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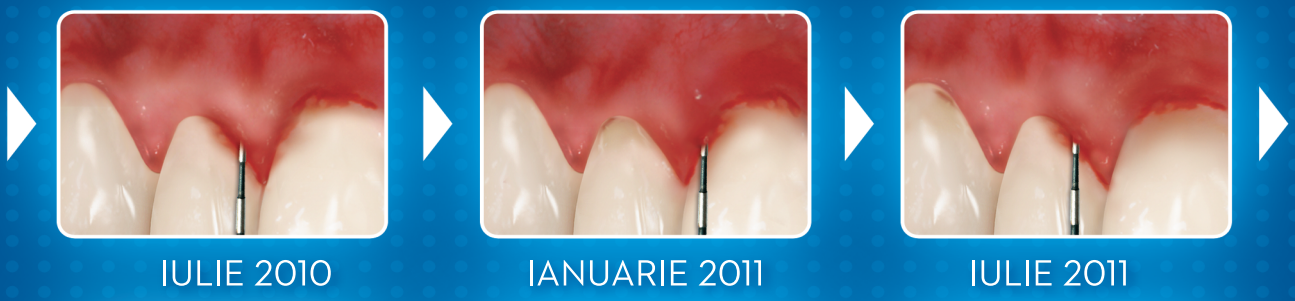
REDUCE ŞI AJUTĂ LA PREVENIREA PROBLEMELOR GINGIVALE ÎN 4 SĂPTĂMÂNI PENTRU A ÎNTRERUPE CICLUL GINGIVITEI



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blend-a-med | Oral-B | CLINIC LINE GUM PROTECTION SYSTEM

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P12125.01

Continuă îngrijirea ce începe în cabinetul dumneavoastră

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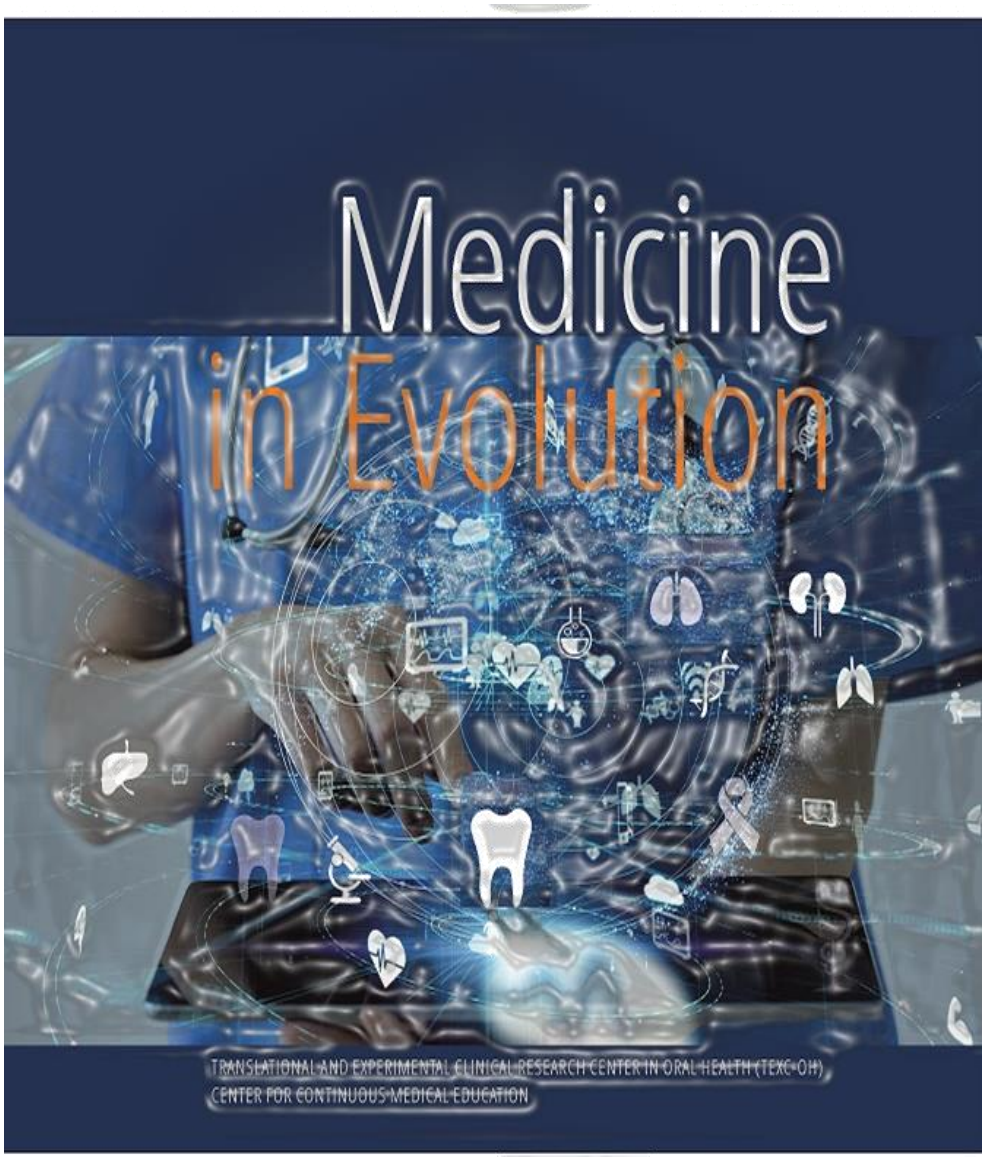

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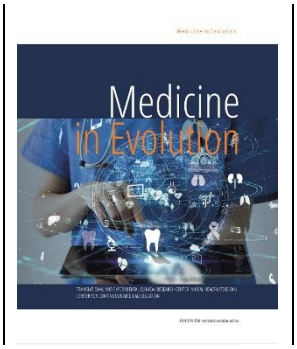

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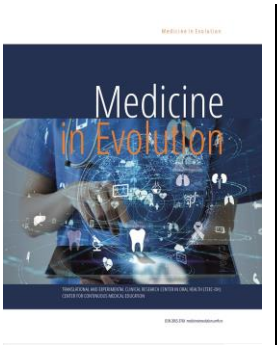

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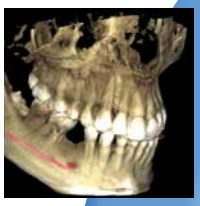

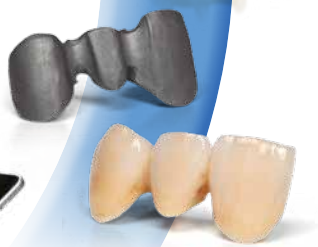

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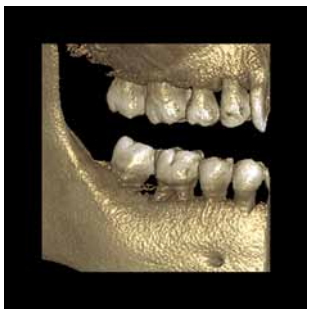

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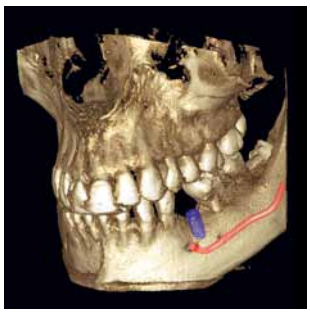
Ø42 x 42 mm–90 x 60 x 130 mm



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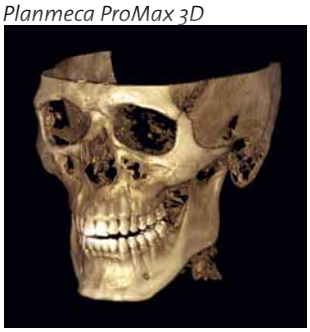
Planmeca ProMax 3D



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Clinical study of analysis of deviation from the mean of Bennett angles using electronic condylography measurement

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Abstract

The study was carried out on a group of 140 Romanian patients to analyze the deviation from the average (15°) of the Bennett angles in order to identify some potential common aspects. Based on the exact values of the Bennett angles sent to the dental laboratory, customized prosthetic works will be carried out later.

The measurements were made by condylography, a method of recording mandibular dynamics and all the functions of the craniomandibular system: breathing, speech, swallowing, mastication, aesthetics, stress-management. An ARCUSDigma condylograph from KaVo Dental GmbH was used for diagnostic condylography, and biacrylic composite, fixed with Temp-Bond NE temporary cement from Kerr Dental, was used to create the clutch.

After the study we found that 25% of the patients had a Bennett angle of at least 4° and another 9% had values close to 4°, which demonstrates the existence of repetitive common aspects.

Keywords: Bennett's angle, condylography, lateral movement, recording of mandibular dynamics

INTRODUCTION

140 patients participated in this study (of which 100 were female and 40 were male), who underwent diagnostic condylographies using the ARCUSDigma condylograph from KaVo Dental GmbH.

All measurements were made with the same device, by the same doctor, in the same office.

With this group of patients we intended to identify the pattern of Bennett values found on the patients having deviation from the average (15°) of the Bennett angles.

The Bennett angle is the angle formed between the sagittal plane and the condyle, during lateral movement of the mandible. The Bennett angle is identified on the non-working (swing) side, in other words when we perform left laterality we have a Bennett angle on the right side and vice versa.

The lateral movement is a complex, translational movement, the most complex that is performed in the human body. The Bennett angle has one horizontal component and one vertical component: when we perform the lateral movement, at the beginning of it, the condyle makes a movement towards sagittal plane (immediate ISS, Shift) and then starts moving forward and down, supporting the lateral movement on the non-working side. The Bennett angle is influenced by the anatomical structures and the ligaments and muscles that are creating and supporting this complex movement.

That is why it is very important to obtain exact values of the Bennett angles (left-right) in order to be able to share them later with the dental laboratory and carry out personalized prosthetic work.

Given the complexity of this translational movement and the importance of the mechanical relationship between the Bennett angles and the anatomy of the glenoid fossa, we initiated this study to analyze the values obtained on this group of Romanian patients. This analysis will allow us to determine if common repetitive aspects along the measured values can be identified from a statistical point of view. The results obtained in the measurements are exact, mathematical, demonstrating clear causality between the anatomy of the skull, the glenoid fossa, the eminence and the shape of the condyles.

We analyzed the deviation from the mean Bennett value to identify what are the common values, if any, and the percentage in this batch of patients. If any common values are found, may become useful statistical data in our daily practice.

Aim and objectives

The objectives are the measurement with condylography of Bennett angles, the collection of data resulting from condylography of mandibular dynamics, the introduction of the obtained data in a table - the ratio of the articulator - the analysis of the deviation from the average of 15° of each electronic record, the interpretation from a statistical point of view of the data obtained from the mandibular dynamics recording and the identification of potential quantitative informational aspects towards a certain mathematical value. The data is obtained and processed in the KaVo KiD software from ARCUSDigma (KaVo Dental GmbH).

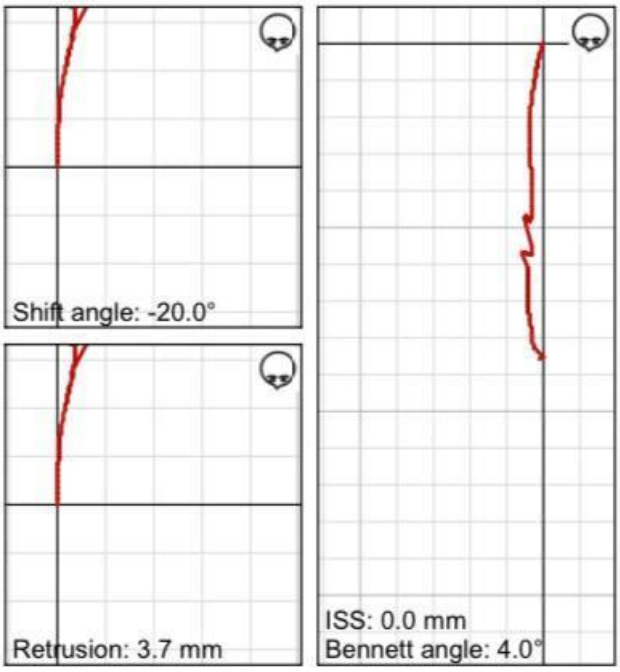

Figure 1. Bennett Angle

The aim is to identify potential repetitive values, which would demonstrate the existence of common points in the anatomy of the skull of the examined patients and in terms of the masticatory reflex, which is achieved through lateral movements, directly related to the Bennett angle. All this information will later be used to carry out direct or indirect prosthetic work on natural teeth or implants.

When we understand and control this lateral movement and have a record of it, the patient will benefit from a functional treatment plan, and not a random one, given that this exact, mathematical information about mandibular dynamics is shared by the dental office with the laboratory, so that the dental technique applies it to perform prosthetic works.

MATERIAL AND METHODS

The patients are Romanian and have participated voluntarily in the study. They all are beneficiaries of prosthetic works on natural teeth or implants.

In a first stage, the impressions of the 2 arches, upper and lower, was made using Speedex additive silicone, manufacturer Coltene/Whaledent AG.

On the basis of these impressions, the 2 models (upper and lower) were realised in the laboratory from class IV Fujirock plaster from GC Europe N.V. Also in the dental laboratory, the clutch was made using Silatray photopolymerizable base plate, manufacturer SILADENT Dr. Böhme & Schöps GmbH and the prefabricated metal clutch from ARCUSDigma from KaVo Dental GmbH.

The clutch is made on the lower model and copies the vestibular faces of the lower teeth without interfering with maximum intercuspation.

Light curing of the base plate and finishing of the composite material (base plate) are also laboratory steps.

Afterwards, a check is made so that they do not press on the gum and the interdental papillae and that there is sufficient friction between it and the vestibular surfaces of the lower teeth.

The clutch check is done in situ in the dental office and is done with 40µ articulation paper, manufacturer Dr. Jean Bausch GmbH & Co.KG, positioned between the 2 arches on the left-right occlusal plane.

After this check, the clutch is provisionally fixed with Kerr Dental's Temp-Bond NE cement or with VOCO GmbH's Structur Premium biacrylic composite. The excess cement or biacrylic composite is removed.

On the upper metal plate, which has a marking for the median of the upper teeth, we put bite silicone and fix it on the occlusal faces and incisal edges of the upper teeth. This plate transmits to us, in the mathematical system and software, the position of the three-dimensional jaw bone in the virtual articulator or analog articulator.

The lower part of the kinematic bow from ARCUSDigma is attached to this clutch. On this lower device there are 4 emitters that produce ultrasound. Fixing is done magnetically.

The kinematic bow is fixed at the level of the clavicle and the 2 auditory pathways, left-right, after which it is connected via the module and the connection cables to the condylograph and computer.

The actual condylography consists in the recording of mandibular dynamic movements: protrusion, retrusion, left laterality and right laterality.

Each dynamic movement will be recorded 3 times, this means 3 consecutive separate recordings, and the KaVo KiD software will average the 3 values for each movement.

After the registration is finished, the software will generate a file, report for the articulator that contains all the information about the anatomy of the skull. This report is important because it actually represents the prosthetic or pre-prosthetic treatment plan.

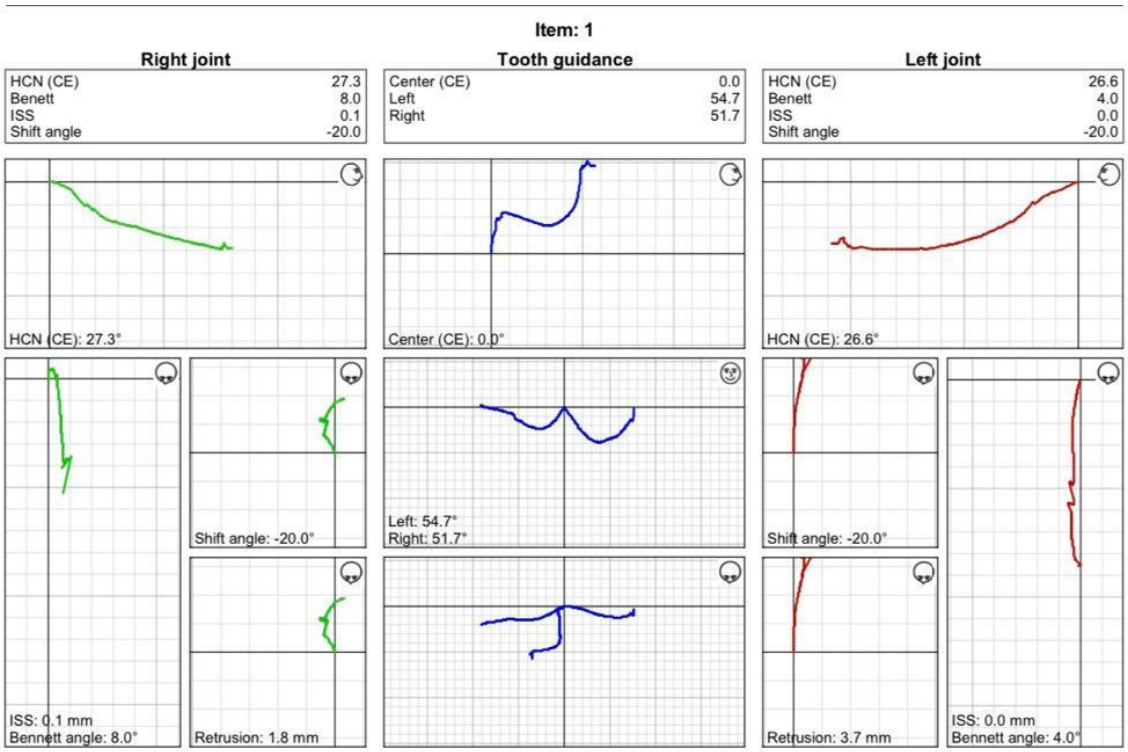

Figure 2. Articulator Report

The next step is to remove the kinematic arch from the patient's skull, manually remove the clutch, and clean the lower teeth with cement or biacrylic composite.

Also, the kinematic bow shows us in the mathematical system the position of the skull through the upper metal plate.

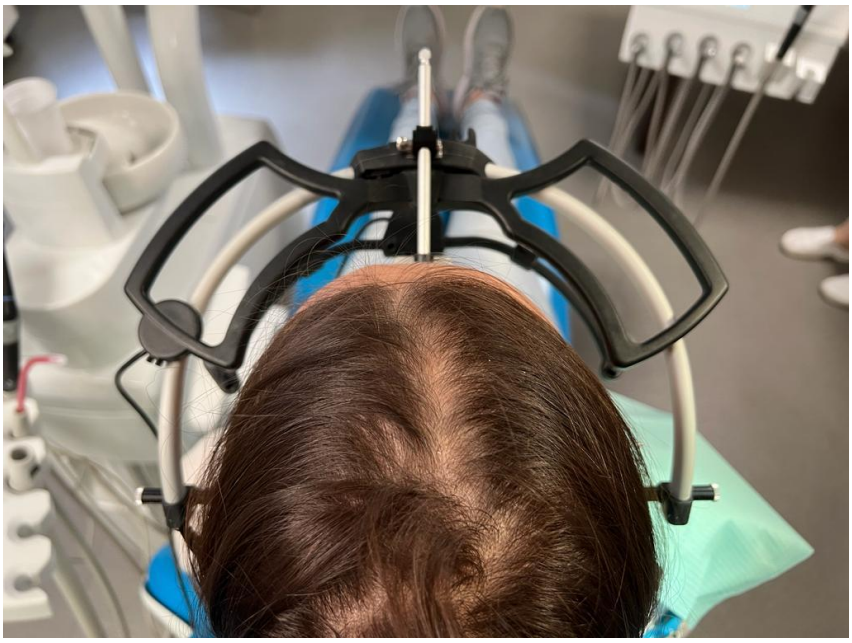

Figure 3. Kinematic Bow – Top view

Figure 4. Kinematic Bow – Lateral view

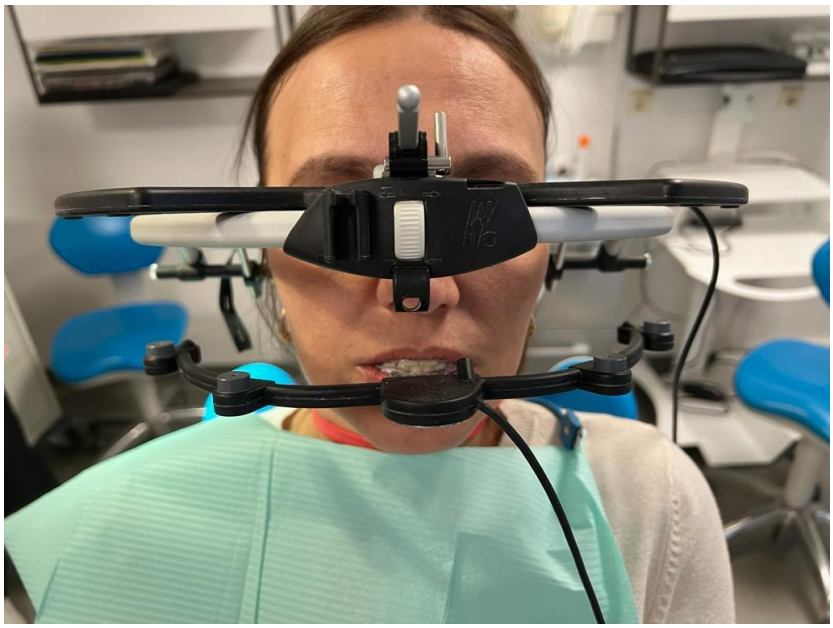

Figure 5. Kinematic Bow – Front view

RESULTS

The interpretation of the condylography, of the tracings, show us if there are neuromuscular and occluso-articular imbalances, if we have intra- and extracapsular changes in the 2 temporomandibular joints, what is the position of the left-right articular discs and if there are changes in their position, median, vestibular or posterior.

Table I. The results of condylography

Id	Anonymous Name	Gender	RIGHT BENNETT	LEFT BENNETT	Right Deviation	Left Deviation	Left-right difference
1.	A.A.	F	21.3	4.0	+6.3	-11	+17.3
2.	A.E.	F	7.7	4.0	-7.3	-11	+3.7
3.	B.N.	F	4.0	4.0	-11	-11	0.0
4.	B.C.	M	28.5	9.2	+13.5	-5.8	+19.3
5.	B.C.	M	_	20.6	-	+5.6	-
6.	B.C.	F	12.8	6.7	-2.2	-8.3	+6.1
7.	B.I-M.	F	4.0	8.0	-11	-7	-4.0
8.	B.I-A.	F	_	10.8	-	-4.2	-
9.	B.B.	M	30.0	6.7	+15	-8.3	+23.3
10.	B.D.	F	4.0	4.2	-11	-10.8	-0.2
11.	B.D.	M	17.2	11.7	+2.2	-3.3	+5.5
12.	B.M.	M	15.9	15.4	+0.9	+0.4	+0.5
13.	C.S.	F	4.0	23.5	-11	+8.5	-19.5
14.	C.N.	F	4.0	6.5	-11	-8.5	-2.5
15.	C.M.	F	10.8	_	-4.2	-	-
16.	C.M.	F	10.7	_	-4.3	-	-
17.	C.G.	F	_	4.6	-	-10.4	-
18.	C.I.	M	_	6.0	-	-9	-
19.	C.L.	F	6.2	4.0	-8.8	-11	+2.2
20.	D.A.	F	4.0	14.3	-11	-0.7	-10.3
21.	D.I.	F	5.0	4.0	-10	-11	+1.0
22.	F.V.	F	_	6.5	-	-8.5	-
23.	F.P.	M	21.8	13.6	+6.8	-1.4	+8.2
24.	G.C.	F	4.0	_	-11	-	-

25.	G.M.	F	18.1	4.0	+3.1	-11	+14.1
26.	G.S.	F	_	4.9	-	-10.1	-
27.	G.I.	M	13.6	8.4	-1.4	-6.6	+5.2
28.	I.A.	F	4.0	4.0	-11	-11	0.0
29.	J.G.	M	12.0	5.2	-3	-9.8	+6.8
30.	M.M.	M	16.5	4.0	+1.5	-11	+12.5
31.	M.S.	F	8.9	11.8	-6.1	-3.2	-2.9
32.	M.A.	F	12.4	4.0	-2.6	-11	+8.4
33.	M.T.	F	4.0	4.0	-11	-11	0.0
34.	M.V.	M	6.8	11.8	-8.2	-3.2	-5.0
35.	M.A.	F	_	10.8	-	-4.2	-
36.	M.G.	F	8.7	_	-6.3	-	-
37.	M.M.	M	4.0	4.3	-11	-10.7	-0.3
38.	N.G.	M	17.3	17.5	+2.3	+2.5	-0.2
39.	N.V.	F	12.1	9.9	-2.9	-5.1	+2.2
40.	N.C.	F	7.7	4.0	-7.3	-11	+3.7
41.	N.A.	F	4.9	4.0	-10.1	-11	+0.9
42.	N.O.	F	_	18.7	-	+3.7	-
43.	O.C.	F	30.0	5.6	+15	-9.4	+24.4
44.	P.E.	F	4.0	4.0	-11	-11	0.0
45.	P.A-M.	F	10.2	8.4	-4.8	-6.6	+1.8
46.	P.I.	F	13.9	30.0	-1.1	+15	-16.1
47.	P.A.	F	6.3	_	-8.7	-	-
48.	P.B.	F	6.0	2.9	-9	-12.1	+3.1
49.	P.Z.	M	12.3	19.4	-2.7	+4.4	-7.1
50.	P.A.	F	_	5.7	-	-9.3	-
51.	R.A-M.	F	8.4	15.4	-6.6	+0.4	-7.0
52.	R.A.	F	9.0	4.0	-6	-11	+5.0
53.	R.M.	F	11.5	6.8	-3.5	-8.2	+4.7
54.	S.V.	M	8.7	22.3	-6.3	+7.3	-13.6
55.	S.V.	F	_	16.6	-	+1.6	-
56.	S.R.	F	8.9	_	-6.1	-	-
57.	S.A.	F	4.0	4.0	-11	-11	0.0
58.	S.S.	M	4.0	17.7	-11	+2.7	-13.7
59.	S.B.	M	18.5	21.6	+3.5	+6.6	-3.1
60.	T.G.	F	_	4.0	-	-11	-
61.	T.C.	M	4.0	10.2	-11	-4.8	-8.2
62.	T.C.	F	13.6	4.0	-1.4	-11	+9.6
63.	U.M.	F	_	4.0	-	-11	-
64.	B.V.	F	8.0	4.0	-7	-11	+4.0
65.	S.V.	F	13.0	_	-2	-	-
66.	D.W.	M	17.5	4.0	+2.5	-11	+13.5
67.	Z.V-G.	M	4.4	6.3	-10.6	-8.7	-1.9
68.	Z.D.	F	4.0	4.4	-11	-10.6	-0.4
69.	A.L.	F	8.5	_	-6.5	-	-
70.	B.G.	F	_	4.7	-	-10.3	-
71.	B.S.	F	30.0	4.0	+15	-11	+26.0
72.	B.D.	M	7.9	17.2	-7.1	+2.2	-9.3
73.	B.S.	F	5.4	4.0	-9.6	-11	+1.4
74.	B.B.	F	6.2	_	-8.8	-	-
75.	B.C.	M	18.1	_	+3.1	-	-
76.	B.E.	F	4.0	_	-11	-	-
77.	B.V.	F	4.0	4.0	-11	-11	0.0
78.	B.C.	F	5.6	_	-9.4	-	-
79.	C.L.	M	6.7	5.9	-8.3	-9.1	+0.8
80.	C.L.	F	15.6	4.0	+0.6	-11	+11.6
81.	C.E.	F	6.7	10.2	-8.3	-4.8	-3.5
82.	D.A.	F	4.0	10.2	-11	-4.8	-6.2

83.	P.D.	M	18.5	4.0	+3.5	-11	+14.5
84.	B.D.	F	_	5.4	-	-9.6	-
85.	D.F.	M	16.4	4.0	+1.4	-11	+12.4
86.	D.E.	F	16.6	4.0	+1.6	-11	+12.6
87.	D.C.	F	4.0	_	-11	-	-
88.	H.C.	M	5.6	4.0	-9.4	-11	+1.6
89.	H.G.	F	_	6.3	-	-8.7	-
90.	H.M.	F	12.6	_	-2.4	-	-
91.	I.R.	M	4.0	14.0	-11	-1	-10.0
92.	J.J.	M	5.9	10.1	-9.1	-4.9	-4.2
93.	L.A.	F	4.0	10.1	-11	-4.9	-6.1
94.	M.I.	F	7.2	_	-7.8	-	-
95.	M.V-E.	F	4.0	_	-11	-	-
96.	N.G.	M	17.3	17.5	+2.3	+2.5	-0.2
97.	N.R.	F	13.9	4.0	-1.1	-11	+9.1
98.	O.A.	F	18.2	11.9	+3.2	-3.1	+6.3
99.	P.O.	F	4.0	4.0	-11	-11	0.0
100.	P.A.	F	6.1	_	-8.9	-	-
101.	P.A-M.	F	6.5	_	-8.5	-	-
102.	S.M.	F	13.6	17.2	-1.4	+2.2	-3.6
103.	S.M.	F	4.0	7.5	-11	-7.5	-3.5
104.	S.C.	F	7.1	17.5	-7.9	+2.5	-10.4
105.	P.S.	F	_	11.1	-	-3.9	-
106.	S.K.	F	4.9	_	-10.1	-	-
107.	T.E.	M	17.1	12.7	+2.1	-2.3	-4.4
108.	T.G.	F	_	4.8	-	-10.2	-
109.	T.A.	F	4.0	_	-11	-	-
110.	T.S.	F	4.0	4.0	-11	-11	0.0
111.	T.P.	M	15.3	_	+0.3	-	-
112.	V.S.	F	4.3	4.0	-10.7	-11	+0.3
113.	V.P.	F	7.5	13.6	-7.5	-1.4	-6.1
114.	A.B.	F	2.0	4.0	-13	-11	-2.0
115.	A.O.	M	3.0	13.0	-12	-2	-10.0
116.	A.I.	F	8.0	4.0	-7	-11	+4.0
117.	B.I.	F	1.0	0	-14	-15	+1.0
118.	B.A.	F	0	0	-15	-15	0.0
119.	B.L.	F	8	4	-7	-11	+4.0
120.	C.B.	M	13	15	-2	0	-2.0
121.	C.L.	F	22	0	+7	-15	22.0
122.	C.S.	M	8	7	-7	-8	+1.0
123.	D.A.	F	7	0	-8	-15	+7.0
124.	G.M.	F	3	0	-12	-15	+3.0
125.	K.M.	M	8	0	-7	-15	+8.0
126.	L.A.	M	6	10	-9	-5	-4.0
127.	M.C.	F	3	19	-12	+4	-16.0
128.	M.M.	F	10	0	-5	-15	+10.0
129.	M.C.	M	5	6	-10	-9	-1.0
130.	M.I.	F	0	20	-15	+5	-20.0
131.	G.O.	F	7	0	-8	-15	+7.0
132.	P.I.	M	4	10	-11	-5	-6.0
133.	R.M.	F	0	1	-15	-14	-1.0
134.	F.D.	F	12.1	9.9	-2.9	-5.1	+2.2
135.	R.A-M.	F	3	1	-12	-1	+2.0
136.	H.S.	F	6	13	-9	-2	-7.0
137.	S.E.	M	14	9	-1	-6	+5.0
138.	T.G.	F	8	16	-7	+1	-8.0
139.	Z.M.	F	0	10	-15	-5	-10.0
140.	O.I.	M	9	0	-6	-15	+9.0

DISCUSSIONS

From the data obtained, we observe a percentage of 83% below the Bennett value of 15 degrees. If the prosthetic works are carried out using an average value of 15 degrees for the left/right Bennett angle, then the positioning of the volumes represented by the artificial teeth will be distalized. Similarly, the canine guidance will have a distalized path, which in situ will result in interference and loading of the canines, because the laterality achieved in the laboratory on the programmable articulator will not be the same as the laterality movements perfomed by the patient.

