symptomatic cases.

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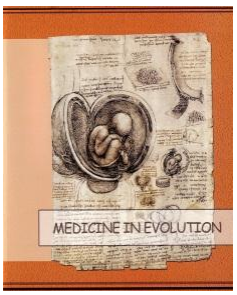
Clinical and paraclinical correlations in metformin treatment



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Abstract

Aims: Determining the degree of risk in patients with type 2 diabetes, with antidiabetic therapy, respectively with Metformin, with associated diseases.

Type of study: Retrospective study of patients with diabetes mellitus and anemia in metformin therapy.

Location: Arad County Clinical Emergency Hospital - Hematology Section

Study participants: 351 patients (aged 18-75 years), type 2 diabetes (termed Lot DZ) admitted to the Arad Hematology Clinic from 2013 to 2015, with duration of diabetes mellitus about 1-15 years.

Methods: Patients admitted to the hematology department with anemia diagnosis (feripriva, biermer, normocytar, and other anemias) were evaluated, who also received metformin treatment.

We associate the study with age, sex, consumption of toxic substances, associated diseases, type of anemia and metformin treatment that the patient follows.

Results: Women (61.15%, 60.53% and 57.14% respectively) predominate in the study group, the women / men ratio being 1.6: 1, 1.5: 1 and 1.3: 1 respectively; there are no significant differences between the three groups in terms of gender distribution (p = 0.445), age (p = 0.943) (mean age 54.63 years in the Metformin group, 54.95 years in the group without Metformin and 56.65 years in the group with diabetic insulinonecites).

In the three subgroups, the most common conditions were cardiovascular (61.87%, 64.91% and 56.12%, respectively). Other disorders include osteoarticular disorders, thyroid disorders and psychiatric disorders (especially low or medium intensity depression).

Unbalanced / very unbalanced metabolic balance was encountered particularly in patients with respiratory diseases (31.03%), cardiovascular (26.51%) and hepatic (21.95%).

Conclusions: Management of type 2 diabetes mellitus (DZ2) requires aggressive treatment to achieve the proposed glycemic and cardiovascular goals and to reduce the incidence of risk factors. Metformin, an old and widely accepted first-line agent, stands out not only for its anti-hyperglycaemic properties, but also for its effects outside glycemic control, such as improving endothelial dysfunction, hemostasis and oxidative stress, insulin resistance, redistribution of adipose tissue and the very important role in the vitamin B12 economy and balance within the human body.

Keywords: *Diabetes, Metformin, vitamin B12, therapy*

INTRODUCTION

Metformin is classified as the only anti-diabetic agent associated with the improvement of cardiovascular morbidity and mortality, being a powerful agent of medical therapy along with lifestyle modification in most patients with diabetes. Currently, several clinical practice guidelines for type 2 diabetes patients, including the American Diabetes Association (ADA) and the European Diabetes Study Association (EASD), recommend that metformin therapy be started when diabetes is diagnosed with the change lifestyle, in the absence of contraindications [1-6, 20]

Metformin is slowly and incompletely absorbed in the small intestine; maximum absorption takes place at one hour and a half-two hours, and completely at six hours. The lowering effect of glucose occurs after 1-2 weeks of treatment. Drug distribution is uniform; 90% of the kidneys are eliminated, so maximum caution is needed in people with kidney problems. Action is performed in the liver in the presence of insulin, reducing gluconeogenesis. The side effects of metformin are: gastrointestinal disorders; very rare: lactic acidosis, hypoglycemia, decrease in thyroid hormone concentration, increase in homocysteine, vitamin B12 malabsorption [20-25]

The etiology of red blood cell fragility in diabetic patients is multifactorial and includes a worsening of preexisting factors, various impairments, immune system diseases accompanying basic pathology, different classes of drugs, and hormonal changes in the context of renal dysfunction. [5-7]

The World Health Organization defines anemia as a hemoglobin concentration <13g / dl in men and <12g / dl in women. If mean corpuscular volume (MCV) greater than 100fL is added to these elements, macrocytic anemia is discussed [15-20]

In Arad in 2013, there were 1235 new cases compared to 2012 when there were 1220 new cases of DZ. And new cases of anemia have increased 20 times more than previous years.

The most common cause of macrocytic anemia is considered to be megaloblastic anemia, which is the result of an alteration in DNA synthesis (deoxyribonucleic acid). Although DNA synthesis is impaired, the synthesis of RNA (ribonucleic acid) is not affected, and this determines the accumulation of cytoplasmic components in a cell with a slow rate of division, resulting in a larger cell than normal. The nuclear chromatin of these cells also has a modified appearance [15-17, 27].

Clinical presentation symptoms of macrocytosis in diabetic patients may be attributed either to anemia itself or to the underlying condition causing anemia. These may include the following: dyspnea, a consequence of anemia - in acute or severe anemia, the amount of hemoglobin in the blood is inadequate to ensure adequate oxygenation of the tissues; migraines / headache, a symptom of anemia due to decreased oxygenation of tissues; fatigue that can be attributed to the underlying disease, if present, or to an inadequate blood volume; inflammation of the mucosa of the tongue, which may reflect glossitis or atrophy of the tongue, common in folic acid deficiencies and vitamin B12 [15]; diarrhea or other gastrointestinal symptoms that may also be present in tropical sprue patients, sprue that may cause folate deficiencies or vitamin B12 [26]; paresthesia or walking disorders that suggest vitamin B12 deficiency.

It has been noticed that with long-term treatment with metformin, some patients have typical symptoms of anemia. [12, 18]

Vitamin B12 deficiency has been recognized since the past as an important side effect in patients with diabetes who are receiving metformin over a period of 5-10 years [18]. Vitamin B12 and folate coenzymes are required for the synthesis of purines and thymidylate; their deficiency leads to a faulty synthesis of DNA. In the deficiency of vitamin B12 and folic acid, the defect in DNA synthesis affects rapidly dividing cells; Clinically, it can also manifest with glossitis, skin changes and flatulence of intestinal villitis.

A significant number of diabetic patients are not treated with metformin alone for glycemic control; there have however been few studies on the effect of hypoglycaemic agents with metformin on vitamin B12 deficiency. [23]

Metformin is the most prescribed medicine used to treat diabetes in the world (usually type 2 diabetes). Its efficacy is equal to or greater than many other available medicines and has an excellent safety profile for most individuals. However, over the last ten to fifteen years, the question arises as to whether metformin causes a vitamin B12 deficiency in those taking this drug for long periods of time.

It should be borne in mind that vitamin B12 deficiency leads not only to megaloblastic anemia and neuropsychiatric disorders, but also has deleterious effects on the health of the cardiovascular system due to iatrogenic hyperhomocysteinemia. [25-31]

MATERIALS AND METHODS

We conducted a retrospective study using data from patients admitted to the Arad County Emergency Clinical Hospital, hematology, during 2013-2015.

Patients were clinically and paraclinically examined by blood counts (erythrocyte count, hemoglobin count), serum cobalamin, Hb A1c, fasting blood glucose, body mass index (BMI), and anamnesic personal history (other associated diseases), duration of treatment with metformin, duration of type II diabetes (1-5 years), diagnosis with berry anemia or other type, age, sex, consumption of toxic substances.

Exclusion criteria were: pregnant women, neoplastic patients, patients with hepatic, renal or cardiac insufficiency, patients with vitamin B12 deficiency anemia known prior to Metformin.

Patients admitted to the hematology department were diagnosed with anemias.

The diagnosis of anemia was highlighted with the help of blood counts and other adjacent functional explorations. [15-18]. To determine the influence of Metformin on the prevalence of Biermer anemia, a study was conducted on 139 diabetic patients who received Metformin alone or in combination with other oral antidiabetic agents.

Over 50% of patients had a metformin duration of 2-3 years (51.08%), and in over 45% of patients the dose was 1000-2000 mg / day (45.32%).

Metformin was administered in the majority of patients as monotherapy (55.40%), with triple therapy being given only 5.76%.

The 351 cases were structured in 3 sublots:

- DZMet Lot - includes type 2 diabetic patients who received Metformin treatment - 139 cases
- DZFMet Lot - includes type 2 diabetic patients who received oral antidiabetic therapy, including Metformin - 114 cases
- Lot DZIns - includes type 2 diabetic patients who did not receive Metformin treatment - 98 cases

We compared the three groups according to BMI: underweight, normoponderal and obesity. They have also been subdivided into subgroups according to gender, age, duration of treatment with Metformin, metabolic control, and associated pathologies.

According to laboratory data, patients with good metabolic control were overweight and obese, whereas those underweight and over 60 years of age had metabolic imbalances.

These were patients requiring emergency treatment with a low degree of absorption at the intestinal level due to age.

RESULTS

Women (61.15%, 60.53% and 57.14% respectively) predominate in all three subgroups, women / men ratio being 1.6: 1, 1.5: 1 and 1.3:1. There are no significant differences between the three groups in terms of sex distribution (p = 0.445).

There are no significant differences between the three age groups (p = 0.943), the median age being 54.63 years in the Metformin group, 54.95 years in the group without Metformin and 56.65 years in the group with diabetic insulinoneceptors.

Most patients in the 3 sub-classes came from urban areas (51.80%, 52.63% and 50.00% respectively), with the urban / rural ratio being approximately 1.1: 1. There are no significant differences between the three groups in terms of environmental distribution (p = 0.816).

Daily consumption of alcohol is recognized by a relatively small percentage of patients (between 10.07% in the Metformin group and 12.24% in the insulin group). Also, smokers represent only 7.91% of the Metformin group and 6.12% in the insulin group, the differences being insignificant.

In both the batch and the 3 subgroups, about 8% of patients work or worked in a toxic environment (7.91%, 7.89% and 8.16% respectively).

Normoponderal patients are also the majority in all three sublots (51.08%, 50.88% and 54.08% respectively) (p = 0.646). However, overweight and obesity accounts for approximately 40% of the total of the three groups (41.73%, 42.11% and 38.78% respectively).

In the 3 sub-classes, the heredo-collateral history was mainly in the form of cardiovascular disease (24.46%, 23.68% and 24.49%, respectively). Diabetes mellitus was found in AHC in percent between 6.14% in the ADO group and 7.19% in the Metformin group.

In the three subgroups, the most common conditions were cardiovascular (61.87%, 64.91% and 56.12%, respectively). In the group of other conditions were found diseases of the osteoarticular apparatus, thyroid and psychiatric disorders (especially depression of low or medium intensity).

In the two oral hypoglycemic sublot, where the duration of diabetes evolution was 1-5 years, the mean was 3.08 years in the Metformin group and 3.39 years in the non-metformin group, while in the group with mean insulin was 8.46 years, with the duration being between 6-15 years.

Metabolic control, assessed with HbA1c, performed in all patients in the three groups.

In the Metformin group, good and very good metabolic control was recorded in 73.38% of patients, in the non-metformin group at 77.20% and 75.51% in the insulin group (p = 0.363).

Over 50% of patients had a metformin treatment duration of 2-3 years (51.08%).

Over 45% of diabetic patients treated with Metformin received a dose of 1000-2000 mg / day (45.32%) and 33.09% daily dose was 33.09%.

Unbalanced / very unbalanced metabolic balance was encountered particularly in patients with respiratory diseases (31.03%), cardiovascular (26.51%) and hepatic (21.95%).

Table 1. Distribution based on a heredo-collateral history

HCA	**Diabetes group**	
	Nr.	%
Cardiovascular disorders	85	24,22
Respiratory disorders	17	4,84
Digestive problems	10	2,85
Renal conditions	3	0,85
Diabetes	24	6,84

Table 2. Distribution according to associated pathology

Associated diseases	Diabetes group	
	Nr.	%
Cardiovascular disorders	215	61,25
Respiratory disorders	29	8,26
Hepatic disorders	41	11,68
Digestive problems	52	14,81
Renal conditions	35	9,97
Other affections	126	35,90

Table 3. Metabolic control according to associated pathology

Associated diseases	Very good		Good		Unbalanced		Very Unbalanced	
	Nr.	%	Nr.	%	Nr.	%	Nr.	%
Cardiovascular disorders	56	26,05	102	47,44	38	17,67	19	8,84
Respiratory disorders	9	31,03	11	37,93	9	31,03	0	0,00
Hepatic disorders	15	36,59	17	41,46	5	12,20	4	9,76
Digestive problems	21	40,38	24	46,15	3	5,77	4	7,69
Renal conditions	12	34,29	18	51,43	2	5,71	3	8,57
Other affections	33	26,19	63	50,00	21	16,67	9	7,14

DISCUSSIONS AND CONCLUSIONS

The present study had three main objectives: to determine the prevalence of Biermer anemia in patients with type 2 diabetes, the influence of antidiabetic therapy and Metformin on the prevalence of Biermer anemia.

As for feriprious anemia and normocytar anemia, these are not influenced by the association or not of other ADOs with Metformin.

A clinically more practical approach would be to administer each patient treated with metformin with an annual injection of 1000 micrograms of vitamin B12. This is sufficient to cover the needs of vitamin B12 for at least one year. An alternative therapy would be the prophylactic administration of calcium carbonate (1.2 grams per day), which could correct the enteral deficiency associated with metformin therapy [1,3,4,18-20,26-28].

There were no significant differences between the three age groups ($p = 0.943$), the mean age being 54.63 years in the Metformin group, 54.95 years in the group without Metformin and 56.65 years in the batch with diabetic insulin requiring patients..

Patients with increased BMI, obesity or overweight, according to laboratory data had better metabolic control, whereas those underweight and over 60 years of age had metabolic imbalances.

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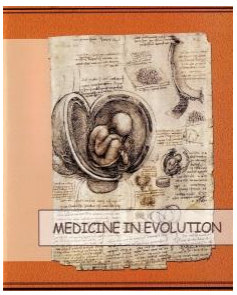
How to collect data in the Neonatal Intensive Care Unit?



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Abstract

Data collection requires impressive resources using both human and technological tools. In the HealthCare System in general, and the Neonatal Intensive Care Unit (NICU) in particular, there is an impressive amount of valuable data lost during continuous patient monitoring. The aim of this study is to bring a new technological means of continuous data collection (in the NICU) during patient monitoring using open source hardware and software. Material and methods. For creating a data collection system in the NICU we used: a Raspberry Pi 3B (RPi), a pulse oximeter for neonatal use (Masimo Radical 7 Rainbow Pulse CO-oximeter) and Python v. 2.7 as programming language. Results: Real time data collection from the NICU during continuous patient monitoring was performed. The collected data consists of the patient's heart rate, oxygen saturation and perfusion index. Conclusions: In Neonatology and any other medical field most scientific research requires a large amount of data that can be easily acquired using open-source hardware and software with a great accuracy and low costs.

Keywords: Neonatal Intensive Care Unit (NICU), patient monitoring, Raspberry Pi, Internet of Things (IoT), open-source hardware and software

INTRODUCTION

Technological advances are made rapidly in almost every domain, particularly in the healthcare system.

The Internet of Things (IoT) is defined as”a self-configured dynamic global network infrastructure with standards and interoperable communication protocols where physical and virtual ‘things’ have identities, physical attributes, and virtual personalities, and are seamlessly integrated into the information infrastructure" [1].

In other words, IoT is a system composed of numerous identifiable smart objects that may communicate and interact among each other, with other users or other entities of the network [2]. And it should allow: new applications to be built on top of the existing system and add an adequate level of interoperability, so that innovative and competitive cross-domain systems and applications can be developed [3,4].

For this there are various products available that allow end-user programming. Thus, the use of open-source hardware and software make it possible at low costs to control and create devices [4] and systems. What is more an open-source device increases safety, security and robustness by allowing more people to inspect and improve its designs [5].

The most popular considered IoT hardware platforms are:

- Arduino - an open-source physical computing platform based on easy-to-use hardware and software [3],
- BeagleBone Black - a low power single-board computer based on Texas Instruments processors [6],
- Phidgets - a set of”plug and play" building blocks for interfacing the physical and the virtual worlds via low cost USB sensing and control from PC [7],
- Udoo - a family of Open Source Arduino-powered Mini PC, compatible with Android and Linux, that can be exploited both as embedded systems for DIY (do it yourself)-electronics projects and as low power consumption, fanless computers for everyday use [8],
- Raspberry Pi (RPi) - a small, powerful, cheap, education-oriented computer board. It operates in the same way as a standard PC, requiring a keyboard for command entry, a display unit and a power supply [9].

In the Healthcare System, there are various wards in which the patients' vital functions are constantly monitored. One of these wards is the Neonatal Intensive Care Unit (NICU) where patients (preemies and newborns) need continuous monitoring due to the comorbidities associated to this fragile age. Among the most frequent items monitored is the oxygen saturation (SpO2), heart rate (HR) and the tissue perfusion index (PI) using a pulse oximeter.

Most of this data is stored automatically in the Electronic Medical Record (EMR) or manually in the patients' medical record [10], as it is done in most of the Romanian NICUs.

Aim and objectives

The aim of this paper is to present a data collection system designed for the NICU using a Raspberry Pi as an IoT object.

MATERIAL AND METHODS

For this project we used:

Raspberry Pi 3B (Figure 1) with the following specifications:

- Quad Core 1.2GHz Broadcom BCM2837 64bit CPU
- 1GB RAM

- BCM43438 wireless LAN and Bluetooth Low Energy (BLE) on board
- 40-pin extended GPIO
- 4 USB 2 ports
- 4 Pole stereo output and composite video port
- Full size HDMI
- CSI camera port for connecting a Raspberry Pi camera
- DSI display port for connecting a Raspberry Pi touchscreen display
- Micro SD port for loading your operating system and storing data

Upgraded switched Micro USB power source up to 2.5A [11].

Figure 1. Raspberry Pi 3 B [11]

Masimo Radical 7 Rainbow Pulse CO-oximeter (Figure 2):

The Radical-7 Pulse CO-Oximeter is a noninvasive, arterial oxygen saturation, total hemoglobin concentration and pulse rate monitor. The Radical-7 Pulse CO-Oximeter can be used as either a Handheld or a Standalone monitor. The Radical-7 Pulse CO-Oximeter features a backlit Liquid Crystal Display (LCD) that continuously displays numeric values for SpO2, SpMet®, SpCO®*, SpHb®, SpOC™*, pulse rate, Perfusion Index (PI) and Pleth Variability Index (PVI).

It also provides graphical displays for plethysmographic waveform, Signal Identifi cation and Quality Indicator (Signal IQ®). The Radical-7 Pulse CO-Oximeter can be used to interface with a multiparameter patient monitor to provide Masimo SET SpO2 and pulse rate information to that monitor for display [12].

Figure 2. Masimo Radical 7 Rainbow Pulse CO-oximeter [12]

FTDI RS232-usb convertor (Figure 3), network cable and a notebook.

Figure 3. FTDI RS232-USB convertor [13]

We connected all components as shown in figure 4 and ran the data collection program created with Python v. 2.7.

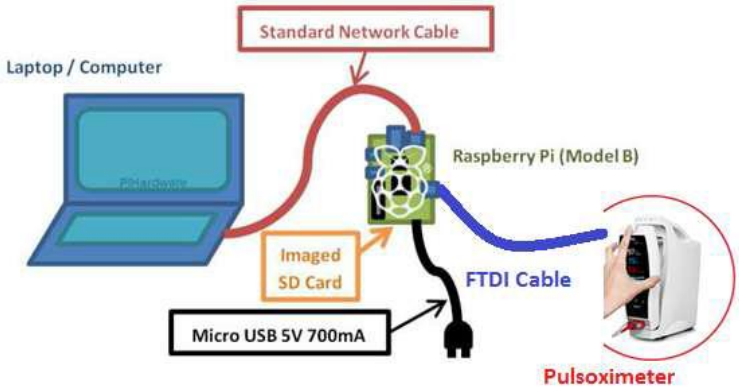

Figure 4. Connecting components [14]

RESULTS

The data collection system works based on a code that will run from the file *sox.py*, after all the system is connected to the patient through the pulse oximeter. In return, data will be collected in real time on the Rapsberry Pi 3 B as shown in Figure 5.

Figure 5. Real time data collection using the *sox.py* code

The collected data that consists of the patient's HR, SpO2 and PI is automatically saved in a folder called READS when the patient is disconnected from the pulse oximeter.

The data is saved on the disc, in the Reads folder in individual.csv files with the date and time as file name.

DISCUSSIONS

According to the WHO, 70–90% of all medical devices donated to the developing world never function as intended [15, 16] due to small faults like the absence of the user's manual or a broken fuse, and creating new technology using open source hardware and software, with low cost components represents a solution. Thus using IoT objects like Raspberry Pi have been already used in the healthcare system: Fechko's peristaltic pump, Wijnen et al's syringe pump, e-Health sensor platform and many other [17-19].

As a IoT object, according to Maksimović *et. al.*[4]the Raspberry Pi is considered to bring the advantages of a PC to the domain of sensor network, and this makes it the perfect platform for interfacing with a wide variety of external peripherals, implying low costs. We chose the RPi due to its low costs and possibility of interfacing with many different devices and using in wide range of applications [4].

There is no standard on expressing the output of a data when collecting it into a data base, however the CSV (Comma Separated Values) format is the most common import and export format for spreadsheets and databases. What is more, no standard format for the CSV has been defined, so it may be defined by the many applications which read and write it. However, the csv module implements classes to read and write tabular data in CSV format. [20]. Reason for which the data collected with the sox.py code is saved under a CSV file for each patient.

As a limit for this project is the fact that through this system there is no data recorded about the personal information or the clinical status of the patient, however correlations can be made as the filename consists of the time and date when the patient was disconnected from the monitor.

Another arguable issue would be the lack of uploading online the data in real time, and make it accessible to other researchers too. Problem that can be solved by using a cloud application.

CONCLUSIONS

Most medical departments, with emphasis on the NICU, lose valuable data concerning the patients vital signs in every second of the continuous monitoring; data that can be included in studies in which large amounts of such information is needed. Reason for which we created the NICU data collecting system. The use of low cost and high performance hardware and software plus its open-source character and small dimensions makes this system usable and perfectable in every NICU bringing plus value to any study conducted in the NICU.

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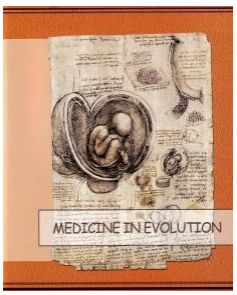
Bone regeneration by means of bioactive glasses – an experimental study



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Abstract

In the last years, alloplastic materials became more and more studied. They are in needed for bone defect augmentation treatments, whether they are congenital or have occurred after traumatic injuries, tumor resection, or regarding implant restoration of the alveolar crest. The main advantage of alloplastic materials is that they have no risk of infection dissemination, being completely synthetic.

This experimental animal study aims to follow the type of bone regeneration after preforming standardized bone defects and augmenting them with bioactive glasses.

The study involved six New Zeeland white rabbits. The bone defects were produced in the left tibial bone, by drilling five monocortical holes with a small round bur, 1 mm diameter. The defects were augmented with bioactive glasses and they were covered with collagen membranes. The animals were sacrificed after six months and we made a histopatological evaluation.

In all cases it can be observed that a partial resorption takes place even to a total resorption of the bioactive glasses granules, their occupying space not being replaced by new bone. Therefore, shallow optical spaces have been created within the cortical bone.

The quantity of newly formed bone is significantly reduced, demonstrated also by the small amount of osteoblastic cells present.