When we perform indirect prosthetic work on natural teeth or implants, it is necessary to transmit the exact measurements from the condylography to the dental technician. In the dental laboratory, the process of performing prosthetic works requires understanding the specifications of the case and its limitations. The maximum intercuspation position is a static position and everything related to the masticatory reflex is part of the dynamic occlusion where the programming of the Bennett angles can determine the functionality in the oral cavity. Erroneous programming of Bennett angles can lead to neuromuscular and occluso-articular imbalances.

CONCLUSIONS

242 results from 140 patients are recorded in the statistical table. In the case of patients where the value of the Bennett angle could not be recorded on one of the sides, we interpreted it as a missing measurement.

We considered the deviation from the average of 15°: those lower than 15° are minus, and the largest are plus. Only 42 results are positive, i.e. over 15°, which represents 17% of all measurements. The rest, i.e. 83%, are less than or equal to 15.

The frequency with which -11 appears, that is 4°, is surprising. There are 62 such results, which represents 25% of the total measurements. So a quarter of the patients had at least a 4° Bennett angle. There are another 20 values near 4 (that is, strictly greater than 3 and strictly less than 5), which brings the number of occurrences of a value near 4 to about 34%. This observation can be generalized, statistically speaking, at the level of the entire population.

In total we have:

- between 0° and 5°: 97 values, i.e. 40%
- between 5° and 10°: 63 values, i.e. 26%
- between 10° and 15°: 38 values, i.e. 15.7%
- between 15° and 20°: 31 values, i.e. 12.8%
- between 20° and 25°: 8 values, i.e. 3.3%
- between 25° and 30°: 5 values, i.e. 2%

Right-Left differences (these could only be done for 102 patients, both measurements were possible):

- between 0 and 5°: 32 positive values and 21 negative values, total 53, i.e. 52%
- between 5 and 10°: 14 positive values and 14 negative values, total 28, i.e. 27.4%
- between 10 and 15°: 7 positive values and 4 negative values, total 11, i.e. 10.7%
- between 15 and 20°: 2 positive values and 4 negative values, total 6, i.e. 5%
- between 20 and 25°: 3 positive values and 0 negative values, total 3, i.e. 3%
- between 25 and 30°: 1 positive value and 0 negative values, total 1, i.e. 1%

Of the 9 0.0 Right-Left differences, 8 are given by the 4-4 angles and one by 0-0.

In 38 patients, i.e. 27.1% of the total, due to temporomandibular joint problems, only one measurement could be performed. Of these, 17, i.e. 44.7%, could not be performed on the right side, and 21, i.e. 55.3%, on the left side.

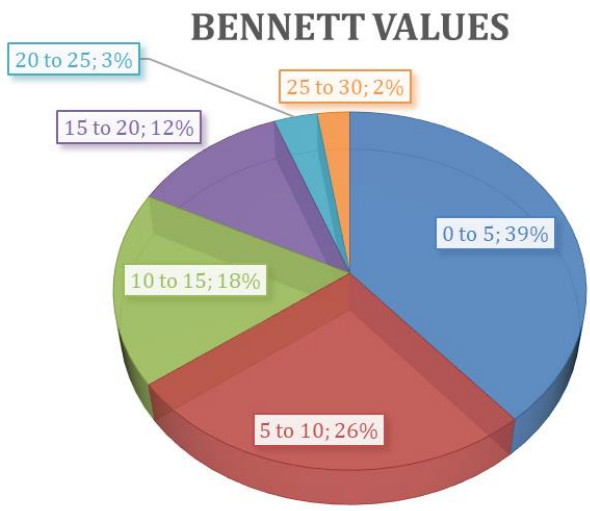

Figure 6. Chart – Bennett Values

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A detailed study on the antitumor effects of consecrated drugs - digoxin and labetalol

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Abstract

Cardiotonic glycosides and beta-blockers are drug classes intensely known for their benefits in cardiovascular diseases, having therapeutic utility in certain conditions and in pregnant women. Due to their established actions, in recent years attention has been directed towards the antitumor effect of cardiotonic glycosides and non-selective beta-blockers. Thus, the aim of the present study was to highlight the anticancer activity of digoxin and labetalol, both in vitro and in vivo, to continue evaluating their effects and to study in more detail their mechanisms of antitumor action. Analyzing the data, it can be say that digoxin, but also non-selective beta-blockers, including labetalol, are promising anticancer agents.

Keywords: cardiotonic glycosides, digoxin, beta-blockers, labetalol, anticancer effect

INTRODUCTION

Digoxin is part of the class of cardiotonic glycosides derived from Digitalis plant species. It is one of the most used drugs in therapeutic practice, being known for its beneficial effects in heart diseases such as heart failure and cardiac arrhythmias. The mechanism of action consists in its positive inotropic effect (increases the contractility of the myocardium), the increase of blood volume and blood pressure and, in addition, the reduction of heart rate [1]. The positive cardiac inotropic effect is exerted by inhibiting the Na+/K+ ATPase pump, resulting in an increase intracellular concentration of calcium ions [2]. According to the classification of the risks of pharmaceutical preparations, stipulated by the FDA (Food and Drug Administration), digoxin is part of risk category C. Digoxin can be administered during pregnancy, if the potential benefits justify the potential risks. Cardiomyopathy in pregnancy can be catastrophic for the mother's health, accounting for up to 11% of maternal deaths. Therefore, the cardiotonic glycoside can be administered to pregnant women who have persistent symptoms of heart failure, despite the treatment instituted with beta-blockers or other cardiovascular drugs. During pregnancy, digoxin can also be used to treat maternal tachycardia, an arrhythmia with rapid ventricular response [3]. Digoxin is a substance that easily crosses the placenta, but in normal doses, it has a minimal negative effect on the child.

Another category of drugs analyzed in terms of administration among pregnant women with cardiomyopathy is that of beta-blockers, synthetic drugs, included in risk class C. Beta-blockers are considered safe drugs during pregnancy; however, some studies suggest that they may limit intrauterine growth. Selective beta-1 compounds are preferred to be used, such as metoprolol, compared to non-selective ones that can stimulate uterine contractions. However, labetalol, a non-selective beta-blocker (alpha and beta-blocker), is routinely administered to pregnant women for the treatment of hypertension and cardiomyopathy, preserving uteroplacental blood flow. Although it has a favorable safety profile, labetalol induced several adverse effects in pregnant women, such as: bradycardia, arterial hypotension, or maternal hepatotoxicity [4,5]. After birth, newborns of mothers who have treated with beta-blockers must be monitored for up to 3 days to evaluate the potential adverse effects that may occur [6].

Recently, attention has focused on the potential anticancer effects of existing drugs in therapy for the treatment of various pathologies. Specific cardiovascular medication has demonstrated its effectiveness in heart diseases even in certain physiological states, such as pregnancy, but today it is desired to study in detail their toxic effects and especially their anticancer properties through in vitro and in vivo studies.

Cancer is considered a major health problem that affects the entire population of the world. In the last decades, numerous studies have been conducted to establish the mechanisms of carcinogenicity, but especially to identify the antitumor potential of natural compounds [7].

Standard cancer treatments consist of chemotherapy, radiotherapy, and surgery. The basic goal of anticancer therapy is to kill the tumor cell without affecting the healthy cell, but in the case of standard therapy, this is not fully achieved, as the healthy cells are also affected and numerous adverse effects occur such as anemia, peripheral neuropathy, and loss of appetite [8]. Starting from these inconveniences, it was desired to develop a treatment as effective as possible, with targeted action and with reduced side effects [9]. Thus, the study of natural compounds in the treatment of carcinomas began; observing that they are better tolerated, with few adverse reactions, and can be administered even in particular physiological situations, such as pregnancy. An example of an intensively studied natural compound is betulinic acid, a pentacyclic triterpene, which exhibits numerous biological

activities, including antitumor effects against several types of cancer cells. In addition, several conventional antitumor agents are derived from natural sources such as Taxol, vinca alkaloids [10]. Studies in recent years have suggested that cardiac glycosides and beta-blockers may exhibit antitumor activity [11-13].

Aim and objectives

The aim of this study was to highlight the anticancer activity of cardiotonic glycosides and non-selective beta-blockers, more precisely digoxin and labetalol, both in vitro and in vivo, in order to continue the study of their effects and in detail the mechanisms of action the basis of their antitumor activity.

MATERIALS AND METHODS

Systematic searches were performed on PubMed, Google Scholar to identify relevant studies on the anticancer effect of cardiotonic glycosides and beta-blockers, especially digoxin and labetalol respectively. Data related to the antitumor activity of cardiotonic glycosides and β-blockers through in vitro and in vivo studies were extracted.

The searches in the specialized literature were carried out using the following terms: cardiotonic glycosides, digoxin, beta-blockers, labetalol, cancer, anticancer/antitumor effect, in vitro/in vivo studies. The titles and abstracts of the identified studies were checked in detail to finally exclude irrelevant studies. Relevant articles were assessed to determine whether they were eligible or should be removed. References from eligible articles were screened to further pick out potentially relevant studies.

RESULTS AND DISCUSSIONS

The initial search revealed a number of 3378 results for cardiotonic glycosides and 18167 for beta-blockers in the PubMed database from the past 10 years, which were then sorted to select information specific to our study, as can be seen in figure 1.

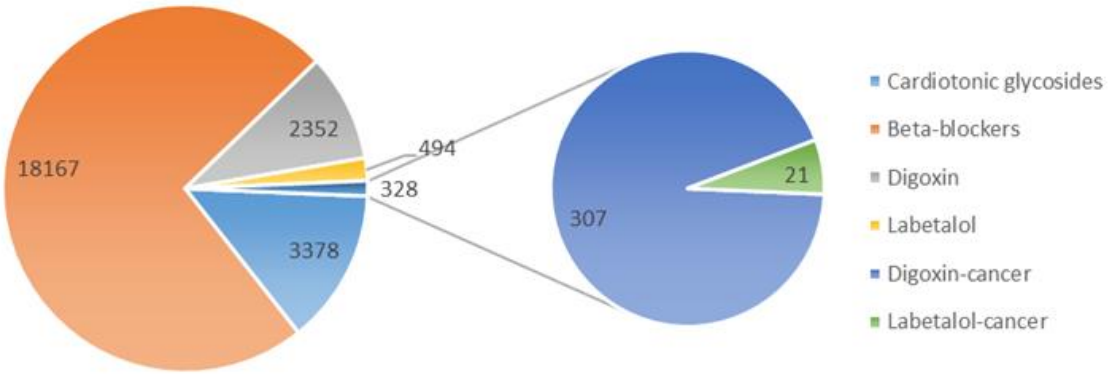

Figure 1. Diagram of systematic database searches

In the following, we will present the articles from which we began our research to analyze the anticancer effect of digoxin and the beta-blocker, labetalol.

Now, worldwide, cancer is one of the main causes of mortality. More precisely, cancer is the second cause of mortality in the population under 70, immediately after cardiovascular pathologies [14].

In recent years, research studies have focused on investigating the anticancer potential of several molecules used in therapy to treat various pathologies. Thus, cardiotonic glycosides and especially digoxin came to the fore, as promising molecules in the treatment of cancers,

their targeted effect being investigated at the molecular level [15]. Digoxin has attracted attention regarding its potential antitumor activities, highlighting its capacity to inhibit cancer cell proliferation and induce apoptosis [16].

Moreover, there is evidence that beta-blockers, both the non-selective ones (labetalol, propranolol, carvedilol) and the selective ones (nebivolol, atenolol), show activity in the treatment of cancer. Most studies have highlighted the effect of non-selective molecules, especially propranolol [17-19].

The cytotoxic effect of digoxin was exposed by our research group through *in vitro* studies on melanoma cells and *in ovo*, in association with betulinic acid, known for its antitumor activity [20]. From these first studies carried out, we want to continue closely investigating the antitumor mechanism of digoxin in skin cancer. This can be accomplished by evaluating and summarizing its antitumor potential in other types of cancer.

Cardiotonic glycosides - digoxin - candidates for cancer treatment. Preclinical studies

Cardiotonic glycosides are molecules that show antitumor properties against lung cancer at relatively low concentrations [21,22]. Digoxin has demonstrated that inhibits the development of the primary tumor and, in addition, inhibits the metastasis of tumor cells from the breast to the lung, by implantation in severe combined immunodeficiency mice [23]. It was observed, at the molecular level, that digoxin decreases NDRG1 (N-Myc Downstream Regulated 1) and VEGF (Vascular endothelial growth factor) by inhibiting HIF-1α (Hypoxia-inducible factor 1-alpha) in lung adenocarcinoma cells (A549) under low oxygen conditions [24]. Other studies have strengthened the potential of digoxin's antitumor activity on lung cancer. The study led by Lin revealed that digoxin inhibited the proliferation, migration, and colony formation of A549 cancer cells and was found to suppress Src (Proto-oncogene tyrosine-protein kinase) activity and its protein expression in a dose (50-500 nM) and time (2-24 hours) dependent manner and, moreover, it decreases the activity of EGFR (Epidermal growth factor receptor) and STAT3 (Signal Transducer Moreover, activator of transcription 3) [25]. Another study, carried out on human non-small cell lung cancer cells (A549 and H1299), showed that digoxin induces autophagy in the two cancer lines by inhibiting the phosphorylation of Akt (Protein kinase B), mTOR (Mechanistic target of rapamycin) and p70S6K (Ribosomal protein S6 kinase beta-1) [26].

On the other hand, digoxin inhibits the proliferation of lung cancer by hampering the expression of subunit α-1 and exerts discriminatory antitumor activity in lung cancer cells with STK11 (Serine/threonine kinase 11) mutation; mutation considered a new biomarker in the treatment of lung cancer for cardiotonic glycosides [27].

Lately, different scientific research groups have suggested that cardiotonic glycosides have the potential to inhibit the proliferation of breast cancer, with a selective effect only on cancer cells. It has been shown that digoxin together with other glycosides such as: peruvoside, strophanthidin, ouabain, oleandrin and lanatoside C suppress the development of breast cancer [21, 28-30]. Glioblastoma is considered one of the most aggressive carcinomas in the world, often relapsing even after chemotherapy and surgery [31]. In this direction, digoxin has been shown to target HIF-1α in human glioma stem cells and induce apoptotic effects in brain cancer [32,33].

The antitumor effect of digoxin was studied on neuroblastoma xenografts from mice, as well as Lewis's lung and colon cancer. SH-SY5Y neuroblastoma grafts were inhibited in the highest proportion of 44%, respectively 19% for Neuro-2a, while lung and colon cancer grafts were less sensitive. Digoxin revealed an inhibitory effect (50% at 53 ng/ml) on angiogenesis *in vitro* on bovine endothelial cells and *in ovo* through the chicken chorioallantoic membrane assay [34]. On the other hand, it was observed that the administration of low and long-term

doses of digoxin, digitoxin and ouabain inhibits the expression of the PSA gene (Prostate-Specific Antigen) by changing the expression of the PDEF gene (Prostate-derived Ets factor) in human prostate cancer cell lines (LNCaP) [35]. Following a systematic screening of 2000 drugs, it was revealed that five cardiotonic glycosides, such as: digoxin, digitoxin, peruvoside, strophanthidin and ouabain, cause the death of anoikis-resistant PP-C1 prostate cancer cells. In addition, digitoxin and ouabain produced apoptosis in prostate cancer cells (PC3) by reducing the expression of Hoxb-13, hepatocyte nuclear factor-3α, hPSE/PDEF and SURVIVIN [36].

The most used cardiotonic glycosides, with the most proven actions in the treatment of cancer, are digoxin and digitoxin. The structural difference between digitoxin and digoxin is an additional hydroxyl group on digoxin, which changes the pharmacokinetic and pharmacodynamic of the molecule. Therefore, digitoxin is a more lipophilic substance, metabolized mainly in the liver and with a longer half-life than digoxin [37].

According to the above, table 1 shows the mode of action of digoxin and digitoxin on cancer cells.

Table 1. Digoxin and digitoxin and their mode of action in cancer cells

Cardiotonic glycosides	Mechanism of action	References
Digoxin	inhibits HIF-1alpha synthesis	[32]
	inhibits androgen-dependent/independent mechanism	[38]
	inhibits Src signaling pathways	[39]
Digitoxin	↓ anti-apoptotic proteins Bcl-xL and Bcl-2	[40]
	↑ cytochrome c release and Caspase activation	[41]
	inhibits topoisomerase I	[42]
	↑ Ca2+ uptake	[43]
	inhibits p53 synthesis	[44]
	inhibits general protein synthesis	[45]
	caspase 9 mediated apoptosis	[46]
	MAPK pathway mediated apoptosis	[47]

The presented preclinical investigations have suggested that cardiac glycosides, including digoxin, may exert anticancer activity. As well as the preclinical studies, there are also numerous clinical studies that reinforce the idea of studying in depth the anticancer effect of cardiotonic glycosides.

Cardiotonic glycosides - digoxin - candidates for cancer treatment. Clinical studies

It is well known that cardiotonic glycosides are effective in the treatment of cardiovascular diseases. But as we can see, this drug class is increasingly shaping its anti-tumor effect, an effect also supported in clinical studies. Several cardiotonic glycosides have been included in clinical trials, including digoxin, Anvirzel (aqueous extract of *Nerium oleander*), PBI-02504 (CO_2 extract of *Nerium oleander*), and UNBS-1450 (semisynthetic derivative). The first results of the phase I studies were promising. More precisely, Anvirzel has shown that it has an anticancer effect with a safe and effective administration up to 1.2 mL/m^2/day. This pharmaceutical form has been clinically studied for its effect on non-small cell lung cancer in combination with chemotherapy medication [48,49]. Regarding the PBI-

05,204 extract, the maximum tolerated doses evaluated (0.6–10.2 mg/day) in phase I studies were shown to be effective and it was recommended to proceed to phase II studies in the treatment of colon cancer, rectum, breast, and bladder. Following these studies, the safety, pharmacokinetics, and pharmacodynamics of the product were monitored, and the most tolerated dose of 0.2255 mg/kg was identified [50].

Digoxin has so far been included in 32 clinical studies to evaluate the antitumor effect in several types of cancer (breast, prostate, pancreatic, etc.), alone or in combination with other immunotherapeutic drugs [51]. A clear example is the association of digoxin with cisplatin in head and neck cancer, where a stronger effect of the combination was observed than in the case of using the compounds separately [52].

Cardiotonic glycosides, especially digoxin and digitoxin, have been intensively evaluated regarding their anticancer potential in numerous preclinical and clinical studies, figure 2 shows this information.

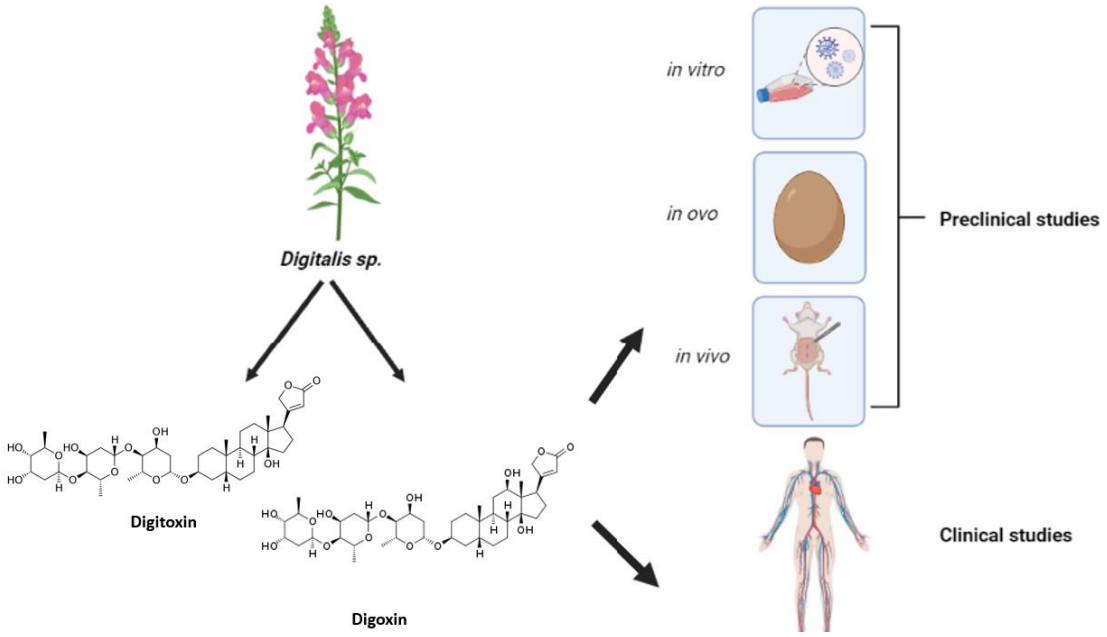

Figure 2. Digoxin and digitoxin - preclinical and clinical studies

Digoxin, a compound long used in cardiovascular diseases, has shown potential in the treatment of cancer. We want to supplement the data obtained by our research group and those from the literature with other more detailed studies, especially regarding the mechanism of digoxin's cytotoxic action at the level of skin cancer cells. Moreover, we wish to continue studying another drug used in cardiac pathologies, labetalol, considered safe in pregnancy, regarding its antitumor action.

A first study carried out by our research team showed that labetalol does not show cardio and hepatotoxicity *in vitro* on healthy cells, willing to deepen the effect of the beta-blocker on cancerous cell lines [53].

Beta-blockers - labetalol - candidates for cancer treatment. Preclinical studies

Beta-blockers are a heterogeneous pharmacotherapeutic class that presents multiple benefits in cardiovascular diseases leading to the reduction of mortality caused by these pathologies [54]. Furthermore, to the proven benefits, in recent years this drug class has sparked interest in studying its antitumor effects.

Regarding the effect on cancer cells, propranolol and other β-blocker drugs have been observed to reduce MAPK activity in pancreatic carcinoma [17,55,56]. It has also been

reported that propranolol decreases the viability and migration of breast cancer lines, to the greatest extent when co-administered with metformin. Thus, it was concluded that the two drugs decrease tumor development, improving survival, an effect observed after studying two models of triple breast cancer. Besides these, the evidence suggests that non-selective beta-blockers, more precisely propranolol, potentiate the anti-angiogenic and antitumor effects of chemotherapy medication [17,57]. In breast cancer biopsies isolated from patients who received propranolol, changes in cancerous proliferation were observed. More precisely, on the MDA-MB-231 cell line, it was demonstrated that propranolol after 24 hours of treatment produces changes in cell viability, observed with the help of flow cytometry [58].

To support the *in vitro* effect of beta-blockers, additional studies and especially clinical studies are needed.

Beta-blockers - labetalol - candidates for cancer treatment. Clinical studies

In a phase II, placebo-controlled, triple-blind study, the research group noted that the administration of propranolol before surgical removal of breast cancer was associated with an important decrease in the expression of metastasis markers [59]. Thus, this evidence supporting the survival benefits of beta-blockers should pave the way for a phase III clinical trial. The study by Watkins et al., which included a large number of patients (>1400), evaluated the effect of β-blockers in ovarian cancer. Beta-blockers showed an increase in overall survival compared to patients who were not given the drugs. Moreover, it was reported that this increase in survival was characteristically associated with non-selective beta-blockers [60].

Another study conducted on the Swedish population indicated that patients with pancreatic cancer who received beta-blockers had a lower mortality specific to adenocarcinoma [61]. In another type of cancer, prostate cancer, it was observed that beta-blockers decrease pathology-specific mortality, results that were obtained after 4 observational studies that included 16825 patients [62].

Also, the administration of non-selective beta-blockers was correlated with a longer survival in patients with metastatic melanoma compared to those who were administered selective beta-blockers [63,64]. Beta-blockers have shown their benefits in several types of cancer; however, new preclinical and clinical studies are needed to establish the utility of this drug class in cancer management. Beta-blockers have been evaluated for their antitumor potential in various preclinical and clinical studies, figure 3 outlines this.

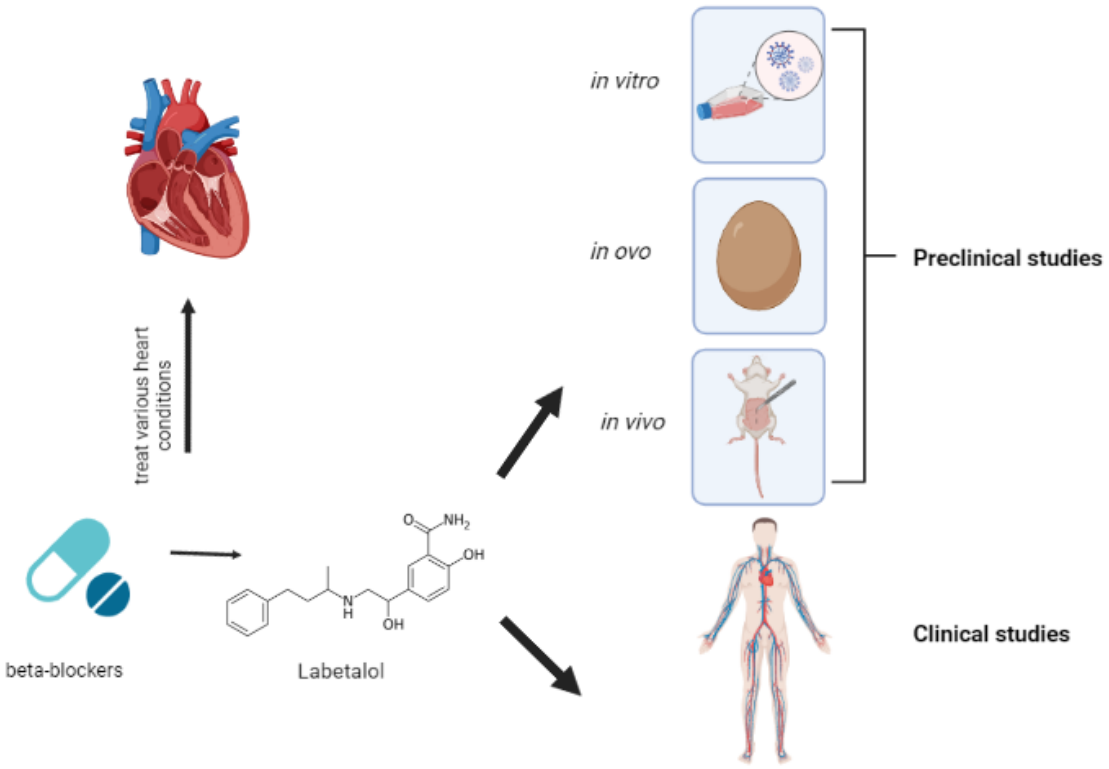

Figure 3. Beta-blockers- labetalol - preclinical and clinical studies

CONCLUSIONS

Cardiotonic glycosides and beta-blockers have been used in the treatment of cardiovascular pathologies, but studies in recent years on cancer cell lines and animal systems have revealed other new therapeutic actions, supported by clinical studies. Analyzing the data, it can be noted that digoxin, but also non-selective beta-blockers, including labetalol, are promising anticancer agents according to the information from the specialized literature. The antitumor effect of labetalol has not been intensively debated, but the beneficial effect of propranolol in the treatment of cancer, which is part of the same class of non-selective beta-blockers, has been highlighted. Therefore, our research group will focus on the study of the labetalol molecule. Although there is clear evidence for both substances, further studies are needed to support their cytotoxic effects and to understand in detail their mechanism of action.

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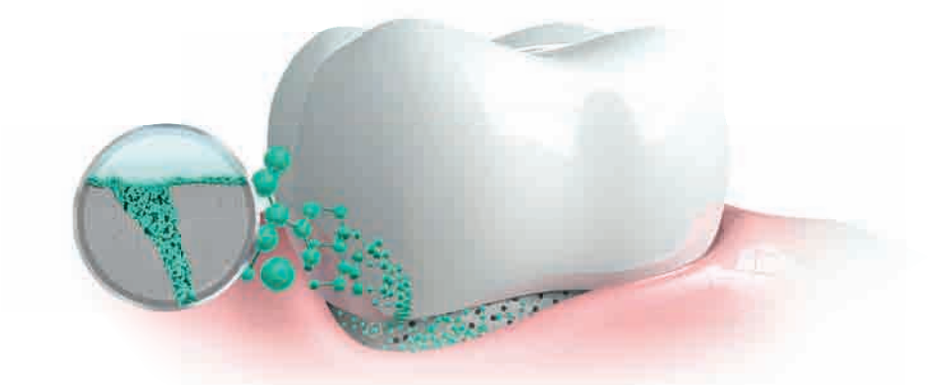
Noul elmex®SENSITIVE PROFESSIONAL cu tehnologia PRO-ARGIN

Calmarea **imediată* și de durată** a durerii din sensibilitatea dentară[1,2]



- În contact cu saliva, se formează un strat bogat în calciu, care obturează instant[1,*] tubulii dentinari deschiși
- Stratul rămâne intact în timp, chiar după expunerea la acizi, asigurând calmarea de durată a durerii din sensibilitatea dentară[2,3]

93% dintre pacienți confirmă calmarea durerii din sensibilitatea dentară[4]

93% dintre pacienți — confirmă reducerea hipersensibilității dentinare[4]

91% dintre pacienți — apreciază recomandarea medicului stomatolog[4]

Calmarea imediată* a durerii din sensibilitatea dentară[1]

Calmarea imediată* și de durată începe cu recomandarea dumneavoastră**

*Pentru calmare imediată, aplicați direct cu degetul pe dintele sensibil și masați ușor pentru 1 minut;
**Doar în legătură cu pasta de dinți

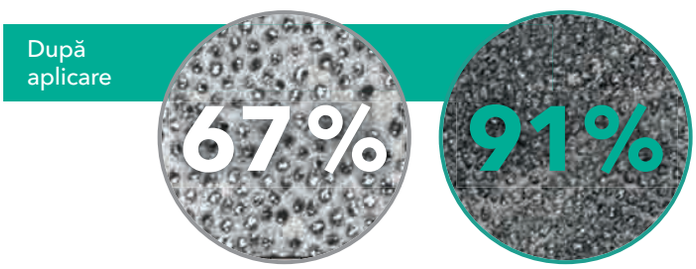
Referințe: 1. Nathoo S, et al. J Clin Dent. 2009;20(Spec Iss):123 –130; 2. Docimo R, et al. J Clin Dent. 2009;20(Spec Iss): 17– 22.; 3. Report Deon Hines-0003, 2016; 4. Studiu Ipsos cu privire la utilizarea produsului elmex® SENSITIVE PROFESSIONAL Repair & Prevent, efectuat în Polonia, rezultate după 2 săptămâni de utilizare, cu 325 de participanți (2017).

elmex® SENSITIVE PROFESSIONAL realizează obturarea superioară a tubulilor dentinari în comparație cu tehnologiile concurente[1,2,*]

Studiul 1[1,*]

Tehnologia cu fluorură de staniu/ fluorură de sodiu

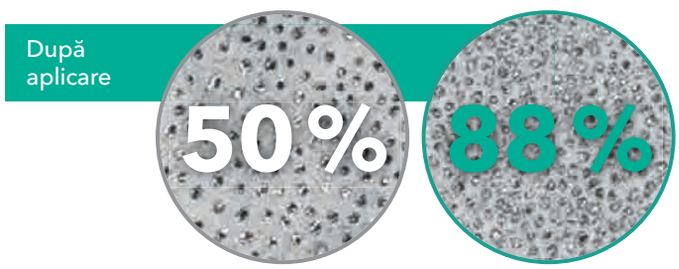
Tehnologia PRO-ARGIN



Studiul 2[2,*]

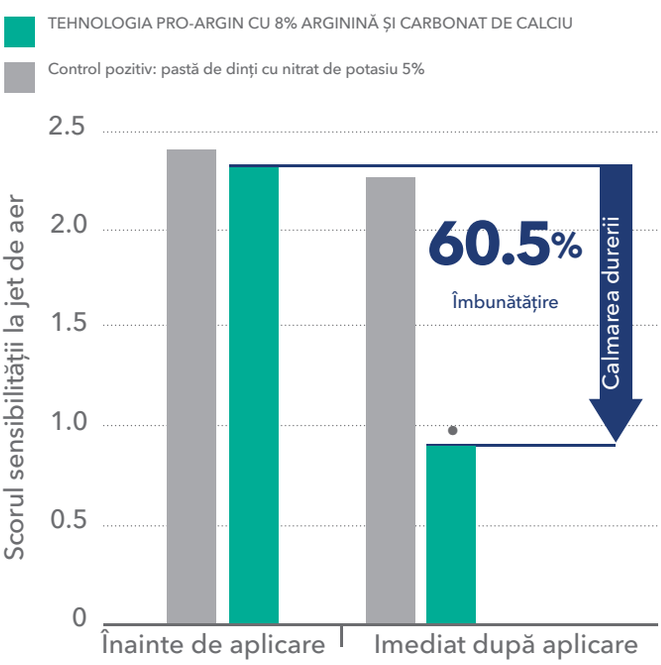
Tehnologia Novamin/ fluorură de sodiu

Tehnologia PRO-ARGIN



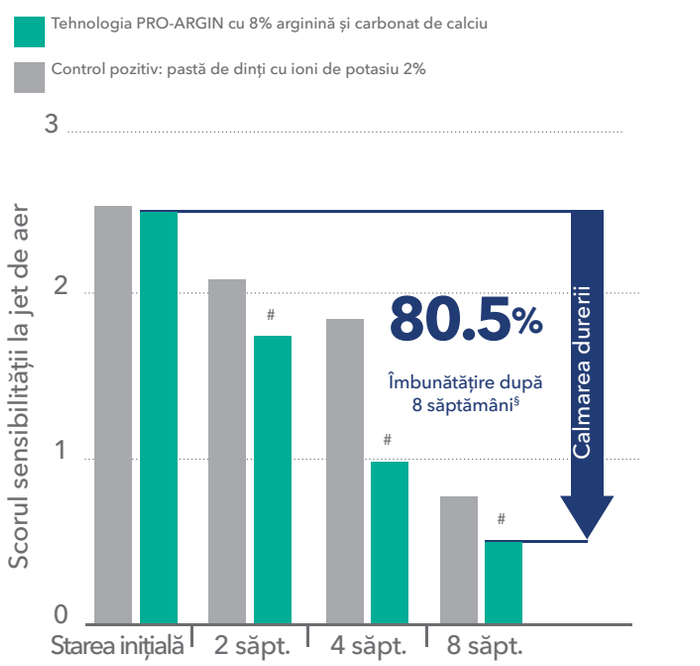
elmex® SENSITIVE PROFESSIONAL oferă calmare semnificativă imediată** și de durată a durerii din sensibilitatea dentară[3,4]

Calmarea semnificativă a durerii din sensibilitatea dentară instant[3,‡,**]



‡ În comparație cu starea inițială (sunt prezentate doar datele relevante)
• Semnificativ statistic (p<0,001)

Calmarea semnificativă de lungă durată a durerii din sensibilitatea dentară după 2, 4, și 8 săptămâni de utilizare[4,§,&]



§ În comparație cu starea inițială
& În comparație cu o pastă de dinți comercială desensibilizantă, ce conține 2% ioni de potasiu și 1450 ppm de fluor (NaF)
# Semnificativ statistic (p<0,05)

*Studiu in vitro, imagini reale de microscopie confocală după 5 aplicări (p<0,05%);
**Pentru calmarea imediată aplicați direct pe suprafața sensibilă și masați ușor cu vârful degetului timp de 1 minut.