Keywords: bone defect augmentation, alloplastic materials, bioactive glasses

INTRODUCTION

On an yearly base, million people find themselves in need of bone defect augmentation treatments, whether they are congenital or have occurred after traumatic injuries, tumor resection, or regarding implant restoration of the alveolar crest (1,2). Ideal standard is autolog bone, but it presents few limitations regarding its availability, form of graft not always optimal, necessity of a second surgical intervention for prelevation, thus increasing patient recovery time (3). Alografts and xenografts can represent an alternative but present the risk of infection, as well as loss of part of their biological properties once processed, and their cost can be rather high (4). Therefore, alloplastic materials became more and more studied; their main advantage is that they have no risk of infection dissemination, being completely synthetic. Today, their chemical composition can be controlled down to the smallest level, the molecular level, as well as the form and size of the particles.

The alloplastic materials can be divided in three groups: polimers, bioactive glasses and calcium fosfate (5). Bioactive glasses are materials which have the capacity of obtaining a biological response at the interface between them and bone tissue around, thus engaging in a direct connection (6). Bioactive glasses have proven to be efficient materials for bone augmentation in oro-maxillo-facial surgery (7).Their success is mainly due to their bioactivity, as result of their composition: 45% SiO_2, 24.5% CaO, 24.5% Na_2O si 6% P_2O_5 (8). Their unique composition helps the appearance of a layer of hydroxyapatite gel on the surface of the particles which attracts osteoblastic cells, stimulating bone formation as well as bonding with the collagen fibers (9).

This experimental animal study aims to follow the type of bone regeneration after preforming standardized bone defects and augmenting them with bioactive glasses.

MATERIAL AND METHODS

The study involved six New Zeeland white rabbits (three male, three female) with an average of 6 months of age and an average weight of 2.5 kg, from" *Cantacuzino*" National Institute of Imunologic and Microbiologic Research, Bucharest. The animal study protocol was approved by the Ethical Committee of Animals from Bucharest. The animals were housed in special rooms (temperature 18^{o}C - 24^{o}C, humidity 50%-70%, and a 12 hours light/dark cycle) and fed with a standard diet. The animals were anesthesiated with 10mg/kg xylazine and 50mg/kg ketamine. The bone defects were produces in the left tibial bone. The animals were sacrificed after six months using 200mg/ml IV Phenobarbital.

1. Surgical procedure

After the general anesthesia, the left tibial area was shaved and the skin was sterilized with povidone iodine solution. Using a 5 cm incision of skin, the subcutaneous and muscular tissues were dissected and the periosteum was removed from the bone. A standardizated defect was created by drilling 5 monocortical holes with a small round bur, 1 mm diameter. The defects were augmented with bioactive glasses and they were covered with collagen membranes. After placement of the membrane, suture was done in three layers (periosteum, muscular tissue and skin). The postoperatively wounds have been monitored daily, for two weeks. We took x rays of each animal after three days from surgery and then again after six months, from surgery.

2. Histopatologic evaluation

The animals were sacrificed after 6 months. The left tibia was harvested and fixed with formaldehyde 10%. After fixation of each specimen in formaldehyde, they were decalcified by using formic acid for 20 days, the solution was changed constantly. After decalcification, we harvested the areas of interest and continued with the histopatological evaluation. The specimens were introduced in paraffin blocks, then using a microtome several serial cross

sections were made. The sections were fixed in hematoxylin-eosin and evaluated under the microscope (Microscope optic Olympus xc30). We evaluated the number of osteoblasts and osteocytes around bioactive glasses particules and we analyzed the resorbtion of grafts particules, in program Olympus CellSens Dimension.

RESULTS AND DISCUSSION

The histopathological analysis, in all cases it can be observed that a partial resorption takes place even to a total resorption of the bioactive glasses granules, their occupying space not being replaced by new bone. Therefore, shallow optical spaces have been created within the cortical bone, spaces which in time may undermine the bone resistance. The bioactive glasses particules have not determined inflammatory reactions. This observation being also proven by the radiological images (*Figure 1*).

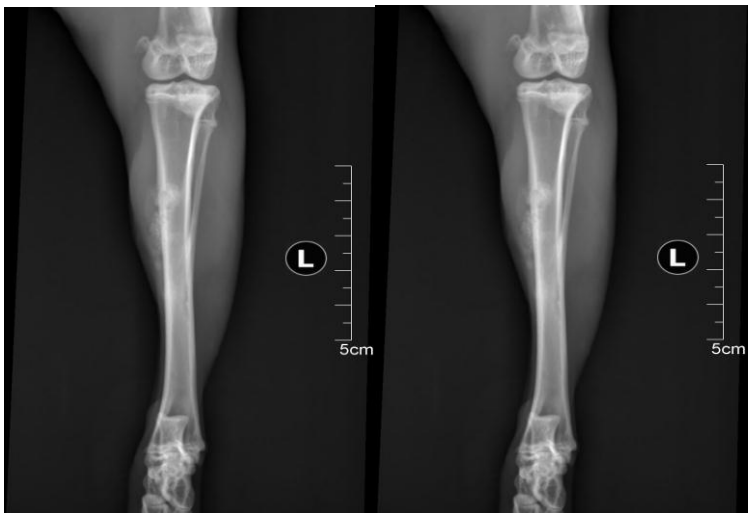

Figure 1. Radiological examination three days after surgical intervention (left) and at six months (right) at the same specimen

The number of osteoblasts and osteocytes has not been significantly higher around the particles of the addition material in comparison to normal cortical bone: therefore the osteogenesis process was reduced; overall osteoblastic and osteoclastic activity being reduce (*Figure 2, Figure 3*).

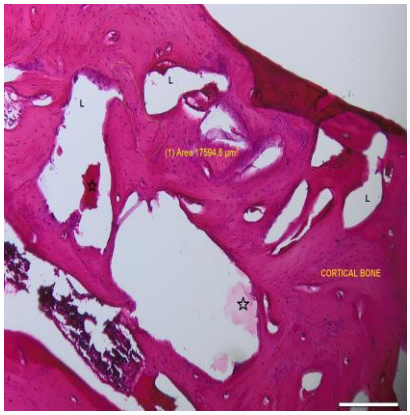

Figure 2. Transversal section through the tibia in the addition region with bioactive glasses and collagen membrane. In the cortical bone optical shallow spaces can be observed (L) or which contain small fragments of exogen material being resorbed (black starts), the surrounded area being osteocytes

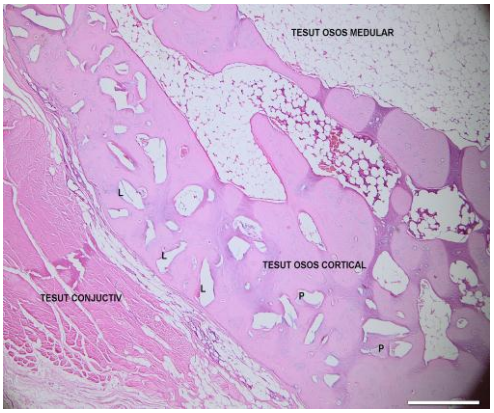

Figure 3. Transversal section through the tibia in the addition region with bioactive glasses and collagen membrane. At the level of the cortical bone a disorganized architecture can be observed by the optical shallow spaces (L) and particles of bioactive glasses in different stages of resorption (P)

Although the thickness of the cortical bone was greater, in comparison to a normal cortical size, its was of a lower quality, by the presence of the shallow spaces where no bone formation took place, even if the addition particle materials have been resorbed. (*Figure 4, Figure 5*).

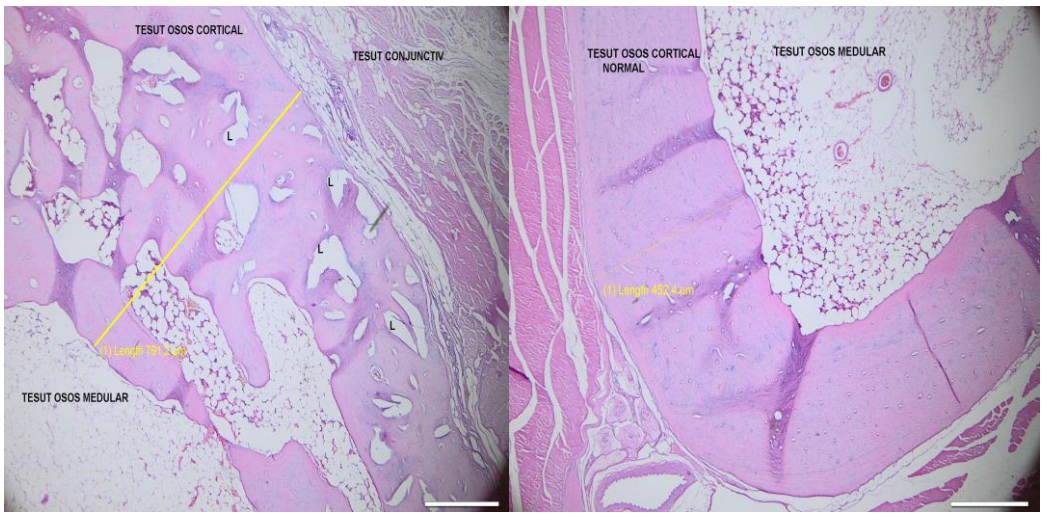

Figure 4. A: Transversal section through the tibia in the addition region with bioactive glasses and collagen membrane. The disorganized bone architecture can be seen by the presence of numerous optical shallow spaces (L). B: transversal section through the tibia where the cortical bone presents no pathological modifications.

In the speciality literature there are a few essential criteria for an alloplastic material to be of success (10,11,12):

- its matrix needs to be bioactive, to adhere to the surrounding bone;
- the material needs to be biocompatible, to avoid an negative imun response and thus fibrous incapsulation;
- the osteogenic cells need to be capable to proliferate on the surface of the particles as well as between them;
- the distance between the particles should be more than 100 μm, to permit the formation of a vascular network;
- the cells which adhere to the material's matrix should be stimulated to become osteoblastic cells;
- the alloplastic material matrix should resorb in the same time as bone healing, too fast would lead to a decrease in bone resisdence, and too slow would determine a prolonged immunological response with fibros tissue formation.

The most common synthetic materials are beta-tricalcic fosfate and bioactive glasses (13). Both form a bond with the bone by means of an active surface of hydroxyapatite. The disadvantage of the tricalcic fosfate is that it disintegrates faster that the formation of the new bone (14).

The bioactive glasses are materials based on silicate, introduced for use in 1970. It is considered that silicate plays a critical role in its bioactivity, thus being very biocompatible materials (15). Due to their granular and non-porous nature, bioactive glasses have a reduced grade of interconnectivity (16). Silcate forms a network that unites all components of bioactive glasses, by help of the oxygen atoms. After addition of this materials to the bones, an ionic dissolution takes place between Na and Ca at the level of the material and H and H_3O surrounding ions. This ionic flux determines an increase in local pH, and over the value of 9, the O-Si-O bonds start to break thus beginning the resorption of the bioactive glasses (17). Therefore a hydroxi-apatite gel layer forms on the surface which attracts osteoblastic cells (18).

The studied material is a bioactive glass which comes in particles, which adapts easy to different forms of bone defects, having a high surface-volume ratio, thus enhancing the osteo-conductive properties as well as the ionic dissolution and surface reactivity (19, 20). Its main disadvantage is the difficulty in maintaining them at the defect site and their poor mechanical properties (21). It has been demonstrated that larger particles are optimal for bone regeneration, in cases of critical bone defect, while particles under 310 μm determine the formation of a scar tissue at the defect site (22).

The guided osteogenetic phenomena of the bioactive glasses depends mainly also on the dimension of the particles. Thus, the glass particles and the neighbouring tissue form a silicate gel which is rapidly covered by calcium fosfate. The macrophage cells penetrate this gel, destroying it into smaller pieces and initiating the resorption process. The mezenchimal cells appear in the interior which will later transform in osteoblasts and will determine bone apposition. (Schepers, Ducheyne, Barbier 1993)(23). The size of the bioactive glass particles should be between 300 μm and 360 μm. (Schepers, de Clercq, Ducheyne si Kempeneers 1991)(24) If they would be greater, they wouldn't resorb, and if they would be smaller, they would completely resorb without guiding the appearance of the mezenchimal cells. (Schepers, Ducheyne, Barbier 1993)(23).

Bioactive glasses are an alloplastic material which creates a bond with the bone tissue as well as with the adiacent conjunctive tissue. (Wilson 1993)(25). Bioactive glasses are indicated more for the treatment of the bone defects. (Quinones si Lovelace 1997) (26). It can be used for socket preservation, bone defect augmentation after cyst removal, sinus lift etc. (27) It has two major properties: biocompatibility and ability to realize hemostasis. (Fetner, Hartigan si Low 1994).(28)

CONCLUSIONS

The used material in this study resorbs a lot faster that the needed time of the osteoblasts to produce new bone. Therefore, empty bone areas result by the resorption of the bioactive glasses, which cause decrease in bone strength. The quantity of newly formed bone is significantly reduced, demonstrated also by the small amount of osteoblastic cells present.

The obtained data need to be interpreted while correlating to the studies limitations. Due to the rather small number of experimental animals used in this study, the results did not permit a statistical analysis.

All authors have had equal contributions in this study.

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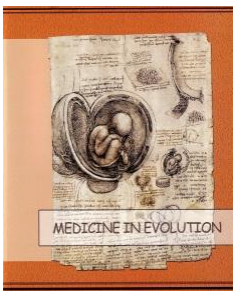
Osteoporosis in postmenopausal women



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Abstract

Osteoporosis is defined as a bone cell deregulation, being characterized by a reduction of bone mass and bone tissue integrity, leading to bone fragility and decreased bone hardness. This loss of performance in bone cells leads to a higher risk of fractures, predominantly in the hip and spine. In terms of percentage, 40% of osteoporosis cases occur in postmenopausal women and 15% occur in elderly men.

Keywords: bisphosphonates, postmenopausal women, osteoporosis

INTRODUCTION

Bone undergoes a continuous process of formation during the course of life, constantly changing. There is a constant balance between bone deposition and resorption, to which osteoblast cells (young cells with a role in bone renewal) and osteoclasts (mature cells with a role in resorption) have an important contribution. When this balance is disturbed by systemic diseases (osteoporosis), alterations of bone geometry (at the level of hydroxyapatite) occur.

BONE BIOLOGY IN THE CURRENT CONTEXT

Osteoblasts form a (collagen or non-collagen) bone matrix termed osteoid. These can remain on the bone surface, initiating bone apoptosis (1). Osteoclasts are formed from hematopoietic cells of monocytes or macrophages. During bone resorption, hydroxyapatite and the organic matrix are removed by multinuclear osteoclasts. Both bone deposition and bone resorption are coordinated and controlled by endocrine and biological mediators with a role of stimulation (parathyroid hormone PTH, parathyroid-related peptide PTHrP, prostaglandin E2, vitamin D3) and inhibition (calcitonin, estrogen, interferon, transforming growth factor β) (2,3).

Bone metabolism is regulated by RANK (receptor activator of nuclear factor Kβ), RANKL (receptor activator of nuclear factor Kβ ligand), and OPG (osteoprotegrin). The balance between RANKL and OPG is crucial in the control of osteoclasts in the bone microenvironment. RANK is expressed in the osteoclast plasma membrane, RANKL is expressed in the osteoblast plasma membrane, and OPG is produced by osteoblasts, acting as a decoy receptor through its binding to RANKL, thus preventing RANK action (4).

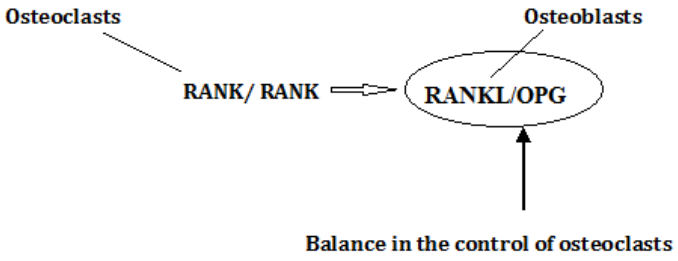

Figure 1. Schematic representation of molecular interactions between osteoclasts and osteoblasts

ETIOPATHOGENY

Osteoporosis is defined as a bone cell deregulation, being characterized by a reduction of bone mass and bone tissue integrity, leading to bone fragility and decreased bone hardness. This loss of performance in bone cells leads to a higher risk of fractures, predominantly in the hip and spine. In terms of percentage, 40% of osteoporosis cases occur in postmenopausal women and 15% occur in elderly men (5).

Regarding the classification of osteoporosis stages, there are four stages as shown in the table below (6):

Table 1. Stages of development of osteoporosis according to Harris H. Mcllwain

Stage 1	- usually develops around the age of 30 to 35 years, it has no visible symptoms
Stage 2	- usually develops after the age of 35 - when the decrease of bone density occurs at a faster rate than bone renewal - it also has visible symptoms, it can be detected by densitometry tests
Stage 3	- usually develops after the age of 45 to 55 - at this stage, bones become more fragile

	- the incidence of bone fractures increases in this stage - most cases of osteoporosis are diagnosed during this stage
Stage 4	- occurrence of continuous bone fractures - increase of pain - risk of disability - deformities of the spine and other areas that may become more obvious - difficulties in moving and performing daily activities - this stage is less frequent, because of available treatment to prevent future fractures

In premenopausal women, ovaries represent the main source of estradiol. This functions as a circulating hormone and acts on target tissues. On the other hand, in postmenopausal women, when ovaries stop producing estrogen, estradiol is no longer just en endocrine factor. Thus, this is produced at a number of extragonadal sites and acts locally at these sites as a paracrine or even an intracrine factor. These sites include mesenchymal cells in adipose tissue, including breast adipose tissue, osteoblasts and chondrocytes in bone tissue, vascular endothelium and smooth muscle cells in the aorta, and many sites in the brain. Thus, circulating estrogen levels in postmenopausal women do not represent action mechanisms of estrogen; on the contrary, they are more reactive than proactive. This is due to the fact that in these cases, circulating estrogen has its origin in extragonadal sites where it acts locally, and in case it leaves local metabolism and enters the general circulation, this will reflect in its direct action on bone tissues (7).

According to recent studies, estrogen deficiency is the main causative factor in the development of osteoporosis both in women and men (8). Estrogen deficiency present at an advanced age is associated with an increase of bone resorption to the detriment of bone formation, which results in excessive bone loss.

From a molecular point of view, it has been recently discovered that the receptor activator of nuclear factor kβ (RANK)/RANK ligand (RANKL)/ OPG triggers an important signal that regulates osteoclast formation. Thus, RANK/RANKL binding inhibits osteoclast formation and differentiation and implicitly slows bone resorption (9). Recent studies have shown that regulation of RANKL activity in bone cells and estrogen deficiency in postmenopausal women are responsible for bone resorption (10,11). Furthermore, experiments conducted on animal models (ovariectomized mice) for the induction of osteoporosis have shown that OPG, in addition to preventing bone resorption, increases bone mineral density and in excess, can even lead to osteopetrosis. It was demonstrated that a single injectable OPG dose administered to postmenopausal women leads to a rapid and marked reduction of bone turnover within 12 hours; this could be proved by biochemical markers and collagen products (NTX urinary N-telopeptide, DPD deoxypyridinoline) (12,13).

TREATMENT

According to current clinical studies, bisphosphonates are effective in reducing bone mass loss and implicitly, in increasing bone mineral density in osteoporotic postmenopausal women. Through their action, they improve the biomechanical properties of bone affected by osteoporosis and during hormone replacement therapy, finally leading to a significant improvement of the general bone structure (14).

Osteoporosis is a health problem reported worldwide. Its treatment is represented by drugs that are generically termed *bisphosphonates*, which through their action at cellular level stop the action of osteoclasts and even improve bone architecture. Bisphosphonates administered per os are effective in reducing the risk of osteoporotic fractures, being successfully administered to women diagnosed with different stages of osteoporosis (15).

CONCLUSIONS

The general dental practitioner must explain to the patient the advantages and disadvantages of this type of treatment both from a general clinical point of view and from a local point of view, at the level of the oral cavity (16). At the same time, it is imperative to closely monitor the patient throughout the duration of bisphosphonate therapy, as well as after the completion of treatment, for an early detection of potential complications in the oral cavity, and also, to apply the clinical protocols required in these cases.

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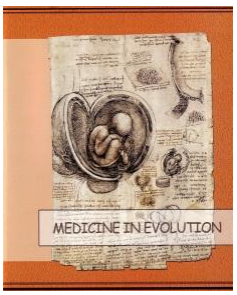
Treatment with ozone before sealing pits and fissures



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Abstract

Carious lesions frequently appear on occlusal surfaces, and their progression can be rapid. Pit and fissure sealants are safe and effective in preventing dental caries. Ozone is a very good alternative and/or an additional disinfectant for standard antiseptics, due to its undeniable disinfection power over other antiseptics. By applying ozone, 99.9% of bacteria present in carious lesions are inactivated, and proteins that affect remineralization are destroyed in seconds. By early detection of fissures and superficial caries, it is even possible to heal them completely, thus maintaining the integrity of the dental structures.

The purpose of this study is to demonstrate the effectiveness of ozone treatment on microorganisms located at the pit and fissure level, which most often prevents adhesion of the sealing material to the dental surface, thus leading to the loss of sealing and then to the continuation of the carious process deep inside dental tissues.

For this study, a total of twenty 20 children were selected, showing permanent molars and premolars and who did not have carious lesions of cavities. Patients were divided into two groups: the first group of ten patients, on whom 27 sealing operations were performed after having brushed their teeth professionally and cleaned them with Healozone, and the second group of ten patients on whom a number of 25 sealing operations were performed after the teeth had been cleaned only by professional brushing. Patients were asked to come back in 6 and 12 months after sealing to verify their integrity.

Comparing the results obtained from the 12-month study, it was found that within Group 1, retention and integrity of the seals are far superior to those in Group 2.

As a result of this study, it can be said that ozone has a beneficial role in maintaining the sealing of pits and fissures for a longer period of time, thoroughly cleaning them and thus ensuring better adherence between the dental surface and the sealing material used.

Keywords: *ozone therpy, sealants, caries prevention*

INTRODUCTION

The presence of caries in the pits and fissures of molar occlusal surfaces is accountable for approximately 67-90% of caries in children aged between 5 and 17 years. Carious lesions frequently appear on these surfaces, and their progression can be rapid. The main factor of occlusal caries is the uneven relief of occlusal surfaces in lateral teeth. Thus, the appearance of caries is directly related to the shape and depth of occlusal pits, and the existence of deep and narrow pits is the best environment for the emergence and development of caries. Pit and fissure sealants are safe and effective in preventing dental caries [1].

Sealing materials have been developed to protect pits and fissures against caries by preventing the impact of food residues and bacteria, which produce acid, resulting in the initiation of carious lesions. These pit and fissure sealants are widely accepted as an effective, non-invasive treatment for preventing or stopping occlusive caries. The effectiveness of sealing materials in caries prevention has been associated with the duration and degree of retention of the sealant [2]. This is why pits and fissures should be as clean as possible before applying the sealing process. A new concept in dental medicine that can lead to a better retention of sealing materials at the pit and fissure level is ozone therapy applied before the sealing itself.

The onset of the mechanism causing occlusal caries in pits and fissures takes place at the occlusal pit hole through two independent bilateral lesions in the enamel of opposite cuspal slopes. The lesion then extends across pit walls [3]. In its progress, the process follows the prismatic structure, expanding. The base of the pit demineralizes after the two bilateral lesions unite at its base. It is believed that the hole and walls of the pit demineralize before the pit, because the presence of an organic body can act as a buffer against acid metabolites of the dental plaque, as well as a diffusion barrier, resulting in the reduction of the acid attack at the pit base. Usually the presence of high amounts of protein at the base of the pit influences the evolution of the lesion. Proteins provide resistance to caries progression by favouring re-deposition of the mineral phase and limiting the access of acids produced by bacterial plaque to enamel crystals [4].

Ozone therapy is an innovative treatment method used in many medical fields such as: orthopaedics, treatment of rheumatic diseases, vascular and neurological diseases, dermatology, urology, gynaecology, aesthetic treatments and dentistry. This therapy is based on the ability of ozone (ozone or trioxygen is an oxygen form, O_3) to destroy the microorganisms involved in various diseases.

Ozone is an unstable blue gas found in large quantities in the stratosphere, with a concentration of 16-20 mg/m. Due to its instability, it has the highest oxidation potential, about 150% more than chlorine, when used as an antimicrobial agent. This powerful oxidation property has led to the use of ozone in many medical and dental areas. [5]

Applications of ozone therapy in dental medicine: Ozone is a very good alternative and/or an additional disinfectant for standard antiseptics, due to its undeniable disinfection power over other antiseptics. In dentistry, ozone can be used: as a powerful disinfectant; to control bleeding; to clean the wounds in soft bones and tissues; to improve healing by increasing the local supply of oxygen to the surface of the wound; to increase metabolic processes related to wound healing; as a diagnostic method - vitality test; in dental prosthetics - for crown disinfection; in dental conditions, carious lesions, enamel fissures, canal treatments, dental whitening, dentinal hypersensitivity, abscess, granulomas, fistulas, aphthae; in surgery - for implants, replanting, extraction, wound healing, coagulopathy; in orthodontics and orthopaedics - in temporomandibular joint dysfunctions, trismus, muscle relaxation.

In dental medicine, HealOzone is used for safe and rapid disinfection in the oral cavity. A large dose of ozone can be used in many dental applications. It even goes into the smallest pits and fissures of teeth to destroy bacteria, fungi and viruses.

By applying ozone, 99.9% of bacteria present in carious lesions are inactivated, and proteins that affect remineralization are destroyed in seconds. By early detection of fissures and superficial caries, it is even possible to heal them completely, thus maintaining the integrity of the dental structures [6].

HealOzone works as follows: ozone penetrates infected enamel and dentine; 99.9% of bacteria and their acid are inactivated; a fluid is deposited to reduce and neutralize the remaining acid, adding minerals and fluorides; full remineralization is achieved from 4 to 12 weeks.

The purpose of this study is to demonstrate the effectiveness of ozone treatment on microorganisms located at the pit and fissure level, which most often prevents adhesion of the sealing material to the dental surface, thus leading to the loss of sealing and then to the continuation of the carious process deep inside dental tissues. This is why we have conducted a comparative study on pit and fissure sealing on teeth that were first cleaned using ozone therapy, compared to sealing conducted on teeth that were cleaned only by professional brushing.

MATERIAL AND METHODS

For this study, a total of twenty (20) children out of a total of 28, aged from 7 to 12 years, were selected, showing permanent molars and premolars and who did not have carious lesions of cavities. Patients were divided into two groups: the first group of ten patients, on whom 27 sealing operations were performed after having brushed their teeth professionally and cleaned them with Healozone, and the second group of ten patients on whom a number of 25 sealing operations were performed after the teeth had been cleaned only by professional brushing. Patients were asked to come back in 6 and 12 months after sealing to verify their integrity.

Clinical examination and data collection:

Dental status for all teeth was recorded according to WHO criteria [7]. Dental caries were clinically diagnosed and visually detected. Study registration conditions did not include signs of cavity caries, so that 8 patients out of 28 were excluded from the study. First, information on brushing habits and eating habits of the children was also collected in a questionnaire to identify important differences. For the first group of 10 patients, professional brushing was performed using prophylactic cleansing paste (Clean Polish, Kerr), after which ozone was applied to the occlusal surface for 10 seconds.

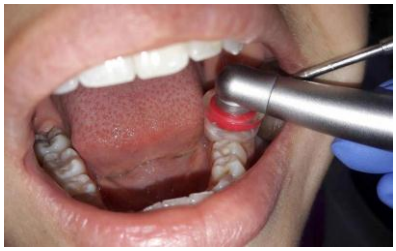

Figure 1. Applying ozone to the occlusal surface at 3.6

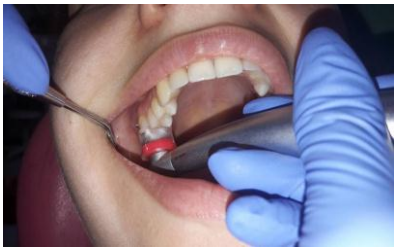

Figure 2. Applying ozone to the occlusal surface at 1.6

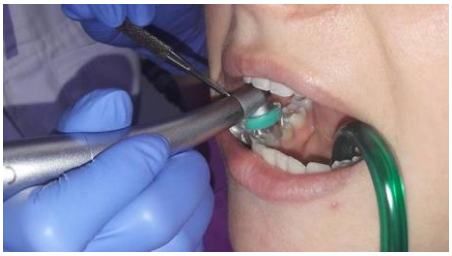

Figure 3. Applying ozone to the occlusal surface at 4.4

After the therapy was completed, teeth treated with ozone were sealed. A demineralising gel containing 37.5% phosphoric acid for enamel demineralisation (Etchant Gel, Kerr) was applied to the pits and fissures for 15 seconds after which they were rinsed with water. After the surface has dried, a sealant for pits and fissures (Clinpro, 3M ESPE) was injected, which was photopolymerized for 20 seconds with the curing light guide as close as

possible to the sealing, but without touching it. Finally, articulating paper was used to check occlusal contacts, and high points were removed with a finishing bur. Patients were asked to come back in 6 and 12 months to assess the status of the sealing.

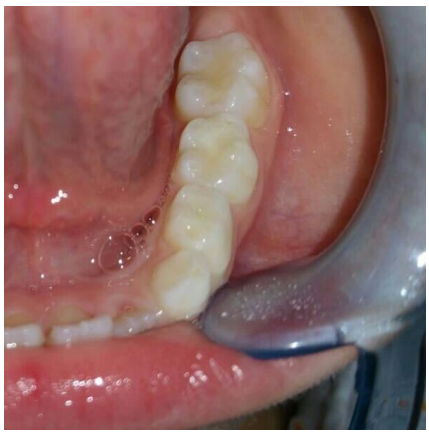

Figure 4. Sealing of pits and fissures after ozone therapy 3.6

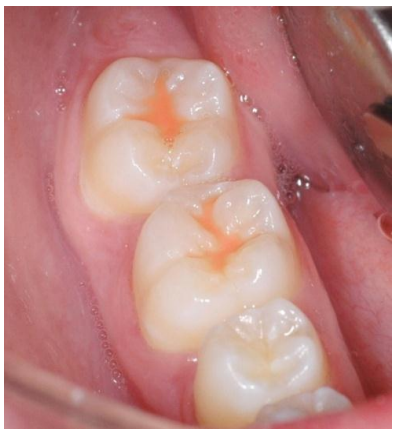

Figure 5. Seals with colour pigments after ozone therapy 4.6, 4.7

For the second group of 10 patients, the experimental study started in the same way by professional cleansing, and then the sealing according to the previous protocol was performed. Patients were asked to come back in 6 and 12 months to assess the status of the sealing.

RESULTS

The following figure shows a schematic diagram showing the design of the sample. Of the 28 participants, 8 exclusions from the study were recorded and 20 remained for follow-up in 6 and 12 months. The number of teeth available for sealing retention evaluation was 52.

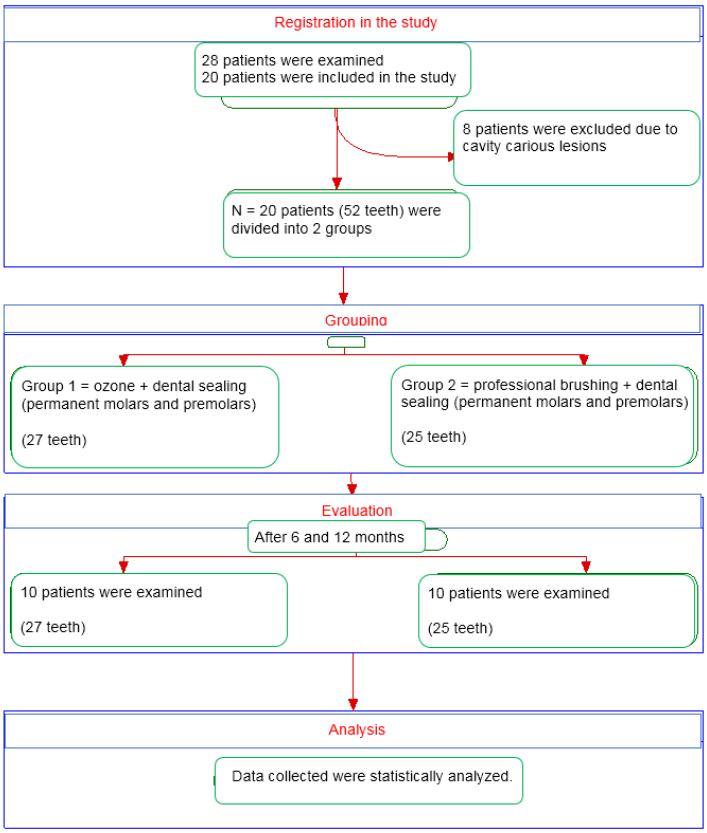

Figure 6. Diagram showing the design of the sample

Comparing the results obtained from the 12-month study, it was found that within Group 1, retention and integrity of the seals are far superior to those in Group 2.

Table 1 shows the results of the comparative study, so that for Group 1, after the first 6 months from making the sealing following ozone therapy, 25 teeth out of the 27 had a complete retention of sealing, and on 2 teeth the sealing were partially lost. There was no total loss of sealing.

With regard to Group 2, after the first 6 months of sealing following a professional brushing, the differences compared to Group 1 are not very significant. A complete retention of sealing was recorded on 22 teeth out of the 25 teeth, partial retention on 2 teeth and complete sealing loss on 1 tooth.

Twelve months after the seals were made, the differences between the two groups were more pronounced. In Group 1 there was a complete retention of 22 teeth out of 27, a partial retention on 4 teeth and only one teeth sealing was completely lost. Instead, in Group 2, only 14 teeth showed complete retention of sealing, 7 teeth showed partial retention, and sealing on 4 teeth was completely lost.

In conclusion, after 12 months, 81.48% of the sealing made on the teeth treated with ozone kept their integrity, and on the teeth sealed after a professional brushing, only 56% of the sealing was completely preserved.

Table 1. Comparison between retention of sealing - Group 1 versus Group 2

Evaluation period	Retention	**Group 1 (n=27 teeth)**		**Group 1 (n=25 teeth)**	
		No. of teeth	Percentage	No. of teeth	Percentage
6 months	Complete retention	25	92.59%	22	88.00%
	Partial retentions	2	7.41%	2	8.00%
	Complete loss	0	0,00%	1	4.00%
12 months	Complete retention	22	81.84%	14	56.00%
	Partial retentions	4	14.81%	7	28.00%
	Complete loss	1	3.70%	4	16.00%

The comparison between the two groups was also shown in Figure 7.

As a result of this study, it can be said that ozone has a beneficial role in maintaining the sealing of pits and fissures for a longer period of time, thoroughly cleaning them and thus ensuring better adherence between the dental surface and the sealing material used.

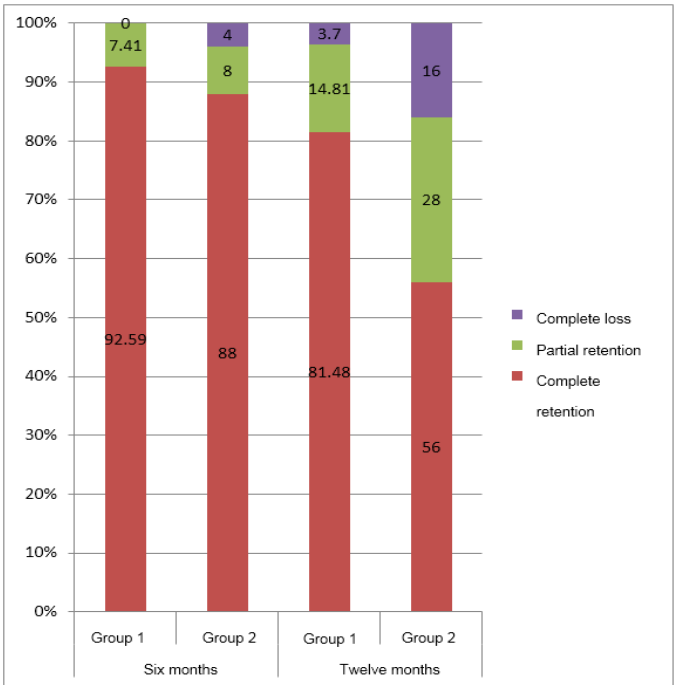

Figure 7. Percentage comparison between retention of sealing - Group 1 versus Group 2

So far, several studies have been conducted, which focused on improving the success of pits and fissures. An important factor to consider in the success of sealing materials is the prevention of microinfiltration, penetration of bacteria and oral fluids into the space between tooth and restorative material. Since microinfiltration can lead to the development of caries under the sealing, its inhibition is essential for a successful sealing [8], [9].

Despite the oral hygiene procedures, the optimal fluoride environment and a realistic approach to dietary changes, occlusal dental caries are inevitable in most children and adolescents as a result of the anatomy of pits and fissures, which favour stagnation of bacteria. Sealing the pits and fissures of caries-prone teeth with a composite resin forms a protective layer that prevents demineralization of the enamel by blocking the interaction between the cariogenic bacteria and their nutrient substrates, thus eliminating the harmful acid secondary products, which is considered a definitive treatment method in the prevention of tooth decay [10].

The ability of sealants to resist caries attack is to a large extent determined by the integrity of the enamel sealing interface, which prevents microinfiltration at its periphery. Otherwise, the carious process can be sustained and continued under the sealing. This, in turn, depends on an optimal clinical technique performed by the dentist. Therefore, the assessment should not be limited to the physical, chemical or biological acceptance of the material used for sealing, but also to the technique of cleaning and preparing the tooth surface to accept the placement of the sealant.

On the basis of the study, it has been found that the success of the pit and fissure sealing depends on their long-term retention on teeth surface.

Castillo et al. have evaluated the antimicrobial effect of ozone gas on *Streptococcus mutans*. Their results showed that the application of ozone for 10 seconds and 20 seconds produced a significant reduction in the number of bacteria. When the exposure lasted for 40 seconds, the total elimination of bacteria was noted. Both the application time and the previous bacterial concentration influence the antimicrobial effect of ozone [11].

Johansson et al. assessed the antibacterial effect of ozone on cariogenic bacterial species with or without saliva, and a possible effect on salivary proteins. The study has shown that the tested cariogenic species are affected to varying degrees by ozone gas, with almost 100% killing after just 60 seconds of ozone application. It has also been demonstrated that the presence of saliva has reduced the antibacterial effect of ozone. Detection of altered salivary proteins indicated that most salivary components are additional targets for ozone molecules [12].

Recently, Polydorou et al. evaluated the antimicrobial effect of ozone on the two most important cariogenic species, *Streptococcus mutans* and *Lactobacillus casei*, in 4 weeks and 8 weeks after the treatment, using a dental cavity model. The results have shown that the ozone effect differs between the two types of microorganisms. It has been shown that the viability of *Lactobacillus casei* has not been affected by the application of ozone. By contrast, the viability of *Streptococusmutans* significantly decreased. Applying ozone resulted in a reduction in bacteria after 4 weeks. As for the effect over the 8-week period, it appeared to be stable over time. It is suggested that the application of ozone in addition to the use of other antibacterial methods after caries excavation could be more successful in eliminating bacteria remaining under restorations [13].

Ozone could be a useful tool for reducing and controlling oral infectious microorganisms in the dental plaque and dental cavity [14]. However, the results of *in vitro* studies are controversial, although some researchers have reported that ozone therapy has had little or no effect on the viability of microorganisms, others have suggested that ozone is very effective in killing gram-positive and gram-negative oral microorganisms [15], [16].

CONCLUSIONS

Applying ozone before sealing the pits and fissures has proven to be an effective solution for cleaning teeth and retaining sealing material for as long as possible. This painless preventative method can have a great influence on remineralization by increasing the salivary mineral concentration.

Although we have achieved positive results in this study, clinical evidence on ozone application is not extensive. Therefore, more evidence is needed before ozone can be accepted as an alternative to current methods of dental decay management and prevention.

Ozone therapy allows for a new vision that respects patients' needs and requirements for a non-invasive and effective dental care, and is truly a change in dental practice. It is applicable to a wide range of soft and hard intraoral tissue conditions.

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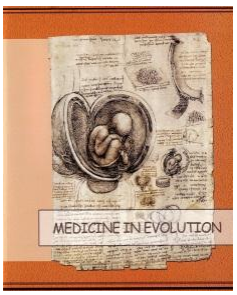
Assessment of Removable Partial Dentures Using Finite Elements Analysis



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Abstract

Aim and objectives. This study is focused on finite element analysis to dynamic load due to the action of the forces which operate in case of removable partial dentures and aims at making predictions about the areas with highest fracture risk. Material and methods. An upper class I Kennedy edentation with the fixed component represented by semi-physiognomic crowns on 2.4, 2.5, 1.4, 1.5 teeth and the mobile component made of two saddles and a palatinal connector, joined by precission millings and interlocks was taken in consideration. For the manufacture of the metallic framework Herenium Sun (Heraeus Kulzer) Co-Cr alloy was used. The Autodesk® Inventor® Professional software was used for visualisation, simulation and digital representation. Results. When a static load is applied at saddle level, the main stress appears at the joining areas of the metallic saddles with the interlocks and at the distal extremity of the main connector. A frequency of the load higher than 9535.17 Hz, applied at saddle level leads to fracture. Conclusions. Finite element analysis permits noninvasive testing in dental technique. The software enables the dental technician to import scannings of any prosthetic piece so the future resistance may be determined since the pattern stage.

Keywords: *finite element analysis, stress distribution, removable partial denture*

INTRODUCTION

The connections between removable partial dentures and teeth or tissues are not rigid ones, so they are subject to movements in response to functional loads, their design requiring biomechanical considerations. [1]

These possible movements do not occur singularly or independently, they show a certain dynamic and occur simultaneously. [2] The complex geometry of the removable partial dentures makes stress distribution analysis very complicated. Among the different methods of assessing complex removable partial denture biodynamics, the finite element method enables to experimentally and noninvasively test a particular design of the removable partial denture. It provides information on minimum resistance areas of the metal framework and allows corrections before manufacturing the denture. The method is based on the idea of building a complicated object with simple blocks, or dividing a complicated object into small and manageable pieces (finite elements). By analyzing what happens with each finite element, as part of the whole system, the response of the system to external actions can be predicted. [3] Subsequently, predictions regarding possible failure can be made. [4]

Aim and objectives

The present study is focused on finite element analysis to dynamic load due to the action of the forces which operate in case of removable partial dentures in order to make predictions regarding the areas with highest fracture risk. Our objective is to answer the question: which is the reaction of the denture framework structure when it is subjected to external actions?

MATERIAL AND METHODS

An upper class I Kennedy edentation was analysed. The fixed component is represented by semi-physiognomic crowns on 2.4, 2.5, 1.4, 1.5 teeth. The mobile component consists of two saddles and a palatinal connector. Joining the two components is made by precission millings and interlocks. (Figure 1)

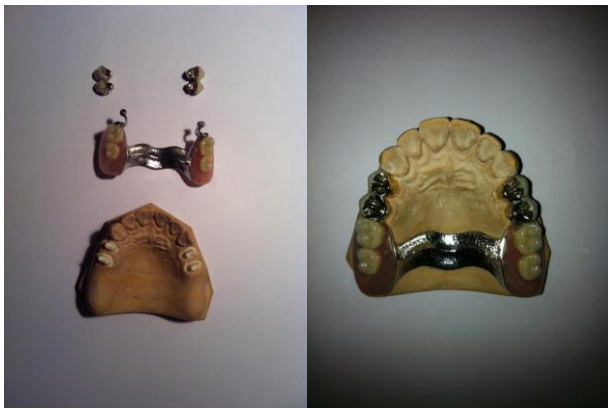

Figure 1. The removable partial denture

Finite element analysis includes computerized preprocessing, processing and post-processing. A continuous body is meshed in a finite number of elements with a finite number of joints, which are interconnected by lines or planes. The resulting forces that act on an element are taken into consideration as concentrated forces applied in its joints. The balance and compatibility conditions for each loaded joint lead to an algebraic system of equations in which the unknown elements can be the joint movements, the inner forces (efforts) or both, according to the method used. [5]

Two main stages may be described when analysing an object by finite element method:

1. Obtaining the model of the studied structure or system
2. Simulation of the actions which interact with the system. [4]

The finite element analysis involves the creation of a computer-simulated model. This consists in considering the entire structure as an entirety of individual structural elements. Therefore, each part of the model is divided into individual elements (finite elements). Adjacent elements are connected at specific points (nodes) on their common boundaries. [6] In our case the mathematical model was completed and the finite element model was developed by dividing it into 68.038 elements, connected in 120.616 points.

For manufacturing the metallic framework a Co-Cr alloy was used: Herenium Sun (Heraeus Kulzer) with the main properties described in table 1. The volume of the piece is 966.259 mm^3 and it weighs 0.00792332 kg.

Table 1. Alloy's properties

General properties	Density	8.2 g/cm^3
	Yield strength	490 MPa
	Tensile strength	861.25 MPa
Stress	Young modulus	250Gpa
	Poisson's ratio	0.31ul
	Shear coefficient	95.4198GPa
Thermic Stress	Expansion coefficient	$0.000018ul/C^0$
	Thermal conductivity	10w/(mK)
	Specific heat	42 $J/(kg\ C^0)$

An occlusal load of 4.337 N was applied to the occlusal surface of the teeth (Figure 2), considered to be the highest value of human bite ever recorded, in accordance to the Guinness Book of Records, established in 1992, with a length of 2 seconds. The Autodesk® Inventor® Professional software was used for visualisation, simulation and digital representation.

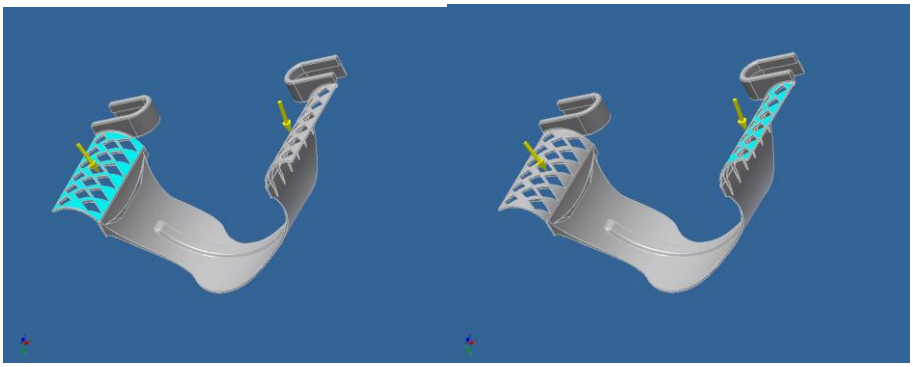

Figure 2. Force localization

RESULTS

When a static load of 4.337N is applied at saddle level, the main stress appears at the joining areas of the metallic saddles with the interlocks and at the distal extremity of the main connector. (Figure 3) Due to the fact that heat-cured acrylic resins are not characterised by increased elasticity, in this area cracks of the acrylic structure may occur even if the metallic framework remains intact.