Referințe: 1. Hines D, et al. Poster acceptat, July 2018 IADR. Colgate- Palmolive Company 2018.; 2. Hines D, et al. Poster #0742, March 2018 AADR. Colgate-Palmolive Company 2018.; 3. Nathoo S, et al. J Clin Dent. 2009;20(Spec Iss):123 –130; 4. Docimo R, et al. J Clin Dent. 2009; 20(Spec Iss): 17– 22.

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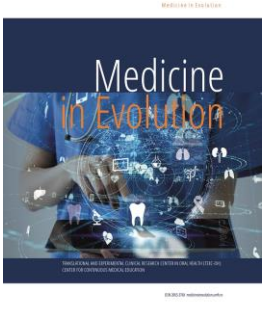
Enameloplasty in interdisciplinary treatment of dental injuries – case report



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Abstract

Case presentation: Traumatic lesions of the upper incisor group can target only one of the dental topographical areas, being represented by crown fractures with or without affecting the pulp chamber, crown-root or root fractures or they can also involve the alveolar process. Another category of dental trauma can be represented by complete or incomplete dental dislocations, as well as traumatic tooth avulsion.

Material and method: In this study we presented the case of the 12-year-old patient with traumatic avulsion of the two upper central incisors. The interdisciplinary treatment performed was orthodontic and direct restorative. We used Herculite dental composites system from Kerr, Germany.

Discussions/Conclusions: The direct restorative composites are able to perform as an intermediate solution during the complex treatment when morphological dental transformations are required and to facilitate the objectives of the orthodontic treatment in frontal traumatic injuries.

Keywords: traumatic avulsion, orthodontic, restorative, composite, incisors

INTRODUCTION

In the last period, there is an increased frequency of dental-facial traumatic accidents in children and young people, by increasing the number of traffic accidents, sports accidents, and especially playgrounds accidents. It seems that this pathology is directly related to the intensification of road traffic, congestion and daily agitation, both in urban and rural environments.

It was found that the traumas of the frontal teeth represent, second to untreated dental caries, the major cause of the occurrence of large crown destructions in child and adolescent patients. According to Andersson [1, 2], the prevalence of traumatic dental injuries (TDIs) in children and adolescents is approximately 20% and varies little. Petti et al [3] found that traumatic dental injuries occur in both primary and permanent dentitions, although the prevalence in primary dentition is higher. So traumatic accidents in children and young people can affect temporary teeth, but also permanent teeth. According to some authors, the period of maximum frequency would be between 1-10 years, and according to others between 7-18 years, with the higher incidence in males [4, 5].

From the dental trauma classification system provided by Andreasen [6], the pathologies that can be treated by ameloplasty/ enameloplasty (associated with orthodontic treatment) are: enamel cracks and crown fractures without complications. But enameloplasty also finds its application in the treatment of dental avulsions, when the limiting teeth of the traumatically edentulous space are orthodontically moved in order to redistribute the space. As a result they require a "disguise" to be as close as possible to the shape, size and color of traumatic lost teeth.

The mechanism of producing dental-periodontal lesions can be directly (the traumatic forces acting on the dental structures) or indirectly, usually in forced occlusions, in the case of falls or hits on the chin, leading in some situations to the avulsion of the involved teeth [7-10].

Aim and objectives

The aim of this case report was to emphasize the use of direct composite restorative adhesive materials in a situation of traumatic injury of frontal upper incisors, with following partial avulsion. First the edentulous traumatic space was the subject of orthodontic treatment to re-distribute the remaining teeth for an improved occlusion and to prepare proper dental abutment axis for the future definitive prosthetic work. During the orthodontic treatment, due to aesthetic considerations, and to facilitate the orthodontic occlusal achievement, we „transformed" an upper lateral incisor into upper central incisor or an upper canine into an upper central incisor using direct adhesive composites placed into a conforming crown.

CASE REPORT

I. Anamnesis

This is the case of PM, 12-year-old female patient. She presented to the dental office after a fall in the street, with open mouth. The patient was clinically sound.

II. Clinical examination data

At clinical examination we discovered the following:

- the traumatic avulsion of the both upper central incisors
- the avulsed 2.1 remained gingivally embedded in a horizontal position
- the absence of the upper right lateral incisor (1.2)
- a treated carious lesion on 7.5

III. Paraclinical investigations

The initial OPT confirmed the absence of the bud of 1.2, and especially the 2.1 enclaved in gingival mucosa (Figure 1, arrow).

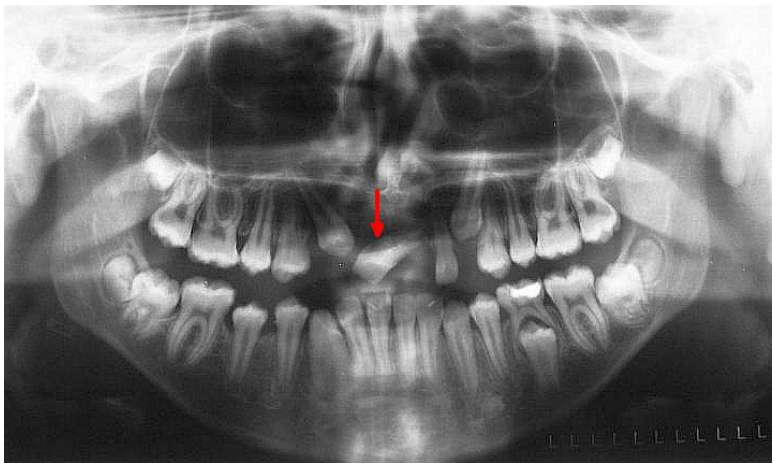


Figure 1. Patient PM, female, 12 years old, with traumatic avulsion of 1.1, 2.1 and anodontia of 1.2 (initial radiological appearance)

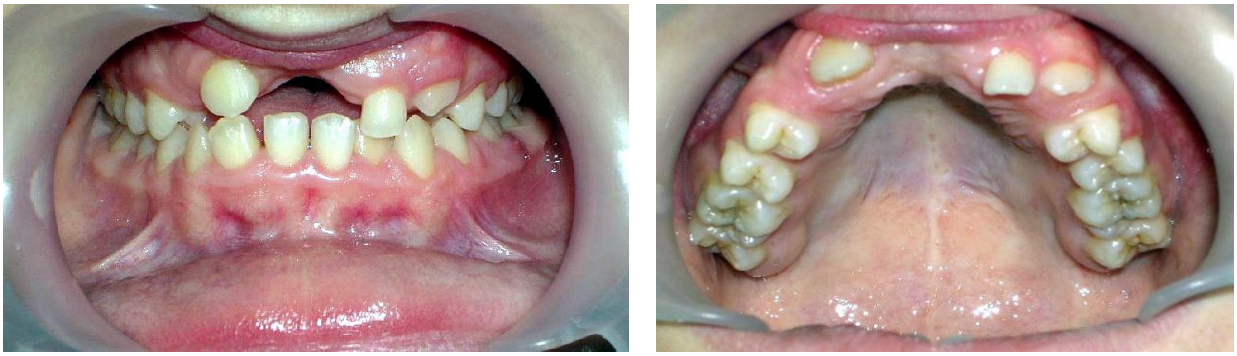
In a first stage, for the dental trauma with avulsion, the indication was for an emergency extraction of 2.1, the patient remaining under observation until the wound in the upper frontal area was completely healed.

Three months after the accident, the oral examination revealed the superposition of the lower frontal group through egression with the inversion of the incisal line, due to the lack of antagonists (Figure 2a) and an atypical swallowing by interposing the tip of the tongue in the edentulous space.

The complex diagnosis was:

- anodontia of the upper right lateral incisor (asymmetry),
- frontal open occlusion,
- occlusal-articular dysfunction,
- atypical swallowing, of traumatic etiology;

alteration of masticatory, physiognomic and self-maintenance functions.



a b

Figure 2. Intraoral appearance of patient PM, female, 12 years old, 3 months after the avulsion of 1.1 and 2.1 (a – occlusal, b – upper arch)

IV. Treatment and evolution

In this situation, the orthodontist followed the objectives of judicious redistribution of the existing spaces. This was performed in order to establish a final fixed prosthetic solution,

with the favorable placement of the future abutment teeth. So the orthodontic and restorative treatment were pre-prosthetic treatments.

After two years of orthodontic treatment, the mesial displacement of the lateral groups was obtained. In order to maintain the results, the orthodontist chose a palatal plate, with an artificial tooth next to 1.1 for physiognomic reasons, also acting as a temporary prosthesis. An important role in reaching this stage was played by the upper wisdom molars, which in their eruption process generated true mesialization impulses of the lateral teeth.

For the insertion of the lower frontal group, the orthodontist used a fixed appliance on the lower arch.

As far as we are concerned, after applying the device, we transformed 1.3 and 2.2 on their initial positions into approximate central incisors. This step was dictated by their morphology (Figure 3 and 4) and performed to obtain a minimum frontal overlap:

- 1.3 with a very high gingival margin and a large vertical dimension, and
- 2.2 with a smaller vertical dimension, the gingival border being approximately next to the lower portion of the cervical third of the vestibular face of 1.3 (Figure 3).

Figure 3. Patient PM, female, 14 years old, occlusal aspect with ameloplasty of 1.3 and 2.2 with composite materials placed in the celluloid cap/transparent crown

We used the method of direct enameloplasty with composite materials applied to the tooth surface by means of celluloid caps, with an increased interest in building the incisal angles and less in covering the vestibular face.

The work phases were:

- teeth isolation,
- demineralization of the working area with ortho-phosphoric acid 34% (UltraEtch, Ultradent, USA), for 20 s, washing with water and drying,
- application of the adhesive (OptiBond, Kerr, Germany) according to the manufacturer's instructions, then photopolymerized for 20 seconds.
- the choice from the celluloid caps kit (Frasaco, Italy) of two incisor-shaped caps that we adapted up to half of the gingivo-incisal distance, so that they cover only the incisal half of the crowns of the targeted teeth. We practiced at the incisal level 3 holes for the evacuation of the surplus material. Then we filled the caps with composite (A2, Herculite XRV, Kerr, Germany) taking care not to retain air voids, and applying them with pressure on the two teeth. After removing the excess composite, it was photopolymerized for 40 s (20 s on the vestibular side and 20 s on the palatal side). When the hardening of the composite resin was obtained, we removed the caps with one dental probe. [11, 12]

- occlusion adaptation (static and dynamic) of the obtained surfaces and finishing with finishing discs (OptiDisc, Kerr, Germany), points, cups and brushes with polishing paste.

We left most of the vestibular faces intact in order to place brackets to move the reshaped teeth towards the midline. One of the reasons for adopting this solution was to fix the bracket directly on the tooth enamel and not on a composite construction, in order to have an intimate control over the dental movements.

Until that prosthetic phase was reached, we found with satisfaction that after another two years of orthodontic treatment (fixed and mobile) the two modified teeth reached the frontal median area, with a point of contact, and the composite restorations by enameloplasty in the celluloid cap behaved honorably throughout this interval (Figure 4).

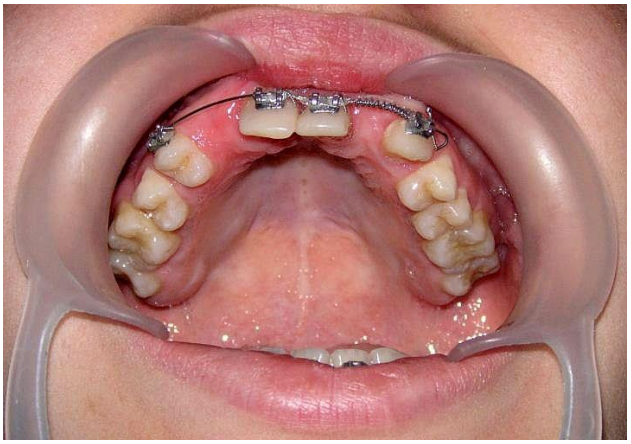


Figure 4. Patient PM, female, 16 years old, stage of orthodontic treatment, with placement of 1.3 and 2.2 on the space of the upper central incisors and their crowns remodeled by enameloplasty

DISCUSSIONS

In these "traumatizing" situations enameloplasty finds its usefulness, managing to bring simple, fast, relatively rapid solutions through the use of adhesive composite materials. These solutions can be temporary, but sometimes also "definitive". In support of what has been stated [13-15], we believe that the presented case can be an argument.

Insertion of the composite material with the help of a transparent celluloid cap/ crown matrix as a conformer, adapted to the dental structure (in the case of restoration of the entire dental morphology) or of a half adapted to the dental structure and proximal to the prepared surface (in the case of restoration of only a portion of the dental morphology) applied to the tooth that is to be restored can lead to favorable and quick solutions.

As general indications for manipulation, the literature and manufacturers propose that on the preparation for adhesion, a quantity of composite is applied with the help of a spatula moistened in adhesive, after which the crown matrix is filled with composite material and placed on tooth in the correct position and with pressure [12]. It will be photopolymerized for a longer time (60 s) vestibular and oral, and the excess will be removed. In the case of using an integral celluloid cap, small holes can be made in the incisal portion to facilitate the evacuation of excess material. Surface finishing is done with sharpened diamond cutters, and marginal finishing with flexible discs. The restoration must be checked in the centric relation position, in propulsion and laterality.

CONCLUSIONS

A particularization of the techniques of applying direct composite materials by layering are the veneers.

Most likely, the final prosthetic solution in our case will be through esthetic bridges or prosthetics on implants for the morpho-functional restoration of the traumatized area.

Although this time the enameloplasty was a temporary, intermediate solution during the complex treatment, the mechanical qualities of the micro-hybrid composite resin - Herculite XRV, Kerr, Germany – such as high resistance to compression / bending or wear resistance, as well as the color adaptation made this type of material to be chosen by us as a ultimate solution for crown remodeling of the incisal portion of the front teeth, we hope successfully.

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Anticoagulant therapy in patients with dental treatment needs. A literature study

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Abstract

Aim and objectives: The aim of this literature study was to review relevant articles regarding the specificity of dental treatments, especially oral surgery and implantation in anticoagulated patients. Material and methods: Using relevant MeSH terms, a search in PubMed database was performed in order to find publications about the particularities of dental treatments in patients who are anticoagulated, particularly with non-vitamin K antagonist oral anticoagulants (NOACs). Results: The practitioners must act taking into account the bleeding risk and the extent of the surgical procedure. Conclusions: The main conclusion is that the non-vitamin K antagonist oral anticoagulant (NOAC) therapy does not represent a contraindication for surgical dental procedures.

Keywords: anticoagulated patients, dental treatment, bleeding risk

INTRODUCTION

Non-vitamin K antagonist oral anticoagulants (NOACs), also known as direct oral anticoagulant drugs (DOACs) are considered nowadays safe and effective, and have dramatically increased the quality of life of the treated patients. NOACs are considered world-wide the medication of choice in many clinical situations, such as acute venous thromboembolic disease (deep vein thrombosis and pulmonary embolism), prevention of thromboembolism and stroke in patients with non-valvular atrial fibrillation, prophylaxis in the postoperative setting, and in the acute coronary syndrome. The dental treatments in clinical practice may rise sometimes difficulties because dentists face with patients requiring surgical procedures. Some of these patients have multiple comorbidities and, moreover, the dentists are more often performing invasive dental procedures in patients with anticoagulants. The rapid trigger of action, their relatively short half-life and predictable pharmacokinetics make the periprocedural use of the NOACs more simple and safer [1,2,3,4,5].

Clinical studies have demonstrated that NOACs have a safe efficacy and a predictable anticoagulant effect. They do not need a routine coagulation monitoring, although they require a good understanding of their effects, side-effects and interactions [6,7].

Aim and objectives

The aim of this article is to review the literature regarding the therapeutic attitude of the dentist with patients undergoing NOACs therapy and need surgical procedures of different extents.

MATERIAL AND METHODS

A literature review was conducted using PubMed database and applying relevant MeSH terms (between January 2011-December 2021). The primarily identified studies were screened independently by 2 reviewers using the following criteria: surgical dental treatment, patients taking anticoagulants and hemostatic intervention. After removing duplicates and irrelevant publications, the search identified 19 studies, which were reviewed and included in this work.

RESULTS

It is generally recognized, that the practitioners must make the difference between the therapeutic attitudes in invasive surgical procedures which require temporary discontinuation of NOACs, and the less invasive procedures with a low bleeding risk. These ones require minimally- or uninterrupted NOAC therapy [8].

For instance, in an extensive review, Steffel et al. concluded that dental extractions can generally be performed in the dental office using local hemostatic measures, without interrupting anticoagulation or by just omitting the morning dose of the NOAC (where applicable). The hemostatic techniques refer to the use of sutures, oxidized cellulose or resorbable gelatin sponge or compressive gauze soaked in tranexamic acid [8].

Additionally, getting into details, some authors recommend that dental extractions of 1 to 3 erupted teeth, implantation, root canal procedures, subgingival scaling may require a preprocedural temporary interruption period of 12 – 24 hours. The intervention may be scheduled 18 – 24 hours after the last NOAC dose, with a restart 6 hours later (i.e.not skipping a dose of rivaroxaban). The same authors reported that the patients with low or moderate

bleeding risk should take the last NOAC dose ≥24 hours before multiple tooth extractions of more than 3 teeth. Also, the creatinine clearance has an influence on the moment at which the last NOAC dose should be taken [8,9,10,11].

In cases of high risk of bleeding (extractions of more than 5 teeth, extensive surgery procedures in patients with comorbidities, or surgical procedures lasting more than 45 minutes), the intake of dabigatran, rivaroxaban and apixaban should be suspended 24 hours before surgery or even longer, depending on the renal function, and should be resumed 24 hours after. The authors provide no information about the use of edoxaban [12].

Another study, which included patients under treatment with dabigatran, apixaban and rivaroxaban, showed that continuing the medication at the time of teeth extractions led to bleeding similar to patients on warfarin with an INR between 2.0 and 4.0. (under local hemostasis). The authors concluded that there is no need to adjust the doses prior to dental extractions, or to schedule the extractions around doses, thus eliminating the thrombotic risk associated with anticoagulant interruption [13].

In contrary, other authors recommend that tooth extractions in patients with comorbidities taking direct oral anticoagulants may be safely managed when they are performed at least 4 hours after the last intake and do not involve 2 or 3 contiguous premolars and molars [14].

Delayed extractions of at least 6 hours after the last dose (in patients under dabigatran or rivaroxaban) are also recommended from some authors. They also concluded that an interruption of medication is not necessary [15].

A study of Miclotte et al. concluded that omitting the morning dose (where applicable) of NOACs (dabigatran, rivaroxaban, or apixaban) may avoid extensive bleeding during and early after the dental extractions. One must be aware that patients undergoing anticoagulation therapy exhibit a higher risk of delayed bleedings [16]. Moreover, before invasive surgical procedures, which may be linked with a higher risk for bleeding or in which bleeding may have important clinical consequences, it is advisable to take the last NOAC dose 48 hours or longer before surgery but this decision should take into account all clinical-related factors, including renal function and the measurement of NOAC plasma levels [8].

A retrospective study conducted by Al Sheef et al. in 2021 had concluded that in case of dental extractions the higher bleeding risk was observed in patients under warfarin treatment compared with those who were treated with clopidogrel. The bleeding surgical areas were treated just with local hemostatics [17].

Regarding the implant insertion, in a prospective study including patients receiving dental implants, Gómez-Moreno et al. found no statistically significant differences in bleeding episodes during and after implant insertion among patients receiving continuous rivaroxaban therapy and healthy volunteers receiving placebo. After the surgical procedures, the implant sites were sutured with nonabsorbable material, and all patients bit gauze soaked in 5% tranexamic acid for 30-60 minutes [18].

A retrospective study evaluated the incidence of bleeding events and healing complications in patients with Rivaroxaban (20 mg) treatment, who needed implants and immediate implant-supported restorations. The implants were inserted in mandible, either in healed sites or fresh extraction alveoli. The medication was interrupted for 24 hours, at the physicians' recommendations. No major postoperative bleeding was observed. In three patients (25%) a slight immediate postoperative bleeding was noticed and controlled just under compression. The authors concluded that implant placement with an immediate loading does not pose any significant risk in patients with a 24 h discontinuation of Rivaroxaban, in agreement with the patient's physician [19].

DISCUSSIONS

The non-vitamin K antagonist oral anticoagulant (NOAC) therapy does not represent a contraindication for surgical dental procedures. The practitioners must do a careful preprocedural evaluation of the patient, in order to choose the best attitude regarding the anticoagulant treatment. It must be always assessed, which is the best option for the patient: a bleeding at the surgical site or a life-threatening alternative.

CONCLUSIONS

Within the limitations of this literature study, the following conclusions can be drawn:

1. The non-vitamin K antagonist oral anticoagulant (NOAC) therapy must not always be interrupted before oral surgery.
2. A delayed surgical procedure after the last dose might be a clinical alternative.
3. Patient's comorbidities must be always taken into consideration.
4. The local hemostatic measures limit or even avoid the postoperative bleeding.

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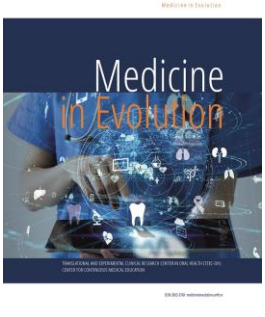
How dental restorations influence plaque-induced gingivitis (a cross-sectional study)?



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Abstract

Aim and objectives: This study aims to establish if oral distribution of dental restorations in close contact to gingiva can influence the risk, severity or distribution of gingivitis. Material and methods: The data presented in this study are part of the PAROGYM cross-sectional study developed on a sample of 1595 Bucharest schoolchildren aged 11 to 14 years. The students were clinically examined and gingival scores were recorded. The Löe GRI index (gingival restoration index) was used for the assessment of dental restorations in close contact to gingiva. Results: The first molars are the teeth that have most often dental restorations in relation to gingiva and can provide some reasons for the prevalence value of gingivitis from this area.

Keywords: gingivitis, dental restorations, children

INTRODUCTION

Dental caries and plaque-induced gingivitis and are the most prevalent oral diseases among children [1]. Caries and gingivitis have a prevalence more than 70% and 90% respectively, among schoolchildren from Bucharest, Romania [2], [3].

Gingivitis may be influenced by many factors besides dental plaque, such as caries, tartar, hormonal background or dental restorations.

Löe retention index GRI (gingival restoration index) was used in previous studies for measuring the effect of dental restoration in the pathology of gingivitis. The GRI scores from Bucharest schoolchildren population prove that dental restauration may influence the prevalence of gingivitis [3]. When a part of a dental restoration is close to gingiva, dental plaque may be attached faster to the tooth (restoration) and be present in a larger amount. However, if the restauration has a good designed and it is polished enough having a smooth surface, this risk is minimum.

Aim and objectives

The main role of this study is to "map" the dental restorations which are near or in a close contact with the gingival tissue and may increase the amount of local dental plaque and gingival inflammation.

MATERIAL AND METHODS

The data presented in this paper are part of the PAROGYM study developed between 2008 and 2009 on Bucharest gymnasium schoolchildren population. 1595 students aged 11 to 14 years from 56 different schools were investigated in order to establish their oral health status. Some of the data related to caries and gingivitis were previously published [2], [3].

EpiInfo software (Centers for Disease Control and Prevention, Atlanta, GA, USA) was used to estimate the proper length of the sample from the total of 58,000 schoolchildren population from 5th to 8th grade (data from 2008). The sample was built for an assumed prevalence of gingivitis of 50%, a 95% confidence interval and a 2.4 estimation error. We used classes as clusters in a single-stage cluster sampling method. The students were also stratified by city regions, grades, and the presence (or not) of a dental unit in school.

The dental examinations were performed in school dental or medical units by one experienced examiner who was calibrated prior to this study. The role of dental restorations in relation to gingiva was measured using GRI – *gingival restoration index* [4]:

- "0": no dental restoration margin closer than 1 mm to the gingival margin (supragingival restoration)
- "1": supragingival margin of a dental restoration extending less than 1 mm below the gingival margin
- "2": subgingival margin of a dental restauration extending more than 1 mm below the gingival margin
- "3": grossly insufficient marginal fit of a dental restoration in a supra and/or subgingival location

GRI and other indexes used for gingival condition assessment (GI – *gingival index,* PlI – *plaque index,* GCI – *gingival caries* index) were scored in this study counting all the teeth surfaces except occlusal.

The study was approved by the Ethics Committee of "Carol Davila" University of Medicine and Pharmacy and every student enrolled in the study had to have an informed consent sign by one of the parents.

The data presented in this paper were processed using the SPSS software, version 24 (IBM, Armonk, NY, USA).

RESULTS

The distribution of dental restorations in relation to gingiva (GRI scores) are exposed on teeth surfaces in tables I and II and graphically shown in figure no. 1.

Table I. GRI scores distribution on upper teeth

Upper teeth					
Tooth	**Surface**	**GRI**	**Tooth**	**Surface**	**GRI**
17	V	0.00	27	V	0.00
17	M	0.00	27	M	0.00
17	D	0.00	27	D	0.00
17	P	0.00	27	P	0.00
16	V	0.01	26	V	0.01
16	M	0.02	26	M	0.02
16	D	0.01	26	D	0.02
16	P	0.01	26	P	0.02
15	V	0.00	25	V	0.00
15	M	0.00	25	M	0.00
15	D	0.01	25	D	0.00
15	P	0.00	25	P	0.00
14	V	0.00	24	V	0.00
14	M	0.00	24	M	0.00
14	D	0.01	24	D	0.00
14	P	0.00	24	P	0.00
13	V	0.00	23	V	0.00
13	M	0.00	23	M	0.00
13	D	0.00	23	D	0.00
13	P	0.00	23	P	0.00
12	V	0.00	22	V	0.00
12	M	0.01	22	M	0.00
12	D	0.00	22	D	0.00
12	P	0.00	22	P	0.00
11	V	0.00	21	V	0.00
11	M	0.01	21	M	0.01
11	D	0.01	21	D	0.01
11	P	0.00	21	P	0.00

Table II. GRI scores distribution on lower teeth

Lower teeth					
Tooth	**Surface**	**GRI**	**Tooth**	**Surface**	**GRI**
37	V	0.00	47	V	0.00
37	M	0.00	47	M	0.00
37	D	0.00	47	D	0.00
37	L	0.00	47	L	0.00
36	V	0.01	46	V	0.02
36	M	0.02	46	M	0.02
36	D	0.03	46	D	0.02
36	L	0.02	46	L	0.01
35	V	0.00	45	V	0.00
35	M	0.01	45	M	0.00

35	D	0.01	45	D	0.00
35	L	0.00	45	L	0.00
34	V	0.00	44	V	0.00
34	M	0.00	44	M	0.00
34	D	0.00	44	D	0.00
34	L	0.00	44	L	0.00
33	V	0.00	43	V	0.00
33	M	0.00	43	M	0.00
33	D	0.00	43	D	0.00
33	L	0.00	43	L	0.00
32	V	0.00	42	V	0.00
32	M	0.00	42	M	0.00
32	D	0.00	42	D	0.00
32	L	0.00	42	L	0.00
31	V	0.00	41	V	0.00
31	M	0.00	41	M	0.00
31	D	0.00	41	D	0.00
31	L	0.00	41	L	0.00

(mean values)
D – distal, M – mesial, V – buccal, P – palatal

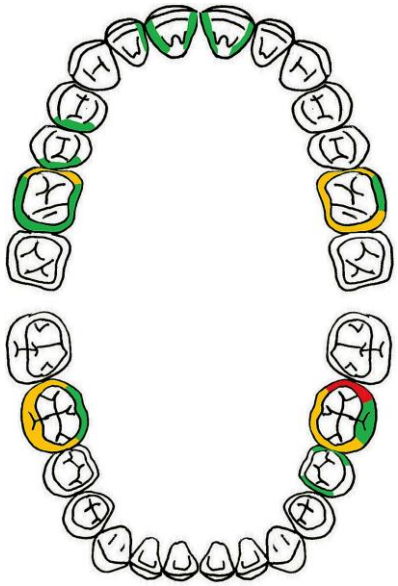

Figure 1. Distribution of GRI mean scores: red – GRI = 0.003, yellow – GRI = 0.002 and green – GRI = 0.001

DISCUSSIONS

The previously results of this study shown there it is a link between gingivitis and dental plaque, caries and dental restorations [3]. This paper shows the oral distribution of dental restorations in contact to gingiva, in this way being able to compare to oral distribution of gingivitis.