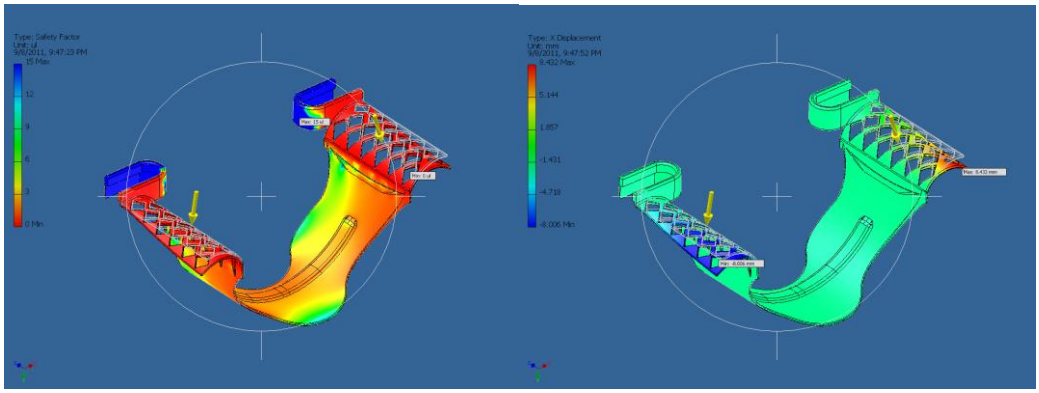

Figure 3. Tensions which appear in the metallic framework and saddle deformation

In conditions of fixed interlocks, the distal extremity of the metallic framework tends to clogg with a maximum value of 8,432 mm. This value changes in a dynamic environment such as the mouth, depending on the characteristics of the soft tissues which form the alveolar ridge (thickness, type, mobility). In case of dynamic load, a force of 4.337N is applied repeatedly with a certain frequency. Figures 4 and 5 show the deformation of the metallic framework at different random frequencies.

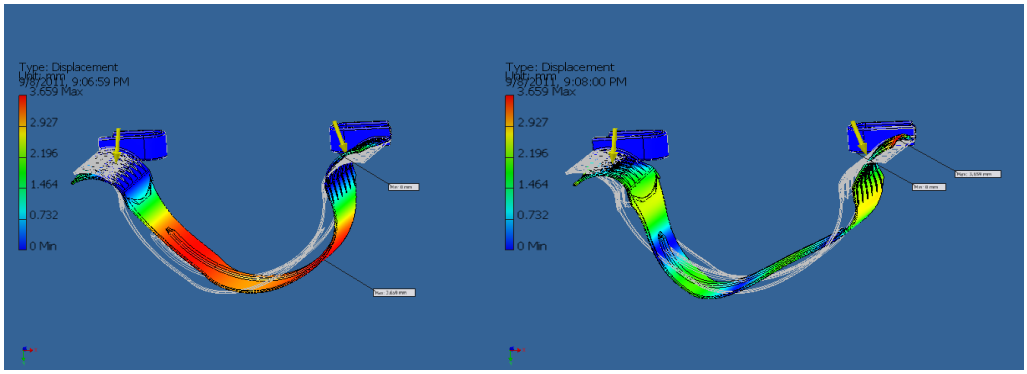

Figure 4. Framework deformation at a frequency of 1018.48 Hz and 4997.77 Hz

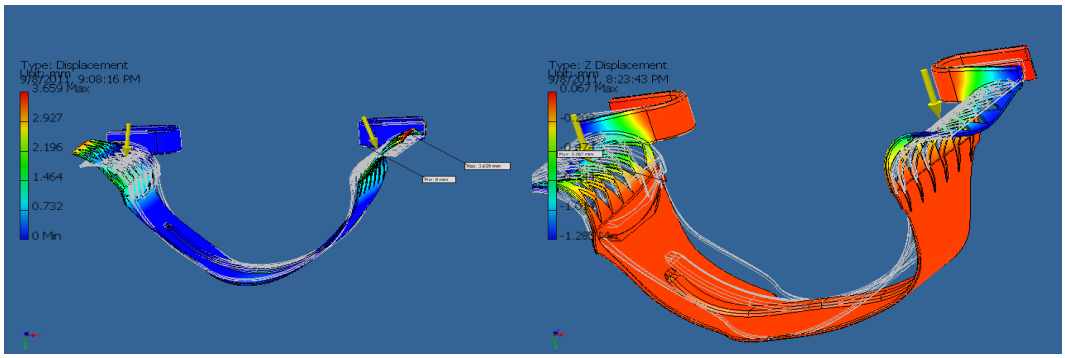

Figure 5. Framework deformation at a frequency of 6339.08 Hz and 9535.17 Hz

A frequency of the load higher than 9535.17Hz applied at saddle level leads to fracture.

The displacement tendency of the removable partial denture when submited to forces in the mouth is shown in Figure 6.

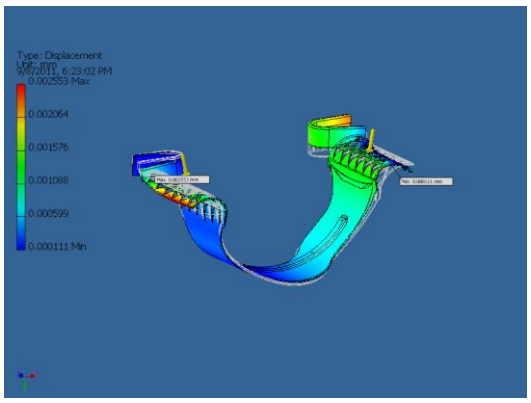

Figure 6. Framework balance when submited to forces in the mouth

DISCUSSIONS

In case of upper dentures the loading system is more complicated, because of the fibro-mucous resilient areas, which are different for the alveolar ridge (0.2 mm) and for palate (torus 0.1 mm; distal third 0.4 mm, rest of the palate 0.2 mm). The forces that displace the denture towards the prosthetic field are usually applied on the oral cusps of the maxillary sustaining area. [7]

One may observe that, when clogging in the distal area of the saddles, the interlocks are displaced in a mesial to distal direction. In the fixed component area, when a load is applied on the working side, the opposite side tends to rise, involving traction forces. In case of high paraxial forces, due to a difficult sustaining polygon, thick foliation, balancing ridge, premature contacts in the molar area, situations which permit excesive clogging of the saddles, the prosthetic piece may be compromised. [4]

A higher frequency of pressing force on the saddles area may result in the fracture of the framework. This in unlikely to happen in the mouth as long as the thickness of the framewok is mantained in normal parameters. However, in certain conditions, cracks may occur at the level of the heat-cured acrylic resin area.

CONCLUSIONS

Finite element analysis permits noninvasive testing in dental technique. The software enables dental technicians to import scannings of any prosthetic piece so the future resistance may be determined even in the pattern stage, helping them in choosing the lightest material and the minimum thickness possible. Finite element analysis shows that in case of a properly rebuilt occlusion by a removable partial denture with precision milling retentions, the forces are transmitted in the axis of the pillar teeth, the paraxial forces being of low intensity.

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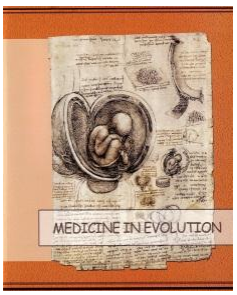
Epidemiologic study on dental injuries in primary teeth



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Abstract

Objective. *To assess the prevalence and distribution of traumatic dental injuries (TDI) in primary teeth in patients treated at a university clinic.*

Material and method. *Retrospective study on 1231 children (687 boys) aged 1- 6 years. Age, gender, affected teeth, type of injury, aetiology, place of occurrence and treatment were registered.*

Results. *162 (13.16%) children, of which 89 (54.94%) boys had TDI. Mean number of affected teeth=1.48 (boys=1.57, girls=1.37, NS). 72.84% of children with TDI were aged 1-3 years. Central incisors were the most affected (82.08%). Falling was the most common etiology (86.41%), 54.90% of incidents occurred inside. The most frequent types of injury were subluxation (20%) and lateral luxation (19.58%). The most common treatment method was"monitor only" (57.08%).*

Conclusions. *Dental trauma were more frequent in boys and in 1-3- year-old children. Parents and educators must be informed regarding the high frequency of dental trauma in small children and about the necessity of early treatment.*

Keywords: *traumatic dental injuries, primary teeth, epidemiology*

INTRODUCTION

Traumatic dental injuries (TDI) in children represent a public dental health problem because their frequency, occurence at a young age, costs and because treatment may continue for the rest of the patient's life [1]. TDI in primary teeth could have a great impact on quality of life, affecting children physically, esthetically and pshychologically [2]. In addition, these can lead to alterations in the succedaneous teeth, especially in cases of intrusive luxations and avulsions [3].

In Romania most of the studies about dental trauma were performed on permanent teeth or both primary and permanent dentition. For this reason, there are no reported data about the prevalence of dental injuries in primary teeth, there are only few data about their distribution [4-6]. Therefore, the aim of the study was to assess the prevalence of TDI in primary teeth and to analyze distribution of traumatic episodes in patients treated at an emergency pedodontic clinic over a 6 years period.

MATERIAL AND METHODS

A retrospective study was carried out using dental records of 1231 children (687 boys, 544 girls) aged between 1 and 6 years (mean age = 4.01±1.58 years), referred to Pedodontics Department, Faculty of Dental Medicine, Carol Davila University Bucharest (Romania) between 2010-2015. Age, gender, affected teeth, type of injury, etiologic factors, place where the injury occurred, treatment were registered for each patient. TDI were diagnosed according to classification adopted by the World Health Organization and modified by Andreasen et al. (2007) [7]. Were analized: prevalence of trauma in primary teeth, distribution of trauma according to age, sex and type of trauma, distribution of traumatized teeth according to topography and number of affected teeth, distribution of traumatic events related to the place of occurence and etiologic factor and treatment methods used.

Quantitative analysis of the collected data was performed using program SPSS 20.0 for Windows (Chicago, IL, USA). Data were analyzed using ANOVA and independent variables T-test, with the level of significance set at 5%.

RESULTS

Of the 1231 children analyzed, 162 had TDI in primary teeth, resulting a prevalence of 13.16% (12.95% - boys, 13.42% - girls, NS, p=0.633). Among the 162 children with TDI, 89 (54.94%) were boys, with a male:female ratio of 1.22: 1. A total of 240 primary teeth were injured. Mean number of affected teeth/child=1.48 (1.57 in boys, 1.37 in girls, NS p=0.065).

More than 2/3 of dental injuries were registered in children aged between 1-3 years, children aged 1 being most affected (30.24%)(fig. 1).

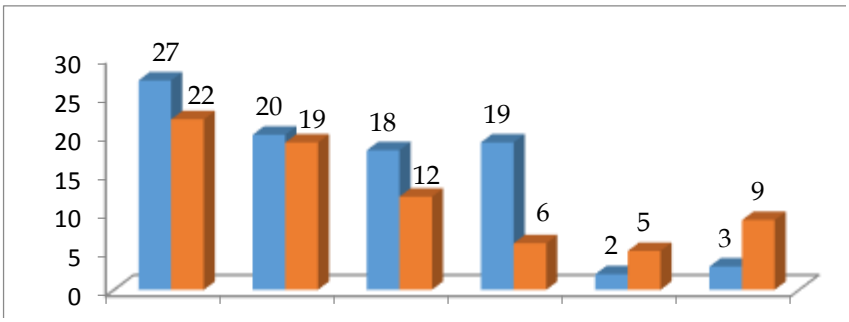

Figure 1. Age and sex distribution of children with dental injuries (n=162 children)

Luxation injuries were found in 66.67% of cases (n=160 teeth) and dental fractures in only 33.33% (n=80 teeth) (SS, p=0.000). Dental fractures were more prevalent in children aged 1 and 2 years (fig. 2). Mean age of children with luxation injuries was SS higher than mean age of children with dental fractures (p=0.022).

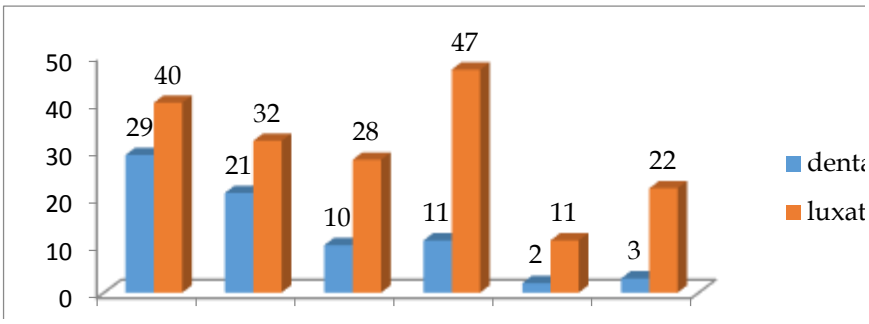

Figure 2. Age distribution of dental fractures and luxation injuries (n=240 teeth)

Boys were the most affected by injuries to the periodontal tissues (fig. 3)

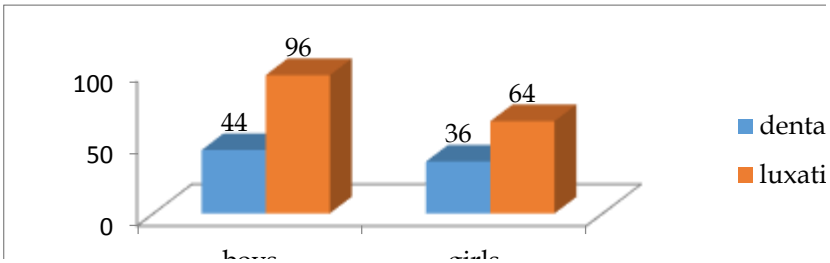

Figure 3. Sex distribution of dental fractures and luxation injuries (n=240 teeth)

There was correlation between types of injuries and age (p=0.017) and no significant relationship with gender (p=0.453).

All types of dental traumatic injuries were found. Subluxation was the most common type of injury, followed by lateral luxation and intrusive luxation (Table I).

Table I. Distribution of affected teeth according to the type of injury (n=240 teeth)

Type of injury	n	%
Enamel fracture	12	5
Enamel-dentin fracture, without pulpal involvement	27	11.25
Enamel-dentin fracture, with pulpal involvement	13	5.41
Root fracture	15	6.25
Crown-root fracture	13	5.41
Concussion	2	0.83
Subluxation	48	20
Lateral luxation	47	19.58
Intrusive luxation	33	13.75
Extrusive luxation	5	2.08
Avulsion	25	10.41

All affected teeth were anterior teeth, except for two cases. 94.17% of injured teeth belonged to maxillary arch and maxillary central incisors were most affected (82.08%).

In most cases, traumatic injury involves 1 tooth (61.73%), seldom 2 teeth (30.25%) and rarely 3 or 4 teeth (8.02%). When trauma occured at a smaller age, one tooth was more frequently involved (fig. 4).

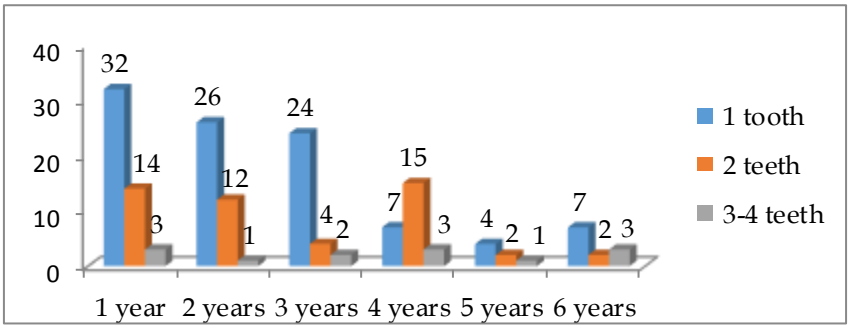

Figure 4. Distribution of traumatic events according to the number of teeth involved

54.90% of traumatic incidents occurred inside the house or kindergarten and 45.10% outside. At the age group 1-3 years, most of the events occured indoors (62.04%), while in the age group 4-6 years trauma occured outdoors were more prevalent (72.73%).

The most common cause of injury was falling while walking or running (Table II).

Table II. Etiologic factors of trauma events (n=162 children)

Etiologic factors		n	%
Falls	while walking or running	73	45.06
	from high objects	19	11.73
	against objects	33	20.37
	from moving objects	15	9.25
Collisions		14	8.64
Playing accidents		4	2.47
Car accidents		4	2.47

There is no significant correlation between type of trauma (dental fractures or luxations) and place (p=0.682) or etiology of trauma (p=0.410).

Regarding the treatment provided for injured primary teeth, the most common was"monitor only", followed by root canal treatment and extraction (Table III).

Table III. Distribution of the different methods of treatment

Treatment method	n	%
Monitor only	137	57.08
Extraction	26	10.83
Pulp capping and restoration	6	2.5
Root canal treatment	33	13.75
No treatment	25	10.41
Smoothing of fratured incisal edge	1	0.41
Repositioning	11	4.58
Repositioning and splinting	1	0.41

DISCUSSIONS

The results of the present study generally confirm data reported from previous studies. The value of prevalence of TDI in primary teeth found in present study is between figures reported in literature (Table IV).

Table IV. Prevalence of TDI in primary teeth in studies conducted in pedodontics clinics

Authors	Year	Country	Sample	Age	TDI (%)
Chowadry *et al.* [8]	2014	India	65870	< 6 y	1.03
Skaare & Jacobsen [9]	2005	Norway	20000	1-8 y	1.3
Present study	2016	Romania	1231	1-6 y	13.16
Cunha *et al.* [10]	2001	Brazil	1654	0-3 y	16.3
Mendoza-Mendoza *et al.* [11]	2015	Southern Europe	879	1-7 y	21.7

Almost all studies raported a slight higher frequency of dental trauma in primary teeth in boys than in girls [3, 9, 12-14]. Thus, Arikan *et al.* [12] found that boys were 1.5 times

more likely to receive a dental injury than girls. Vukojevic *et al.* [14] found that the occurence of dental trauma was higher in boys (58.4%), as well as Assuncao *et al.* [3] and Rassmusson & Koch (15) - 57% and de Jesus *et al.* [13] – 54%. In the present study a higher frequency of dental trauma in boys was also found (almost 55%). This higher prevalence may be associated with differences in the types of games played by boys and girls [12], or with more agitated nature of boys compared to girls [13]. However, some studies showed that in primary teeth there does not appear to be a difference between genders [5,16].

Mean number of affected teeth/child was 1.47 and there were no statistically significant differences between sexes. This value was lower than those reported by other authors: de Jesus *et al.* [13] – 1.81; Assuncao *et al.* [3] – 1.57; Vuletic *et al.* [16] -1.69; Vukojevic *et al.* [14] - 2.01.

In this study, dental injuries in primary teeth were more frequent in children from the age group 1-3 years. Children aged 1 were the most affected. Previous studies confirmed that younger children are more susceptible to dental trauma when they are learning to walk, due to the poor muscle coordination. Additionally, their curiosity and lack of danger perception contribute to an increased risk of facial trauma [3,10,12]. These results agree with the findings of other studies [3,12-15]. However, some researches found an increased susceptibility in children between 3 and 5 years, when children' physical activity increases [7,17].

Because of the resilient bone surrounding the primary teeth, the majority of injuries are tooth luxations [7,13]. In this research, luxation injuries were twice more frequent than dental fractures. In studies conducted in pedodontics clinics or emergency centers, luxations were the most prevalent type of trauma in primary teeth: Arikan *et al.* [12] – 72.73%; de Jesus *et al.* [13] – 85%; Vukojevic *et al*. [14] – 84.5%.

Among all types of dental injuries, subluxation, lateral luxation and intrusive luxation were more prevalent. Also, Assuncao *et al.*, in a study performed in 2011 on 679 primary teeth with luxation injuries, reported that the most common types of luxations were subluxation (32.6%), followed by intrusive luxation (29.7%) and avulsion (20.6%) [3]. In change, de Jesus *et al*. [13] and Kovacs *et al.* [5] found that most common injuries were lateral luxation, followed by concussion. Another study conducted by Arikan *et al*. [12] on 99 traumatized primary teeth reported that the most common type of injury was lateral luxation (33.3%), followed by subluxation (14.1%).

According with all previous studies [2,3,8,12,13], dental trauma occured more frequently in the maxillary arch, central incisors being the most affected. The majority of patients had one tooth affected by trauma (61.72%). This finding is consistent with many studies: Rodriguez [18] – 70.9%; Skaare & Jacobsen [9] – 58%. In contrast, Arikan *et al.* [12], in a research conducted on 51 patients, found that most of the patients (58.8%) had more than one tooth injured.

Most of trauma events occured at home or in kindergarten, where children spend the greatest part of their time. This situation was more frequent in children younger than 4. This result underlines the need to inform parents and preschool teachers about injuries in primary teeth. Higher frequency of dental injuries occured at home/kindergarten was also reported by other researchers [9,12].

Falls were the most frequent etiologic factor in traumatized teeth (86.41%), this result being in agreement with other studies [3,5,9,14,16,17]. When considered separately, falling from the child' own height (by walking or running) was the most prevalent cause of dental trauma (45.06%), followed by falling against objects (20.37%). Assuncao *et al*. (2011) found a similar result, but Garcia-Godoy *et al*. (1983), cited by Assuncao *et al*., reported that falling against an object was the most frequent cause of dental injuries [3].

„Monitor only" was the most common treatment among the analized cases, followed by root canal treatment and extraction. In similar studies, Eyuboglu *et al.* [17] and Arikan *et al.* [12] reported that"examination and follow-up" and extraction were the most frequent

treatment methods used. In the study on luxation injuries in primary teeth, Assuncao *et al.* [3] found that"monitor only" was the most common treatment, followed by splinting. Also, Cunha *et al.* [10] reported that"follow-up only" was the most used treatment for dental injuries among babies and todlers.

CONCLUSIONS

1) Dental trauma were more frequent in boys and in children aged 1-3 years;

2) It is necessary to inform parents and educators regarding the high frequency of dental trauma in small children and about the necessity of early treatment.

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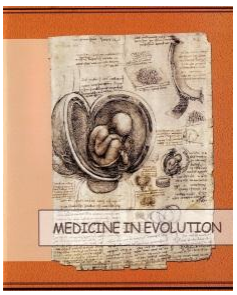
Tooth loss and survival rate in chronic moderate to severe periodontitis. A synthetic search of surgical non-regenerative therapy studies.