This study shown that first molar presented the most dental restorations with margins extended under gingival margins. However, the first permanent molar is tooth considered to be most affected by caries due to its period of mineralization coinciding with early childhood diseases and being one of the first teeth to erupt [5], [6]. We also can see dental restorations on upper incisors and premolars. Comparing to "map" of gingivitis [3] there are some similarities: First of all, dental restorations and gingivitis seems to be located generally on/near interdental surfaces. Secondly, they are most prevalent on the upper teeth. One big

different is that dental restorations are generally located on first molars and the gingivitis is located mostly on the upper anterior teeth. However, the dental restorations in relation to gingiva are not the only factor which can influence the frequency and the extent of gingivitis. Dental plaque is the main cause for gingivitis and the way children brush and floss may give the main model for the oral distribution of plaque-induced gingivitis.

It is obvious that dental restorations rise the risk for gingivitis or increase its extent. The differences appear when we deal with a well-designed dental restoration or with an overhanging dental restoration. Both cases lead to more dental plaque accumulation and provide high risk for gingivitis. However, while a well-designed dental restoration close to the gingival margin increase the risk for gingivitis, an overhanging dental restauration rise in addition the extent of gingivitis and may be positively related to the severity of periodontal disease [7], [8].

CONCLUSIONS

The dental restorations in close contact to gingiva may influence the risk and prevalence of gingivitis especially increasing the rate of plaque accumulation. However, they are not the only risk factor for the gingivitis, dental plaque and oral hygiene quality and routine remaining the most important issues.

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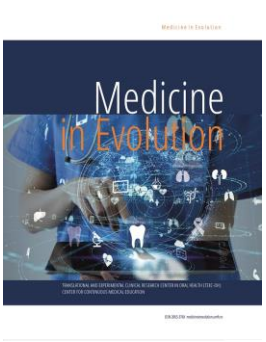
Use of dōTERRA essential oils for periodontal manifestations in mature adult type I diabetes mellitus – case report



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Abstract

Case presentation: Diabetes is similar to periodontal diseases, with a common, multifactorial disease process involving genetic, environmental, and behavioural risk factors. The aim of current periodontal therapy is to remove the bacterial deposits from tooth surface and to shift the pathogenic microbiota to one compatible with periodontal health.

Materials and method: Traditionally, various species of herbs are used to control and cure some of dental problems or systemic diseases. The literature documents that many plants themselves have anti-inflammatory, antioxidant, antibacterial, astringent and other useful properties. We presented a 59 years old female with type I diabetes mellitus case. The patient presented a mild diabetic periodontitis. We introduced in the oral therapy, besides periodontal manoeuvres, a specific recipe with essential oils from dōTERRA. In parallel with clinical surveillance there were performed microbiological tests with samples from oral biofilm.

Discussions/Conclusions: In this case report we successfully used topical extracts from plants, such as essential oils, manufactured by dōTERRA. The microbiologic lab tests showed no pathological flora.

Keywords: essential oils, plants, periodontal disease, diabetes

INTRODUCTION

The multi-microbial nature of the periodontal disease, results in making the detection and treatment a challenging task, especially when the diabetes in present. Diabetes mellitus is currently classified under two major types: type I (former called insulin-dependent diabetes mellitus), and type II (former called non-insulin-dependent diabetes mellitus) [1-3].

The scientific researches on the pharmacological properties of volatile oils from different plant species have demonstrated their effectiveness in various diseases due to their antibacterial, antiseptic, antiviral, antispasmodic, analgesic, antioxidant, anti-hemorrhagic, hypotensive, antimicrobial, sedative or skin regeneration properties, etc. [4]

In this study the dōTERRA essential oils are obtained by one of the two primary extraction methods: steam distillation or cold pressing (unique process for citrus peel and tree bark). The final product is an essential oil with a high therapeutic degree. By contrast, lower grade essential oils are often extracted by chemical processes or using solvents to increase profit [5-7].

Aim and objectives

The aim of this study was to assess the influence of some of dōTERRA essential oils/ products in addition to the traditional periodontal treatment in a case of diabetes mellitus type I installed in a mature adult patient.

CASE REPORT

I. Anamnesis

The patient CI, female, 59 years old, from the urban environment, with insulin-dependent diabetes mellitus and AHT, presented to the dental office for gingivo-periodontal manifestations.

The medical analyzes performed before the dental consultation revealed the following: the patient had diabetes mellitus type I (insulin-dependent) under control, AHT grade 2 with a very high CV risk, mixed heart disease, mixed dyslipidemia. The patient had a history of treatment with Arcoxia for 8 days for anti-inflammatory reasons, under prescription.

The patient already has used products based on essential oils (without specialist consultation), for internal use.

II. Clinical examination data

At the clinical examination (Figure 1) a good oral hygiene was found, with an oral mucosa in a functional state, without apparent periodontal damage, despite the existence of a lower diastema (over 5 mm). The presence of simple carious lesions, partially treated, was also found.

The patient had specific halitosis, grade 2 dental mobility, without heavy gingival bleeding.

The periodontal diagnosis was diabetic periodontitis, stage I, grade A.

In the dental office we considered that a microbiological diagnosis was needed. In addition, we followed the development of pathogenic bacteria (beta-hemolytic bacteria).

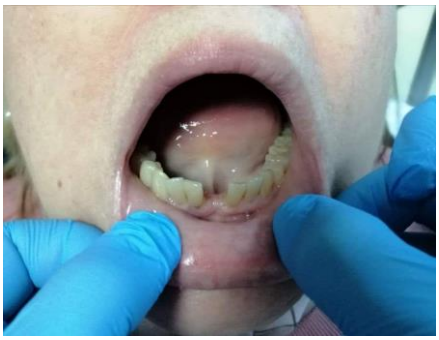

Figure 1. Initial appearance of the lower arch with the presence of diastema (CI, female, 59 years old)

III. Laboratory data

The microbiological analysis consisted in taking of two samples (Figure 2) from the immediate location of the carious lesions, with the help of a sterile swab, but insisting on the area of the gingival sulcus.

Figure 2. Intraoral aspect before microbiological sampling (CI, female, 59 years old)

The plates were kept incubated at 37°C for 72 hours, following the daily bacterial growth, and insisting on the development of pathogenic (beta-hemolytic) microorganisms. There were used plates with culture media (Figure 3) as: blood agar; Chapman; MacConkey; ADCL and Sabouraud (for fungi).

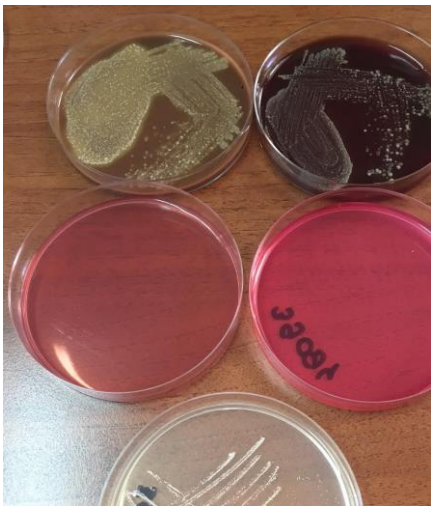

Figure 3. Microbiological culture environment (CI, female, 59 years old)

The data of the laboratory analysis were the following: beta-hemolytic and pathogenic colonies on enterobacteria media did not develop, also there were no fungal colonies.

As result we concluded that the positive clinical results are due to the observation of this case in a phase after using essential oils, and before the presentation at the dentist's office.

IV. Treatment and evolution

The case confirmed a controlled insulin-dependent diabetes with normoglycemia, which led us to only add oral solutions for prevention of future periodontal lesions. So our main therapeutic objective was to maintain the results at the oral level.

In this case, the oral working protocol consisted in initial periodontal therapy then we added products based on essential oils with oral use, one of them according to an original prescription.

Thus, we created the following administration scheme:

1. Incense essential oil - Frankincense® (dōTERRA): 1 drop sublingually, in morning and evening (with pipette), internal use.

2. Myrrh Essential Oil - Myrhh® (dōTERRA): prepared as a mouthwash according to an original recipe (1 liter in a glass container). The mouth was rinsed at least 2 times a day, actively, with a dose of 40-50 ml. In addition, a small amount of mouthwash was swallowed for maximum effect. It was supplemented with gingival massage with a clean finger.

3. Toothpaste with On Guard® Essential Oil Blend (dōTERRA): the toothpaste was used 2-3 times a day. Each group of teeth was brushed for at least 10 seconds, with back and forth movements from the gum to the tooth, thus preventing food debris or biofilm from being inserted under the gum. The tongue and mucosa of the cheeks were washed as well. The On Guard® Mouthwash was then used for complete hygiene [8, 9].

4. On Guard® Mouthwash (dōTERRA): was used at least 2 times a day, in morning and evening, after dental brushing. The mouth was rinsed actively with a dose of 40-50 ml mouthwash, spited out, without rinsing again with water. As an alternative method, mouthwash could be used before dental brushing [10].

5. Original mouthwash prepared with dōTERRA essential oils according to our own recipe:

In a glass container we pour 1 liter of distilled water and we added the following essential oils:

- 5 drops of mint, tea tree, wild orange and spearmint essential oils;
- 3 drops of clove, and cinnamon essential oils, and
- 2 drops of incense, and myrrh essential oils.

The mouthwash was used in a similar mode like On Guard® Mouthwash. For maximum effect a small amount of prepared mouthwash could be swallowed.

Thanks to the stable clinical situation and the microbiological results through which no pathogenic flora was detected, the patient was kept under surveillance by periodic checks once every 3 months. The patient previously administered herself essential oils (internally). We added original products based on essential oils with action on the oral cavity. Therefore we considered that it was only necessary to maintain the clinical situation and regular monitoring every 3 months.

At the next check session (after 3 months) the patient presented stabilized periodontal parameters. We performed another laboratory microbiological test, and its results showed no signs of oral pathogens (Figure 4).

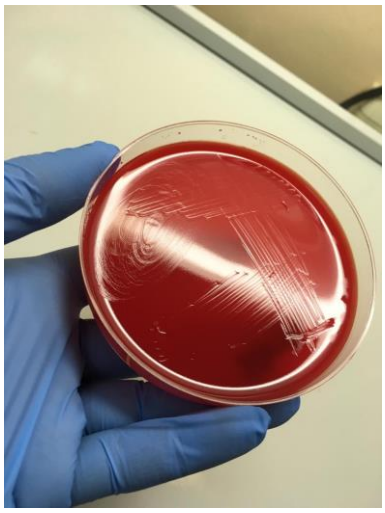

Figure 4. Second lab examination with no pathological development after 3 months (CI, female, 59 years old)

DISCUSSIONS

The action of diabetes itself on the gums is based on disruption of local metabolism and accumulation of toxic intermediates (tissue acidosis), and vascular and nerve changes (meiopragy, arterial and venous vascular suffering, diabetic neuritis). According to the literature, the periodontal pathology in diabetes has a particular form. The microorganisms frequently detected in insulin-dependent diabetes are: Streptococci, Actinomyces/ Aggregatibacter, Veillonela parvula or Fusobacterium [1, 3, 12, 13].

Precursors of the chemical compounds contained in phytotherapeutic products, the essential oils can be considered first-line effective in the treatment of periodontal diseases, partly due to their antifungal and antibacterial nature [11, 12]. Frequently used in aromatherapy or massage, pure and chemically unaltered essential oils are today studied in numerous scientific articles. To maintain general health, essential oils are included as supportive supplements in internal administration. They also can be used as initial-local or complete treatment, in our case – diabetic periodontal manifestations [6, 7, 13].

Different essential oils combinations can be obtained through formulas specifically stated in manuals and guides [14-16]. The use of essential oils is specific to each organ/system, addressing primarily the cause, but following the symptoms. Therefore they can be used in standardized preparations, prepared according to the original recipe of the manufacturer (dōTERRA in the presented case) or can be prepared according to personal/ original formulas (mouthwash, ointments or toothpaste). Local and topical modes of administration can be combined with other (internal) routes of administration of other essential oils for better results.

In our case, in the presence of type I diabetes, incense, myrrh, mint, tea tree, wild orange, spearmint, clove, and cinnamon dōTERRA essential oils contributed to stabilize the diabetic periodontitis. They acted by controlling and inhibiting the oral biofilm in synergy with the classic periodontal therapy (biofilm mechanical elimination; supra and subgingival scaling; use of chemical and physical agents). Their positive effect was proved through the microbiologic lab tests performed in our study.

CONCLUSIONS

The bacteria with a predisposition for the gingival area and those that colonize the subgingival space are incriminated in the maintenance of many systemic diseases, not only periodontal diseases. Keeping them within limits of non-pathogenicity can be achieved by

appropriate oral hygiene (prophylaxis and maintenance of oral health), and moderate and limited quantitative consumption of sweet or intensely acidic foods.

In this case of a mature adult diabetes mellitus type I, the establishment of oral essential oil treatment proved to be a real support for the health of the oral cavity, and the body as a whole.

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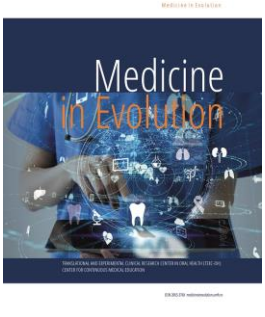
Innovative methods of enamel remineralization in the treatment of early carious



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Abstract

In enamel, especially on free smooth surfaces, under the influence of certain factors, a dissolution of inorganic hydroxyapatite crystals can occur, and in this area, the enamel loses its translucency, becomes chalky, matte and rough, and the resulting structure is called a white spot lesion, this being the first objective clinical sign of caries also named the incipient carious lesion.

For this white spot lesion can be used the concept of minimally invasive dentistry, a very conservative way of intervention against enamel demineralization and any further substance loss.

An example of this minimally invasive dentistry concept is the use of the self-assembling peptide P11-4, one of the promising biomimetic alternatives for enamel remineralization. We showcase two clinical cases of white spot lesions treated with Regenamel®, a medical product that uses Curolox® Technology, based on self-assembling peptides.

Keywords: incipient carious lesion, remineralization, tooth enamel, Regenamel®, Curolox®

INTRODUCTION

Tooth enamel is the translucent, thin outer covering of the tooth and the hardest tissue in the human body [1]. Enamel development and mineralization is an intricate process tightly regulated by cells of the enamel organ called ameloblasts. During enamel development, enamel matrix proteins are known to control the disposition, morphology, and growth of the hydroxyapatite crystals [2]. The impact of developmental insults on enamel is critical because, unlike bone, once mineralized, enamel tissue is acellular and hence does not remodel [3].

Caries are considered a continuous dynamic process [4]. Enamel caries always starts through a process of subsurface demineralization leaving a microporous surface of lost minerals in-between the hydroxyapatite crystallites [5,6]. In enamel, especially on free smooth surfaces, under the influence of certain factors, a dissolution of inorganic hydroxyapatite crystals can occur, and in this area, the enamel loses its translucency, becomes chalky, matte and rough, and the resulting structure is called a white spot lesion, this being the first objective clinical sign of caries also named the incipient carious lesion [7]. For this white spot lesions can be used the concept of minimally invasive dentistry, a very conservative way of intervention against enamel demineralization and any further substance loss [5,8]. An example of this minimally invasive dentistry concept is the use of the self-assembling peptide P11-4, one of the promising biomimetic alternatives for enamel remineralization. The P11-4 peptide structure consists of natural amino acids: glutamine, glutamic acid, phenylalanine, tryptophan, and arginine. The resulting higher molecular structure has a high affinity for tooth mineral, and the high affinity for tooth mineral structure is based on the correspondence of the Ca ion binding site distances on P11-4 and the Ca spacing in the hydroxyapatite crystal lattice. Matrix formation is controlled by pH, therefore allowing control of matrix activity and site of formation [2,9,10]. The self-assembling peptide promotes the de-novo formation of hydroxyapatite within the carious lesions and is sold as Curodont™ Repair or Regenamel® [11]. Curodont™ Repair is marketed in Switzerland under the brand name Regenamel® [12]. This medical product uses Curolox® Technology, based on self-assembling peptides, forming a 3-dimensional matrix with a high affinity for the dental mineral [12]. When Regenamel® is applied to a tooth, the peptide diffuses into the subsurface micropores, forming a three-dimensional scaffold of tiny fibers. These scaffolds resemble teeth development proteins and promote hydroxyl apatite crystallization around them to restore tooth enamel over a three-month period [13].

Aim and objectives

In this case study, we aim to treat white spot lesions using a minim-invasive approach rather than a radical method of treatment.

MATERIAL AND METHODS

We showcase two clinical cases of white spot lesions.

The first one is an eight-year-old patient, with mixed dentition. The patient presents two removable orthodontic appliances (upper and lower), with anchoring elements for stability on 6.5 and 7.5. In the past, he presented dental sensitivity to strong stimuli. The teeth to which Regenamel® was applied are 6.5 (the upper left temporary second molar) and 7.5 (the lower left temporary second molar). They present carious lesions that are not detectable radiographically, as occlusal radiolucency is not present, but the clinical inspection reveals 6.5 superficial carious lesions located occlusally, in the middle (Fig. 1) and distal pits 7.5 superficial cavitary carious lesions located in the distal fossa (Fig. 2).

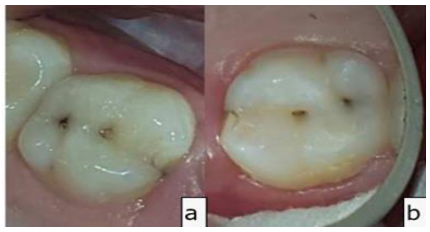

Figure 1. a, b The initial and final appearance of the carious lesion on tooth 6.5

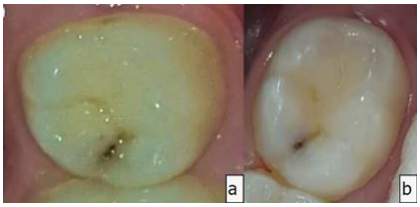

Figure 2. a, b The initial and final appearance of the carious lesion on tooth 7.5

The second one, is another eight-year-old patient, with mixed dentition. In the antecedents, he presents pain in the temporary teeth, with deep carious lesions, which indicates an increased susceptibility to caries. Radiological examination of the teeth to which Regenamel® was applied is 2.6 (the upper left permanent first molar) and 3.6 (the lower left permanent first molar). They present early carious lesions, which are not detectable radiographically, as no occlusal radiolucency is present. Clinical examination indicates that 2.6 shows multiple superficial carious lesions, non-cavitation, located in the distal, central fossa and in the occlusal-palatine groove (Fig. 3), and 3.6 shows multiple superficial carious lesions, non-cavitating, located at the level of grooves and pits of the occlusal surface (Fig. 4).

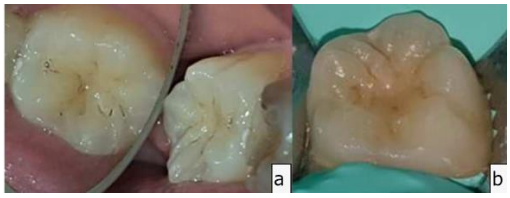

Figure 3. a, b The initial and final appearance of the carious lesion on tooth 2.6

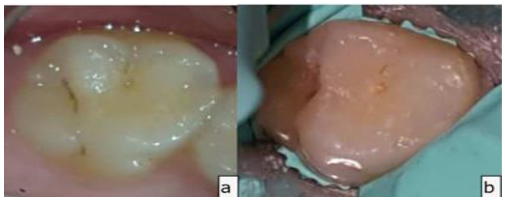

Figure 4. a, b The initial and final appearance of the carious lesion on tooth 3.6

For both patients, the same protocol was used as described: professional dental cleaning, removal of the pellicle using 2% sodium hypochlorite for 20 seconds, removal of the inorganic deposits using 35% phosphoric acid for 20 seconds, rinsing of the tooth surface with water, the drying the tooth surface with air and then applying of Regenamel®.

Regenamel® must be used exclusively by medical personnel. In the case of advanced carious lesions, Regenamel® produces only superficial mineralization and through repeated uses at 12-week intervals, remineralization becomes more effective. Topical applications with fluoride are only allowed 5 minutes after applying Regenamel® if applied before it can inhibit the action of Curolox® technology.

Currently, no side effects have been identified, but they cannot be completely excluded; as in the case of any dental treatment, this treatment can induce gingival

inflammation, pulp, and dentinal hypersensitivity. There is not enough data on side effects in pregnant women or during breastfeeding, therefore Regenamel® products should not be used in this case.

RESULTS

From a clinical point of view, the lesions are: diminished in terms of size, the appearance of the surrounding enamel is less infiltrated, and the color is darker, a sign of the chronicity of the lesion and the halt in evolution. When inspecting with the dental probe, the contour of the lesion is harder and smoother compared to that of the initial lesion, this fact being more obvious in the first case (in the two analyzed temporary teeth).

Repetition at certain time intervals, in order to increase the enamel remineralization rate could not be achieved due to the conditioning in terms of time, and in addition, the use of a combination of products containing Curolox® technology (e.g. toothpaste) is indicated. The results must be monitored at certain intervals and repeated as needed to facilitate enamel remineralization and the maintenance of the result largely depends on the patient's cooperation in terms of respecting oral hygiene, which is a decisive factor, instead, the dentist must very carefully evaluate the evolution of the process carious and establishing the application intervals of Regenamel®.

DISCUSSIONS

Technological evolution and the desire for minimally invasive treatment forced the creation of new treatment methods based mainly on the remineralization of carious lesions rather than on the removal of the carious process. Also new methods of discovering in advance the white spot lesions can be used before they progress to larger cavities. Quantitative light-induced fluorescence is a recent method that employs the use of fluorescent light to identify demineralized areas [14,15].

Fiber optic trans illumination-digital fiber-optic transillumination (FOTI/DIFOTI) is another new technique in which infrared light (780nm wavelength) is used to identify white spot lesions without the use of ionizing radiation [20]. Another recent method developed for the early identification of white spot lesions is near-infrared light transillumination (NILT), which uses optical fibers to transmit light (780nm wavelength) to the tooth via the root [16, 17]. A new technique known as Fluorescence Induced Theragnosis is very useful in diagnosing and helping manage white spot lesions, initial caries, and biofilm identification [18,19].

Chli and collaborators [20] state that the clinical trials about the efficacy of self-assembling peptides in masking the color of white spot lesions for achieving patient satisfaction appear to be insufficient for clinical guidance. Alsamolly, [21] assessed that the remineralization potential of self-assembling peptides increased by increasing the storage time (three months and six months).

Doberdoli D. and collaborators [22] concluded that using the self-assembling peptide with fluoride varnish or twice weekly application of Curodont Protect (self-assembling peptide matrix containing P11-4, fluoride, and calcium phosphate), had improved the enamel repair and arrest WSLs over fluoride varnish alone. This statement was in agreement with Alkilzy and collaborators [23] who stated that there was a statistically significant overpowering from the combination of the self-assembling peptide with fluoride, over the use of fluoride alone.

CONCLUSIONS

The approach of carious lesions is based in recent years mainly on the concepts of prevention, minimally invasive, and remineralization, which Regenamel® fully respects, that is why this material and its technology are in the first places, thanks to the results obtained from the point of histological view, through a multitude of studies carried out in vitro and on clinically obtained results, but we are still far from achieving a true restoration of the lost enamel, clinically detectable. Unfortunately, there is still no clear evidence to support the theory and long-term studies showing the stability of the "regenerated" enamel over a long period of time, which could be a direction in which research should continue.

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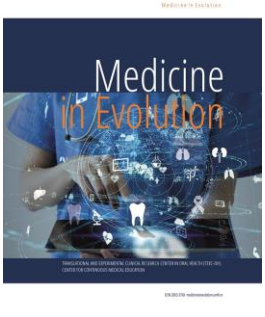
Antibiotic therapy in pedodontic practice-antibiotic administration guide



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Abstract

Aim and objects: The main idea of this article is to establish a guideline for the administration of antibiotics.

Methods: In our methodology we used studies on antibiotic therapy in pedodontic practice and compared the guidelines found with their use nowadays. The selection criterion was by the keywords used "antibiotics, pedodontic therapy, guide to the use of antibiotics",

Results: The type of condition and the need to administer antibiotics as well as the daily administration dosage were presented.

Conclusions: Appropriate and correct use of antibiotics is essential to ensure effective and safe treatment. Practices that may increase microbial resistance should be avoided. To improve standards of treatment, dentists need to be up-to-date in their knowledge of pharmacology.

Keywords: antibiotics, pedodontic therapy, antibiotic use guide

INTRODUCTION

The discovery of antibiotics revolutionized contemporary medicine in 1928, Alexander Fleming identified penicillin, the first chemical compound with antibiotic properties.

Research has continued, and there are now a whole series of antibiotics, classified according to different criteria. However, the administration of antibiotics has been a problem since ancient times. From the beginning until today, there has been an impressive increase in the the use of antibiotics. However, antibiotics have a limit in use, many patients are not aware of. (2)

The choice of the child's medication requires even more caution, which is determined by the dentist, so a guide to the administration of antibiotics must be present in the office of any paediatric dentist, facilitating the decision whether or not to prescribe antibiotics to a child, depending on the pathology. (3) (4)

In dentistry, antibiotics are administered for prophylactic and therapeutic reasons, playing an adjuvant role in preventing the spread of dental and oro-facial infections. (2) (5) The antibiotic's effect is short-term and not permanent. (6)

The use of antibiotics in paediatric practice requires certain conditions of administration and is based on certain selection criteria depending on the individual child. The conditions of antibiotic administration and dosage are the criteria underlying the guidelines developed by various studies around the world. (3) (7)

At the same time, the adverse effects of antibiotics should not be forgotten, which is a very delicate and important subject to address, especially when dealing with a child, who is different in many ways from an adult. In pedodontics, we can discuss from the newborn stage up to the age of 15-16 years, and the area of approach includes mainly temporary teeth, as well as young permanent teeth. (8) (9)

It has been reported in studies that the unjustified use of antibiotics in children, especially in the control of ENT disorders and dental infections, can lead to increased. This problem stems from the inappropriate use of antibiotics by both physicians and parents. (2) (10)

Antibiotic resistance is an inevitable consequence of antibiotic misuse and is the ability of a type of germ to survive, multiply and grow in the body presence of an antibiotic, even under the conditions of a maximum drug concentration. (4)

Bacteria causing dental infections are generally saprophytic. The microbiology in this respect is varied, with multiple microorganisms with different characteristics involved. (4) (11)

According to Dr Toma J. Pallasch, the inappropriate use of antibiotics in dentistry involves in particular recommending them in the "wrong situations" or for too long, which includes giving antibiotics after a complete and correct dental procedure to a generally healthy patient to "prevent" an infection, which in all likelihood will not occur. (5) (12) (13)

The conditions of antibiotic administration and the criteria for antibiotic selection in the child must be considered. Appropriate use of antibiotics depends on correct nomination of the diagnosis of the present oral disease and proper knowledge about the general condition of the patient and knowledge of antibiotic therapy. (14) (15)

Aim and objectives

The main idea of this article is to create an antibiotic administration guide which will include, depending on the pathology, what kind of antibiotic is to be administered, the dose and the time interval required. Updating and modernising guidelines of any kind makes the

dentist's work easier. With new and updated information at hand, we are able to offer the best possible treatment appropriate to the little patient.

MATERIAL AND METHODS

In our methodology we used studies on antibiotic therapy in paediatric dentistry and compared the guidelines found with their use nowadays.

The selection criterion was by the keywords used "antibiotics, paediatric therapy, guidelines for the use of antibiotics" on the medical websites Pubmed, Free Medical Journals, Oxford Academic, Cochrane Library.

Another criterion was the publication period, selecting a 16-year interval,2005-2021. There is a wide variation in dosages for all prescribed antibiotics and different dosing periods, which do not correspond to modern day recommendations.

With the information collected from each study, we have managed to produce a comprehensive guide and provide new and improved information.

The studies included were non-clinical or clinical studies, surveys cross-sectional surveys, case reports.

The exclusion and inclusion criteria for the studies are presented in Tables 1 and 2.

Table 1. The inclusion

Children or teenagers up to 18 years old
Antibiotic therapy in medicine dental medicine
Antibiotic therapy guidelines
Articles on resistance to antibiotics and adverse effects

Table 2. The exclusion

Studies on adults
Studies unrelated to pedodontics
Articles older than 10 years

15 articles with useful information have been selected to produce a complete and up todate guide to antibiotic administration in children.

The information in each study was chosen according to drug therapy, dose and pathology.

RESULTS

Table 3. Guide to antibiotic administration in paediatric dental therapy

Condition	Antibiotic	Daily Dose	Time interval	Commercial Name
Acute Pulpitis	Does not require	-	-	-
Cronic Pulpitis	Does not require	-	-	-
Cellulite	Amoxcillin	Children>3months and <40kg-20-40 mg/kg/day Children> 40 kg-250-500 mg Childre <40kg: 20-45mg/kg/day	-8 hour -8 hour	Amoxicilina MIP Pharma 500 mg tablet Augmentin

	Amoxcillin+ clavulanic acid For allergy sufferers to penicillin Metronidazole Azithromycin Clarithromycin Erythromycin	Children >40 kg: 250-500 mg/kg/day 30/mg/kg/day Children>6months to 16years-5-12mg/kg/day 7.5 mg/kg Children with age between 6-12 years: 30-50mg/kg/day	-12 hour -8 hour 6 hour 12 hour 12 hour 6h/8h	875/125 mg Metronidazole Arena 250 mg Azithromycin Sandoz 500mg Clarithromycin 200-250 mg Erythromycin Sandoz 200mg
Ulcerative gingivitis necrotic	Amoxicillin Metronidazole For those allergic to penicillin-Erythromycin Azyithromycin	50 mg/kg/day 30 mg/kg/day Children aged 6-12 years: 30-50mg/kg/day 10 mg/kg/day	8 hours 8 hours 6/8hours 6-8 hours	Amoxicillin MIP Pharma 500 mg50 Metronidazole Arena 250mg Erythromycin Sandoz 200mg Azythromycin Sandoz 500mg
Virus infections herpes (gingivostomatitis herpes)	Does not require antibiotic administration-Only antivirals are given	-	-	-
Eruption and Exfoliation of teeth	Does not require	-	-	-
ProphylaxisAntibiotics	Amoxcillin Allergy to.penicillin	Dose recommended is 1500 mg with a hour before a intervention dental surgery and 750 mg every 6 hours after surgery Children over 6 years old and adolescents up to under the age of 14 years-Clindamycin 15 mg/kg with one hour before intervention		Amoxicilin MIP Pharma 500 mg tablets Clindamycin-MIP 150 mg/ml
Abces	Amoxicillin	*Children>3months and <40 kg-20-40mg/kg/day *Children > 40 kg-250-500 mg	8 hours 8 hours	Amoxicillin MIP Pharma 500 mg tablet

	Metronidazole Amoxicillin and Clavulanic acid For.those allergic to Penicillin-Erythromycin	Children 30/mg/kg/day Children with weight<40 kg:20-45 mg/kg/day Children with weight >40 kg: 250-500 mg/kg/day Children aged between 6-12 years: 30-50 mg/kg daily	8 hours 12 hours 8 hours 6 hours	Metronidazole Arena 250 mg Augmentin 875/125 mg Erythromycin Sandoz 200 mg
Concussion	Does not require	-	-	-
Subluxation	Does not require	-	-	-
Dislocation	Does not require	-	-	-
Intrusion	Does not require	-	-	-
Extrusion	Does not require	-	-	-
Avulsion and Replantation	Amoxicillin	Children>3 months and<40 kg-20-40 mg/kg/day Children > 40 kg-250-500 mg	8 hours 8 hours	Amoxicilin MIP Pharma 500 mg tablet
Plaque gingivitis	Does not require	-	-	-
Periodontal disease associated with systemic diseases	It is preferable to consult your doctor treating the disease in concerned.	-	-	-

DISCUSSIONS

The realization of this guide comes to the aid of doctors, to facilitate the choice of antibiotics, depending on the specific pathology of each patient. We also considere children allergic to penicillin, offering other options that are not lethal.