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Abstract

Introduction: *in patients suffering of chronic severe generalized periodontitis, there are teeth at borderline, rising up the question of retaining or extracting. According to systems for assigning periodontal prognosis, these are classified as having questionable, unfavorable or hopeless prognosis. It has been shown, that the prognosis can be improved in most of the cases.* ***Objective*** *of this research was to review in a synthetic search the literature reporting the survival analysis (survival rate, tooth loss) of teeth with severe reduced attachment apparatus, and to assess, according to this literature, the ability of long term supportive periodontal care to modify the prognosis from hopeless to unfavorable or questionable.*

Methods: *articles were electronically searched in PubMed and in relevant scientific journals. The filters used referred to full text articles and human studies. The query used in the advanced search offered 1,486 results. Studies were considered for inclusion if limited to patients with moderate to severe periodontitis, who underwent active periodontal therapy (APT) and followed a supportive periodontal care (SPT) program for at least 5 years. Also, they had to report data on tooth loss, diagnosis, prognosis, treatment approach, supportive periodontal treatment, treatment outcome.*

Results: *from the electronic database search and the screening of the reference list of included publications, 18 articles were selected and grouped according to the treatment approach: non-surgical; surgical, non-regenerative therapy; surgical regenerative therapy. 3 articles were selected for the topic non-surgical therapy, and 15 for surgical therapy. In patients treated with surgical non-regenerative procedures alone, the* ***conclusions*** *were: The tooth retention was related to the case type, rather than the surgery performed. Periodontal therapy in conjunction with regular SPT at 3 or 4 months decrease tooth morbidity in patients with advanced periodontitis. Not the bone loss, but bone loss relative to total length is the significant factor for tooth loss. Studies in this this paper were selected for the surgical non-regenerative treatment regimen, and data are synthetized and briefly commented.*

Keywords: *survival rate, tooth loss, long term survival, maintenance, chronic periodontitis, severe periodontitis, questionable teeth, hopeless teeth, surgical regenerative treatment*

INTRODUCTION

The first studies on the importance of supportive periodontal care program were conducted by Oliver (1) and Ross et al. (2). In 1978, Hirschfeld & Wasserman (3) stated that"the main goal of periodontal treatment is the retention of as many teeth as possible in health, function and comfort". Periodontal maintenance care (PMC), also known as supportive periodontal therapy (SPT), is an essential part of the long-term success periodontal treatment, and immediately follows the completion of active periodontal therapy (APT). Periodic recall visits form the base of the maintenance program. Preservation of periodontal health status acquired in the active periodontal phase needs time and efforts from the part of the dentist and the staff. Another essential component is compliance, and this belongs to the patient.

In a systematic review from 2008, Gaunt et al. (4) find that supportive periodontal care delivered in specialist compared with general dental practice will likely result in greater periodontal stability and higher tooth survival rates. In the same review, the cost evaluation analysis based on the Axelsson & Lindhe article from 1981 (5) showed that, for the patient the difference between SPT delivered by the general dentist is an extra 210€ (equivalent) per extra tooth per year over 30 years. PMC includes a group of procedures: update of medical and dental history, extra-and intra-oral soft tissue examination, dental examination, periodontal evaluation, radiographic review, removal of biofilm and calculus, treatment of new or recurrent sites of periodontal disease, establishment of an individualized interval for periodontal maintenance treatment. The purpose of these procedures is to prevent the progression or recurrence of periodontal disease, to reduce the incidence of tooth loss and to increase the probability of diagnosing and treating other diseases found within the oral cavity (AAP 2001). Long-term tooth retention is a fundamental objective of periodontal therapy. Most patients with a history of generalized severe chronic periodontitis that has been recently treated and stabilized are initially placed on a periodontal maintenance therapy program with a 3-month recall interval. The basis for this relatively short interval is the fact that people with a history of severe disease are, by nature, at high risk for recurrence. (6). The predictability of maintenance care program may be associated with diverse conditions, mainly when a patient is exposed to one or more risk factors that influence the host response (7,8). It is worldwide acknowledged that poor compliance with the recall and recare intervals is associated with recurrence/progression of periodontal disease, clinical attachment loss, increasing of probing depths, root caries and tooth loss (5).

Due to the frequency of severe periodontitis among Romanian patients, and the amount of extractions performed by general dentists in severe compromised periodontal patients, a synthetic search was conducted in in the literature, to assess the predictability of different type of periodontal treatment (non-surgical; surgical non-regenerative; surgical regenerative) and the outcomes of these clinical procedures. Therefore, the objective of this paper is to characterize the quantity and quality of the available literature in order to show that severely compromised teeth can be predictably long-term maintained if they are included in a qualitative supportive periodontal treatment. Studies in this paper were selected for the surgical non-regenerative treatment regimen, and data are synthetized and briefly commented.

METHODS

Development of a protocol

This synthetic search was conducted following with modifications a protocol imagined by Miron et al. (9), made prior to the initiation of this search. This protocol included definition of the focused question; a PICO (patient, intervention, comparison, outcome)

question; a defined search strategy; study inclusion criteria; determination of outcome measures; screening methods, data extraction and comparison.

Defining the focused question

How far can be extended the survival rate of teeth with severe reduced attachment apparatus due to periodontal disease, how long and which procedure is more predictable?

PICO question

P: Can patients with severe periodontal disease and severely compromised teeth support

I: undergoing non-surgical/surgical, non-regenerative/ surgical/ regenerative procedures

C: when compared with not treated patients

O: maintain their teeth on long-term?

Search strategy

Articles were electronically searched in the PubMed database and in scientific relevant journals. The filters used referred to full text articles and human studies. Combination of search terms and search strategies were used to find appropriate studies (Table 1).

Table 1. Search criteria for non-surgical treatment

Search Terms
'severe periodontitis' OR 'severe periodontal disease' OR 'moderate periodontotis' OR 'moderate periodontal disease' OR 'periodontal maintenance' OR 'maintenance program' OR ' supportive tratment' OR 'tooth loss' OR 'survival rate' OR 'survival tee' OR 'periodontal prognosis'
AND
'nonsurgical' OR 'non-surgical'

Table 2. Search criteria for surgical but non-regenerative treatment

Search Terms
'severe periodontitis' OR 'severe periodontal disease' OR 'moderate periodontitis' OR 'moderate periodontal disease' OR 'periodontal maintenance' OR 'maintenance program' OR ' supportive tratment' OR 'tooth loss' OR 'survival rate' OR 'survival tee' OR 'periodontal prognosis'
AND
'surgical' OR 'open flap' OR 'open- flap' OR 'gingivectomy' OR 'resective surgery' OR 'osseous surgery' OR 'widman flap' OR intrabony defect' OR 'intra-bony defect' OR 'intrabony pocket' OR 'intra-bony pocket' OR 'infrabony defect' OR 'infra-bony defect' OR 'infrabony pocket' OR 'infra-bony pocket' OR 'intraosseous defect' OR 'intra-osseous defect'

Table 3. Search criteria for surgical, regenerative treatment

Search Terms
'severe periodontitis' OR 'severe periodontal disease' OR 'moderate periodontotis' OR 'moderate periodontal disease' OR 'periodontal maintenance' OR 'maintenance program' OR ' supportive tratment' OR 'tooth loss' OR 'survival rate' OR 'survival tee' OR 'periodontal prognosis'
AND
'surgical' OR 'open flap' OR 'open- flap' OR 'regenerative surgery' OR intrabony defect' OR 'intra-bony defect' OR 'periodontal regeneration' OR 'intrabony pocket' OR 'intra-bony pocket' OR 'infrabony defect' OR 'infra-bony defect' OR 'infrabony pocket' OR 'infra-bony pocket' OR 'intraosseous defect' OR 'intra-osseous defect' OR 'guided tissue regeneration' OR 'GTR' OR ' guided bone regeneration ' OR 'GBR'

The query used in the advanced search offered 1,486 results, according to the topic of this search:

((((periodontal [All Fields] AND (care[All Fields] OR ("maintenance"[MeSH Terms] OR"maintenance"[All Fields]) OR program[All Fields])) or survival[Title/Abstract]) or loss[Title/Abstract]) AND ((moderate[All Fields] OR severe[All Fields]) AND ("periodontitis"[MeSH Terms] OR"periodontitis"[All Fields]))) NOT apical[All Fields].

A hand search was conducted through the Journal of Clinical Periodontology, Journal of Periodontology, Journal of Periodontal Research, Periodontology 2000 from November 2016, until August 2017. The reference list of the selected articles was screened.

Criteria for study selection and inclusion

All the studies selected had to be written in English. They had to be full-text articles and to be human studies. No reviews were included. Studies were considered for inclusion if were limited to patients with moderate to severe periodontitis, who underwent active periodontal therapy (APT) and followed a supportive periodontal care (SPT) program for at least 5 years. Also, they had to report data on tooth loss, survival rate, diagnosis, prognosis, treatment approach, supportive periodontal treatment, treatment outcome. In the end, from the electronic database search and the screening of the reference list of included publications, 18 articles were selected. The 9 articles were grouped according to the treatment approach: surgical, non-regenerative therapy.

Outcome measure determination

The main outcome was tooth loss during SPT. Second endpoints were the change of prognosis and the survival rate.

Screening method

Titles and abstracts of the selected articles were screened by the first author (VR) based on the question:"which are the long term results of different treatment procedures involving non-surgical/surgical but non-regenerative/surgical regenerative procedures at severely periodontal compromised patients? Full-text articles were obtained if the follow-up period was at least 5 years, and if the outcome of the treatment was described in at least two terms of the following: tooth loss during SPT, tooth loss during APT, change of prognosis, survival rate.

Data extraction and analysis

The following data were extracted: the main author's name, the study design, the number of patients, the number of teeth, the setting where the clinical procedures were performed, the presence of systemic diseases, initial SPT prognosis, last SPT prognosis, the period of SPT, recall intervals, compliance, administration of antibiotics, the population of the study description (age range, mean age, gender), smoking habits, inclusion of the third molar, if the teeth considered in the study were abutment teeth or not, the furcation involvement, the kind of treatment the patient underwent, initial extraction, tooth loss during SPT and which of them were lost for periodontal reason and survival rate. Due to the reduced number of articles, no meta-analysis was performed. Instead, the data is reported in a synthetic fashion with an overview of all studies fitting the search descriptions. The articles selected for this synthetic search were summarized in tables, according to the type of the treatment the patient underwent: surgical non-regenerative.

RESULTS AND DISCUSSIONS

For this approach, the search criteria resulted in 9 relevant studies. The survey of Hirschfeld & Wasserman (3) is a summary of long term tooth survival. It is considered the landmark study of tooth loss due to periodontal reason. 600 patients were re-examined in a private practice, with 1464 teeth after APT and SPT. A tooth was considered to have a"questionable prognosis" if there were present: furcation involvement, a non-eradicable pocket, severe bone loss and marked mobility with pocket depth. Only tooth-related factors were considered. The severity of periodontitis at the initial exam was classified: early, intermediate and advanced. The response to the treatment differed among patients and they were grouped into"response groups": well-maintained (0 to 3 teeth lost), downhill (4 to 9 teeth lost) and extreme downhill (10 to 23 teeth lost). Regarding the surgical treatment, surgically fibrotic cases were treated more often than edematous cases. The mobility was treated by selective grinding, occlusal night guards or fixed splinting. During the mean 22 years period of supportive therapy, 7.1% of teeth were lost due to periodontal reasons, while 1.2% due to other reasons. Despite that in the well-maintained group half of the sample lost no tooth during 22 years of regular supportive therapy did not prevent the loss of 20.5% teeth,

which had initially an early disease form. Only 31.1% of the teeth marked with questionable prognosis were lost, each group having a different pattern of loss. From the 387 mandibular molars with furcation involvement, 246 were retained over 22 years. 83% of patients treated for periodontal disease and maintained for more than 15 years in a specialist practice lost fewer than 4 teeth (well-maintained). However, the rate of tooth loss varied from 12% in well-maintained, 55% in downhill group and 92% in the extreme downhill group. A bilateral symmetry of loss on the right and left side and a predictable order according to their position on the arch were remarked. Regarding the periodontal surgery, the tooth retention was related to the case type, rather than the surgery performed.

In 2000, Tonetti et al. (10) investigated the prevalence of tooth loss and the dental pathologies associated with tooth extraction during active periodontal treatment (APT) and supportive periodontal therapy (SPC). The reasons for extraction were classified as following: periodontal disease, caries, endodontic problems and technical failures (root fractures). Severe periodontal disease was associated with 57%, perio was associated with 14%, and caries, endodontic or technical failures with 29% of tooth extractions in the studied population. It was noted that an increased number of extractions during APT decreases the incidence of tooth loss during SPC, while maintaining compromised teeth increases the incidence of tooth loss during SPC. The incidence of tooth loss was 0.17 per patient per year, relatively similar with the 0.11 teeth per patient per year of Hirschfeld & Wasserman study from 1978. The study suggested that initial extraction should be considered to compare the overall impact of comprehensive therapy on tooth loss.

Checchi et al. (11) assessed the dental prognosis at the beginning of SPT and at the end of observation period as follows: questionable in 26.54% and 24.04%, respectively; hopeless in 8.91% and 7.78% respectively. In their study, each patient received surgical therapy consisting of osseous surgery to recreate positive bony architecture, or open flap debridement without bone contouring in advanced lesions. The results yielded 0.07 teeth per year lost due to periodontal reasons, which is comparable with the data of the Hirschfeld & Wasserman study from 1978, (0.08 teeth/year). These results suggested that periodontal therapy in conjunction with regular SPT at 3 or 4 months decrease tooth morbidity in patients with advanced periodontitis. Also, it was concluded that a low mortality rate appears in patients following APT combined with a strict and regular periodontal care.

Table 4. Details of the included studies from 1978 - 2002: surgical, non- regenerative therapy

Study	Hirschfeld & Wasserman	Tonetti et al.	Checchi et al.
Year of publication	1978	2000	2002
Study design	Retrospective	Retrospective	Retrospective
Number of patients	600	273	92
Number of teeth	1464	6503	2310
Operator	University	University	Private
Diagnosis	Generalized Chronic Periodontitis early: PD< 4mm, 7%, intermediate: PD 4-7mm, 16.5% advanced: PD > 7mm 76.5%	48.4% moderate 24.9% advanced	9.8% moderate 90.2 advanced
Systemic disease	Not reported	Excluded	Not reported
Initial SPT Prognosis	Questionable teeth 2139 at baseline	Not reported	Questionable 26.54% Hopeless 8.91%
Last SPT Prognosis			Questionable 24.04% Hopeless 7.78%
SPT	15- 55 years Mean: 22 years	67	80.4
Recall interval	4- 6 months	3 months	3-4 months

Compliance	Well-maintained 83.2% Downhill 12.6% Extreme downhill 4.2%	Not reported	64% regular attenders 36% irregular
Antibiotics	No	No	No
Age range	12- 73	16-81	28-65
Mean age	42.2	Not reported	45
Gender		59% female	Not reported
Smoking	Not reported	Current 39.6% Former 27.8%	Not reported
3rd molar inclusion	Included	Excluded	Not reported
Abutment teeth	Fixed and removable prostheses	Determined but not reported	Not reported
Furcation involvement	Multirooted maxillary 867/ mandibular 597 with FI were lost 284/176	Not reported	Root resection Tunneling Hemisection
Surgical treatment	Gingivectomy Osteoplasty Flap surgery 16% of each group had surgery	Modified Widman Flap	OFD Respective osseous surgery
Initial extraction (APT)		311	126
Teeth loss during SPT	8.3%	263	50
No of teeth loss during SPT per year	0.08	Not reported	0.07
Periodontal reason	7.1%	64%	44%
Survival rate	68.8%	Not reported	Not reported

Fardal et al. (7) investigated factors associated with tooth loss due to periodontal reasons during SPC in a Norwegian specialist periodontal practice. In the study, 1.5 % of the teeth present at the end of APT were lost during SPT. 9% of those with poor prognosis and 67% of those with hopeless initial prognosis were lost during the observation period. Smokers, older age and male gender showed the highest rate of tooth loss in the sample studied. The change in prognosis between the APT and at the end of observation period was assessed: 202 teeth were considered to worsen over the period, and it was not always possible to anticipate a tooth loss, even for teeth with initial good prognosis.

Chambrone et al. (8) noted that from the population of their study, 120 subjects with 2,927 teeth, only 53 teeth (1.8%) were lost during the average duration of SPT of 17.4 years, and thus, only a minority of treated patients (8.4%) was responsible for more than a half of tooth extractions (51.3%) during SPT. For periodontitis, the average of tooth loss per patient was 0.44. The authors found that smokers, older subjects, males, patients who followed periodic SPT for at least 20 years and patients who returned once a year for maintenance recall visits had experienced the highest percentage of tooth loss due to periodontal reasons.

Carnevale et al. (12) described in their study the prevalence and reasons of tooth extraction during APT and SPC in periodontal patients. During APT, non- surgical periodontal treatment and fiber retention osseous resective surgery were performed (FibReORS, Carnevale et al. 2007) where needed, in order to obtain sites with PD≤3 mm. During APT, 576 (7.5%) teeth were extracted, 44% of them due to advanced periodontitis. The number of tooth extractions was higher in cases with severe periodontitis. During SPT, 67 teeth were removed (0.95% of the present teeth, following completion of APT), the average being 0.22 teeth per patient.

Table 5. Details of the included studies from 2004 to 2007: surgical, non- regenerative therapy

Study	Fardal et al.	Chambrone et al.	Carnevale et al.
Year of publication	2004	2006	2007
Study design	Retrospective	Retrospective	Retrospective
Number of patients	100	120	304
Number of teeth	2436	2927	7696

Operator	Private	Private	Private
Diagnosis	81% moderate 8% severe	Generalized chronic periodontitis	Moderate periodontitis 45% Severe periodontitis 41%
Systemic disease		Excluded	Not reported
Initial SPT Prognosis	Uncertain 14.2% Poor 4.2% Hopeless 0.4%	Not reported	Not reported
Last SPT Prognosis	25% from uncertain to poor	Not reported	Not reported
SPT	9-11 years	10-36 years	3-17 years
Recall interval	3-6 months	Mean frequency 9.4 months	Mean 3.4 months
Compliance	98% well maintained 2% downhill	Not reported	
Antibiotics	Yes	Not reported	Not reported
Age range	25-69	20- 72	25-85
Mean age	46	38.9	52
Gender	68 females, 32 males	47 males, 73 females	193 females, 111 males
Smoking	Current 38% Nonsmoker 62%	Nonsmokers 100 Smokers 20	Current, former, never
3rd molar inclusion	Included	Included	37% of the exctraction during APT- 3rd molar
Abutment teeth	Not reported	Not reported	59.8% of pockets
Furcation involvement	Not reported	Not reported	Recorded but not reported
Surgical treatment	When needed Not specified what type	When indicated	Apically positioned flap with osseous respective surgery and gingival fiber retention
Initial extraction (APT)	Not reported		576(44% perio, endopario)
Teeth loss during SPT	36	111	67(60% prosthetic abutment)
No of teeth loss during SPT per year	0.04	0.05	0.02
Periodontal reason	75%	47.7%	30% perio
Survival rate	Not reported	Not reported	Not reported

Tooth-related factors contributing to teeth loss were assessed by Pretzl et al. (13). The evaluation was conducted at tooth level (baseline bone loss, tooth type, furcation involvement, abutment status) and patient level (Interleukin- 1 polymorphism, compliance to SPC, mean plaque scores during SPC). In patients attending recall visits regularly, 93% of teeth exhibiting baseline bone loss 60-80% of root length survived 10 years. Authors found that furcation-involved teeth have worse prognosis (13% tooth loss) than single-rooted teeth (5%) or multirooted teeth without furcation involvement (10%). Teeth used as abutments for fixed or removable dentures before periodontal treatment showed higher mortality than teeth that were not abutments, removable dentures having a worse effect than fixed dentures. This observation should be considered before extracting"hopeless" teeth. It was found that some of these"hopeless" teeth may have had a better prognosis than those teeth that were required and used as abutments. This observation confirmed and underlined the significance of the concept of"shortened arches". Authors stated that"not the bone loss, but bone loss relative to total length is the significant factor for tooth loss". Only 14% of the teeth considered

initially"hopeless" at initial exam were lost in regular SPT group due to periodontal reasons, and 86% of"hopeless" teeth survived 10 years. In the irregular PST group, 39% of"hopeless" teeth were lost.

In 2008, Matuliene et al. (14) investigated the influence of residual probing pocket depth (PPD) ≥ 5 mm and bleeding on probing (BOP) after APT on the progression of periodontitis and tooth loss. The prevalence of PPD=4 mm was reduced from 8.0% to 5.8%, while the prevalence of PPD≥5 mm increased from 2.9% to 4.3% during the maintenance period. Increased PPD was strongly associated with tooth loss. Authors found that, with the exception of the step between PPD = 5 mm and 6 mm, the increase by 1 mm PPD increased the odds, and therefore the probability, of tooth loss in a statistically significant way. The authors concluded that residual PPD≥6 mm represent an incomplete periodontal treatment outcome and require further therapy.

Ng et al. in 2011 (15) investigated the incidence and reasons for tooth loss during APT and SPC. They grouped the patients in"all compliers" (AC), (regular compliers and irregular compliers) and"non-compliers" (NC)."All compliers" lost during SPC 0.9 teeth/patient/year; the tooth loss due to periodontal reasons was 0.03 teeth/patient/year."Non-compliers" lost 2.7 teeth/patient during discontinuation; tooth loss due to periodontal reasons was 0.22 teeth/patient/year, seven times bigger than"all compliers".

There is a bilateral symmetry of loss on the right and left side and a predictable order according to their position on the arch. The tooth retention was related to the case type, rather than the surgery performed. Initial extraction should be taken into account to compare the overall impact of comprehensive therapy on tooth loss. Periodontal therapy in conjunction with regular SPT at 3 or 4 months decrease tooth morbidity in patients with advanced periodontitis. It is not always possible to anticipate a tooth loss, even for teeth with initial good prognosis. Smokers, older subjects, males, patients who followed periodic SPT for at least 20 years and patients who returned once a year for maintenance recall visits experienced the highest percentage of tooth loss due to periodontal reasons. Not the bone loss, but bone loss relative to total length is the significant factor for tooth loss. Residual PPD≥6 mm represent an incomplete periodontal treatment outcome and require further therapy.

Table 6. Details of the included studies from 2008 – present day: surgical, non- regenerative therapy

Study	Pretzl et al.	Matuliene et al.	Ng MC-H et al.
Year of publication	2008	2008	2011
Study design	Retrospective	Retrospective	Retrospective
Number of patients	100, respondent rate 71%	172	273 compliers 39 non-compliers 34 irregular compliers
Number of teeth	2301	4138 teeth 24828 sites 31> 5 mm	6199
Operator	University	University 98 Private 73	University
Diagnosis	Moderate ChP 30 Severe ChP/AgP 60/10	Severe periodontitis 89%	Mild 64, moderate 211 or severe 37 by attachment loss
Systemic disease	Not reported	Included, diabetes mellitus type 2, rheumatic diseases, HCD(heart and circulation disease)	Diabetes type II included
Initial SPT Prognosis	Good 80% Questionable 385 Hopeless 122	Not reported	Not reported
Last SPT Prognosis	93% of teeth with 60-80% (questionable) bone loss survived 10 years	Not reported	Not reported
SPT	10 years±6 months	3-27 years.	7- 20 years

		Mean 11.3 years	Mean 10.9
Recall interval	3-6 months	3-12 months in private practice	Not reported
Compliance	Regular 1245 Irregular 1056	Increased in University 94.9% 2-4 months interval in SPT	Compliers 239 Non-compliers 39 Irregular compliers 34
Antibiotics	Not reported	Not reported	Amoxicilin and/or metronidazole
Age range	Not reported	16-69	19-80
Mean age	46.5	45±11 years	44.5
Gender	59 females, 41 males	95 females, 77 males	183 females, 129 male
Smoking	Current, former, never	Current 33.1% Former 24.5%	Light smokers, moderate, heavy, ex-smokers
3rd molar inclusion	Excluded	Not reported	Erupted included
Abutment teeth	232 for FDP 67 for removable	Not reported	Not reported
Furcation involvement	390 of 699 multirooted	Not reported	Multi-rooted/ single-rooted 69.9%/ 31.1%
Surgical treatment	If required	If required	When required
Initial extraction (APT)	155 (29 in regular SPT, 126 in irregular)	303 50.8%	308
Teeth loss during SPT	Regular SPT 29 Irregular SPT 126	294 49.2%	228
No of teeth loss during SPT per year	0.15	0.17	0.09
Periodontal reason	Not reported	Not reported	73(32%)
Survival rate	Not reported	Not reported	Not reported

CONCLUSIONS

There is a bilateral symmetry of loss on the right and left side and a predictable order according to their position on the arch. The tooth retention was related to the case type, rather than the surgery performed. Initial extraction should be taken into account to compare the overall impact of comprehensive therapy on tooth loss. Periodontal therapy in conjunction with regular SPT at 3 or 4 months decrease tooth morbidity in patients with advanced periodontitis. It is not always possible to anticipate a tooth loss, even for teeth with initial good prognosis. Smokers, older subjects, males, patients who followed periodic SPT for at least 20 years and patients who returned once a year for maintenance recall visits experienced the highest percentage of tooth loss due to periodontal reasons. Not the bone loss, but bone loss relative to total length is the significant factor for tooth loss. Residual PPD≥6 mm represent an incomplete periodontal treatment outcome and require further therapy.