Each type of condition requires a certain type of antibiotics in order to be treated. In some cases, there are certain patients who have developed over time an increased resistance to a certain type of antibiotic, therefore it is necessary to know exactly which type of antibiotic should be administered in each type of the condition.

So, as a dentist, a lot of caution is needed, depending on the anamnesis and the patient's history. There are also patients who do not know their allergic terrain to certain antibiotics, thus coming into contact with the respective medicine to produce an allergic reaction that can be from mild to the most serious forms, that is why it is indicated for patients who have had in the history of allergic episodes to any type of medicine or even to other antibiotics, an allergy test should be performed to exclude the possibility of this incident.

The dentist must perform a thorough history and ask as many questions as possible related to the use of antibiotics. Unfortunately, many parents administer their own treatment to their children, without knowing the risks of using antibiotics, therefore we recommend that before administering any type of treatment, patients should see a dentist, who has full knowledge in administering the correct treatment.

CONCLUSIONS

Appropriate and correct use of antibiotics is essential to ensure treatment effective and safe treatment. Practices that may increase microbial resistance should be avoided.

To improve standards of treatment, dentists need to be up to date in their knowledge of pharmacology in dentistry, as well as in continuing education, with ongoing evaluation of dental practices, a better understanding of the pathogenesis of these infections, including host immune response to bacteraemia.

The production of this guide is intended to help clinicians, to facilitate the choice of antibiotics, in specific pathology of each patient. We have also considered children allergic to antibiotics, penicillin allergic children, offering other non-lethal options. So, as a dentist you need to have great caution, depending on the patient's history and medical history.

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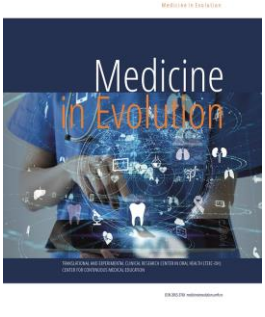
Management of anterior dental crossbite in mixed dentition: case presentation



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Abstract

Case presentation: Aim of this study is to describe the treatment of a patient with mixed dentition and anterior dental crossbite. The objectives of treatment were to correct the malocclusion, to align the incisor, to control the permanent teeth in a good eruption and improve aesthetical conditions.

Materials and Methods: This study presents an interceptive therapy which can use to treat the anterior crossbite. In this case, it shows that the use of the myofunctional appliance change the anterior dental crossbite.

Discussion: Various authors present solved clinical examples and recommend the use of removable appliances to treat de anterior dental crossbite.

Conclusions: Anterior crossbite is a malocclusion that must be diagnosed and treated early to establish well-balanced occlusal development.

Keywords: anterior crossbite, removable appliances, interceptive therapy

INTRODUCTION

Cross bite in the anterior area represents deviations from the ideal occlusion that occurs in the sagittal direction at the level of the anterior segment. It is a malocclusion caused by the lingual location of the maxillary anterior teeth in relation to the mandibular anterior teeth [1,2] which involves one or more maxillary and mandibular teeth.[3] A correct diagnosis and early management may be beneficial in preventing the progression of this malocclusion in late adolescence.

Many orthodontic interceptive therapy approaches have been offered in order to repair the anterior crossbite, including tongue depressor or tongue blade or popsicle stick therapy, a removable inclined bite plane and eruption guidance appliance (EGA). [4,5]

Tongue depressor or tongue blade or popsicle stick therapy constitutes one of the most basic removable appliances. A force must be delivered in the proper direction and for a sufficient period to move a tooth. When using a tongue depressor, the patient should use it 20-30 times a day. Crossbite can be repaired in two weeks, but it can take up to three months.[5]

Removable inclined bite plane made of self – cure resin is made by thermoforming a plastic film over a mandible working cast. It is a specially designed resin that permits acrylic to be applied without the risk of the material coming away from the appliance. An inclined plane of orthodontic acrylic is constructed over the anterior teeth. Acrylic is used to engage only the upper tooth/teeth in a crossbite at a 45-degree angle to the long axis of the lower incisors and the posterior bite opening are not more than 2mm.[1]

Treating anterior crossbite has a considerable impact on the direction of condylar development and, as a result, mandibular size and form. The functional repair of this malocclusion is accomplished with the use of occlusal pressures, which can shift the occlusal plane angulation and so rectify the jaw relationship.[6,7]

Aim and objectives

The purpose of this study is to describe the treatment of the anterior crossbite, minimize mandibular protruded development, enhance the profile, and adjust the occlusal plane inclination using the eruption guidance appliance.

CASE PRESENTATION

The subject, K.A., a 8 year old man, was selected in our study. Nothing remarkable showed in his medical history, no temporomandibular problems, no oral habits, and good compliance. Clinical examination showed anterior crossbite at the level of the upper central incisors 1.1. and 2.1.

The present therapy technique is centered on collecting a variety of information with the goal of early detection of anomalies and the discovery of essential treatment techniques in minimizing clinical development. The approach of the contemporary notion of non-invasive or minimally invasive, resulting in the preservation of as healthy dental tissues as possible, is the key to success in correcting any structural defects.

An eruption guiding appliance (EGA) was chosen as the orthodontic instrument to treat this patient. For patients with mixed dentition and anterior crossbite, this appliance concentrates on nasal breathing and initial myofunctional correction. It is soft and flexible, providing excellent compliance while adapting to any arch form or malocclusion. This is focuses on arch growth and continuous habit correction.

The first stage of the treatment plan included the use of MYOBRACE i-3® appliance (size medium). (Figure 1)

Figure 1. MYOBRACE i-3® appliance

In the first month, the treatment is divided into four stages: the first week, the device is worn for 30 minutes during the day, after this week, 30 minutes will be added each week, so that at the end of the 4 weeks the device will have to be worn for 2 hours a day. The patient is instructed to bite into the appliance while keeping his lips closed firmly. The active phase of the treatment begins after the first month, with the patient maintaining the appliance for 1-2 hours each day and as much as possible at night (preferably for 8-10 h). During this time, the patient was monitored once a month. This phase is recommended for the first six months of usage.

After this period, we decided it was needed to continue the orthodontic treatment using the successive appliance (MYOBRACE i-3H®), for the arch expansion and to promote the position of the tongue and improve the lip seal for another 6 months. The patient was controlled regularly every month.

The major treatment was to correct the anterior crossbite while also improving the profile and changing the occlusal plane orientation. (Figure 2,3,4)

Figure 2. Extraoral before and after treatment pictures: frontal view at rest, frontal view with a smile, lateral view at rest, lateral view with smile

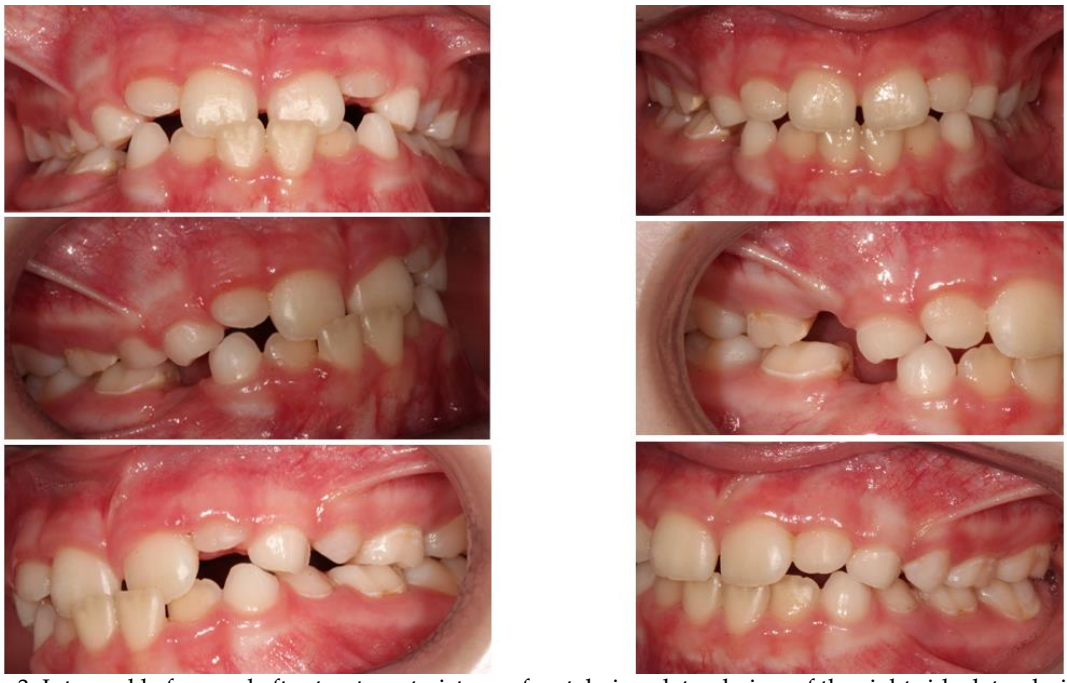

Figure 3. Intraoral before and after treatment pictures: frontal view, lateral view of the right side, lateral view of the left side

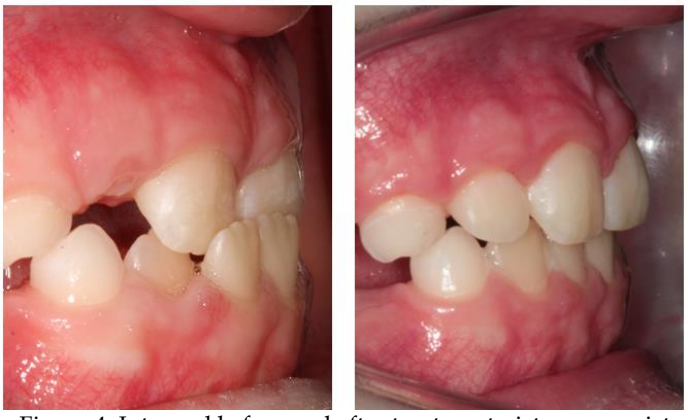

Figure 4. Intraoral before and after treatment pictures: overjet

The treatment length with MYOBRACE i-3® and MYOBRACE i-3H®appliance was of 12 months. (Figure 5)

The patient continues to utilize the EGA as a technique of retention during the night.

Figure 5. MYOBRACE i-3H® appliance

DISCUSSIONS

Anterior crossbite may be quite dangerous in children. It causes significant aesthetic discord and functional damage by disrupting environmental factors in the mouth cavity.[5,8,9]

The current study looked at the importance of the early diagnostic and treatment of the anterior crossbite with an elastodontic appliance in participants who had symptoms of malocclusion in mixed dentition stage.

In 2020, Pellegrino M.[4] et al., in her study describe the importance of the functional device use in an eruption guidance appliance (EGA) in particular, an LM Activator High Short for 18 months. In our study use the MYOBRACE i-3® and MYOBRACE i-3H®appliance for months. In both studies the goal was achieved by correcting the anterior crossbite, improving the profile and adjusting the inclination of the occlusal plane. The fundamental feature of these devices, according to Keski-Nisula[11] et al., is that these devices do not use active pressures to adjust tooth position, but rather use erupting forces to guide the erupting teeth towards an appropriate occlusal position.

Another approach in treating anomalies of the crossbite in the frontal area can also be treated by using the removable inclined bite plane mentioned in the study. Also, Biradar[1] in his study used these devices which are very useful in treating this type of the anomalies.

An alternative treatment can be the use of the Aligners. In his study, Inchingolo[10] illustrates the orthodontic treatment of a 25-year-old patient with skeletal and dental class III malocclusion, anterior crossbite that created functional and aesthetic issues, occlusal trauma, and incisor wear.

In her study, Herawati[5] mentioned that there are numerous possible and suggested treatments for treating basic anterior dental crossbite, one of which is tongue blade therapy. A mild dental crossbite involving only one tooth is treatable. Her research was conducted during the Covid 19 coronavirus pandemic, which prompted her to make her call dentistry is an essential component of our healthcare system.

CONCLUSIONS

Based on the results from this study, it is plausible to conclude that anterior crossbite malocclusion occurs and should be addressed as soon as possible. All of the procedures utilized to correct the abnormalities produce good outcomes, resulting in improvements in occlusion function and improved aesthetics.

The EGA appliance used was able to correct the occlusal plane inclination and harmonize the profile. Because of the little emotional and psychological influence, this therapy option is particularly considerate of the patient's daily life. All of these characteristics provide EGA another option for treating individuals with anterior crossbite at an early age, during incisor eruption.

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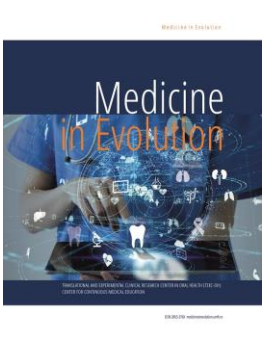
Bacterial colonization of removable orthodontic appliances



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Abstract

Currently, orthodontic treatment represents an interest in biological and microbiological changes at the level of orthodontic devices. This paper presents a synthesis of an investigation into the existence of scientific evidence supporting the hypothesis that the presence of orthodontic appliances influences the oral microflora. The study was carried out in the Paediatric Dentistry Department of the Victor Babeş Timişoara University of Medicine and Pharmacy in the time interval 01.09.2021-01.03.2022, the patients being users of removable orthodontic appliances. Orthodontic appliances significantly influence the oral microflora, independent of the type of appliance, although removable appliances have been shown to have a lower impact on bacteria compared to fixed appliances. Orthodontic appliances are currently considered niches with bacteria, which determine the difficulty of performing oral hygiene, having a direct impact on the development of oral microflora at the level of saliva and supragingival dental plaque

Keywords: orthodontic appliance, elastomeric appliance, microflora, oral hygene

INTRODUCTION

Nowadays, although the continuous development of preventive techniques is advanced, more and more children are faced with poor hygiene, which over time leads to a loss of dental hard tissue due to the presence of bacteria, especially in the case of children who are users of orthodontic appliances [1]. The pathological condition given by the bacterial microflora has a major impact on the quality of life of patients, therefore prevention and awareness of the effects is very important. Removable orthodontic appliances influence the oral microflora, significant changes appear only 15 days after starting the treatment, and the initial increase of microorganisms was followed by a progressive decrease towards physiological values [2].

The composition of the oral microbial flora is influenced by several factors such as: diet, age, oral hygiene, presence of carious lesions, pregnancy, periodontal disease, genetic factors [3]. The oral cavity represents a unique environment in the human body, which is characterized by the presence of saliva, hard surfaces, temperature fluctuations and large variations in nitrogen and carbon intake. It is colonized by a complex microbiota that develops as biofilms on all mucosal and dental surfaces [1].

Bacteria in the oral cavity occupy the ecological niche that is provided by the surface of the teeth and the gingival epithelium. There is a dynamic balance between plaque bacteria and the host's defence system [1].

Saliva has a major influence on bacterial plaque, namely by mechanical cleaning of exposed oral surfaces, by buffering the acids produced by bacteria in the oral cavity and by controlling bacterial activity. Salivary secretions maintain the oral tissues in a physiological state and are considered protective in nature [4].

In the oral ecosystem, saliva contributes in many ways. The absorption of salivary glycoproteins is the result of the formation of the salivary film which results in the facilitation of bacterial adhesion. Saliva is a rich source of proteins and carbohydrates, it inhibits the growth of exogenous organisms, because non-specific defence factors, such as lysozyme and lactoferrin, and specific IgA, salivary leukocyte protease inhibitor (SLPI) are present at its level. Buffer capacity plays a major role in maintaining pH, and the acidity of saliva can favour the growth of cariogenic bacteria [5].

Orthodontic treatments are increasingly used not only to correct malocclusions, but also to improve all functions. Known for their benefits, they also have some disadvantages, namely: they produce a series of disorders in the oral cavity, also injuries. Their presence in the oral cavity modifies the oral ecosystem, as it provides:

- a space for the accumulation and retention of food;
- a different physico-chemical environment;
- surfaces for adhesion and attachment of the oral microflora forming the biofilm [2].

The introduction of an orthodontic appliance into the oral cavity will induce a change in the number and composition of the oral microflora. In addition to the growth of cariogenic bacteria, such as Streptococcus mutans, Lactobacilli, there is also an increase in oral yeasts. Colonization with Candida albicans is of interest among orthodontists due to the possible cariogenic effect of the yeast [6,7].

The modification of the oral microbiota is closely related to the application of orthodontic appliances. Their introduction into the oral cavity greatly inhibits oral hygiene and causes an increase in the number of retentive areas for bacterial plaque. Changes at the oral level are followed by changes such as an increase in bacterial concentration, change in buffer capacity, acid pH, and salivary flow. According to some studies, the influence that orthodontic appliances have on the oral cavity, the increase in the number of bacteria and also

the viability of S. mutans and lactobacilli species has been studied. However, the changes that occurred between the number of bacteria from the beginning of orthodontic treatment and during it vary [8].

Aim and objectives

The aim of the paper is to highlight any correlation between the qualitative and quantitative changes in the oral microflora and orthodontic appliances. Predisposing factors for the appearance of changes are bacterial plaque, carious lesions, periodontal disease as well as other infections that can have an impact on the oral health of patients wearing orthodontic appliances. The results of this work could motivate practitioners on periodic controls regarding oral health, and patients on the importance of oral hygiene to prevent the risks of carious lesions and juvenile periodontal disease.

MATERIAL AND METHODS

The study was carried out in the Paediatric Dentistry Department of the Victor Babeş Timişoara University of Medicine and Pharmacy in the time interval 01.09.2021-01.03.2022, the patients being users of removable orthodontic appliances.

The patients were not informed in advance about the exact date on which the collection was taking place in order not to influence the results by instituting hygiene of the oral cavity and of the orthodontic appliance, different from the usual practice, noted in the patient's record as patients with unsatisfactory hygiene.

1. Criteria for including patients in the study:

- patients aged between 8-14 years, regardless of gender, with unsatisfactory hygiene, without oral lesions, users of removable orthodontic appliances.

2. Criteria for excluding patients from the study

- patients younger or older than the 8-14 years range, patients not wearing appliances, with oral lesions, patients wearing removable appliances but with very good hygiene.

Two kits were used for the collection of microbiological samples, one of the pharyngeal exudate type and a Micro-IDent® and micro-IDent®plus kit.

The pharyngeal exudate kit contains an ethylene-sterilized, cotton-tipped plastic applicator, length 13x165 mm, used for collection from the device and oral cavity, immersed in a liquid of modified Stuart culture medium that allows preservation and transport and a clear plastic tube with a label so that it can be identified in the laboratory. This culture medium allows the identification of pathogens such as Neisseria gonorrhoeae, Haemophilus influenzae, S. mutans, C. albicans, Lactobacillus, etc.

The Micro-IDent® and micro-IDent®plus kit produced by HAIN is presented in a blue plastic box containing 4 sterile plastic containers, coded with the colours yellow, blue, green and red. The 4 containers contain endodontic paper cones, 4% taper, yellow code 15. The micro-IDent® and micro-IDent®plus test system used can identify from 5 and 11 species of periodonto-pathogenic bacteria as well as their concentrations. Simple testing includes the following pathogenic species: Aggregatibacter actinomycetemcomitans (Aa), Porphyromonas gingivalis (Pg), Tannerella forsythia (Tf), Treponema denticola (Td), Prevotella intermedia (Pi). The test of 11 pathogenic species can identify: Aggregatibacter actinomycetemcomitans (Aa), Porphyromonas gingivalis (Pg), Tannerella forsythia (Tf), Treponema denticola (Td), Prevotella intermedia (Pi), Parvimonas micra (Pm), Fusobacterium nucleatum (Fn), Campylobacter rectus (Cr), Eubacterium nodatum (En), Eikenella corrodens (Ec), Capnocythophaga sp. (Cs).

The microbiological collection was carried out using the two kits: pharyngeal exudate and Micro-IDent® from the level of orthodontic devices as follows:

- From the removable orthodontic devices, it was sampled the internal and external base and from the anchoring elements as springs and bows (Fig. 1)

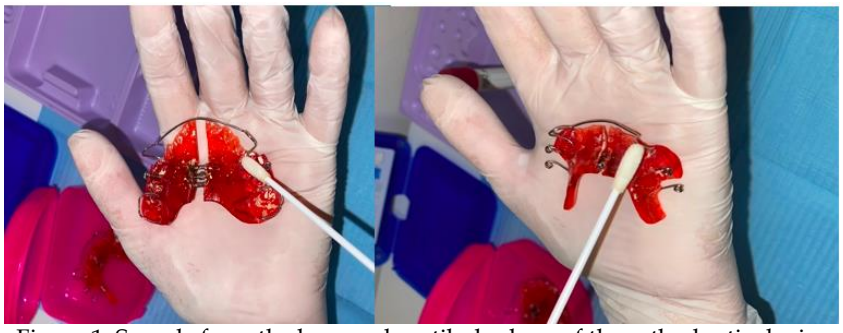

Figure 1. Sample from the base and vestibular bow of the orthodontic device

- Both faces and dental indentations were sampled from the elastomeric removable devices (Fig. 2).

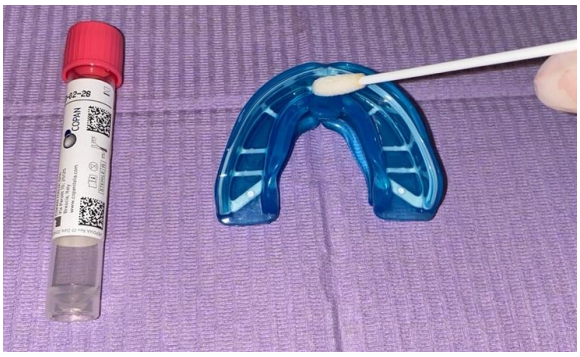

Figure 2. Sample from the elastomeric orthodontic device

The pharyngeal exudate kit was used by brushing the applicator on the described surfaces for 15 seconds (Fig. 1,2), to be immersed in the transport medium from the provided container. The patient's initials were written on the test tube, to be sent within a maximum of 2 hours after collection to the Timişoara Bioclinica Laboratory.

The Micro-IDent® kit was used by brushing paper cones on the described surfaces for 15 seconds and with the help of color-coded containers they were collected from different surfaces as follows: red - bows and springs, yellow – internal base, blue – external base, green – front area of the device (Fig. 3).

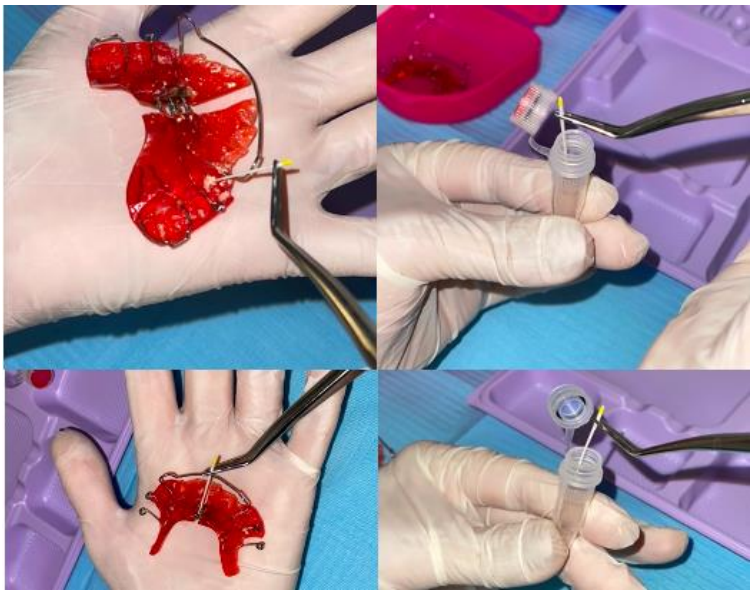

Figure 3. Sample from the base and screw of the orthodontic device

The elastomeric devices were sampled using the following coding: red – maxillary surface, yellow – mandibular surface, blue – maxillary anterior area, green – mandibular anterior area (Fig. 4).

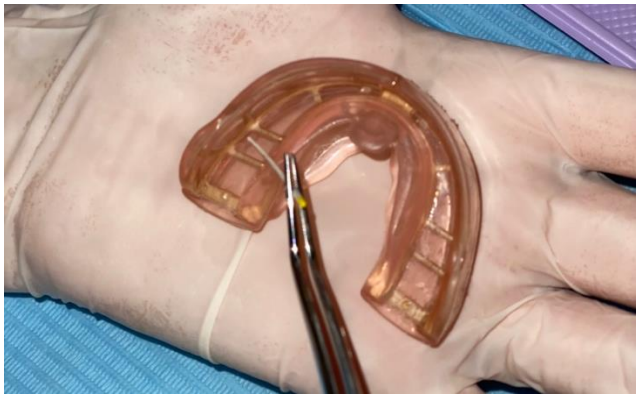

Figure 4. Sample from the elastomeric orthodontic device

Test results were sent within 7 days for the exudate and 10 days for the Micro-IDent® test.

The patients were instructed about the importance of achieving hygiene of the orthodontic device and the oral cavity.

RESULTS

The results obtained after the sampling were received from the Timişoara Bioclinica Laboratory in the form of microbiological analysis (Table 1, Table 2).

Table 1. Results of exudate analyses

Patient	Exsudate results
Patient 1	Candida albicans
Patient 2	Stenotrophomonas maltophilia
Patient 3	Streptococcus mutans, Candida albicans
Patient 4	Staphylococcus aureus, Candida albicans
Patient 5	Lactobacillus acidophilus, Staphylococcus aureus

Table 2. Results of Micro-IDent® analyses. Legend: Very high = +++, Raised = ++, Low = +, Undetectable = –

Patient	Micro-IDent® results
Patient 1	Actinobacillus actinomiycetemcomitans (Aa) – Porphyromonas gingivalis (Pg) – Prevotella intermedia (Pi) – Bacteroides forsythus (Bf) ++ Treponema denticola (Td) + Peptostreptococcus micros + Fusobacterium nucleatum/periodonticum ++ Campylobacter rectus + Eubacterium nodatum – Eikenella corrodes ++ Capnocytophaga spec. +
Patient 2	Actinobacillus actinomiycetemcomitans (Aa) ++ Porphyromonas gingivalis (Pg) + Prevotella intermedia (Pi) – Bacteroides forsythus (Bf) + Treponema denticola (Td) ++ Peptostreptococcus micros + Fusobacterium nucleatum/periodonticum + Campylobacter rectus + Eubacterium nodatum – Eikenella corrodes ++ Capnocytophaga spec. +
Patient 3	Actinobacillus actinomiycetemcomitans (Aa) + Porphyromonas gingivalis (Pg) ++ Prevotella intermedia (Pi) + Bacteroides forsythus (Bf) ++ Treponema denticola (Td) – Peptostreptococcus micros – Fusobacterium nucleatum/periodonticum + Campylobacter rectus + Eubacterium nodatum + Eikenella corrodes + Capnocytophaga spec. +
Patient 4	Actinobacillus actinomiycetemcomitans (Aa) - Porphyromonas gingivalis (Pg) – Prevotella intermedia (Pi) + Bacteroides forsythus (Bf) + Treponema denticola (Td) ++ Peptostreptococcus micros + Fusobacterium nucleatum/periodonticum ++ Campylobacter rectus + Eubacterium nodatum – Eikenella corrodes + Capnocytophaga spec. –
Patient 5	Actinobacillus actinomiycetemcomitans (Aa) – Porphyromonas gingivalis (Pg) – Prevotella intermedia (Pi) ++ Bacteroides forsythus (Bf) ++ Treponema denticola (Td) ++ Peptostreptococcus micros + Fusobacterium nucleatum/periodonticum + Campylobacter rectus – Eubacterium nodatum + Eikenella corrodes ++ Capnocytophaga spec. –

DISCUSSIONS

Following the completion of the study, an increased presence of Candida albicans yeast was observed, in a percentage of 37%, which is part of the normal bacterial flora of the oral cavity but has potential as an opportunistic pathogen in the following situations: low immunity, poor oral hygiene, general diseases [9,10]. Streptococcus aureus has a high pathogenic potential, causing suppurative infections or septicaemia [11]. Patients with Streptococcus aureus need drug treatment, carried out after carrying out the antibiogram type analysis to establish resistance to the different classes of antibiotics. Streptococcus mutans is the main bacterium responsible for the development of carious processes, and the quantifiable number on an exudate type analysis denotes the presence of large numbers of colonies also at the level of the orthodontic device, diagnosing the patient with increased cariogenic potential [12] (Fig. 15).

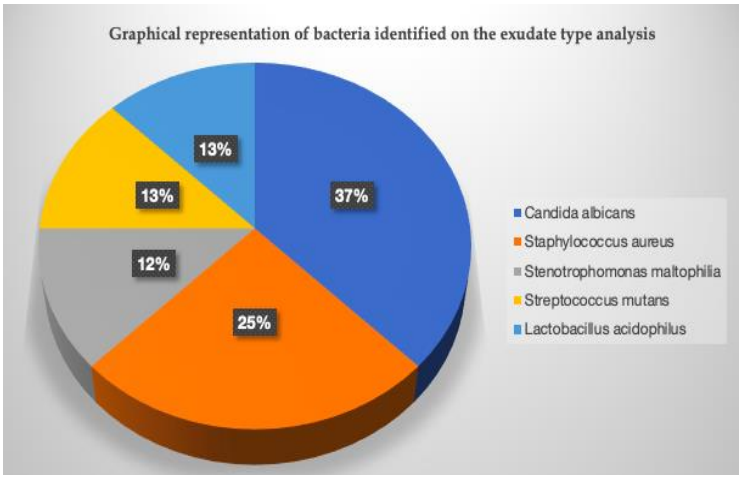

Figure 5. Graphical representation of bacteria identified on the exudate type analysis

Micro-IDent® analysis for the identification of germs associated with periodontitis revealed the majority presence of bacteria in the green and orange complexes that are recognized for inducing periodontal disease. The bacteria in the red complex are responsible for the production of gingival hypertrophy and the appearance of new blood vessels, with gingival bleeding as a clinical sign. The bacteria from all the complexes present in different numbers in the patients included in the study, quantitatively and qualitatively influence the bacterial biofilm, all of which are etiological factors of periodontal disease [13] (Fig. 16).