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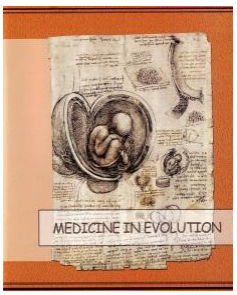
The maxillary and mandibular dental arch forms in different classes of malocclusion in a group of patients from the western part of Romania



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Abstract

Aim: The objective of this study was to determine the shape of the maxillary and mandibular dental arches in Angle Class I, II, and III malocclusions in a group of patients in the western part of Romania. The study was descriptive, non-experimental and transversal.

Material and methods: A total of 75 patients with ages between 12 and 39 years were clinically examined over a period of 3 years and divided into 3 groups (25 patients in each group) according to Angle's classification of malocclusion (Class I, II and III). Exclusion criteria: missing teeth (with the exception of third molar), removable partial denture prostheses, extensive prosthetic restorations, orthognathic surgery and those who refused to participate. The shape of the dental arches was determined on study models using orthodontic archwires overlaid on the occlusal surfaces of the teeth, following the arch perimeter. The archwires were chosen according to the OrthoForm™ (3M Unitek, USA) archwire templates. The results were related to the type of malocclusion.

Results: In all of the three groups, the dominant shape of the maxillary and mandibular arches was the tapered shape, followed by the ovoid and the square shape.

Conclusions: Dental arch shape is a very important factor that must be taken into account in orthodontic treatment planning, because it plays an important role in maintaining the stability of the treatment results.

Keywords: *dental arch form, malocclusion, orthodontic archwire template*

INTRODUCTION

The dimensions and the shape of the dental arches have an important role in orthodontic diagnosis and treatment planning. These parameters influence the aesthetics, the available space and the stability of the dentition [1].

A correlation between the size and the shape of the dental arches and malocclusion (Angle Class I, II and III) may be observed both in the maxillary and in the mandibular dental arches. The literature reported several correlations between the shape of the dental arches, the facial type and the type of malocclusion.

Different methods have been proposed to assess the morphology of the dental arch from simple classifications of the arch form [2] to linear measurements [3,4] and complex mathematical equations [5,6].

Chuck [7] was the first to classify the shape of the dental arches as tapered, square and ovoid.

Orthodontic treatment planning should consider the pre-treatment arch form of each patient and the ethnic group the patient belongs to in order to achieve aesthetic, functional and stable dento-alveolar relationships [1,3].

Aim and objectives

The present study is descriptive, non-experimental and transversal and its main objective was to determine the shape of the maxillary and mandibular dental arches in Angle Class I, II, and III malocclusions in a group of patients from the western part of Romania using arch wires templates on study models.

MATERIAL AND METHODS

A total of 75 patients from the western part of Romania, with ages between 12 to 39 years were clinically examined, over a period of 3 years, in the Department of Orthodontics, Faculty of Dental Medicine, Victor Babes University of Medicine and Pharmacy in Timisoara.

The patients were divided into 3 groups (25 patients in each group) according to Angle's classification of malocclusions (Class I, II and III).

Exclusion criteria: missing teeth (with the exception of the third molars), removable partial dentures, extensive prosthetic restorations, previous orthodontic treatment, orthognathic surgery and those who refused to participate.

The same clinical and paraclinical examination protocol was used to diagnose the type of malocclusion. For each patient, alginate impressions of the maxillary and mandibular arches ware taken and hard plaster study models were cast from the impressions within 6 hours.

The shape of the dental arches was determined on the study models using orthodontic archwires overlaid on the occlusal surfaces of the upper and lower teeth, following the arch perimeter. The archwires were chosen according to the OrthoForm™ (3M Unitek, USA) archwire templates (Figure 1), because these templates covered the most common arch forms. In this study we used Unitek™ Beta Titanium archwires (0.019 by 0.025 inch) corresponding to each type of OrthoForm archwire template. The results were related to the type of malocclusion.

The same method was used to identify the shape of all dental arches on all 75 study models (Figure 2, 3 and 4).

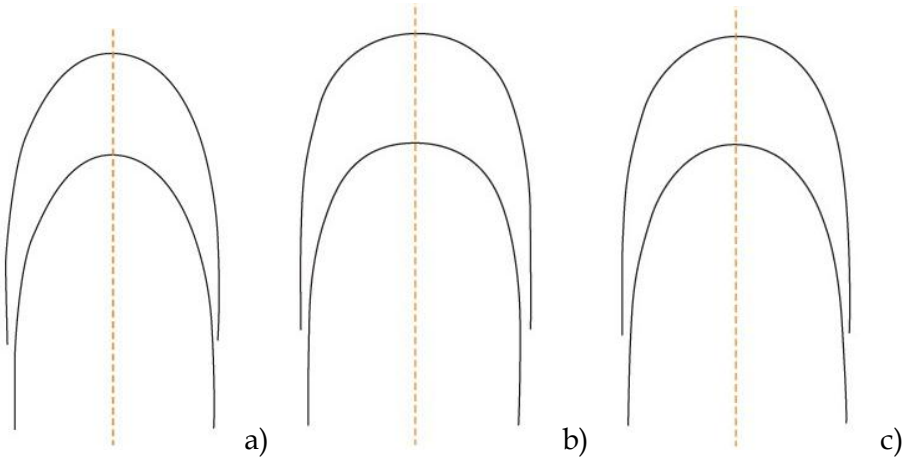

Figure 1. The types of the arch wires templates OrthoForm™ (3M Unitek): a) OrthoForm I (tapered arch form); b) OrthoForm II (square arch form); c) OrthoForm III (ovoid arch form)

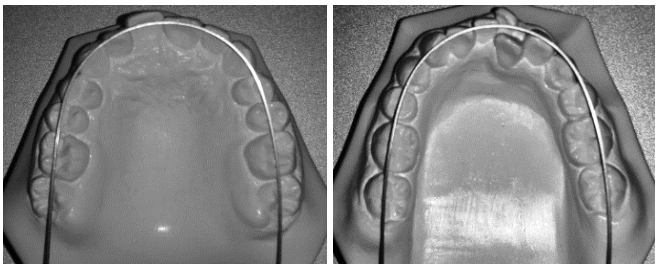
Figure 2. Square shaped maxillary and mandibular dental arches in Angle class I malocclusion

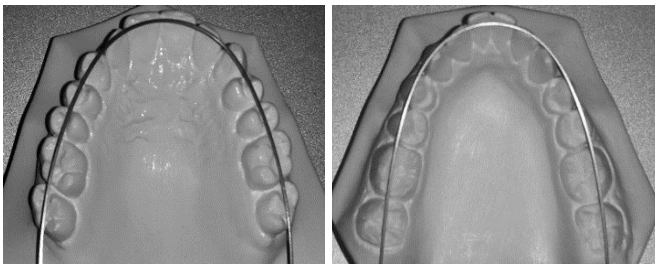
Figure 3. Tapered shaped maxillary and mandibular dental arches in Angle class II malocclusion

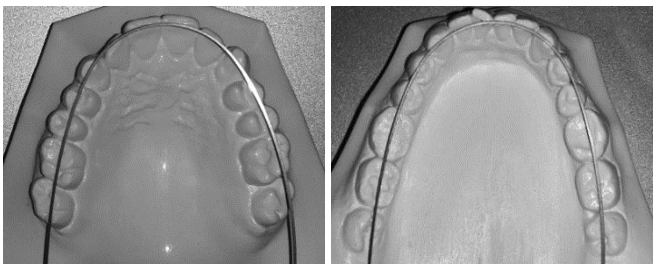
Figure 4. Tapered shaped maxillary and ovoid shaped mandibular dental arches in Angle Class III malocclusion

RESULTS

The 25 patients included in the group with Angle Class I malocclusion (Figure 5) had the following maxillary dental arch forms: tapered (60%), ovoid (36%) and square (4%). In the same group, the mandibular arch forms were as follows: tapered (60%), ovoid (28%) and square (12%).

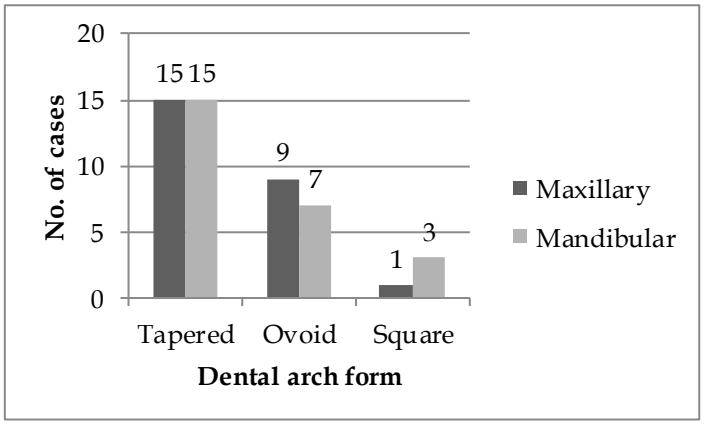

Figure 5. The dental arch form in the group with Angle Class I malocclusion

The 25 patients included in the group with Angle Class II malocclusion (Figure 6) had the following maxillary dental arch forms: tapered (44%), ovoid (36%) and square (20%). In the same group, the mandibular arch forms were as follows: tapered (52%), ovoid (24%) and square (24%).

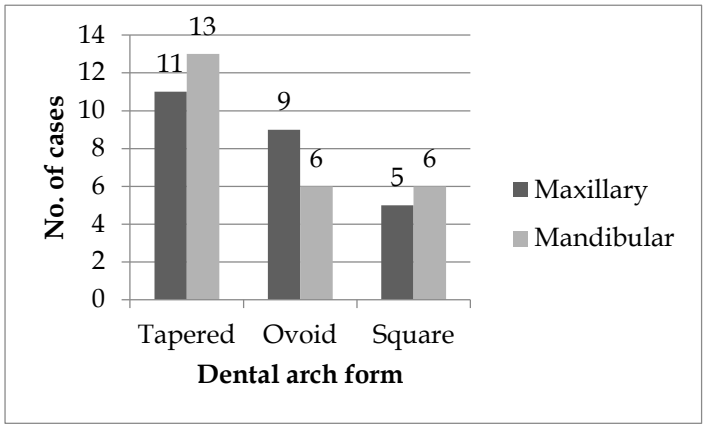

Figure 6. The dental arch form in the group with Angle Class II malocclusion

The 25 patients included in the group with Angle Class III malocclusion (Figure 7) had the following maxillary dental arch forms: tapered (56%), ovoid (36%) and square (8%). In the same group, the mandibular arch forms were as follows: tapered (20%), ovoid (40%) and square (40%).

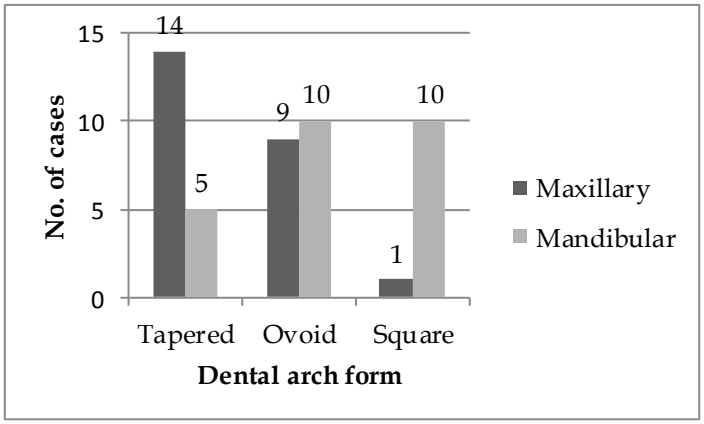

Figure 7. The dental arch form in the group with Angle Class III malocclusion

DISCUSSIONS

The aim of our study was to determine the shape of the maxillary and mandibular dental arches in Angle Class I, II, and III malocclusions and our results showed that in all of the three groups, the dominant shape of the maxillary and mandibular arches was the tapered shape, followed by the ovoid and the square shape.

Olmez and Dogan [3] found similar results in a group from the Turkish population and concluded that the most common dental arch shape is the tapered form, regardless of the malocclusion type. The next most common shape was the ovoid one, followed by the square arch shape. The same study shows that there are no significant differences between Angle Class I and Class II malocclusions.

The shape and size of the dental arches were also analysed in a study published by Burris and Harris [8]. Comparing the dental arches in native white American and Afro-American population, they noticed that the square shaped dental arches were more common in blacks, while the tapered shaped ones were more common in whites. They did not take into consideration the gender differences.

In 2004, Guerrero and Améstica [9] published a research about the mandibular dental arch shape, based on a study conducted on 103 young people in Chile, using 3M Unitek archwires. The tapered shape was found in 26% of the cases, the square shape in 35% of the cases and the ovoid shape in 39% of the cases.

When comparing the maxillary arch forms (square, tapered and ovoid) according to different classes of malocclusion in Jordanian population, the most common arch form in Class I was the ovoid shape, followed by the tapered shape, while in Class II and Class III subjects, the most common arches had a tapered shape [10]. These results suggested that the ovoid shape should be taken into consideration in Class I cases and the tapered shape should be considered when dealing with Class II and Class III cases [10].

There is always a chance for errors when assessing the shape of the dental arches based on the standardized shape decided by the manufacturer, therefore the present study may provide reference data on the arch dimensions of the fully dentate population for future comparisons, since these parameters have a high impact on orthodontic rehabilitation.

CONCLUSIONS

The dominant shape of the maxillary and mandibular arches was the tapered shape, followed by the ovoid and the square shape in all the three classes of malocclusion (Angle Class I, II and III).

Dental arch shape is a very important factor that must be taken into account in orthodontic treatment planning, because it plays an important role in maintaining the stability of the treatment results.

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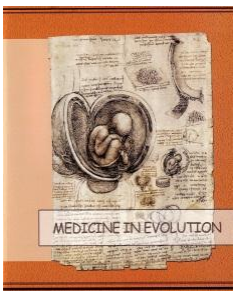
The evaluation of an impacted maxillary canine before and during orthodontic traction using conventional and cbct imaging: a case report



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Abstract

Objective: The aim of this case report was to highlight the advantages of cone beam computed tomography (CBCT) imaging over conventional 2D radiographs in providing accurate data related to the localization of impacted maxillary canines and their relation with the adjacent anatomical structures.

Case presentation: An initial orthopantomography and a CBCT exam confirmed the impaction in palatal position of the maxillary left canine 2.3 in a 15-year-old female patient. The intraoral exam showed the retention of the temporary canine 6.3. After thoroughly assessing the position of 2.3 and the resorption degree of the lateral incisor 2.2, we decided to extract 6.3, to surgically expose the crown of 2.3 and to use the tunnel traction technique combined with orthodontic braces. To minimize the risk of further root resorption of 2.2, we used light disto-occlusal forces, followed by buccal forces. A follow-up CBCT scan was taken after 10 months of treatment to reassess the position of the impacted canine, using angular and linear measurements. After 18 months of active treatment, the impacted canine was aligned in the dental arch.

Conclusions: When compared to conventional 2D radiographs, the use of CBCT imaging offered additional relevant data which positively influenced the treatment planning and the treatment outcome.

Keywords: *impacted maxillary canine, CBCT, orthodontic treatment, tunnel traction*

INTRODUCTION

The permanent maxillary canines have an important role not only in facial and dental aesthetics, but also in functional occlusion and in the proper development of the dento-alveolar arches.

Permanent maxillary canines have the highest frequency of impaction after the third molars, with a prevalence rate of 1% to 3% [1,2]. Impacted canines are twice as prevalent in women than in men [3].

Ericson and Kurol [18] in 1988

defined number of sectors to denote different types of impaction

Ericson and Kurol [18] in 1988

defined number of sectors to denote different types of impaction

Both conventional radiographs and cone beam computer tomography (CBCT) imaging can provide important data, in order to evaluate the degree of difficulty of the treatment and, implicitly, to approximate the time required to align the impacted canine on the arch. Using orthopantomographies, Lindauer et al. [4] devised a simple method to assess the position of the tip of the cusp of the canine in relation with the contour of the lateral incisor.

In order to maintain the periodontal health, Crescini et al. [5] proposed a combined surgical-orthodontic treatment, called the tunnel traction technique, which can be used when the retention of the corresponding temporary canines provides enough space for the guided eruption of the impacted canines.

The aim of this case report was to highlight the advantages of CBCT imaging over conventional 2D radiographs in providing accurate data related to the localization of impacted maxillary canines and its relation with the adjacent anatomical structures.

CASE PRESENTATION

A 15-year-old female patient (C.G.) presented to the Department of Pedodontics and Orthodontics, at The Faculty of Dental Medicine in Timisoara for esthetic and functional reasons.

Anamnesis

The patient had no significant medical history and there were no relevant heredocolateral and personal pathological antecedents. There was no history of trauma or other local factors that could have interfered with the normal development of the dento-maxillary system.

Clinical examination data

The intraoral examination showed the following findings: the retention of the temporary canine 6.3, dental anomalies of position in the anterior region (1.2 in distorotation, diastema with divergent crowns, isolated microdontia of the upper lateral incisors), Angle Class I molar relationships on both sides, Class II canine relationships on the right side, a deep overbite and a normal overjet (Figure 1).

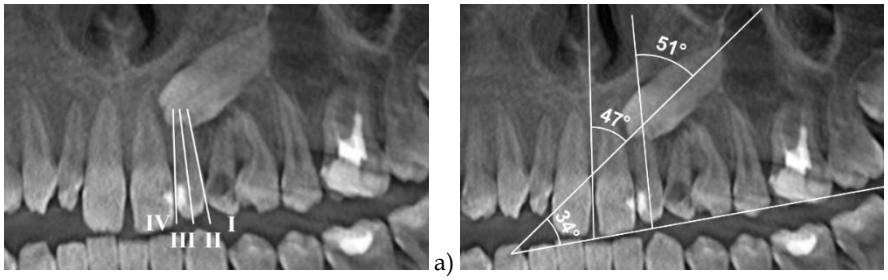
Figure 1. Initial intraoral examination: a) frontal view; b) lateral view (right); c) lateral view (left)

Additional paraclinical investigations

Conventional radiological exams (orthopantomography) and an initial CBCT exam confirmed the presumptive diagnosis of palatal impaction of the permanent upper left canine 2.3.

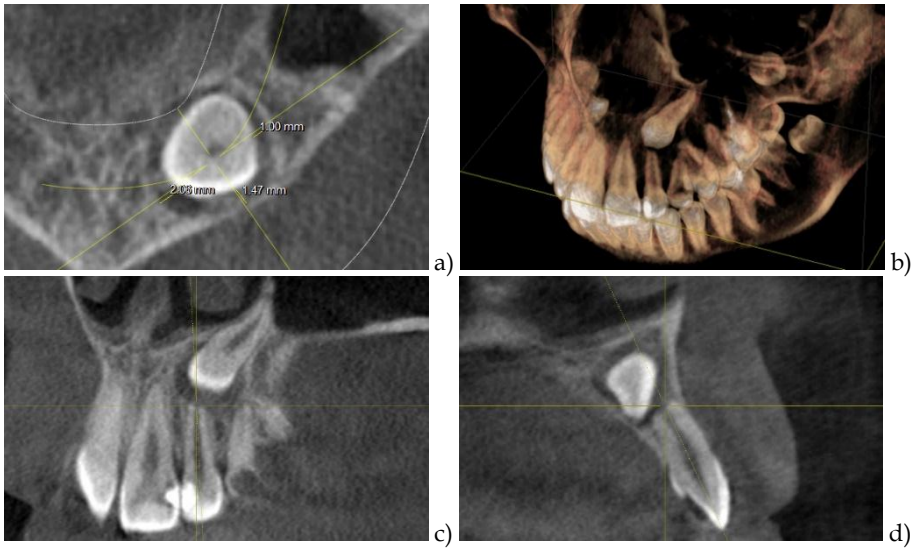
Several angular and linear measurements were done to evaluate the position of the impacted canine in relation with the occlusal plane, the mid-sagittal line and the long axis of the lateral incisor, the position of the crown and the dental follicle relative to the adjacent anatomical structures (Figure 2 and 3).

The impacted canine 2.3 had a palatal position in relation with the apex of the root of 2.2 (Figure 3.d). The dilacerated root (mesially curved) of the upper left first premolar 2.4 was also observed.



a) b)

Figure 2. Initial orthopantomography: a) the tip of the cusp of the impacted canine 2.3 is positioned in sector IV in relation with the upper lateral incisor 2.2; b) angular measurements in relation with the occlusal plane, the mid-sagittal line and the long axis of the lateral incisor



a) b) c) d)

Figure 3. Initial CBCT exam: a) axial view of the crown of the impacted canine 2.3 and the position of the dental follicle relative to the adjacent structures; b) 3D image reconstruction; c) cross-sectional view showing the reduced degree of resorption of the apex of 2.2; d) cross-sectional view showing the palatal position of the crown in relation with the apex of 2.2.

Treatment and evolution

Considering the age of the patient, the treatment of choice was fixed orthodontic appliances (braces) in order to correct the dento-alveolar anomalies.

After thoroughly assessing the position of the impacted canine 2.3 and its relation with the lateral incisor 2.2, we decided to adopt a combined surgical-orthodontic technique to align 2.3 on the arch. The first step was the extraction of the temporary upper left canine 6.3. The next step consisted in the surgical exposure of the crown of 2.3 through a buccal mucosal incision, the ostectomy of the buccal alveolar bone covering the crown of 2.3 and the removal of the follicular envelope. An orthodontic bracket was bonded to the most accessible surface

of the crown (Figure 4.a). We opted for the use of the tunnel traction technique, therefore a ligature wire was attached to the bonded bracket and was guided through the extraction site of 6.3.

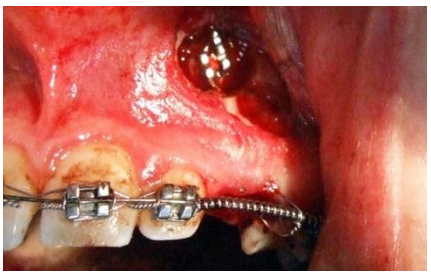
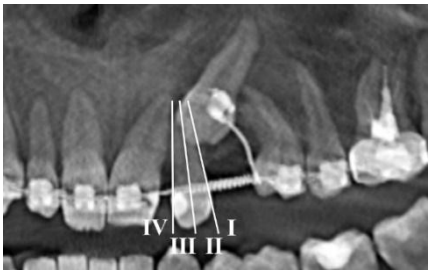


Figure 4. Intraoperative view: the extraction of 6.3, the surgical exposure of the crown of 2.3; a wire ligature was used to traction 2.3 using the tunnel traction technique

We used light disto-occlusal traction forces, followed by buccal forces, in order to reduce the risk of further root resorption in the upper lateral incisor 2.2.