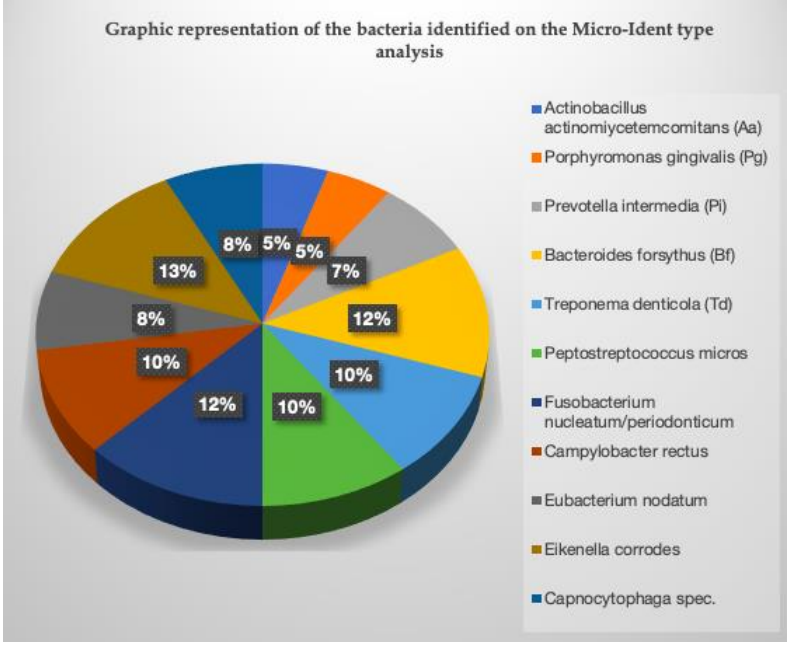

Figure 6. Graphical representation of bacteria identified on the Micro-Ident type analysis

Scientific publications have demonstrated that the presence of removable orthodontic appliances in the oral cavity of patients could change the nature of dental plaque and the colonization of oral microorganisms, leading to an increase in the microbial population, especially Streptococcus and Lactobacillus [14,15,16,17]. These may be associated with intraoral adverse effects on enamel and periodontal tissues. The use of appliances creates a favourable environment for the accumulation of microflora components and food residues, which, over time, can cause caries or aggravate any pre-existing periodontal disease. They can interfere with the practice of oral hygiene and can cover considerable parts of the tooth surfaces, so an increase in microflora has been reported in relation to orthodontic treatment [18,19,20].

According to a study conducted in 2011 by Asli Topaloglu-Ak et al. who investigated the effects of mobile, removable and fixed orthodontic appliances among 69 patients aged 6-17 years on mutant Streptococcus, Candida albicans and Lactobacillus sp. The introduction of any foreign object into the oral cavity, causes changes in the microbiological environment, as it provides multiple adhesion surfaces for the colonization of C. Albicans. The study concluded that orthodontic appliances are capable of increasing the bacterial and fungal population. Their long-term use increases the risk of periodontal disease, carious lesions and has a negative effect on the oral flora. In order to preserve oral health, periodic checks at short intervals, evaluation of oral hygiene to prevent caries are recommended [21].

The oral environment has the ability to adapt when the orthodontic appliance is inserted into the oral cavity. Several studies have shown an increase in stimulating flow, salivary pH and the buffering capacity of saliva, which lead to an increase in its anti-cariogenic property. There are studies that show that orthodontic appliances can increase the number of surfaces where plaque is accumulated by changing the bacterial flora, which leads to an increased risk of carious lesions [22,23,24].

Studies show an increased colonization for the fungal pathogen C. Albicans being frequently detected in patients wearing orthodontic devices. These devices increase the rate of oral carriage of the bacteria, and during treatment lead to a change in their number, our results also coincide with other studies investigating yeast growth [9,10,25].

Orthodontic appliances significantly influence the oral microflora, independent of the type of appliance, although removable appliances have been shown to have a lower impact on bacteria compared to fixed appliances. Orthodontic appliances are currently considered niches with bacteria, which determine the difficulty of performing oral hygiene, having a direct impact on the development of oral microflora at the level of saliva and supragingival dental plaque [26,27]. Compared to patients not wearing orthodontic appliances, patients during treatment reported the existence of qualitative and quantitative changes in supra- and subgingival bacterial plaque throughout the period of orthodontic treatment [28].

CONCLUSIONS

Following this study carried out on 5 patients aged between 8-14 years, we came to the conclusion that the quantitative and qualitative changes in the microbial biofilm present among patients wearing orthodontic removable devices appear from the first week of wearing and become more and more increased during the treatment, with a higher colonization of the following species in order: the orange complex (Fusobacterium, Prevotella and Campylobacter spp), green complex (Eikenella corrodens A. actinomycetemcomitans, Capnocytophaga spp.), and then that of red complex (P. gingivalis, T. forsythia and T. denticola). Patients treated with orthodontic devices are advised to improve their oral hygiene and to attend periodic check-ups, especially in the first months of treatment.

The increased need for orthodontic treatments these days also involves the awareness of family and patients about the need to achieve good hygiene because the specificity of the materials orthodontic removable devices are made of, have an increased porosity and thus, in the absence of compliance with maintenance indications, they contribute negatively to the development and multiplication of a large number of potentially pathogenic and cariogenic bacteria.

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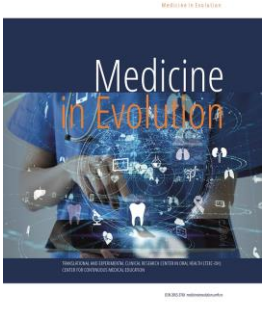
Assessment study of the views on the importance of informed consent in the medical act in dental health services in Timis County



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Abstract

Background: Informed consent is an ethical concept that is codified by law and must be put into daily practice in every health institution. Informed consent is based on the concept of respect for autonomy, which gives adults the right to govern their lives according to their own values and preferences. In Romania, for any type of clinical investigation, medical care or potentially risky treatment we need the written consent of the patient, certified by his/her signature. The objective of the study was to evaluate the signing and use of informed consent to dental health care in Timis County.

Material and method: A retrospective observational epidemiological study was conducted, in which we aimed to evaluate the signing and use of informed consent in current dental practice in Timis County. The research method used was the use of a questionnaire survey, which was put online on a group of dentists in Timis County, between March and May 2022.

Results: The habit of signing informed consent in dental services in Timis County is not present in 45% of respondents.

Conclusions: Our study revealed that the use of informed consent by patients in Timis County is not necessarily a practice habit, especially in rural areas.

Keywords: Informed consent, medical care, treatment

INTRODUCTION

Informed consent is an ethical concept that is codified by law and must be put into daily practice in every health institution. Three fundamental criteria are necessary for an informed clinical consent to be correctly completed: the patient must be competent, be adequately informed and not be coerced by medical staff or relatives. The doctor-patient interaction is rooted in the ethical concept of beneficence, but in the 19th and 20th centuries, jurisprudence and societal changes brought respect for autonomy and, with it, informed consent [1].

Informed consent is based on the concept of respect for autonomy, which gives adults the right to govern their lives according to their own values and preferences. Informed consent has been defined as "the autonomous authorization of a person for a medical intervention or participation in research" and consists of seven elements: patient capacity (also called competence), voluntariness, disclosure of material information (such as risks, benefits and relevant alternatives), recommendation of a plan, agreement, decision and authorization [2,3]. Informed consent can be given verbally or through signed documents, the latter often favoured by institutions when risks are higher (e.g. when anaesthesia/sedation or invasive procedures are required) to protect against liability.

Some accounts of informed consent suggest that clinicians' roles should be limited to providing information and presenting the patient with options. However, a preferred concept of informed consent is the "shared decision-making" model, in which clinicians and their patients or caregivers work together to decide the best care options for the patient, especially if there is more than one reasonable option [4,5].

In Romania for any type of clinical investigation, medical care or treatment with potential risk we need the written consent of the patient, certified by his/her signature. Exceptions to this rule are medical emergencies that put the patient's life at risk, but even in these cases an emergency report must be completed after the intervention justifying the lack of informed consent.

The purpose of the informed consent signing process is to provide patients with sufficient information to enable them to make an informed decision and preserve their autonomy. Patient consent must be obtained prior to each dental medical procedure. Indeed, professional regulatory bodies and other professional organisations issue regularly updated detailed guidance on this process [6]. The pillar of informed consent is an ongoing process whereby the patient is provided with sufficient information to enable them to make decisions voluntarily and without coercion. They must be given explanations (in appropriate language and terminology) to enable them to understand exactly their oral health condition, the type of treatment proposed and other treatment alternatives as well as their benefits and risks, and the consequences if action is not taken.

The name(s) of the doctor(s) responsible for the medical act must be mentioned in the informed consent form. The doctor must thus inform the patient in accessible language about the purpose of the medical intervention/treatment used, the potential risks to which the patient is exposed, the prognosis of the conditions without treatment or the recommended medical/prophylactic care methods, some possible medical/social, psychological, economic consequences, etc., as well as the alternative treatment options that may or may not be provided in the dental service concerned, and the patient must be informed about the right to a second medical opinion.

The objective of the study was to assess the signing and use of informed consent to dental medical services in Timis County.

Aim and objectives

In this retrospective study we aimed to evaluate the signing and use of informed consent in current dental practice in Timis County.

MATERIAL AND METHODS

A retrospective observational epidemiological study was conducted, in which I aimed to evaluate the signing and use of informed consent in current dental practice in Timis County. The research method used was the use of a questionnaire survey, which was put online on a group of dentists in Timis County, between March and May 2022. At the end of the period, it was observed that 89 subjects practicing dental medicine in Timis County responded to the questionnaire, of which 58 were dentists, 21 were prophylaxis nurses and 10 receptionists from dental clinics in Timis County. The mean age of the respondents was 39.21± 8.6 years, with a minimum of 22 years and a maximum of 63 years. 65 of the respondent subjects were female, and 68 stated that they were working in urban areas.

RESULTS

Understanding of the need to complete and the duties of completing informed consent, of health care staff taken in this study. They are described in Table 1 and it can be observed that almost ninety-six percent of the subjects felt that the consent form gives permission to the dentist to perform the procedure and almost 84% felt that confirmed they are given enough data to help the patient decide for themselves. Nearly seventy percent felt that the form is for the protection of the dentist/clinic. 55.8% responded that once the informed consent form is signed, patients will not be able to claim compensation for any events associated with the medical work.

Table 1. Summary of awareness/understanding of the informed consent process by dental medical staff

	YES **No (%)**	**NO** **No (%)**
The consent form gives the dentist permission to perform the procedure	82 (95,34)	4 (4,66)
The consent confirms that sufficient information has been given to the patient so that they can decide	72 (83,72%)	14 (16,28%)
The signed consent is a legal necessity	61 (70,9%)	25 (29,1%)
The consent is filled in to identify the correct part of the procedure	66 (76,74%)	20 (23,26%)
After signing the consent, patients cannot claim compensation for any adverse events associated with the medical activity	38 (44,18%)	48 (55,8%)
The consent is to protect doctors, dentists and medical clinics	60 (69,76%)	26 (30,24%)
The consent form is not compulsory	23 (26,74%)	63 (74,25%)

The habit of signing the informed consent in dental services in Timis County is not present in 45% of the respondents (Figure 1). Of the 41 respondents who said that they do not usually provide informed consent to patients, 21 (80.77%) are in rural areas.

The place of signing the IC was usually the waiting room is in most cases the waiting room (72%) and it is signed before the patient comes in contact with the doctor, for the doctor to consult him or to establish a treatment plan (Figure 2).

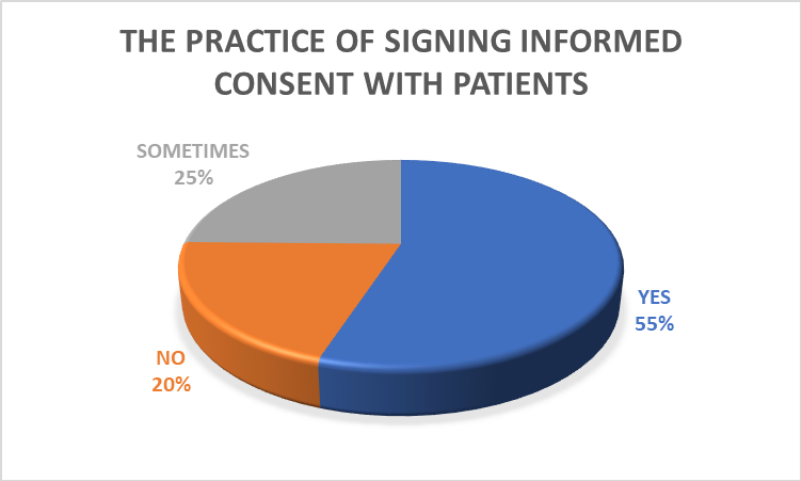

Figure 1. The practice of signing informed consent with patients

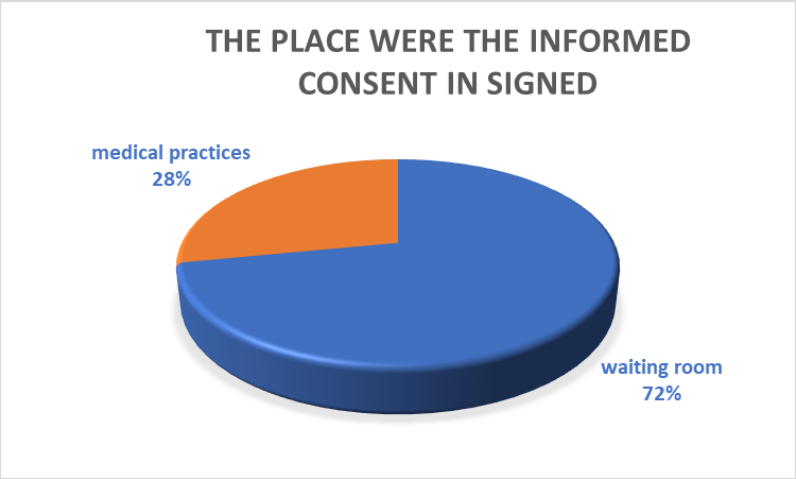

Figure 2. The place where the informed consent is signed

The explanations related to treatment, complications, costs in 69% are given by the doctor and in 31% by the nurse.

The perception of the medical staff who work in Timis county about the importance of the patient's completion of the I.C., 40% say that it is not important to fill in the I.C., and 31% do not believe that it is mandatory (Figure 3).

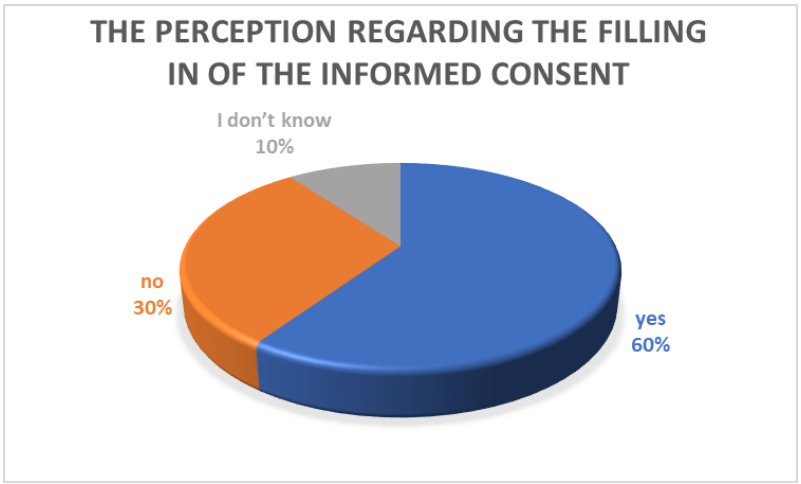

Figure 3. The perception regarding the filling in of the informed consent

DISCUSSIONS

Our study revealed that obtaining informed consent from patients in Timis County is not common practice, especially in rural areas. In many cases although they are filled in, most of the time they are given by the nurse or receptionist, in the waiting room, before any first contact of the patient with the doctor.

For patients with medical risks, assessment and precautions to be taken during treatments are essential. Risk factors include: the increasing number of elderly patients, the increasing use and administration of a wide range of drugs in dentistry and medicine in general, the stress level of patients determined by socio-economic conditions, and last but not least, the lack of health education among the population [6].

As the need for informed consent becomes more evident in the dental profession, a dental professional should know which procedures actually require written informed consent. The answer to this question is relatively simple: any procedure that is "invasive or irreversible" requires informed consent. The fact that a patient visits a dental office for an examination implies that he or she wants the doctor to conduct a clinical examination to determine what treatment might be needed, but most dentists take for granted that over 90% of their procedures are surgical in nature [7]. All procedures, from a simple oral restoration to the removal of a complicated third molar, dental abscess, may require irreversible alteration of body tissues with the risk of complication or unwanted side effect. Even minor occlusal treatments or incisions can affect the surrounding dentition, canine elevation, masticatory function. The mouth is extremely dynamic, subject to the forces of the tongue, lips, cheeks, and teeth. Any change in that environment, even with the physician's best intentions, can lead to undesirable outcomes, and those possibilities must be presented to the patient and documented in writing [8,9].

Although "invasive and irreversible" procedures require information and consent, most diagnostic procedures, such as general clinical examinations, periodontal probing, and radiographs do not require such formal consent [10]. It is assumed, for the most part, that patients want the physician to obtain all the information necessary to make a complete and accurate assessment of their general and oral condition at the initial examination or can determine the reason for any pain in question. Sometimes, however, patients will specifically state that they want to forego diagnostic procedures such as radiographs or periodontal probing. The practitioner's focus should be to obtain immediate "informed refusal" in these cases [9,11].

In one study the difficulties of researching consent for simple dental implants in primary care were presented.4 Previous studies in the UK have shown that many patients are unaware that the informed consent process protects their interests and have had the misconception that it is designed to protect hospitals, clinics and doctors [12,13]. Another study in general practice found that patients had a limited understanding of the legal status of written consent: 46% thought the primary function of consent forms was to protect hospitals and 68% thought consent forms allowed doctors to take control; only 41% of patients thought consent forms made their wishes known [14]. Similar results were reported in a paediatric surgical setting: 51% of patients felt that consent was to protect hospitals and 23% felt that by signing the form they had waived their right to claim compensation if complications occurred [15]. Such findings are also reflected in our study in primary dental care: 60% of health professionals felt that the consent process was to burden them with more paperwork and carried out to protect the hospital/state practice. In addition, 40% mistakenly thought that signing a consent form was a legal requirement [16]. To our knowledge, this is the first study to systematically audit both satisfaction and understanding of the consent process in primary dental care in Romania.

CONCLUSIONS

Our study revealed that the use of informed consent by patients in Timis County is not necessarily prevalent in dental practice, especially in rural areas.

In many cases although it is filled in, most of the time it is given by the nurse or medical registrar in the waiting room before the patient's contact with the doctor.

It is mandatory for dentists to be aware of this legal responsibility to adequately inform patients and obtain informed consent before performing any type of medical care.

Informed patient consent to the benefits and risks of any medical diagnostic and treatment procedure: is mandatory; its absence signifies abuse of the patient by the doctor; if the patient suffers harm, lack of informed consent means liability of the doctor and inoperability of insurance.

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The role of mast cells in inflammatory and malignant lesions of the oral cavity

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Abstract

Mast cells (MC) were described over 100 years ago by Paul Erlich. They are located in the connective tissue in the immediate vicinity of the blood vessels. Mast cells originate from a medullary progenitor cell. It presents in the cytoplasm numerous granules with a variable content of mediators. Different subpopulations of mast cells are described depending on their content in proteases and localization. They are multifunctional cells, being involved both in the body's physiological processes, but also in the pathogenesis of many diseases. Mast cells are involved in the initiation of inflammatory processes in the oral cavity by releasing proinflammatory cytokines. The role of mast cells in cancer is still debatable whether they contribute to tumor progression or have an antitumor effect.

In the future, more in-depth research on mast cells may provide not only insights into their biology, but also a better understanding of their role in various diseases. Mast cells still cause many debates regarding their role in cancer, including oral cancer. The presence of mast cells in oral squamous cell carcinomas has been noted by many authors, but their role remains unclear. However, new therapies targeting mast cells could play an important role in controlling tumor growth and metastasis.

Keywords: Mast cells, inflammation, squamous cell carcinoma

INTRODUCTION

Mast cells form a component of the immune system, playing an important role in host defense. They were first described by Paul Ehrlich in 1878 as cells belonging to the connective tissue. In histological sections, mast cells are round or oval-shaped cells with diameters between 8 and 20μ and have a large number of granules in the cytoplasm.

The content of mast cell granules is very varied. They can produce and secrete a series of substances such as: bFGF (basic fibroblast growth factor), chymase, tryptase, heparin, histamine, TNF-α (tumor necrosis factor alpha), various interleukins (IL-3, 4, 5, 6, 8, 10,13,16), chemokines, matrix metalloproteinases (MMP-2 and 9), TGF-β (transformation growth factor beta), NGF (nerve growth factor), PDGF (platelet-derived growth factor) and VEGF (vascular endothelial growth factor) [1].

They are present throughout the body and play an important role in the maintenance of many physiological functions as well as in the pathophysiology of diseases. Mast cells have been shown to be involved in the initiation of a number of inflammatory conditions. Inflammation is a double-edged sword, responsible for both defense and protection against the carcinogen but at the same time leads to tissue destruction. Also, the pathogenesis of potentially malignant oral diseases and oral squamous cell carcinomas (OSCC) begins with the inflammatory response, mediated by immune cells such as mast cells, neutrophils, lymphocytes or macrophages.

Apart from their role in maintaining homeostasis and inflammation, the association of mast cells with various tumors has been described. In several malignancies, mast cell density has been found to correlate with increased risk of metastasis and poor prognosis. Currently the functional significance of mast cells in various tumors is not yet clearly understood.

Although the presence of mast cells in tumors was recognized more than 100 years ago, only recently has more attention been directed to the role of this cell in neoplastic processes. In the oral cavity, there are few studies on the involvement of mast cells in squamous cell carcinomas, and the results reported in the literature are contradictory.

Back to the history

Mast cells were first described by Paul Erlich in 1878. He called these cells mastzellen because of the tinctorial properties and the intracytoplasmic granules [2-4]. Ehrlich also shows that these cells are located in the immediate vicinity of blood vessels and nerves. He also notes that the number of mast cells is increased in tumors and especially in carcinomas. Studies on the role of mast cells in normal and pathological conditions have a long way to go, Erlich initially suggests that these cells with their granules have the role of "feeding" the surrounding tissues. Today, the role of mast cells in some physiological reactions of the body, wound healing and angiogenesis, defense against pathogens, innate and acquired immunity is known.

Apart from Erlich, other authors also pay special attention to the study of this cell. Among them is Westphall, who in 1891 demonstrated that mast cell granules are soluble in water, and for their preservation the tissues must be fixed in 50% alcohol and stained with alcoholic thionine [5].

In 1935 Jorpes observed the metachromasia of the toluidine blue solution in contact with substances from the heparinoids group and hypothesized that the main component of mast cell granules is heparin [6,7].

The modern literature on the mast cell indicates its active participation in the pathogenesis of numerous diseases, but also in the body's general defense reaction. Among the prestigious personalities who drew attention to this topic was Hans Selye in 1965 [8].

About a century after the discovery of mast cells, Enerback describes, in 1966, two subpopulations of mast cells distinct from a histochemical point of view, thus demonstrating the heterogeneity of the mast cell system [9,10].

Recently, specialized literature pays special attention to the involvement of mast cells in tumor angiogenesis. Thus Grützkau suggests in 1998 that mast cells could contribute to angiogenesis by releasing proangiogenic factors such as VEGF [11]. Since 2009, the idea has been circulating that mast cells could be a therapeutic target for cancer treatment.

The origin of mast cells

For a long time the origin of mast cells was controversial. The origin of mast cells in a medullary progenitor cell, which expresses CD34, is now accepted [12]. In 1978 Kitamura demonstrated for the first time the origin of mast cells. Kitamura also shows that the transcription factors GATA-1 and GATA-2 are involved in the differentiation of pluripotent stem cells into mast cells, and microphthalmia-associated transcription factor (MITF) has an important role in the localization, phenotype and survival of these cells [13,14].

During prenatal development, hematopoietic cells appear in several distinct waves. The first mast cells differentiate from primitive erythromyeloid progenitors in the extraembryonic yolk sac [15]. A second wave of MCs appears together with the first definitive hematopoietic progenitors. The first two waves are mainly connective tissue MCs (CTMCs) [16]. The third hematopoietic wave comes from the aorta-gonado-mesonephros region. Cells formed during this wave produce hematopoietic stem cells that have mast cell-forming potential.

It has long been assumed that MC develops from hematopoietic stem cells in the bone marrow. However, it is now clear that the hematopoietic stem cells in the bone marrow produce only a fraction, not all, of the mast cells. A number of experiments show that bone marrow-derived MCs mainly complement the mucosal MC population (MMC) [17].

Mast cell heterogeneity: how different are they from each other?

Mast cell heterogeneity was first described in the mid-1960s and was based on different characteristics in histochemical staining. Thus the concept of connective tissue mast cells (CTMC) and mucosal mast cells (MMC) was born.

In humans, different subpopulations of mast cells have been defined by their protease content. Thus mast cells containing tryptase (MCT), mast cells containing tryptase and chymase (MCTC) and mast cells containing only chymase (MCC) in cytoplasmic granules are described [18]. The latter were, for a long time, controversial, and the presence of mast cells positive only for chymase remained ignored and practically unstudied. The two distinct subpopulations of mast cells, MCTs and MCTCs, as well as MMCs and CTMCs, differ in localization and mediator content [19].

In addition to dividing mast cells into distinct subpopulations based on their localization or protease content, there are also definitions of mast cells that are either constitutive or inducible, inflammatory (iMC), or pro- or anti-tumorigenic (MC1 or MC2) [20-22]. While the division into constitutive and inducible subpopulations could be related to the prenatal origin of MC, the latter is likely dependent on microenvironmental changes during an inflammation. It is clear that mast cells from different organs differ in receptor and mediator expression, but even within a single tissue there is considerable heterogeneity [23].

The origin and development of different subpopulations of mast cells has raised many questions. For hematopoiesis in the adult, the question was whether there are several different populations of progenitor MCs in circulation or whether there is a progenitor population that has the ability to differentiate and mature into any of the MC subtypes. In other words, heterogeneity is driven by locally produced factors or is driven by the

recruitment of different types of designated progenitors. In a study addressing this question, the results suggested the existence of a common progenitor that gives rise to all subpopulations of mast cells [24]. However, single-cell RNA sequencing and single-cell cultures will likely provide further evidence and insights into this process.

Mast cells in oral inflammation

Mast cells are involved in the initiation of a number of inflammatory conditions in the oral cavity. Gingival inflammation can lead to periodontal disease, where cytokines activate and stimulate mast cells to secrete proinflammatory molecules that play a critical role in inducing inflammation [25]. Increased levels of proinflammatory cytokines, such as IL-1, TNF, and IL-6, are secreted by various cells of the immune system, including mast cells. The role of MC in periodontal disease is not yet clear. However, in this condition, an increase in the number of mast cells and the production of inflammatory cytokines is observed, thus demonstrating their involvement in alveolar bone resorption. In oral tissue, MCs producing cytokines and proteases (tryptase and chymase) favor leukocyte infiltration, causing degradation of the extracellular matrix and leading to gingivitis and periodontitis [26]. In acute inflammation, MCs release various proinflammatory molecules such as histamine, proteoglycans, arachidonic acid metabolites, TNF, and tryptase, a serine proteinase that promotes inflammation. Histamine, acting on the endothelium, mediates vascular permeability and favors platelet adhesion through the adhesion molecule P-selectin.

Mast cells are able to process microbial antigens intervening in acquired immunity and play a key role in inflamed periodontal tissue by producing IL-33 and other pro-inflammatory cytokines. Mast cells play a crucial role in the pathogenesis of allergic and systemic diseases by producing proinflammatory cytokines of the IL-1 family, effects that can be suppressed by IL-37 by forming an extracellular complex with IL-18Rα and IL1R8. In periodontitis, there is a higher expression of pro-inflammatory cytokines, such as IL-33 produced by MC, associated with the pathogenesis of periodontal disease.

Today, IL-37 is known to inhibit innate and acquired immunity and consequently inflammation, an effect that could complement the treatment of acute and chronic gingival inflammation, including periodontal disease [27]. Because IL-37 is a potent blocker of IL-1 and a pro-inflammatory cytokine in periodontal disease, it has been hypothesized that IL-37 treatment of periodontal disease could be an additional therapeutic adjunct to traditional drugs [28].

Mast cells in oral squamous cell carcinoma

The role of mast cells in cancer is still debatable whether they contribute to tumor progression or have an antitumor effect. The presence of mast cells in tumors has been shown to be an independent prognostic factor in prostate cancer, malignant melanoma, pancreatic cancer and leukemia [29]. Increased expression of c-Kit and stem cell factor, which in turn are required for mast cell migration, maturation and survival, has been observed in breast tumors [30]. In addition, increased mast cell numbers and mast cell infiltration in the peritumoral stroma have been observed in Merkel cell carcinoma, lung cancer, hepatocellular carcinoma, colorectal cancer, and Hodgkin's lymphoma [31]. Several cell types, such as tumor cells, endothelial cells, macrophages, and mast cells are involved in increased vascularity in neoplasms [32]. Mast cells are directly involved in the evolution of neoplasia because, beyond their defense functions, they participate in regulating the homeostasis of blood vessels [33]. Their participation in this microenvironment has been suggested in various malignant tumors [34]. Regarding oral squamous cell carcinoma (OSCC) it has been observed that there is an increased density of microvessels and an increased density of mast cells in these tumors, which may be a reason for a poor prognosis [35,36].

Squamous cell carcinoma is the most common malignant lesion in the head and neck region, representing 95% of all malignant lesions in this area. Despite the great progress made in the field of cancer research, the availability of sophisticated diagnostic techniques and improvements in the therapeutic options of patients, the prognosis remains reserved in OSCC. This is probably due to the unpredictable behavior of these tumors, which show a variable aggressiveness independent of the clinico-pathological and histological grade [37].

Because oral squamous cell carcinoma is associated with chronic inflammation in the adjacent connective tissue, immune reaction, and angiogenesis with the progression of dysplastic changes, there is a need to evaluate the role of mast cells in these carcinomas.

Mast cell density in oral squamous cell carcinoma has been reported differently in the specialized literature. Studies by Oliveira-Neto et al. and by Teófilo et al. showed a decrease in the number of mast cells in OSCC [38,39]. The study carried out by Zaidi et al. show that mean mast cell density/mm2 was significantly increased in OSCC cases ($P < 0.05$) compared to normal tissue [40]. This was also demonstrated by the study of Iamaroon et al. and Michailidou and Antoniades. These authors suggested that mast cells release potent pro-angiogenic factors, such as tryptase, which play a significant role in angiogenesis associated with oral squamous cell carcinoma [41,42].

Many studies have been conducted on the role of mast cells in oral cancer and their accumulation in the peritumoral stroma. The involvement of mast cells is linked to the release of important pro-angiogenic factors, which help the interaction of the tumor with the host, thus supporting tumor progression. Not only was its involvement in tumor progression identified, but the progression of leukoplasia with and without dysplasia in oral squamous cell carcinoma was also established. The main factors released are heparin, histamine, chymase, tryptase, bFGF (basic fibroblast growth factor), VEGF (vascular endothelial growth factor) [43].

Other data from the specialized literature show a significant increase in mast cell density in well-differentiated oral squamous cell carcinomas compared to moderately or poorly differentiated ones [44]. A molecular epidemiological study of the mast cell population revealed a significantly higher number of mast cells in squamous cell carcinoma in the skin than in the oral mucosa. In addition, the number of mast cells was higher in squamous cell carcinoma of the lip than in normal oral mucosa. Another study showed that the increase in the mast cell population is not related to the degree of tumor differentiation [45].

The increased density of mast cells and microvessels indicates that mast cells play an important role in regulating angiogenesis in oral squamous cell carcinoma [46]. However, some studies have shown that there is no significant correlation between mast cell density and microvessel density in oral squamous cell carcinoma [47]. On the other hand, Kathuriya et al. showed a significant correlation between mast cell and microvessel density in well-differentiated types, but not in moderately or poorly differentiated types [44]. On the contrary, another study reported a significant correlation between mast cell and microvessel density in poorly differentiated OSCC [35].

On the other hand, another study stated that there was a significant correlation in mast cell and microvessel density in normal oral mucosa but not in oral squamous cell carcinoma regardless of histological grade [48]. However, another study showed that in oral squamous cell carcinomas mast cells in the peritumoral and intratumoral stroma express CD105, VEGF, VEGFR1 and VEGFR2 and showed a positive correlation with the angiogenic activity of the tumor. Also, this study shows that a mast cell influences tumor progression and growth [49].