After 10 months of treatment, follow-up radiological exams were performed to reassess the position of the impacted canine (Figure 5 and 6). No further discernable root resorption was observed in the adjacent teeth.

After 18 months of active treatment, the impacted canine was aligned in the dental arch (Figure 7).



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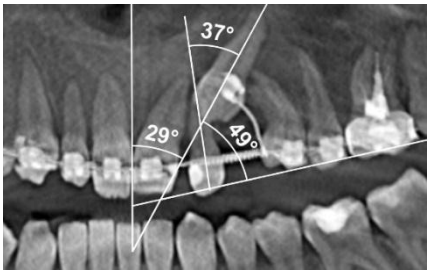
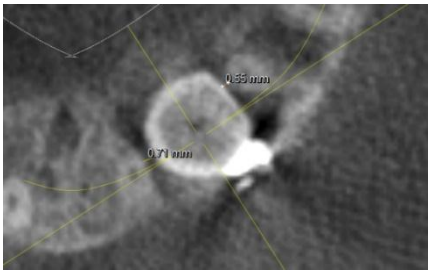


b)

Figure 5. Follow-up (10 months) orthopantomography: a) a more favorable position of the tip of the cusp of the impacted canine 2.3, which was located in sector II in relation with the upper lateral incisor 2.2; b) angular measurements showing the improved position of the impacted canine 2.3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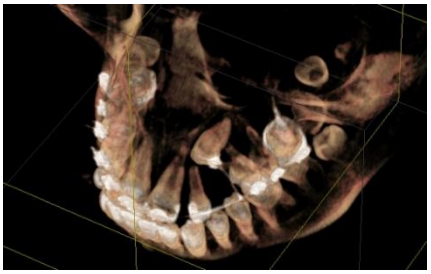
b)

Figure 6. Follow-up (10 months) CBCT exam: a) axial view showing the close proximity of the crown of 2.3 to the apex of the root of 2.2 and 2.4; b) 3D image reconstruction

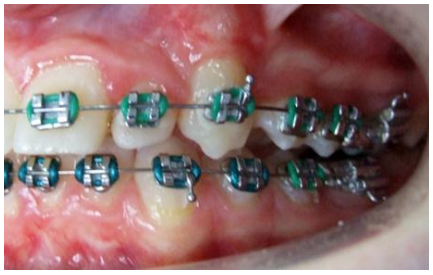

Figure 7. Follow-up (18 months) intraoral exam: the impacted canine was aligned in the dental arch

DISCUSSIONS

Comparative studies between the conventional 2D and the more advanced 3D imaging techniques have demonstrated the advantages of the latter in offering additional relevant data related to the impacted maxillary canines (e.g. a more precise localization and the degree of root resorption in the adjacent permanent teeth), which are essential in choosing the optimal treatment plan for the patient [6].

In order to assess the position of the tip of the cusp of the canine in relation with the contour of the lateral incisor, using conventional orthopantomographies, Lindauer et al. [4] defined four sectors I-IV delimited by three lines (one line tangent to the distal contour of the crown and root of the lateral incisor, one line bisecting the mesiodistal width of the lateral incisor and one line tangent to the mesial contour of the crown and root of the lateral incisor). In our case we observed an improvement in the position of the canine from sector IV to sector II during a period of 10 months of treatment.

In the same period of time, the angular measurements we used also showed an improvement of the angulation of the impacted canine relative to the mid-sagittal line, which decreased from 47° to 37°.

Impacted canines can play an important role in the external root resorption process of the adjacent teeth. Impacted canines in a palatal position are more frequently associated with the resorption of the root of the adjacent lateral incisors [7,8,9]. In our case a reduced degree of apical resorption was observed on the initial CBCT scan, but the resorption did not progress after applying orthodontic traction forces on the impacted canine, even though the crown of the canine came in very close proximity (0.7 mm) to the apex of the lateral incisor, after 10 months of active treatment.

The dilacerated root (mesially curved) of the upper left first premolar 2.4 posed a therapeutic challenge, reducing the available space for the initial phase where disto-occlusal traction forces were used in order to minimize the further resorption of the root of the lateral incisor.

The root resorption of the maxillary first premolar is uncommon and is often misdiagnosed or diagnosed too late, when the tooth is already severely affected by external resorption [10]. In our case the root of the adjacent premolar was not affected during treatment, but the crown of the canine was very closely positioned to the root of the first premolar (0.6 mm).

In conclusion, when compared to conventional 2D radiographs, the use of cone beam computer tomography imaging offered additional relevant data which positively influenced the treatment planning and the treatment outcome.

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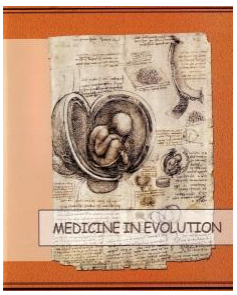
Infiltration treatment of white spots lesions. A case report



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Abstract

White spot lesions can appear on the tooth surface due to plaque presence, when the demineralisation caused by bacteria is higher than the reminalisation, leaving behind porosities that refract the light differently. Fixed orthodontic appliances can participate to plaque accumulation in absence of a correct and regular brushing technique.

The presented case report is a treatment alternative for a patient with demineralisation that appeared during the orthodontic treatment due to lack of hygiene. After the braces were removed, the ICON product developed by DMG was used. Icon-Etch was used first to demineralise the surface, and after 2 minutes the tooth was washed and dried. This faze was followed by applying Icon-Dry. The use of the first two products is repeated if needed. The last product applied was Icon-Infiltrant in a double layer, each cured 40 seconds.

The patient was a perfect candidate for this certain infiltration technique. In absence of a cavity, removing the white spot would imply a high enamel sacrifice. Using ICON we have managed to eliminate the roughness of the enamel and give back the initial shine, with good aesthetic and functional results.

Keywords: *ICON, white spot lesion, demineralisation, orthodontic treatment risk*

INTRODUCTION

White spots and demineralisation associated with non-cavity lesions can appear on the inter-proximal areas of the tooth and on the gingival area of the buccal surface. Various risk factors can contribute to the development of these lesions including poor oral hygiene, low salivary volume and a high sugary based diet. Orthodontic treatment with fixed appliances can be considered a risk due to plaque accumulation around the brackets and difficulties for a correct tooth cleaning.[1,2]

Based on the International Caries Detection and Assessment System, these lesions can be classified as:

Code 1- if no lesion is apparent on a smooth surface when the tooth is wet, but a non-cavity lesion appears when the tooth is adequately dried.

Code 2- if the lesion appears when the tooth is either dry or wet.[3]

The treatment of the white spots can be achieved in several ways, depending on the severity of the lesion. Topical fluoride can be applied on the lesions if they are qualified as Code 1, but the result are not always as expected. Direct application of a high concentration of fluoride is not recommended as it causes rapid remineralisation of the enamel surface, which restricts the passage of ions into the deeper, more affected layers, and limits their complete recovery. For the lesion that classify as Code 2, these measures are unable toremineralize the enamel and more invasive techniques such as erosion–infiltration, bleaching, and microabrasion have to be considered.[2,4,5]

DMG has developed a technique by which these early lesions can be infiltrated with an unfilled low viscosity light cured resin and halt the progress of the demineralization. The kit contains Icon-Etch, Icon-Dry and Icon –Infiltrant, products that war used in the presented case.[6, 7, 8]

CASE REPORT

A 14 years old patient started presenting white spots lesions during orthodontic treatment with fixed appliances. Although various prophylaxis techniques like professional cleaning and topical fluoride were applied, and the correct brushing techniques were explained several times, the poor hygiene led to enamel demineralization and gingivitis. (Fig.1).

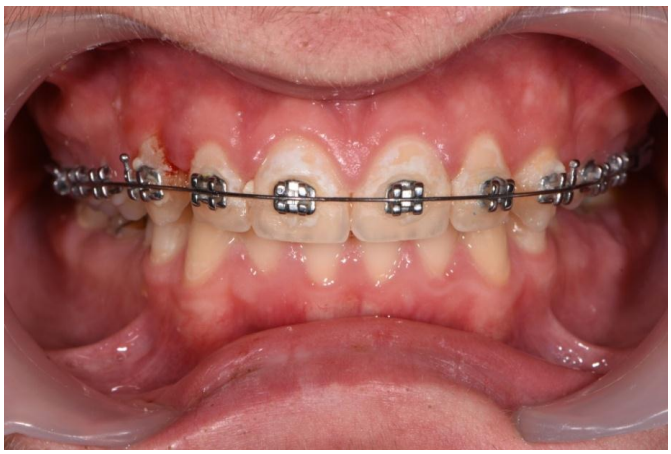

Figure 1. Demineralization and gingivitis

After the fixed appliances were removed, the specific lesions could be observed on multiple teeth, surrounding the place where the brackets use to be, extending towards the gums and inter-proximal, in the same areas where the plaque accumulation reached the

highest levels. The parent was informed about the DMG Icon technique and gave their consent for the treatment.

The first stepof the process consists in the correct cleaning of all teeth. Even if the gingivitis is still present, any type of bleeding is not accepted, considering that it could contaminate the interested areas. Also, a very important part is preventing saliva to reach the buccal part of the teeth. In this case, the patient refused rubber dam placement, so an astringent solution was offered to rinse, which lowered the salivary flow, and combined with soft tissue retractors and suction provided a dry work field. (Fig. 2)

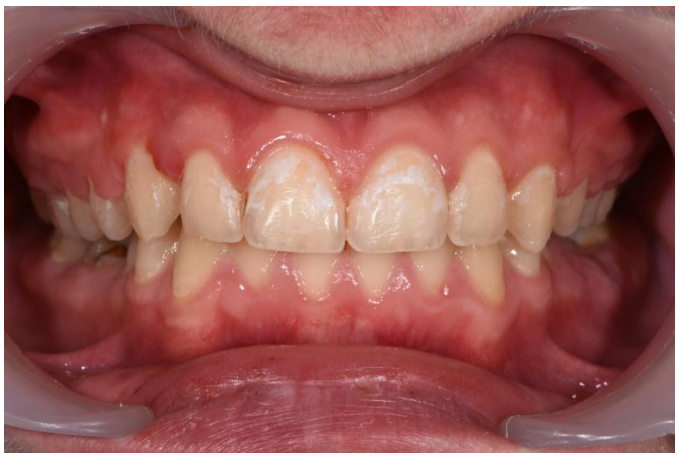

Figure 2. Dry work field

All the products and times recommended by the producer were followed. Icon-Etch was applied on the tooth surface by twisting the syringe after a smooth surface tip is attached. The 15% hydrochloric acid has to be extended 2 mm beyond the edges of the white spot area, and it was set for 2 minutes, being constantly agitated with the brush tip as it buffers after making contact with the tooth surface. (Fig. 3)

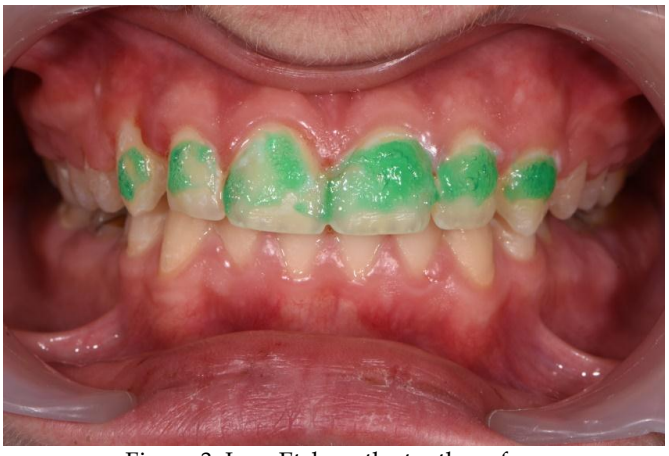

Figure 3. Icon-Etch on the tooth surface

Icon-Etch was rinsed with water for 30 seconds and to dry the surface was used oil- and water-free air. If in this stage, the interested enamel does not have a chalky white aspect, it means that the surface was contaminated and the process must be repeated.

Icon-Dry is a syringe that contains 99% ethanol. It was applied on the tooth, leaved undisturbed for 30 second then dried completely with air. The producers advise that when Icon-Dry is applied, while wet, the white spot does not diminish, the etching part should be repeated two or three times. In our case, it was enough to do these steps once.

An ample amount of Icon-Infiltrant was applied on the tooth surface and let set for 3 minutes, then was light-cured for 40 seconds. A second layer of material was applied, set for 1

minute then light-cured for another 40 seconds. In the end a polishing cup with polish paste was used on the area.

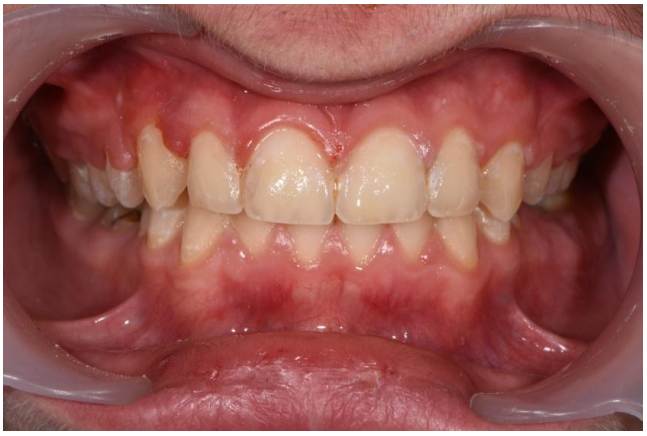

Figure 4. Icon-Infiltrat on the tooth surface

DISCUSSIONS

The patient had a history of orthodontic treatment and poor oral hygiene and did not present the lesions before, which demonstrates that the white spots were indeed a result of demineralisation and not hypoplasia, hypocalcification or fluorosis. Infiltration treatment cannot be applied to the last reminded situations. Also, the absence of cavitated enamel and dentin exposure made the patient eligible for this technique.

Even if correct prophylactic measures were applied, without the patient`s collaboration, the demineralisation still appeared. The plaque accumulated on the upper half of the maxillary teeth, over the limit of where the brackets and arch-wire were situated. The lower half is often protected plaque accumulation through food chewing.

In the presented case, the white spots were categorised as a Code 2 lesion. That meant that a topical fluoride treatment would not chance the appearance of the tooth. Even worse, fluoride use before this technique blocks the surface of the lesion. That way the product cannot get through the deeper layers of the affected enamel, and visually the spot would still be present.

The patient and the parents were extremely satisfied of the outcome of the treatment. The lack of enamel sacrifice, the absence of drilling and the rapidity of the technique are a few of the advantages of this product. The only disadvantage is the need of a good isolation and in absence of that, the risk of gum burn caused by etching.

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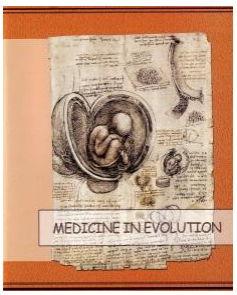
Correcting positional imperfections in the dental aesthetic area: technical step



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Abstract

Intro: The smile is a nonverbal communication tool, associated with exposing the dental arches. Determining the link between the upper lip, the lower lip and the labial commissure with the dental arches during the act of the smile, constitutes one of most important analyses of examining for dental aesthetics (1).

Case presentation: Positional disharmony at the 11 and 21 level in an adult patient, corrected by means of fixed solo full ceramic crowns. The properly executed laboratory steps together with the clinical try ins in the dental office, contributed to a full rehabilitation of the frontal aesthetic area, never omitting the dental mucosal and the aesthetic principles governing the oro-maxillo-facial territory.

Conclusions: the aesthetic result always depends on the materials used in manufacturing the crowns. The pressed ceramic is a modern frequently used material in todays general dental aestetics.

Keywords: *aesthetic area, disharmonies, pressed ceramic*

INTRODUCTION

Dental presses ceramics is an excellent option for front teeth restorations, giving a natural beauty to ones natural smile. The full pressed ceramic crowns are made without any metal support. (2)

The base structure is a synthesized nucleus, melted and pressed in the oven at high temperatures. The ceramic nucleus is plastered with a ceramic mass, by means of a step-by-step stratification technique. The pressed ceramic artificial teeth obtained by means of this technique present a natural translucency and color. (3)

CASE STUDY

After obtaining the model, we work on the crown prep. For manufacturing the crowns we need a model with removable abutments. (Pindex procedure) (picture 1)

Figure 1. Preparation of work abutments

The first step in the process of obtaining the fixed crown is the aplication of a protetive layer on the abutments, in order to easily remove the was crowns off the working abutments. After isolating the abutments, we begin the wax modeling, using 1mm of wax for marginal adaptation, and the proper modeling using a special modeling wax. (Picture 2).

Figure 2. Layout of future prostetic restauration crowns

The crowns are subdimentioned by 2 mm, modeling a partial morphology, to be followed by a stratification of ceramics after the press.

We apply the tilts for the molding in order to wrap the mock up. The mock up wrapping is done by means of a corect conforming system to avoid errors and a special wrapping material is used and it's coresponding liquid.

For pressed ceramics, the injection oven is set to 920°C and a pressure of 3 bars, also using vacuum (picture 3). This temperature is maintained throughout the injecting process.

After the injection step is done, the unwrapping of the crown is done with the help of a sanding machine.

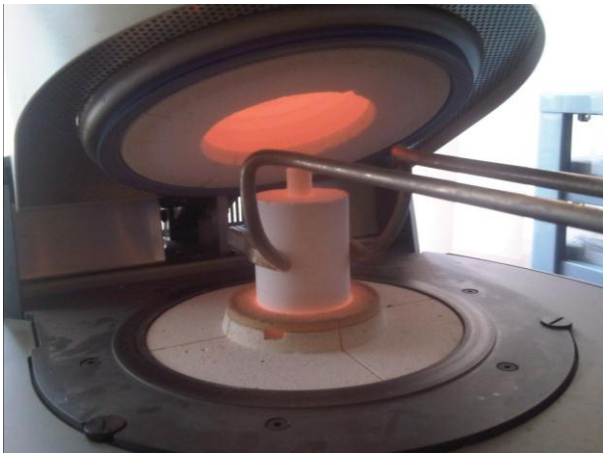

Figure 3. Ceramic press in mold

Adapting the crown to the model is done by means of disks and burrs specialy designed for E-max. At this stage of the process we use the help of the oclusion spray OCCLU-SPRAY, by means of which we notice the interference zones that prohibit the good adaptation of the crowns. (Picture 4).

Figure 4. Adapting crown on abutment

Ceramic stratification was done by means of a brush under vibration the modelation is done in excess, because during the burning, there is a contraction of the ceramic mass of aproximately 25% in all directions. (Picture 5). After applying the dentin mass, and modeling of the corresponding morphological superdimensiones layers, we apply the enamel to obtain a natural incisal transparency. The dentin mass, at the incisal level, is cut in bevel by using a very sharp instrument, (blade). On the vestibular slope, we apply an enamel mass, and on the palatinal slope, we aplly a transparent mass (Vita- Glassklar, Ivoclar- Transparent).

Figure 5. Apllying dentin layer

Finnaly on the entire ceramic surface we apply a glaze, (Vita Ivoclar- glaze Masse) dissolved in a special liquid. (picture 6).

Figure 6. Applying glaze layer

The finishing layer, ensures the final gloss of the ceramic.it is extremely thin and will ensure the crown has a sleek and smooth surface as well as give it's characteristical translucency, that imitates the enamel.

The final glaze will not affect in any shape or form the size of the crown, but this finaly layer can bring slight color modifications. (picture 7)

Figure 7. Final prostetic restoration

DISCUSSIONS

The smile is a main player in the dental aesthetic field, an element that defines the individual as a social beeing.. (4)

The dento-maxilary anomalies, have wide spread, reason for which there is an increades desire and true necesity for aesthetic restauration. in any prosthetic restauration therapy the aesthetic efect is decisive. (5). The aesthetic dentistry treatment solves even the

functional requirements of the oral rehabilitation. No matter how perfect a prosthetic restauration is in terms of functionality, if we do not consider the physiognomic integration and personality fit of the patient, our work may be classified as failure. (6). The key to therapeutic success is ensuring a harmony between the components of the bucal region, facial and oral. (7).aesthetic elements like shape, dimension, symetry, personality, position, allingnement, texutre, color, all have to be considered to obtain optimal results. (8).

CONCLUSIONS

Taking into consideration the abundance and variety of anomaly pathology, the implication of both aesthetic principles that govern the mabilo-facial territory as well as somatic aesthetic principles, requires great care and attention to the dento-mucosal status.in this study we have focused our attention mainly on correcting the allignement of the to front theeth(mezio-rotated). During a correct rehabilitation, we need to respect the functions o the dent0 –maxilary aparatus (mastication, fonetics, endurance), keeping in consideration the points and notions of the aesthetic area.

Ceramics, meets the aesthetic requirements as well as also meets the functionla criteria (biocompatibility. Endurance, maintaiang healthy gum status)

Pressed ceramics is one of the most frequenslty used modern materials, in oral rehabilitations, proving great results in time. the dental tehnician needs to surpass the dentist vision in term os dental physionomy of the dental arches, and and intergate the results whith the facila aesthetics and why not with general aestethics as well.

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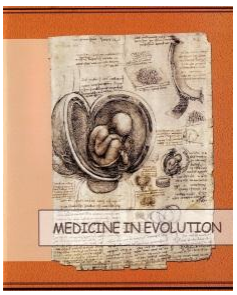
Biomechanical behaviour of the primary reconstruction plates post mandblehemiresection –a finite elements analysis



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Abstract

Objective: Our primary goal is to investigate the biomechanical behavior of the primary reconstruction plates when used to reconstruct a deffect post hemiresection of the mandible, using finite element analysis (F.E.A.). The aim of this paper is to find out if, when used to reconstruct jaw defects after a hemi resection of the mandible without any bone graft, the plate offers enough stability and a good mechanical performance. Furthermore, we investigate material's fatigue.

Materials and methods: Starting with a 3D reconstruction from CT images, we made a study model reproducing the complex geometry of the mandible-primary reconstruction plate binomial, on which we applied forces corresponding to the muscular tractions.

Using F.E.A., we measured the stress generated both in the bone and inside the plate. We realized a static structural analysis to determine the total deformation, as well as the equivalent stress. Also, we investigated the life span of the plate.

Results: Our analysis showed a good biomechanical performance of the mandibular primary reconstruction plates. Also, we observed a good lifespan.

Conclusion: Mandibular primary reconstruction plates can be used, even without any bone graft, for bridging a defect post hemi resection of the mandible, showing good biomechanical performance and stability and a long lifespan.

Keywords: *reconstruction plate, biomechanical behavior, life span, material fatigue, finite element analysis*

INTRODUCTION

The primary reconstruction plate represents, nowadays, a largely utilized method for bridging jaw defects, post mandible hemiresection[1,2]. The specialty literature shows, however, a lot of controversial data regarding both the advantages and the setbacks of this method[1-7]. Furthermore, a vast majority of studies regard the primary reconstruction plate without a bone graft as a temporary jaw bridging method[1-7], though there is data attesting exceptionally good long time results[2]. These controversies justify, in our opinion, a farther analysis of these plates' behavior using the finite element method(F.E.M.), through a static structural analysis concerning the total deformation and the equivalent stress, as well as an investigation of the material fatigue and the plate's life span.