As can be seen from the studies presented, the results from the specialized literature are controversial so that the exact role of mast cells in oral squamous cell carcinomas is not known. The presence of mast cells in oral squamous cell carcinomas has been observed by many authors, but their role in tumor progression and metastasis still remains unclear.

CONCLUSIONS

The biology and function of mast cells, both under normal and pathological conditions, has been a fascinating topic for many researchers over the years. Many fundamental discoveries have been made since the discovery of mast cells in the late 19th century, shedding light on the function of this ingenious cell. However, there are many questions that still await an answer. With the rapid developments in methodology, systems biology in combination with experimental studies and clinical investigations, a rapid development of mast cell research can be foreseen in the coming years. This research will not only provide insights into the biology of mast cells, but also a better understanding of their role in various diseases.

Arguably, mast cells cause much debate regarding their role in a variety of physiological and pathological processes, including cancer. They act as guardians of the immune system and, in turn, respond to many signaling pathways, thus contributing to the process of carcinogenesis and metastasis. Many studies have revealed that the number of mast cells definitely increased with tumor progression. New therapies targeting mast cell mediators and receptors could play an important role in controlling the process of tumor progression and metastasis, thus favoring a good prognosis for the patient.

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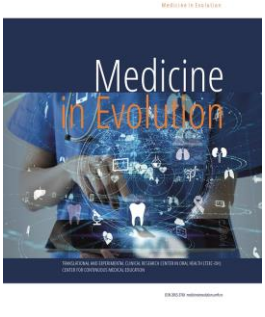
Perioperative management of tooth extraction in patients with antiplatelet and anticoagulant treatment



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Abstract

Patients on anticoagulant or antiplatelet treatment require close monitoring during extraction surgery because of the significant risk of postoperative bleeding. There is no consensus regarding the treatment of patients with anticoagulants, recently dentists opt for a conservative approach, in which the intervention takes place without interrupting the medication, and haemostasis is achieved through local measures.

Discontinuation of anticoagulant treatment during oral surgery increases the risk of thromboembolic events through various mechanisms, such as INR (international normalized ratio), compensatory hypercoagulability and the post-thrombotic effect. Thus, patients are prone to the risk of pre- and postoperative arterial thromboembolism and postoperative venous thromboembolism if the INR value returns to normal shortly after discontinuation of treatment.

This study aims to evaluate the haemorrhagic complications associated with dental extractions in patients under chronic anticoagulant treatment, with the modification of drug therapy and following a standard perioperative management protocol

Keywords: Tooth extraction, anticoagulant, antiplatelet, haemorrhagic complications

INTRODUCTION

Under the name of antithrombotic medication, this group includes drugs useful in the treatment and prophylaxis of thromboembolic conditions. They are indicated both in the treatment of arterial and venous thrombosis, acute or chronic [1].

The category of antithrombotic drugs includes: antiplatelet agents, anticoagulants and fibrinolytics, which play an important role in the phenomenon of atherothrombosis, thus preventing the formation of intravascular thrombi or disintegrating already formed thrombi.

Antiplatelet agents are medicinal substances that inhibit platelet functions in the process of haemostasis (manifested by prolonging bleeding time) and reduce the aggregation capacity of blood platelets, preventing the formation of thrombi. The most common antiplatelet agent is acetylsalicylic acid (Aspirin), it has an antiaggregant effect on platelets.

Oral anticoagulants are coumarin derivatives that act as vitamin K antagonists by inhibiting the synthesis of coagulation factors II (prothrombin), VII, IX and X, preventing the blood coagulation process.

Most practice guidelines consider tooth extractions as minor interventions associated with a low risk of bleeding and self-limited blood loss that can be managed with local hemostatic agents [2]. However, certain surgical interventions in the oral cavity may require temporary discontinuation of antithrombotic therapy [3].

There are both an increasing number of patients prescribed anticoagulation or antiplatelet therapy and drugs for this purpose. There is strong evidence for older drugs (e.g. warfarin, antiplatelet agents), as well as limited evidence for newer direct-acting oral anticoagulant drugs, that for most patients no change in anticoagulant or antiplatelet therapy is necessary before tooth extraction [4].

Planning dental extractions for patients on antithrombotic therapy remains controversial [5].

Aim and objectives

The present work aims to evaluate the haemorrhagic complications associated with dental extractions in patients under chronic anticoagulant treatment, with the modification of drug therapy and following a standard perioperative management protocol.

We analysed the therapeutic management used in the extraction treatment for this category of patients and tried to fit the clinical aspects into the therapeutic protocol. Another objective was to draw the attention of the dentist and the dentoalveolar surgeon to some useful aspects and particularities in the management of these cases, which present a high haemorrhagic risk and require special attention.

MATERIAL AND METHODS

The first stage of the prospective study was to establish the clinical characteristics necessary for patient selection. Patients under antiplatelet or anticoagulant therapy who required extraction treatment and presented themselves at the Timişoara Oral and Maxillofacial Surgery Clinic between January 2019 and December 2019 were included in the study.

The patients were informed about the medical research we are carrying out and expressed their consent in writing, according to Ministry of Health Order 1411 of 12.12.2016, annex no. 1 to the methodological norms - Form for expression of consent of the informed patient.

The selection of patients for inclusion in the study was based on the clinical examination, radiological investigations (orthopantomography) and laboratory examinations (complete blood count, coagulogram, ESR).

Patient selection and inclusion criteria:

1. Adult patients (over 18 years);
2. Both gender;
3. Anticoagulant treatment supervised by the attending physician;
4. Indication of extraction of one or more dental units;
5. INR values between 1 and 3;
6. Admission to the Oro-Maxillo-Facial Surgery Clinic Timişoara for the possibility of monitoring the patient.

Exclusion criteria:

1. Minor patients (under 18);
2. Patients with acute infectious processes, malignant tumors;
3. Administration of an antiplatelet or anticoagulant treatment not supervised by the attending physician;
4. The existence of associated conditions that contraindicate tooth extraction;
5. Too low or too high INR values;
6. Lack of patient compliance and cooperation.

The patients were hospitalized in the Timişoara Oral and Maxillo-Facial Surgery Clinic, where they underwent clinical evaluation and blood sample collection for laboratory examinations: complete blood count, coagulogram (prothrombin time, INR, TTPa), ESR, C-reactive protein, creatinine, urea, blood sugar, followed by referring patients to the specialist consultation, to the cardiologist.

The orthopantomography radiological examination was performed, accompanied by retroalveolar radiography where necessary. All data collected were recorded in the patient record.

Bleeding risk was assessed based on information gathered from the history, clinical examination, and laboratory test results. We attributed an increased risk of bleeding to patients who presented associated comorbidities (which can influence both haemostasis and the patient's predisposition to infections, e.g. diabetes) and those who required multiple extractions, teeth with periodontal problems or ankylosed teeth.

The therapeutic protocol included the modification of the pre-operative treatment scheme, according to the cardiologist's indication, recorded in the patient's observation sheet in the interdisciplinary consultation section, as follows: stop the chronic anticoagulant treatment administered orally and replace it with Clexane 0.6 or 0, 8 depending on the patient's weight up to INR values <1.2. The INR value is checked and when it is <1.2, and the patient has not been administered Clexane at least 6 hours before the intervention, the tooth extraction is performed.

The surgical intervention began with asepsis of the perioral skin using Betadine solution and asepsis of the oral mucosa with Chlorhexidine, followed by local anaesthesia with Articaine anaesthetic with adrenaline 1:200.000. Atraumatic extraction of irretrievable dental units was performed, with minimal detachment of the muco-periosteum and avoidance of extensive denudations of the maxillary bones. Extraction accidents such as dental root fractures, alveolar bone fractures and oral soft tissue wounds should also be avoided due to the intense vascularity at this level. In the cases where it was necessary to make a flap, its expansion was minimal (Figure 1), avoiding its tension or tearing.

In those cases where osteotomy was necessary (ankylosed teeth or root remnants located in the depth of the alveolar bone-Figure 2), an attempt was made to remove as little

bone tissue as possible, in order to keep the alveolar walls intact and facilitate the subsequent stabilization of the blood clot.

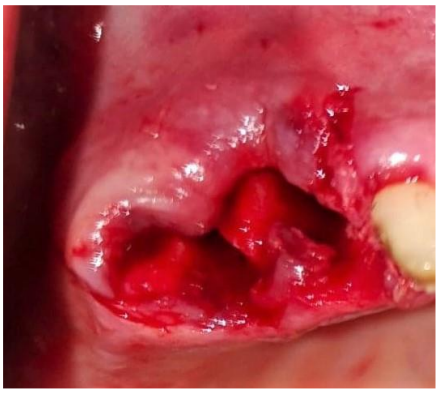

Figure 1. Minimal flap extension

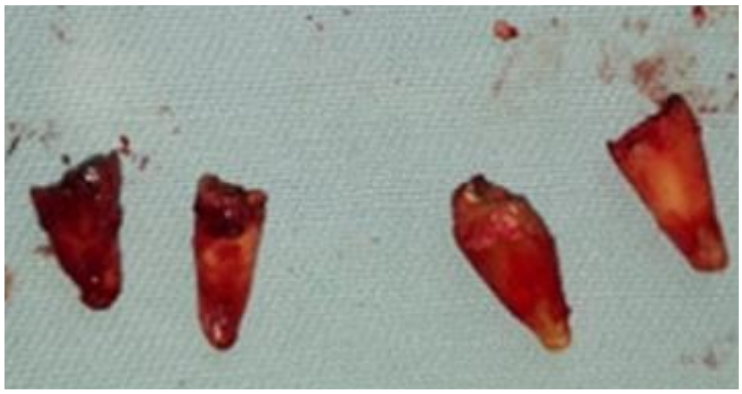

Figure 2. Ankylosed teeth

Regularization of bony margins was performed where necessary to avoid bleeding from mucosal and periosteum injury by sharp bony projections. It was followed by gentle but thorough curettage of the post-extraction alveolus, with careful removal of the remaining infected tissue (to avoid local post-extraction bleeding) and application of the intra-alveolar haemostatic sponge (Figure 3). In all cases, post-extraction wound suture was performed with non-resorbable 4/0 silk thread, triangular needle, made tightly, with the edges flared, followed by the application of a supra-alveolar compressive tamponade for 15-20 minutes post-extraction. Where adhesion of the wound edges was not possible, an "X" suture was performed and a supra-alveolar surgical dressing was applied (Figure 4). It was suppressed 24 hours postoperatively.

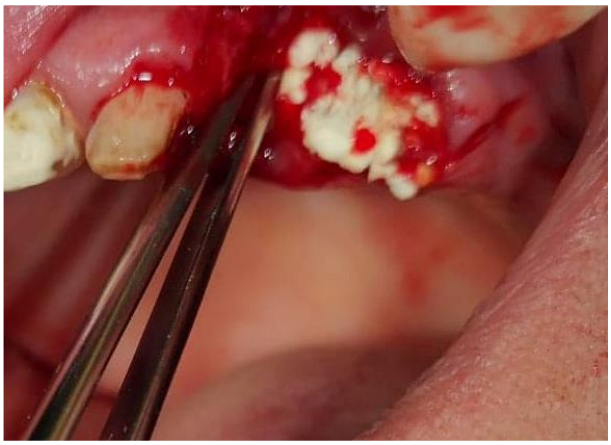

Figure 3. Application of haemostatic sponge

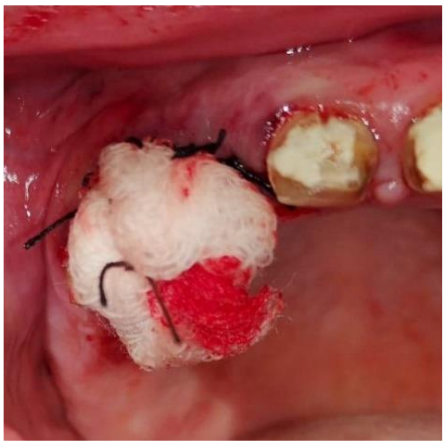

Figure 4. Supra-alveolar dressing

The patients were instructed to follow the post-operative indications to exclude haemorrhagic complications of local origin: maintain supra-alveolar compressive tamponade for 30 minutes; the post-extraction wound will not be explored; vigorous rinsing of the oral cavity is contraindicated to prevent blood clot mobilization; a liquid or semi-liquid and cold diet is recommended for 24 hours; sucking or pushing with the tongue in the wound area is contraindicated; the consumption of hot or thick foods is contraindicated; oral hygiene can be resumed after 24 hours, avoiding touching the wound.

Clexane dose is administered at least 6 hours post-extraction. Any episode of post-extraction haemorrhage is observed and noted on the observation sheet.

The decision to resume anticoagulant treatment is made only after the absence of bleeding from the post-extraction wound. Oral treatment with Sintrom is resumed, overlapping with injectable treatment with Clexane for 3 days. If on the 3rd day the INR is within the target values recommended by the cardiologist, the patient is discharged.

Suture removal was done 7 days after the extraction intervention.

During the intervention, we followed its duration and complexity, the occurrence of haemorrhagic accidents or complications, the cause and duration of the haemorrhage along with the therapeutic behaviour applied in those cases. Intra-alveolar clot formation was assessed at 30 minutes postoperatively, followed by reassessment at 24 and 48 hours.

In cases where post-extraction bleeding was found, the therapeutic approach included (Table 1): haemostasis achieved by renewing the supra-alveolar compressive dressing, held in occlusion for 30 minutes by the patient, in the event of low or medium intensity bleeding; haemostasis achieved by the application of a compressive dressing soaked in haemostatic substances, in the event of the occurrence of a haemorrhage of medium intensity or in the event that haemostasis cannot be obtained by means of a compressive dressing; if the bleeding continued even after maintaining the compression dressing, a new cardiological consultation was performed, with the adjustment of the anticoagulant dose, followed by the surgical revision of the post-extraction wounds. The wound was explored to identify and eliminate the source of bleeding through local haemostasis measures: identification of the source of bleeding (at the level of the soft parts or at the level of the bone), anaesthesia, curettage of the alveolus, washing the wound, ligation/electrocautery of the blood vessel (if applicable), applying haemostatic materials, suturing the wound and applying the supra-alveolar compressive dressing.

Measures of general haemostasis included treatment modification as follows: lowering the dose of Clexane by 2 units; skipping a dose.

Table 1. Measures of local haemostasis

Post-extraction bleeding	Haemostatic technique
Haemorrhage of low or medium intensity	hemostasis achieved by renewing the supra-alveolar compressive dressing, kept in occlusion by the patient for 30 minutes
Moderate bleeding or failure of hemostasis by compression dressing	hemostasis achieved by applying a compressive dressing soaked in hemostatic substances
Severe bleeding	carrying out a new cardiological consultation, with the adjustment of the anticoagulant dose, followed by the surgical revision of post-extraction wounds

RESULTS

The study included 78 patients who presented themselves in the Oral-Maxillo-Facial Surgery Clinic. Of them, 42 were men (54%) and 36 were women (46%). 11 (14.11%) were up to 60 years old, 59 patients (75.64%) were between 60 and 80 years old, and 8 patients (10.25%) were over 80 years old. Patients are evenly distributed according to gender. Regarding the age group, the share of people between 60 and 80 years old is the majority.

Table 2 shows the distribution of patients by age group, depending on gender. The share of male patients is the majority in almost all age groups.

Table 2. Distribution of patients according to gender and age group

Age group	Female patients	Male patients	Total
< 60 years	3	8	11
60-80 years	29	30	59
> 80 years	4	4	8

Regarding the chronic oral anticoagulant treatment followed by the patient on an outpatient basis, in 50 cases (64.1%) it was represented by SINTROM, and in 28 cases (35.89%) by TROMBOSTOP.

Regarding the associated pathology, for which chronic anticoagulant treatment is administered, a number of 42 patients (53.84%) were diagnosed with atrial fibrillation, 8 cases (10.25%) had a history of myocardial infarction and 28 cases (35.89%) have cardiac valvular pathology.

Regarding the associated comorbidities, a number of 39 patients (50%) presented hypertension in their medical history, 11 patients (14.11%) presented strokes in the antecedents, and 28 cases (35.89%) presented type 2 diabetes.

The patients presented chronic osteitis predominantly at the level of the maxillary arch, as follows: 45 patients (57.69%) were diagnosed with chronic odontogenic osteitis in the maxilla and 33 (42.3%) with chronic odontogenic osteitis in the mandible.

From the group of patients, 33 patients (42.3%) required a single extraction, 28 patients (35.89%) between two and four extractions, and 17 patients (21.79%) more than 4 extractions.

Of all the extractions performed, 48 extractions (61.53%) were simple extractions, and 30 extractions (38.46%) required the application of surgical extraction techniques.

Regarding the postoperative evolution of the cases, post-extraction haemorrhage was found in 22 cases (28.2%).

We analysed the dental and therapeutic peculiarities that influenced the occurrence of haemorrhagic accidents. The frequency of bleeding has been increased in the following cases: dental extractions that required the creation of a flap; extractions that required alveolotomy; extraction of large teeth with curved or divergent roots; extraction of ankylosed teeth; extraction of periodontal teeth; the anaesthetic technique did not influence the occurrence of bleeding.

Depending on the moment of the haemorrhage, there were three situations: prolonged haemorrhage: 4 cases; early secondary haemorrhage: 7 cases; late secondary haemorrhage: 11 cases.

The treatment applied in these cases was as follows: in 16 cases out of the 22 haemostasis was achieved with the help of the compressive dressing kept in occlusion by the patient for 30 minutes; in 6 cases, a consistent haemorrhage was found with the formation of massive alveolar clots, which plunged into the oral cavity. These cases required a new cardiological consultation with the adjustment of the dose of anticoagulant treatment and the revision of the post-extraction wounds by alveolar curettage, the introduction of haemostatic material (Gelaspon or Tachosyl sponge) and wound suture. The emergency treatment involved: applying a compressive dressing soaked in Etamsilate 250 mg and rinsing the mouth with tranexamic acid (500 mg tablets dissolved in water).

Resumption of oral anticoagulant treatment was possible in 40 cases (51.28%) after 24 hours postoperatively, in 25 cases (32.05%) anticoagulant treatment was resumed after 48 hours postoperatively, and in 13 cases (16.6 %) resumed more than 48 hours post-operatively.

DISCUSSIONS

The main pathologies involved in the prescription of antithrombotic drugs are atrial fibrillation, followed by deep vein thrombosis, coronary stenting, percutaneous coronary intervention, atherosclerotic cardiovascular disease and prevention of multiple cardiovascular events [6]. This aspect can also be observed in the present study, with 42 patients (53.84%) being diagnosed with atrial fibrillation, and 28 cases (35.89%) showing valvular cardiac pathology.

The management of these patients represents a challenge for dentists as they should carefully balance the risk of bleeding with the risk of thromboembolic complications resulting from the temporary interruption of antithrombotic therapy. Dental procedures are generally associated with a low risk of bleeding. Studies have demonstrated that in the case of dental procedures, the risk of thrombotic events due to altering or discontinuing antithrombotic therapy far outweighs the low risk of potential perioperative bleeding complications among patients treated with single or dual antiplatelet therapy or vitamin K antagonists [7-12].

The management of patients on anticoagulant therapy has changed considerably over time, and there are still differences in approach between dentists, oral and maxillofacial surgeons. Several protocols have been proposed, such as: temporary discontinuation of medication or reduction of administered doses to achieve a subtherapeutic INR, replacement of oral anticoagulants with heparin or low molecular weight heparin, or no change in therapy. None of these approaches is without risks for the patient, and the attending physician must make a clinical assessment of the ratio of risks and benefits, between operative management strategies and the complications that may arise [13]. The balance between drug dose reduction on the one hand and excessive bleeding during surgery on the other are the major issues, especially in outpatient procedures [14].

The patients included in the study follow chronic oral anticoagulant treatment with acenocoumarol (in 50 cases it was represented by Sintrom, and in 28 cases by Thrombostop), benefiting from the advantage of a broad spectrum of action, being a good alternative for long-term anticoagulation due to the rapid onset, long duration of action and stable anticoagulant effect. Acenocoumarol is effective and safe for all age groups and offers an advantage over warfarin in terms of better stability of the anticoagulant effect. After oral administration, a maximal prothrombin time-increasing effect is observed between 24-30 hours [15,16].

INR values should be obtained 24 hours before the extraction procedure. Depending on the reason for anticoagulant therapy, the therapeutic INR target is different [17]. For invasive oral surgical procedures, patients with an INR at the upper limit or greater than 3.5 should be referred for a new consultation with the attending physician for dose adjustment or therapy modification before these [18].

Regarding the pre-operative management of patients, the therapeutic approach was to discontinue medication and administer a short-acting anticoagulant for a few days before surgery, known as "bridging therapy", performed mostly with low molecular weight heparin [19]. In our study the modification of the pre-operative treatment scheme was carried out according to the indication of the cardiologist, by stopping the oral chronic anticoagulant treatment and replacing it with Clexane 0.6 or 0.8 ml (depending on the patient's weight) until the INR value dropped below 1,2. If this value was reached, the extraction intervention was carried out at least 6 hours after the administration of the last dose of Clexane.

Bleeding that may occur in patients on antiplatelet or anticoagulant therapy during dental extractions can be controlled by using local hemostatic measures [20-24] which is why it is recommended not to stop antithrombotic treatment in these patients [21,22,24-27].

In patients under anticoagulant treatment with an INR > 3.5, or who require a major oral surgery, the option of interrupting drug treatment for a period between 0-48h before the intervention can be considered, always consulting the cardiologist [28,29]. International societies and organizations such as the American Dental Association (ADA), American College of Cardiology (ACC), the European Council of Dentists (CED), the Spanish Society of Oral and Maxillofacial Surgery (SECOM), support these recommendations and criteria for the management of these patients [30].

Kwak et al. recommend at least one day interruption of the anticoagulant in cases of multiple dental extractions, implant surgery or deep root scaling, considering the half-life of

the drug and renal clearance, although no significant relationship was reported between the duration of anticoagulant discontinuation and the bleeding tendency [24]. This is not in agreement with other authors, because although there is a low thromboembolic risk when antiplatelet and anticoagulant drugs are discontinued, discontinuation leads to significantly higher morbidity and mortality compared to bleeding events [20,23,25].

CONCLUSIONS

Peri- and postoperative bleeding during dental extractions in patients on antiplatelet or anticoagulant therapy can be easily managed using local hemostatic measures. If any antiplatelet or anticoagulant treatment needs to be changed, this should always be done under the supervision of the responsible hematologist or specialist. In the case of patients with thrombogenic risk, in order to perform dental extractions under appropriate conditions, discontinuation of anticoagulant medication requires hospitalization conditions.

For patients undergoing dental procedures at high risk of bleeding, it is recommended to schedule dental treatment for the morning to allow for monitoring and management of potential bleeding complications, limit the surgical site by performing a single extraction or limit subgingival periodontal scaling to three teeth, and assess bleeding prior to continue and use hemostatic measures to achieve hemostasis as soon as possible.

Based on the type of dental procedure and medical risk assessment, several general treatment approaches can be considered: continuing anticoagulant treatment, scheduling dental treatment as late as possible after the last dose of anticoagulant, stopping treatment for 24 hours or 48 hours. Based on the current reported dental literature, limited dental surgery may benefit from the first two conservative options. However, this needs to be proven in comparative clinical trials.

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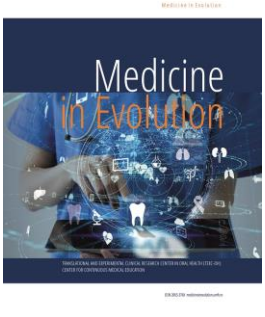
Study on risk factors implicated in post-extraction alveolitis



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Abstract

Post-extraction alveolitis is a complication specific to tooth extraction that can occur during the healing process (usually 24–72 hours after extraction). This complication can occur due to the dislodgement of the blood clot (the first stage of the healing process), following a local infection, poor local hygiene, or factors related to the plasma system. It is estimated that the probability of developing dental alveolitis after an extraction is 3%. In the case of wisdom teeth, the percentage of probability increases to 20% and even 30%.

This paper aims to evaluate one of the complications that can occur after tooth extraction, namely post-extraction alveolitis, as well as on the particularities that can contribute to the development of this complication that leads to the alteration of the patient's general condition and delayed healing.

The retrospective study was carried out on a number of 28 patients hospitalized in Timisoara Oral and Maxillo-Facial Surgery Clinic, who presented post-extraction alveolitis. A series of risk factors are implicated in the evolution of post-extraction alveolitis: surgical trauma, bacterial infections, patient age and sex, oral contraceptives, smoking.

Keywords: post-extraction alveolitis, risk factor, bacterial infection

INTRODUCTION

The links between post-extraction alveolitis and poor oral hygiene, periodontal disease and pericoronitis have led to an extended theory, incorporating a completely extrinsic etiological factor. Certain bacteria show fibrinolytic activity independent of the host response and act directly on the blood clot - Treponema denticola produces its own fibrinolytic enzyme (fibrinolysin) and Prevotella oralis releases proteases that convert plasminogen into plasmin and thus further increase fibrinolysis [1].

The etiopathogenesis of post-extraction alveolitis is not well understood, but it is known that it usually begins around 2-4 days after extraction and is unlikely to occur before the first 24 hours due to the presence of antiplasmin (plasmin inhibitor) which delays fibrinolysis. Only after antiplasmin levels have been reduced does clot lysis occur. Its duration varies between 5 and 10 days [1].

Surgical trauma and the difficulty of the surgical intervention play a significant role in the development of post-extraction alveolitis, this could be due to a greater release of direct tissue activators secondary to bone marrow inflammation following more difficult, therefore more traumatic extractions [2]. Surgical extractions, compared to non-surgical extractions, lead to a 10-fold increase in the incidence of post-extraction alveolitis [2]. In addition, a positive correlation was observed between operator inexperience and increased incidence of post-extraction alveolitis, which could be due to many factors, including prolonged operating time and increased trauma. [1].

Marked or prolonged trauma during an extraction or infection causes increased localized inflammation in the bone that triggers the release of plasminogen activators [1, 2]. They facilitate the conversion of plasminogen to plasmin, which breaks down fibrin and leads to lysis of the blood clot (Figures 1,2) [1, 2]. Plasmin also plays an active role in the production of kinins [1]. Kinins not only propagate the inflammation process by stimulating the release of inflammatory mediators, but have a major role in sensitizing and stimulating pain receptors [1]. All these factors are related to the main characteristics of post-extraction alveolitis, which are clot rupture and severe pain [1].

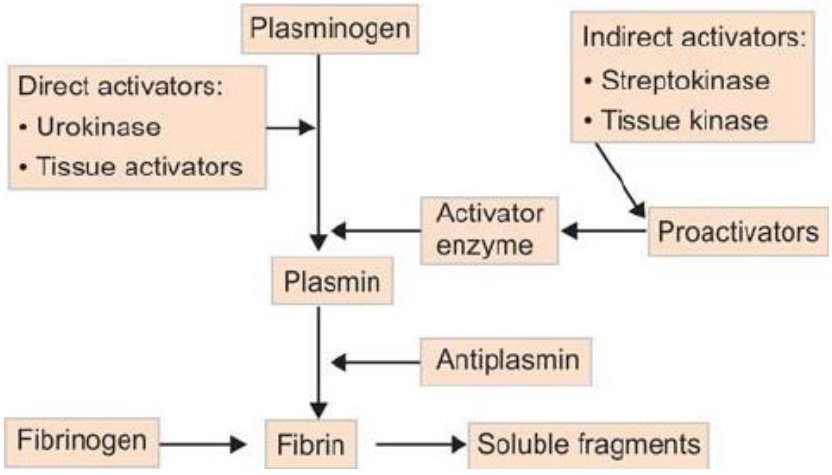

Figure 1. Pathogenesis of post-extraction alveolitis

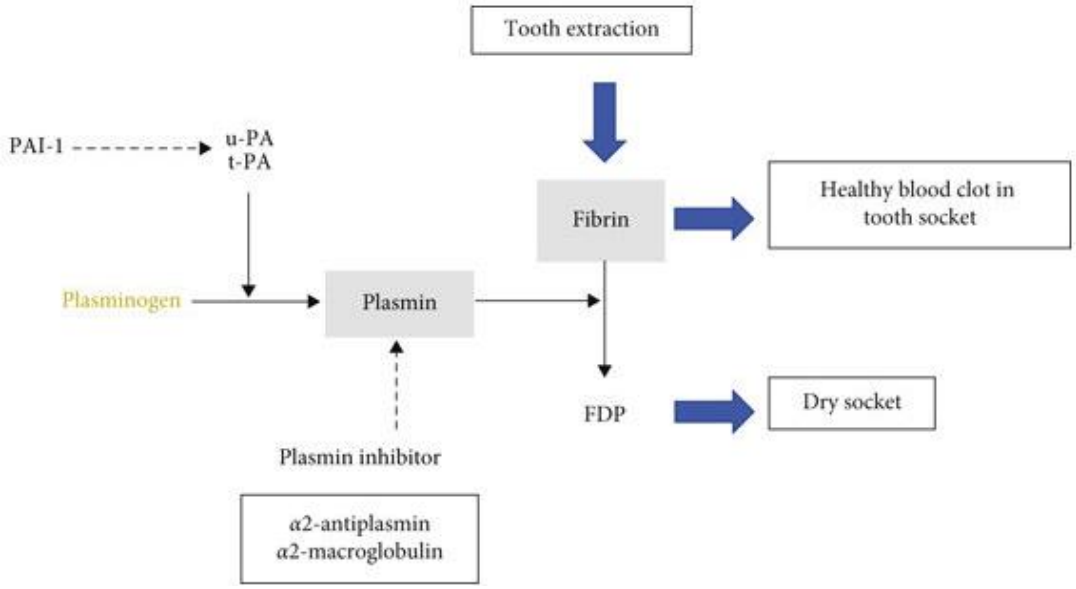

Figure 2. Molecular mechanism of post-extraction osteitis: Plasminogen type-1 is the precursor of plasmin which acts in fibrin degradation. Plasmin inhibitor sterically shields the active site of plasmin, decreasing the access of plasmin to protein substrates. t-PA: tissue-type plasminogen activator; FDP: fibrin degradation products [3]

In the French-speaking literature, a form of wet alveolitis is described that is not found in the international specialized literature [4]. This is characterized by an accumulation of excess granulation tissue at the level of the post-extraction alveolus, moderate pain felt by the patient, the presence of an exuberant, superinfected clot, which can occasionally look like a gingival polyp [4].

Post-extraction alveolitis occurs 2-3 days after extraction. During this period, the blood clot disintegrates, resulting in delayed healing and necrosis of the bony surface of the socket [5]. This disorder is also called fibrinolytic/dry alveolitis and is characterized by an empty cavity, halitosis, bad taste in the mouth, bare bony walls and severe pain radiating to other areas of the head [5].

Aim and objectives

This paper aims to evaluate one of the complications that can occur after tooth extraction, namely post-extraction alveolitis. Another objective is to draw the attention of the dentist and the dentoalveolar surgeon to some aspects and particularities that can contribute to the development of this complication that leads to the alteration of the patient's general condition and delayed healing.

MATERIALS AND METHODS

The first stage of the retrospective study represents the establishment of the clinical characteristics necessary for the selection of patients who presented with post-extraction alveolitis in Timisoara Oral and Maxillo-Facial Surgery Clinic and were included in the study.

Statistics were also made regarding: the total number of patients, the ratio according to sex, the ratio according to age, the distribution of ages according to sex, the ratio of the incidence of dry and wet alveolitis, the number of dental units extracted, the percentage of development of alveolitis at the mandibular and maxillary level, the incidence of associated complications and how many patients presented comorbidities.

The patients were informed about the inclusion in a medical studio and expressed their consent in writing, according to Order of the Ministry of Health 1411 of 12.12.2016,

annex no. 1 to the methodological norms - Form for expression of the consent of the informed patient.