Aim and objectives

Our primary goal is to investigate the biomechanical behavior of the mandibular primary reconstruction plates when used, without a bone graft, as a method to bridge jaw defects post mandible hemi resection. A second goal is to determine, also through F.E.A., the plate's life span.

MATERIAL AND METHODS

For our study, we used CT images which were imported in 3D MIMICS, an image processing software for 3D design and modeling. Thus, we obtained a model to analyze. We allotted the spatial system coordinates XYZ to the model. The origin of the axis system was established in the middle between the two mandibular condyles. A three-dimensional mesh of a mandible reconstruction was constructed. For bone structures, we used a 0.9 mm elements mesh, while for the primary reconstruction plate and for the screws, we used a 0.5 mm elements mesh.

Materials were assigned a Young's modulus as well as a Poisson's ratio (*Table 1*). The bone, as well as the plate and the screws were considered isotropic.

Table 1. Young modulus and Poison ratio

Material	Young module, E (MPa)	Poison ratio
Bone	12000	0.33
Titanium	105600	0.34

The loading and the support conditions were used to simulate the real functioning of the mandible-plate binomial.We applied themuscular forces (Figure 1). A condyles' movement of 2 mm was allowed.

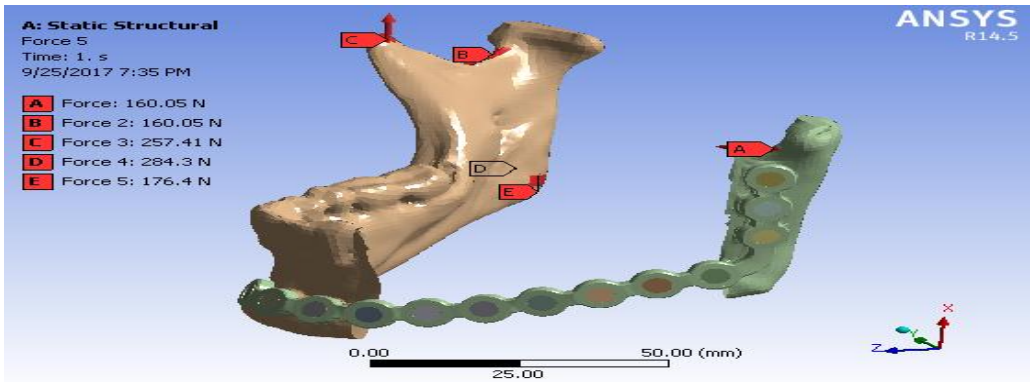

Figure 1. The muscular forces applied

We analyzed the incision (made by the incisors) and the trituration (corresponding to an occlusal loading for the molars on the contralateral side).

F.E.A. aimed to determine the stress and the deformation for all components, i.e. bone, plate and the screws, as well as for the interface between them.

Furthermore, we analyzed the fatigue, which is a weakening of a material based on progressive and localized structural damage that occurs when a material is subjected to cyclic loading, in order to determine the life span of the mandibular primary reconstruction plate.

RESULTS

The results are shown in *figures 2-4*.

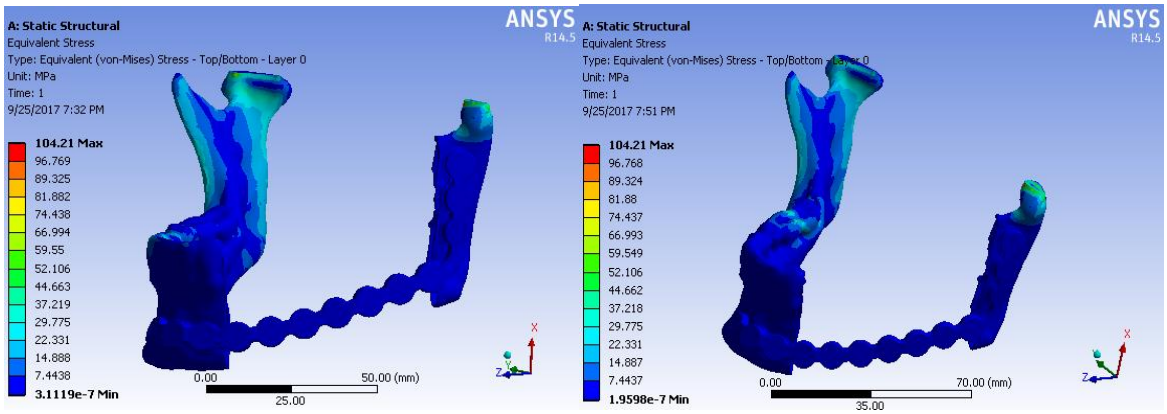

Figure 2. Equivalent stress variation for the incision and triturating movement

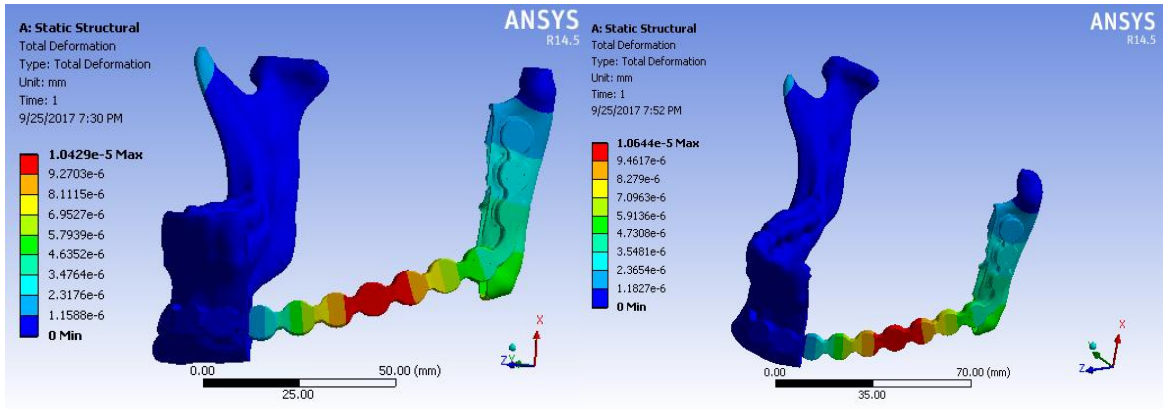

Figure 3. Total deformation variation for the incision and triturating movement

The analyzed data suggest low stress values, which are in the elastic deformation range for the investigated alloy. Also, the displacement recorded at the mandible-plate interface is extremely reduced, which leads us to conclude the good stability of the bone-plate ensemble.

The excellent results concerning material fatigue and the life span are shown in *figure 3*. F.E.A. concluded a risk for fracture due to material's fatigue at more than 14 million cycles. This observation, allows us to consider, from this point of view, the use of mandible primary reconstruction plate (without a bone graft), not as a temporary, but as a long time method for jaw defects bridging.

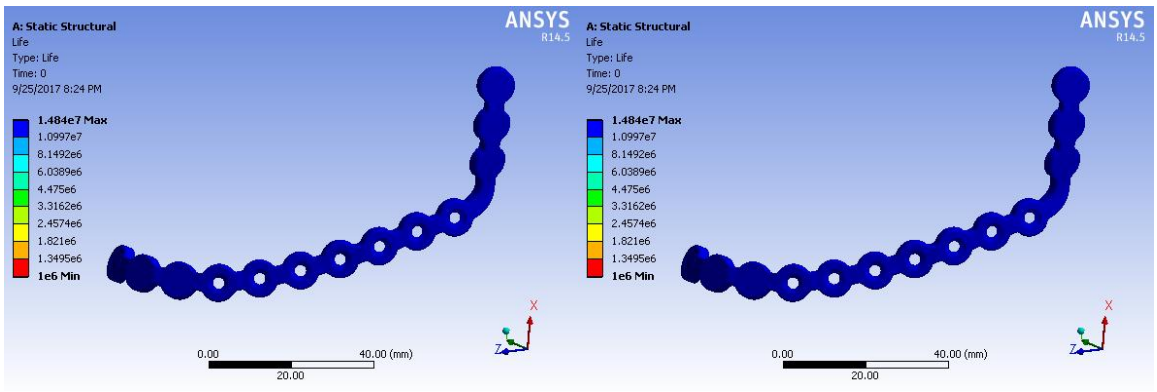

Figure 4. Plate life span, when considering the incisionand triturating movement

DISCUSSIONS

The titanium alloy mandible primary reconstruction plates are devices used for bridging mandibular defects that follow mandible hemi resection. They offer a good positioning for the bone segments (1,8). Ti-6Al-4V is an alpha + beta alloy, being the material of choice for most medical implanting devices, due to its excellent biocompatibility, low risk of fracture and good endurance.The specialty literature does not provide, however, an uniformity of view on the topic of these plates mechanical behavior. So, in the 5-47 percents when, according to Gutwald et al. (1), the complications conducted to plate removal, the main cause was not the plate fracture, but its exposure, tissue necrosis and infection. Navaro-Villa (4) also quotes a series of studies which conclude plate's exposure as the main cause of failure.Militsakh quoted by Gutwald (1) doesn't find any case of plate fracture. Quite opposite, Jia et al. identify a high percent of plate fracture, arround 30 % (3), which does not coroborate with our results. From the point of view of the materials science, we rally to the study made by Paul et al. (2). On 36 pacients, observed for two years postoperatory, the authors conclude an excelent stability of the mandibular primary reconstruction plate, which is consistent with our results concerning the extremely reduced displacement recorded at the mandible-plate interface.

From the point of view of material's endurance, a life span over 14 million cycles allows us to consider the use of mandible primary reconstruction plate without a bone graft, not as a temporary (7), but as a long time method for jaw defects bridging. Considering a number of masticatory cycles between 2000 and 5000 a day (9), the primary reconstruction plate's life span is situated between 8.1 and 20.3 years.Iwasawa et al. (5) also obtain good results concerning jaw defect bridging with mandibular primary reconstruction plates, concluding a good biomechanical behavior of the plates, and insist on the methods to prevent plate's exposure.

CONCLUSIONS

Mandibular primary reconstruction plates represent a method for bridging jaw defects post hemi resection of the mandible which shows good biomechanical performance and stability.

Material's fatigue which leads to a risk of fracture at over 14 million cycles allows us to consider the use of mandible primary reconstruction plate without a bone graft as a long time reconstruction method.

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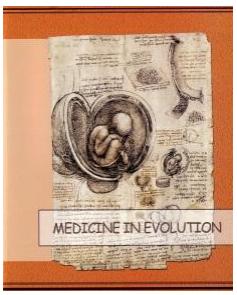
Numeric analysis using finite elements analysisof the ensemble dental crown-implant-bone tissue



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Abstract

The aim of this paper is to underline the mechanical properties of two single retained implant crown materials in order to differentiate the possibility of using each material for typical clinical condition and masticatory load. Objective of the investigation is to highlight the stress distribution over different common dental crown materials by using computer-aided design software and a three-dimensional virtual model. By using finite element analysis it has been highlighted the strength over simulated retained implant single crowns made by metal ceramicand dental resin. The retainedimplant crown models have been created and put on simulated chewing stresses. The three-dimensional models were subjected to axial and oblique forces and both guaranteed expected results over simulated masticatory cycle. Both prosthetic solutions offer long-term success if applied following the manufacture guide limitations and suggestions.

Keywords: *finite element analysis, retained implant crown, bone-implant interface*

INTRODUCTION

The long-term clinical success of dental implantis connected to their connection into newly formed bone (1,2).

A couple of factors plays an important role in load transfer from dental implant to bone, such bone-implant interface and prosthesis type (3). Stress distribution and masticatory forces involving dental implant and implant retained prosthesisis a quite debated topic in the recent literature (4).

During the last years, finite element analysis was widely utilizing for the prediction of stress effect on the implant and its surrounding bone (5,6,7).

The purpose of this study is to assess the biomechanical behavior by determining the tension and deformation on the interfaces implant-bone tissue and dental crown-implant.

MATERIAL AND METHODS

For investigating the mechanical behavior two cases common in dental practice were analyzed:

Case A: metal – ceramic crown

Case B**:** dental resin crown

For both geometrical models a short implant of 6 mm length and 3.5 mm diameter was used.

For defining the geometrical model, we used CAD SolidWorks software, a special design software.In this program, components of the ensemble were generated: fixture, abutment and restauration dental crown.

All these geometrical components were 3D-generated according to each one's dimensions in order to obtain contact points after assembly, without assembling gaps, considering this situation real when the implant is inserted, stabilized and the patient can use it.

To simulate the implant area (mandibula or maxilla), for the current study, it is not necessary to model the whole mandibula or maxilla which would have represented a large and complicated work volume. Consequently, only an area was modeled, the area around the implant, applying the properties of the bone tissue in contact with the implant.

The dental crown was modeled with two components – the outer part (the one in the oral cavity) and the inner part (the one in contact with the abutment). This procedure was necessary for simplifying the numerical simulation according to the two situations – mixed crown and homogeneous crown.

The geometrical model was exported to the numerical analysis software for investigating the biomechanical behavior after implantation with a load of approximately 300 N (simulating the mastication process) applied on the superior area of the dental crown inclined to 30° and an analysis with the axial force (perpendicular on the dental crown) of 300 N.

A numerical model for a simulation using finite element method is composed of:

- A geometrical model
- Applying the contacts between the components of the ensemble. For the model in this study, bonded contacts were applied between the geometrical components, without friction between them.
- The discretization - dividing geometrical components in finite element grid interconnecting through nodes of 1st and 2nd order in order to obtain information from as much areas from the whole model. As the geometrical model is represented tridimensional, formed from volume solid frames, finite elements for the discretization model will be tridimensional (SOLID 187).

Because of the contacts which appear between the constitutive components of the ensemble, two more bondage elements were chosen (elements which mathematically transcript contact properties) CONTA and TARGE elements.After the discretization the whole model was divided in a finite element grid containing 19138 nodes and 28079 elements.

The external load (300 N) was applied on the exterior layer of the dental crown in two ways:

A. The force applied at 30°

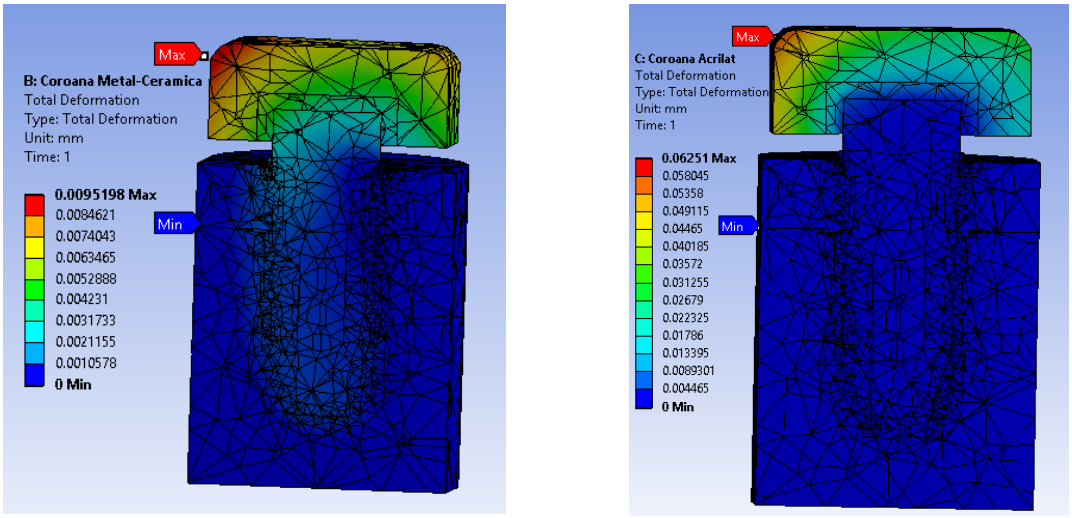
B. The axial compressing force normal to the model

For the blockage model we chose the blockage on the outer surface of the ensemble considering fixed blockage without any degrees of freedom (all six possible moves were nule).

After all stages described earlier were browsed, the resolving command activates and it is followed by the post processing stage which includes presenting the obtained results and their interpretation.

RESULTS AND DISCUSSIONS

In the following, we will present the results for load applied at 30° for the two cases in this study.The magnitude of the displacements in the analyzed ensemble is presented*(Figure 1)*.



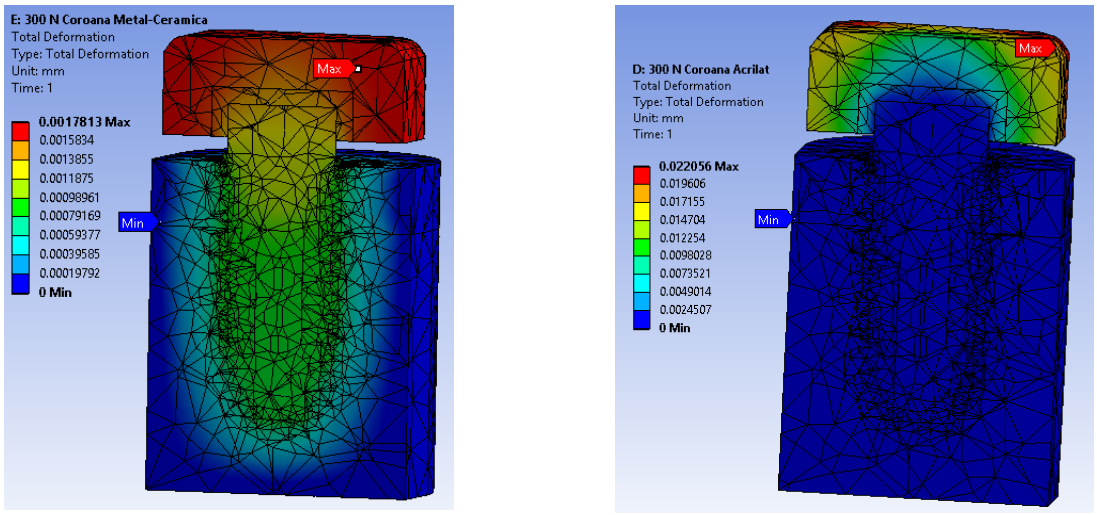
Case A Case B

Figure 1. Magnitude of displacements in the model

Both magnitude and axial displacements of the analyzed model are larger in the case of the dental resin crown in comparison with the bi-component crown (metal-ceramic). Stress level calculated with the von Mises criteria, containing all types of tension which appear during the stress (expansion-compression, torque, shear, bending) is approximately the same. In both cases, maximum values of stress are approximately 441-442 MPa. It is interesting the manner how the tension is distributed in the model. For Case A, the stress is found at the contact between the fixture-cortical tissue and for Case B, the stress is also found at the contact between the fixture-cortical tissue but it is also transmitted to the abutment.

Analyzing next image in Figure 2 we can conclude that for both models, at the interface fixture-bone tissue large forces do not appear, forces which could lead to losing implant stability*(Figure 2)*. Values of these forces situate between 7 and 17 MPa and they are between the limit of plastic deformation of any material used in this numerical study.

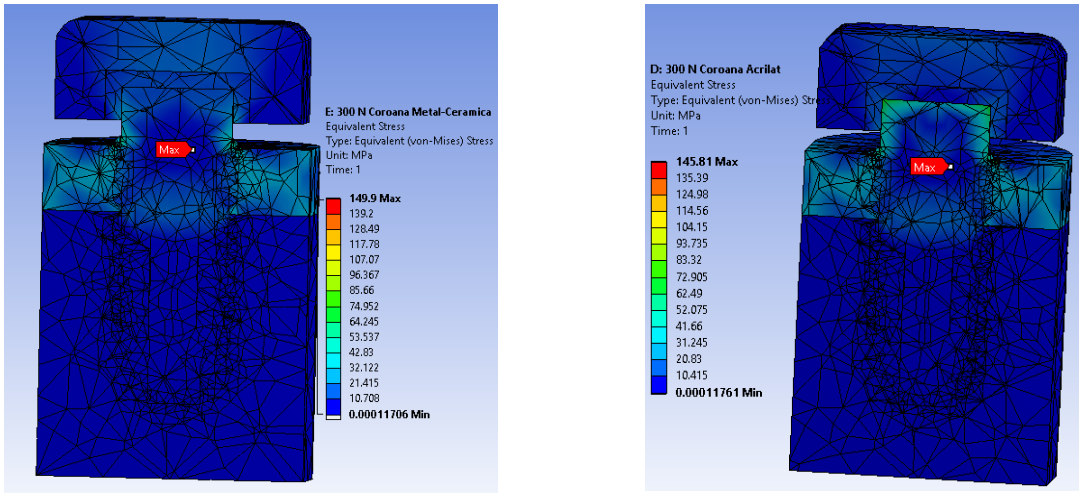
Results for the two models in the case of applying a compression force of 300N equal to the force of mastication. This force could appear in the case when the patient does not follow the dentist's indications and tries to eat rough aliments between molars.



Case A Case B

Figure 2. Stress variation in model

We can observe that in Case A – bi –component crown, the effect of compression force is transmitted in the whole model crown-abutment-fixture, the stress having small values in comparison with the dental resin crown – the stress is in the dental crown*(Figure 3)*.



Case A Case B

Figure 3. Stress variation (*vonMises* criteria) in the analyzed model

These findings are in accordance with our clinical findings where failure is observed more frequently for implant retained dental resin-based restorations than for metal-ceramic restorations.Further studies, using clinically relevant test methods, must be performed to verify the effect of restauration material for dental crown in order to recommend the optimal type of implant retained restoration.

CONCLUSIONS

Finite element analyses have found increased concentration of stress in the implant retained dental resin crown with increased difference compared with the metal-ceramic crown. This findingmay be explained by the differences in mechanical properties between

dental resin and metal-ceramic.All these findings indicate that the results could be clinically relevant and can be used for clinical decision making.

All the authors equally contributed to this work.

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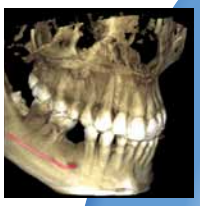

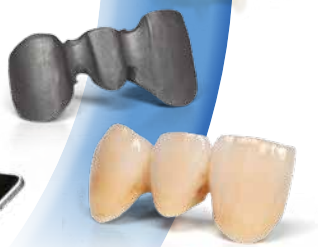

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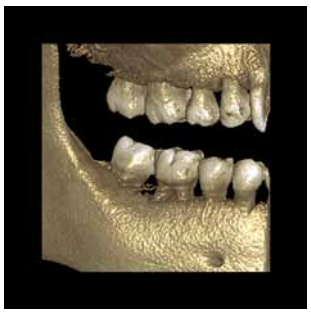

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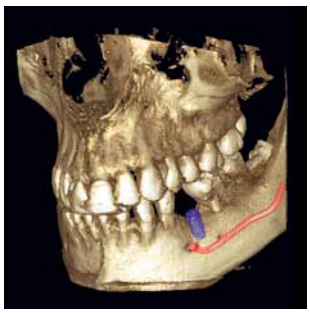

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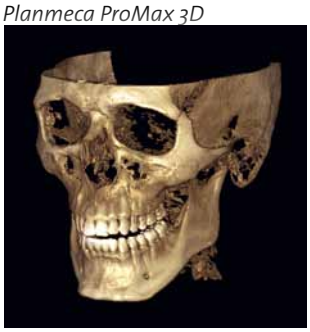

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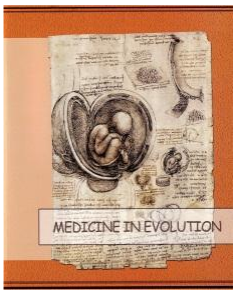

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Introduction presentation of general aspects, in the context of the approached theme.

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