Patient selection and inclusion criteria:

1. Adult patients (over 18 years);
2. Both sexes;
3. The presence of post-extraction alveolitis following the extraction of one or more dental units;
4. Admission to the Oro-Maxillo-Facial Surgery Clinic Timişoara for the possibility of monitoring the patient.

Exclusion criteria:

1. Minor patients (under 18 years);
2. Patients who do not present post-extraction alveolitis;
3. Patients who refused hospitalization;
4. Lack of patient compliance and cooperation;
5. Indiscriminate patients;
6. Patients with acute diseases of the oral mucosa (stomatitis);
7. Patients with acute infectious processes;
8. Patients with malignant tumors cervicofacial located or in the oral cavity;
9. Patients under radio and/or chemotherapy treatment.

The patients were hospitalized in the Timişoara Oral and Maxillo-Facial Surgery Clinic, where they were given anamnesis and clinical evaluation, all data collected to be recorded in the patient file.

Imaging investigations: panoramic radiography or CBCT were requested for imaging evaluation of the case. The role of these paraclinical explorations is to diagnose the presence of alveolar or dental bone fragments at the level of the post-extraction socket, they act as an irritating thorn that prevents or delays the healing of the socket.

During the anamnesis, the patients reported severe, constant pain, with progressively increasing intensity, reaching maximum intensity 2-3 days after the extraction, this being the main reason for presenting to the doctor.

The clinical evaluation highlighted changes in the peri-alveolar oral mucosa, alterations in the healing process located at the level of the post-extraction alveolus, sensitivity to palpation, radiating pain in the neighboring teeth, in the neighboring anatomical areas, pain to touch, irrigation, but no septic process consisting of level of the alveolus or in the surrounding tissues.

RESULTS

The study included 28 patients, 6 men and 22 women, who presented themselves in the Oro-Maxillo-Facial Surgery Clinic Timişoara (Figure 3).

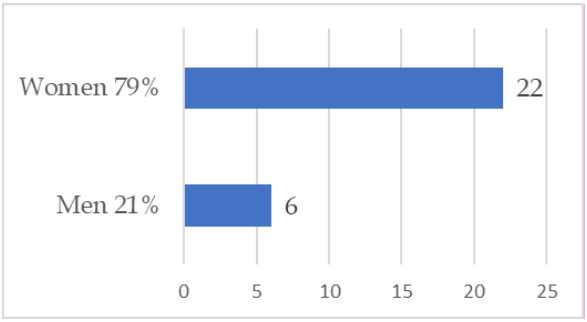

Figure 3. Gender distribution of patients included in the study

Of the 28 patients, 13 (46.43%) were up to 30 years old, 8 patients (28.57%) were between 30 and 49 years old and 7 patients (25%) were over 50 years old (Figure 4).

In the age group <30 years, the number of female patients (9) is higher compared to the number of male patients (4). In the 30-49 age group, patients are only female (8). In the case of the age group ≥50 years, the number of female patients (5) is higher than the number of male patients (2). Therefore, the share of female patients is the majority in all age groups (Figure 5).

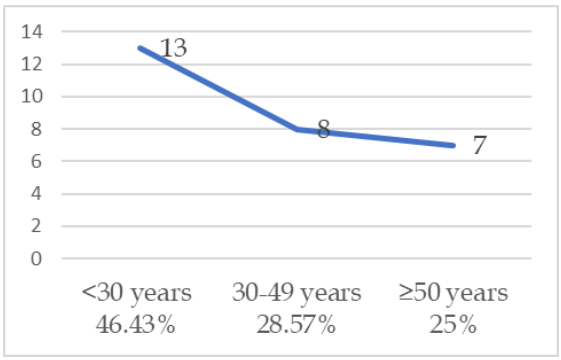

Figure 4. Distribution by age groups of patients included in the study

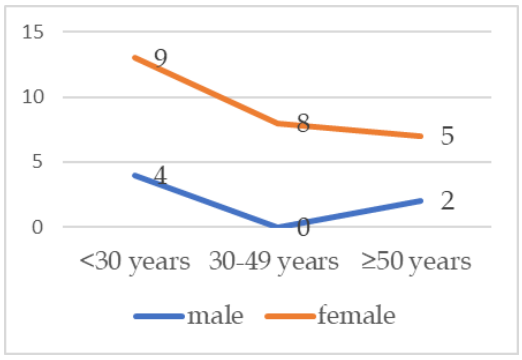

Figure 5. Distribution by age groups and sexes of patients included in the study

Of the 28 patients included in the sample, 6 patients (21.43%) presented wet post-extraction alveolitis, while 22 patients (78.57%) presented dry alveolitis.

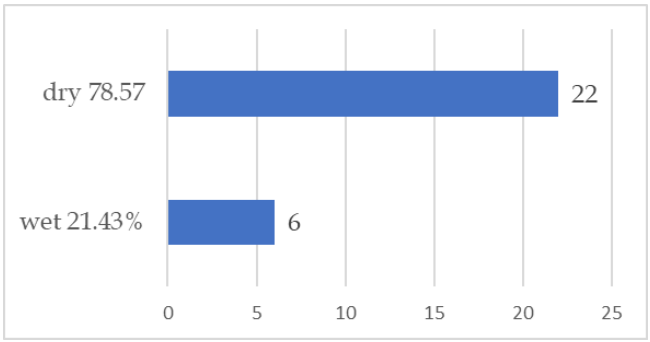

Figure 6. Distribution by type of post-extraction alveolitis

Depending on the number of dental units extracted, 24 patients (85.71%) developed post-extraction alveolitis after a single extraction, 3 patients (10.72%) after two extractions, and one patient (3.57%) among the 28 patients following the extraction of four dental units. In total, a number of 34 tooth extractions were performed (Figure 7).

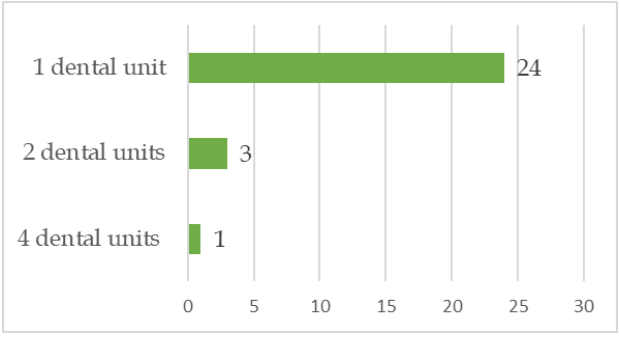

Figure 7. Distribution of patients according to the number of dental units extracted

From the point of view of the position of the extracted tooth, the lower molars represent the highest number of extractions.

From the 34 extractions performed on the 28 patients (Table 1), 22 of the extractions involved molars (64.71%), followed by 9 extractions of premolars (26.47%) and another 3 extractions of anterior teeth (8.82%). In total, 31 extractions of posterior teeth (91.18%). The extractions involving the mandibular third molar were 8 (36.36%) of the 22 molar extractions. Compared to the total of 34 extractions, the extractions of the mandibular third molar represent 23.53%.

Table 1. The distribution of extractions according to the position of the tooth

Position of the tooth		No. of extractions
Posterior	Premolar	9
	Molar	22
	Total	31
Anterior		3
Total		34

The patients presented post-extraction alveolitis predominantly at the mandibular level and are divided as follows: 21 patients (75%) presented mandibular alveolitis, 6 patients (21.43%) presented alveolitis at the level of the maxillary arch and only one case (3.57%) that presented alveolitis at both maxillary and mandibular level (Figure 8).

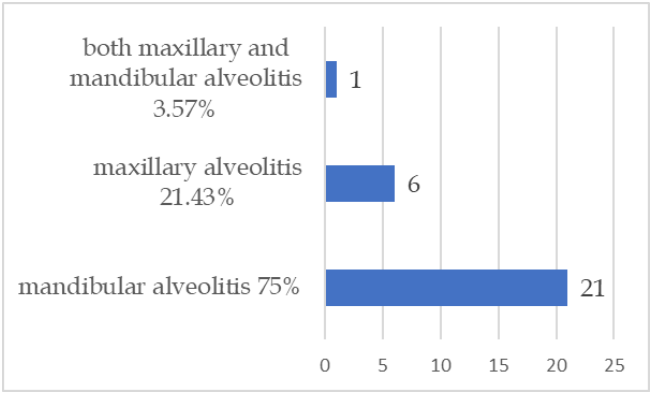

Figure 8. Location of post-extraction alveolitis

From all the extractions performed, 18 patients benefited from simple extractions (64.29%), and 10 patients (35.71%) required the application of surgical extraction techniques, as can be seen in Figure 9.

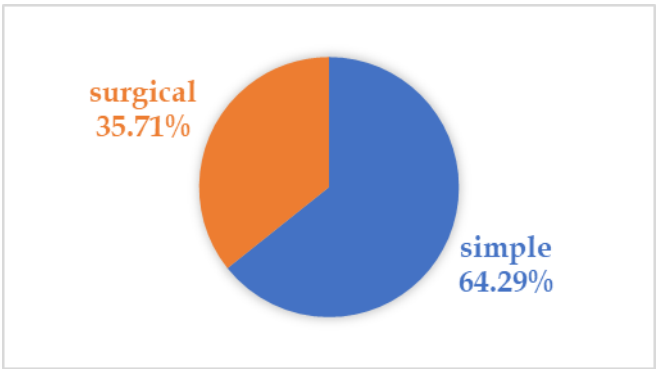

Figure 9. Distribution of patients according to the type of extraction

Also, from the total number of extractions, 7 patients (25%) required the administration of anesthetic in additional doses. In the case of these patients, the average anesthetic administered is 3 carpules.

Of the 28 patients, only one presented the dislocation of the adjacent tooth. Dental trauma and prolonged surgical time are factors that can lead to the development of post-extraction alveolitis.

Regarding the associated complications, a number of 8 patients (28.57%) presented acute cellulitis and 4 patients (14.29%) presented abscess. In total, 12 patients (42.86%) presented associated complications (Figure 10).

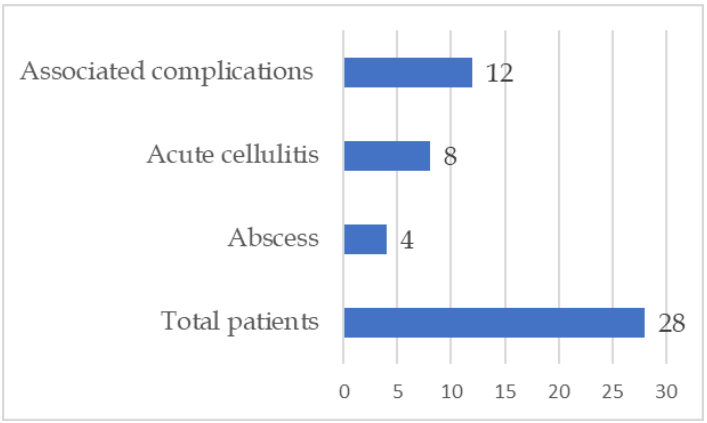

Figure 10. Complications associated with extractions

Regarding the comorbidities presented by the patients (Table2), they are classified according to nature into: cardiovascular-6 patients (21.43%), endocrine and metabolic-3 patients (10.71%), osteo-articular-2 patients (7.14%) and multiple–1 patient (3.57%).

Endocrine-metabolic diseases are represented by type II diabetes (one patient) and thyroid diseases (2 patients), and osteo-articular diseases by chronic osteitis and osteoporosis. The patient with multiple comorbidities presented hypothyroidism and grade II hypertension. In the case of cardiovascular diseases, the most frequent pathologies were myocardial ischemia and arterial hypertension. Also, 3 of these patients also presented anxiety disorders.

Table 2. **Distribution of patients according to comorbidities**

Comorbidity			No. of patients
Cardiovascular			6
Endocrine and metabolic	Type II diabetes	1	3
	Thyroid diseases	2	
Osteoarticular	Chronic osteitis		2
	Osteoporosis		
Multiple	Hypothyroidism and HTN		1

Smoking is one of the risk factors in the development of post-extraction alveolitis, although the mechanism by which it intervenes in the healing of the alveolus is still unclear. Of the 28 patients included in the studied group, 5 patients (17.86%) are smokers (Figure 11).

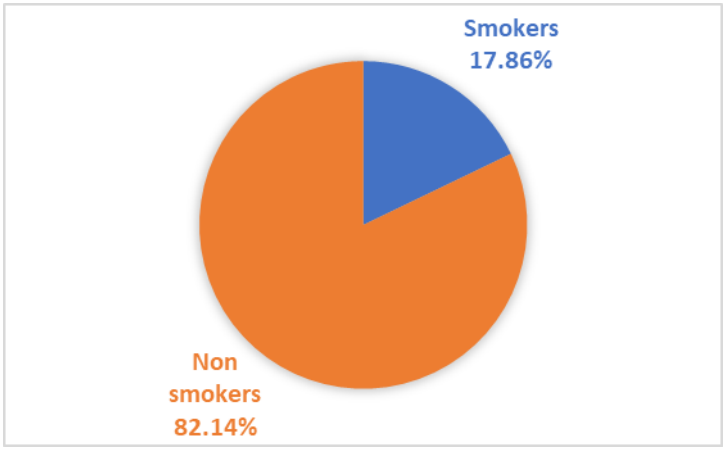

Figure 11. Distribution of patients according to tobacco consumption

From the point of view of the medication administered at the time of extraction, 2 patients (7.14%) were on anticoagulant/antiplatelet treatment, one patient (3.57%) under treatment with bisphosphonates and 4 patients (14.29%) under treatment oral contraceptive (Table 3).

Also, 2 of the studied patients (7.14%) are both smokers and follow chronic oral contraceptive treatment.

Table 3. **Treatment followed at the time of extraction**

Treatment	No. of patients
anticoagulant	1
antiplatelet agent	1
bisphosphonates	1
oral contraceptive	4

DISCUSSIONS

In the study, the percentage of female patients is higher (79%) than male patients (21%). This observation is explained by the literature by highlighting the hormonal differences between the two sexes, more precisely by the presence of estrogen. Even before the introduction of the oral contraceptive pill, the risk of female patients developing post-extraction alveolitis was higher according to studies, but it increased significantly for those using this method of pregnancy prevention. Estrogen is known to increase the production of coagulation factors II, VII, VIII and X, and in particular plasminogen, the precursor of plasmin – the main endogenous factor that leads to blood clot breakdown [1]. This shows how taking oral contraceptive pills can promote early clot breakdown by increasing local plasmin levels. In the female group of patients under study, 4 of them (14.29%) were taking contraceptive pills at the time of extraction. Some studies have also noted a relationship between alveolar osteitis and the stage of the menstrual cycle at which the extraction was performed and reported that the incidence is highest around cycle days 1 to 22 [1].

Although the literature supports the general axiom that the older the patient, the greater the risk of post-extraction alveolitis, this direction was not observed in the studied sample, the highest incidence being in the 18-29 age range (46, 43%), to decrease in percentage with increasing age. These results can be explained by the integrity of the alveolar bone and the low presence of periodontal diseases in the young population, which make the extraction more difficult [6].

It should be highlighted that in each sample made according to age, the percentage of female patients was higher, highlighting once again that the gender of the patient is a risk factor in the development of alveolar osteitis.

It is well documented in the literature that prolonged or particularly traumatic extractions have a higher incidence of post-extraction alveolitis [6]. By analogy, surgical extractions compared to non-surgical extractions have an increased risk of developing fibrinolytic alveolitis. Although in the present study only 35.71% presented alveolar osteitis following surgical extraction, the increased trauma can also be represented by other external factors such as the level of experience of the attending physician, intraoperative accidents, mandibular location and the need for a single extraction.

Bacterial presence has a negative role in the healing of the alveolus both by generating complications of an infectious nature associated with the extraction, and by the fibrinolytic activity exerted on the blood clot by certain bacterial enzymes [7]. Plasmin-like fibrinolytic activity was also observed in colonies of Treponema denticola, a microorganism present in periodontal infection [1]. *In vivo*, the fibrinolytic effect of bacterial pyrogens was highlighted [8]. Of all observed patients, 42.86% presented complications due to bacteria, respectively 14.29% presented abscess - purulent collection caused by the penetration of bacteria into sterile soft tissues under normal conditions, and 28.57% presented acute cellulitis - inflammatory condition what precedes the septic process. The increased presence of bacteria in the oral cavity is promoted by the lack of oral hygiene, another factor incriminating the formation of alveolar osteitis, to which can be added the non-observance of post-extraction food instructions, a series of fermented foods containing bacteria of the genus Bacillus that secrete fibrinolytic enzymes [7].

Related to tooth position, as expected, a significant incidence was observed in posterior tooth extractions (91.18%). Of the posterior teeth extracted, molars occupy the largest part (22 out of 31 extractions). Alveolar osteitis has been shown to be more common following mandibular third molar extraction [9,10]. Some authors believe that increased bone density, decreased vascularity, and reduced ability to produce granulation tissue are responsible for site specificity, although there is no evidence to suggest a link between fibrinolytic alveolitis and insufficient blood supply [1]. The specificity of the area is probably due to the high percentage of surgically extracted mandibular molars and may highlight the effect of trauma due to inaccessibility. Of the total extractions that developed post-extraction alveolitis, 23.53% are represented by the extraction of the mandibular third molar.

In most studies, the mandible is the most frequent site of alveolar osteitis, attributed to difficult and traumatic extractions [6]. From the analysis carried out per batch, the same trend of appearance of fibrinolytic alveolitis at the mandibular level emerged (75%).

Although multiple studies have shown that there is a link between smoking and post-extraction alveolitis, this aspect does not emerge from the data obtained, the percentage of smoking patients being only 17,86%. As the mechanism underlying the process is not fully elucidated, different hypotheses have been suggested that incriminate the high temperature of the inhaled smoke, the toxins it contains and the absorption action of the smoke that creates a negative intraoral pressure with the consequence of breaking the clot. This latter phenomenon is also found when drinking liquids with a straw [1].

The evidence indicating a higher prevalence of post-extraction alveolitis after single extractions compared to multiple extractions is limited, but this conclusion also emerged from the analyzed data, with 85.71% of patients requiring extraction treatment for a single dental unit. This difference could be due to the increased trauma in patients with single extractions compared to patients with multiple extractions whose teeth are damaged at a more advanced level, making the procedure less traumatic [9].

Many studies have shown a significant association between diabetes and alveolar osteitis, this pathology being characterized by lower immunity and delayed wound healing. Fibrinolytic alveolitis occurs due to disruption of blood flow, and in patients with diabetes the incidence is higher due to microangiopathy [11]. Among the observed patients, only one presented type II diabetes as a comorbidity. An increase in blood sugar level above the normal value of ≥126mg/dL could be considered a risk factor for post-extraction alveolitis both in patients with a history of diabetes and in those without this comorbidity [12].

Primary hypothyroidism is a condition characterized by the inability of the thyroid gland to produce enough thyroid hormones. Thyroid hormones play an important role in regulating the growth, development and metabolic functions of the body. Susceptibility to infection, delayed wound healing, and the complication of fibrinolytic alveolitis are common features of hypothyroidism, which may be due to decreased metabolic activity of fibroblasts and longer exposure of the wound to pathogenic organisms. Patients with hypothyroidism are more prone to developing cardiovascular diseases [13]. From the cases analyzed, only one patient classified as having multiple comorbidities presented both hypothyroidism and hypertension.

Anticoagulant patients requiring dental extractions face intraoperative and postoperative bleeding problems that may be difficult to control. If sufficient hemostasis is not achieved after oral surgery, complications such as post-extraction alveolitis, delayed healing and pain may occur [14]. In this study, one patient was being treated with oral anticoagulants. The goal of anticoagulant therapy is to prevent the formation or expansion of clots. Coumarin anticoagulants are vitamin K antagonists required for the synthesis of coagulation factors II, VII, IX and X, as well as endogenous anticoagulant proteins C and S [15].

Antiplatelet drugs are used to prevent arterial and venous thrombosis. In this study, one patient was undergoing antiplatelet treatment. Intra- and postoperative bleeding in patients receiving oral antithrombotic raises many problems, and withholding drug therapy to prevent complications is controversial [16].

Several protocols are used to minimize bleeding complications and to keep the patient's drug dose unchanged, such as suturing the wound or applying various local hemostatic agents [14].

Drug-induced osteonecrosis of the jaws with oral bisphosphonates can result in severe and extensive bone exposure and may require prolonged surgery, therefore patients taking oral bisphosphonates should be treated differently from patients not on this treatment. They are commonly prescribed to prevent complications in malignant bone diseases and in benign bone diseases such as osteoporosis. Only one patient in the study was taking this medication at the time of extraction, who was also diagnosed with osteoporosis. The mechanism by which bisphosphonates influence bone metabolism is not fully understood. However, they are potent inhibitors of osteoclast-mediated bone resorption, inhibit cell function, and induce early apoptosis. Because bisphosphonates have a very high affinity for hydroxyapatite crystals, they have the ability to localize and accumulate on bone mineral surfaces, particularly at sites of high bone turnover. Mammalian jaws are thought to have the ability to regenerate at a rate picked up [17]. Invasive dental procedures should be avoided whenever possible in patients with a history of bisphosphonate use, especially intravenous bisphosphonates for cancer. Discontinuation of oral and intravenous bisphosphonates is recommended before invasive dental procedures and after the development of osteonecrosis of the jaw, provided the systemic condition permits. Limited surgical debridement along with systemic and local antibiotics is the management of osteonecrosis of the jaw, however, cure is not assured [18].

CONCLUSIONS

Following the study carried out over a period of one year, several aspects related to post-extraction alveolitis were concluded.

The highest probability of development is found in young patients, under 30 years old. Due to hormonal differences, women are more prone than men, especially if they take oral contraceptive pills.

Posterior teeth show a higher frequency of development, of which the most numerous cases were represented by molars. The location of the extractions at the level of the mandible can be considered a risk factor because it involves a high trauma. Single extractions present a higher risk of formation due to the integrity and non-alteration of the alveolar bone.

The presence of bacteria can be considered one of the causes of the development of post-extraction alveolitis, but also of complications of bacterial etiology.

Although complications following surgical extractions were less frequent than in simple ones, they present high or prolonged trauma as a common factor.

Patients suffering from type II diabetes and hypothyroidism require additional monitoring due to the slow healing of the lesion. Patients under anticoagulant, antiplatelet and contraceptive treatment have an increased risk of developing fibrinolytic alveolitis. Although the literature supports smoking as a risk factor, in the analyzed data only 17.86% of the patients were smokers, the mechanisms involved in clot dislocation being unexplained.

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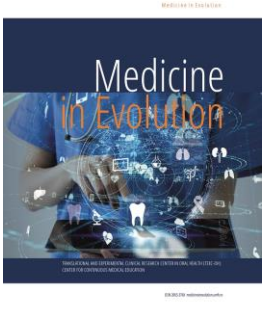
Peculiarities of tooth extraction in patients with diabetes



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Abstract

Tooth extraction is one of the most common procedures in oral and dental surgery, and in the case of diabetic patients this procedure must be managed with greater care.

Several soft and hard tissue disorders of the oral cavity have been reported to be associated with diabetes mellitus. These include periodontal diseases (periodontitis and gingivitis), salivary dysfunction leading to a reduction in salivary flow and changes in the composition of saliva and taste dysfunctions, neuro-sensory mucosal disorders, fungal and bacterial infections and also lesions of the oral mucosa in the form of stomatitis, geographic tongue, benign glossitis, fissured tongue, traumatic ulcer, lichen planus and angular cheilitis. Post-extraction complications such as delayed wound healing, increased risk of bleeding and wound infection have been reported in patients with diabetes.

The present work intends to identify the impact of diabetes on dental extraction, in terms of post-extraction wound healing and the development of complications.

Keywords: Dental extraction, diabetes, post-extraction complications

INTRODUCTION

Diabetes mellitus is a chronic disorder of carbohydrate metabolism characterized by the inability to regulate and control blood glucose levels due to insulin deficiency or resistance.

Oral manifestations and complications of diabetes include dry mouth (xerostomia), dental caries (including root caries), periapical lesions, gingivitis, periodontal disease, oral candidiasis, burning sensations (especially glossodynia), altered taste, geographic tongue, coated and fissure, oral lichen planus, recurrent aphthous stomatitis, increased tendency to infections and poor wound healing (Figure 1). The intensity of diabetes complications is usually proportional to the degree and duration of hyperglycemia [1].

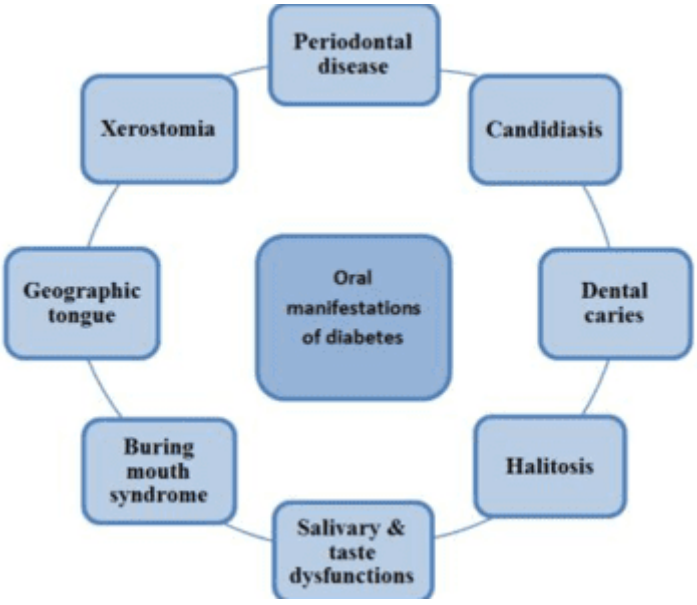

Figure 1. Oral manifestations among diabetic patients [2]

The need for tooth extraction is determined after a thorough clinical and radiological evaluation, taking into account the patient's local and general conditions.

In the specialized literature, there is evidence to support that diabetic patients present an increased risk of infection or delayed healing following surgical procedures [3,4].

Regarding the extraction procedure in diabetic patients, dentists need to better understand the factors that affect glycemic control in order to improve the management of these patients in the dental office. In the specialized literature, there is a lack of information regarding the determination of the maximum permissible blood glucose level recommended for emergency tooth extraction in patients with diabetes.

Based on the diabetes guidelines established by the American College of Endocrinology (ACE), the safety scale of favorable glycemic ranges for patients with diabetes was structured (Table 1) [5].

Table 1. Safety scale of blood glucose levels for patients with diabetes [6]

Blood glucose level	Excellent	Good	Acceptable
Fasting blood glucose	72–109 mg/dl	110–144 mg/dl	145–180 mg/dl
2 hours after meal	90-126 mg/dl	127-180 mg/dl	181-234 mg/dl

On the other hand, there is also a classification for risk assessment in terms of fasting blood glucose levels in diabetic patients (Table 2).

Table 2. Risk assessment based on glycemic levels [6]

Blood glucose level	Assessment of the level of risk
≤ 50 mg/dl	Dangerously low
70-90 mg/dl	Low
90-120 mg/dl	Normal
120/160 mg/dl	Medium
160-240 mg/dl	Grown
240-300 mg/dl	Very high, signals an escaped diabetes under control that requires specialist consultation
≥ 300 mg/dl	Severe, requires emergency medical attention

The fasting blood glucose level of 240 mg/dl is a critical point for any dental treatment. When the blood glucose level reaches 240 mg/dl, the warning signs of diabetes appear: tingling of the hands or feet, dizziness, nausea, vomiting, diarrhea [7]. An emergency tooth extraction at a glucose level of 240 mg/dl will lead to severe infection and delay healing.

To perform a tooth extraction, blood glucose levels may be considered acceptable as long as the dental treatment can be performed with minimal risk, and there are no signs of uncontrolled diabetes. A fasting blood glucose level of 180 mg/dl is considered a cut-off point for scheduled tooth extraction. A blood glucose level (2 hours after a meal) of 234 mg/dl is a cutoff point for an emergency tooth extraction [8,9].

Poor glycemic control predisposes to a number of vascular complications and more. Microcirculatory impairments in particular have a significant influence on postsurgical wound healing. In diabetic patients, changes in capillaries, such as thickening of their walls, lead to altered permeability, preventing leukocyte migration to the site of extraction and amplifying the hyperemic reaction [10,11]. These changes lead to delayed healing and increase the risk of post-extraction wound infection, which can manifest as post-extraction haemorrhage, post-extraction abscess, alveolitis and osteitis [12,13].

Aim and objectives

The aim of this paper is to analyze the frequency and intensity of complications that occur in diabetic patients and in patients with both diabetes and other comorbidities following the surgical procedure of tooth extraction.

Another aim was to draw the attention of dentists and dento-alveolar surgeons to the fact that patients with diabetes represent a risk category in dental treatment, requiring a special pre- and post-operative management, so that they can be reduced to minimum risk of possible complications.

MATERIAL AND METHODS

Patients diagnosed with diabetes who required extraction treatment and presented themselves at the Timişoara Oral and Maxillo-Facial Surgery Clinic were included in the study.

The patients were informed about the medical research and expressed their consent in writing, according to Order of the Ministry of Health 1411 of 12.12.2016, annex 1 to the methodological norms - Form for expressing consent of the informed patient.

Patient selection and inclusion criteria:

1. Adult patients (over 18 years);

2. Both sexes;
3. Patients diagnosed with diabetes who suffered post-extraction complications;
4. Patients who suffer from diabetes, but also have other associated conditions.
5. Patients who have had one or more dental extractions;
6. Patients from the Timişoara Oro-Maxillo-Facial Surgery Clinic database for the possibility of patient monitoring.

Exclusion criteria:

1. Minor patients (under 18);
2. Patients with acute infectious processes;
3. Patients with existing malignant tumors in the head and neck;
4. The existence of associated conditions that contraindicate tooth extraction;
5. Noncompliant patients to treatment.
6. Patients who have not been diagnosed with diabetes.

The data obtained from the anamnesis and those from the observation sheets were noted in the dental evaluation sheet specially designed for this purpose. The data were obtained through clinical examination, questionnaire-interview and paraclinical examination (laboratory analyzes and dental radiographs).

They have registered:

- demographic data: age, gender, occupation, background;
- medical history: general conditions, associated medication, type of diabetes, duration of disease evolution, blood sugar and HbA1c value;
- type of food.

A statistical analysis was also carried out regarding the total number of patients, the ratio according to age and gender, the percentage of development of certain post-extraction complications such as post-extraction hemorrhage, abscess, alveolitis or osteitis and the incidence of the development of these complications in association with other co-morbidities.

Continuous variables in the statistical analysis are presented as mean ± standard deviation. Continuous variables were compared using the Student T test. Categorical variables are expressed as numbers and/or percentages and are compared with the Person Chi-square test.

All statistical tests are 2-tailed and with a $P<0.05$ value considered statistically significant. All statistical analyzes including odds ratio (OR) were performed in IBM SPSS Statistics (Statistical Package for the Social Sciences) version 20.

A number of 102 patients diagnosed with diabetes mellitus (both type 1 and type 2) who underwent the dental intervention of dental extraction were included in the study, the statistical analysis including a variety of demographic parameters, anamnestic or associated with periprocedural complications.

RESULTS

Statistical analysis of demographic data

Age and gender are the main demographic parameters included in the statistical analysis of this study. The gender distribution of the studied group is represented in Figure 2. The average age of the statistically analyzed group was 66.89 ± 9.49 years, the range of values being included between a minimum of 32 years and a maximum of 85 years. The variation of the number of cases correlated with the ages of the patients is represented in Figure 3.

Statistical analysis of anamnestic data

The analysis of anamnestic data was aimed at detecting and dividing patients according to the type of diabetes, but also according to associated comorbidities.

Diabetes – 87.3% of the patients included in the study have type 2 diabetes (89 cases), the percentage of those with type 1 being significantly lower (13 cases, 12.7%) (Figure 4).

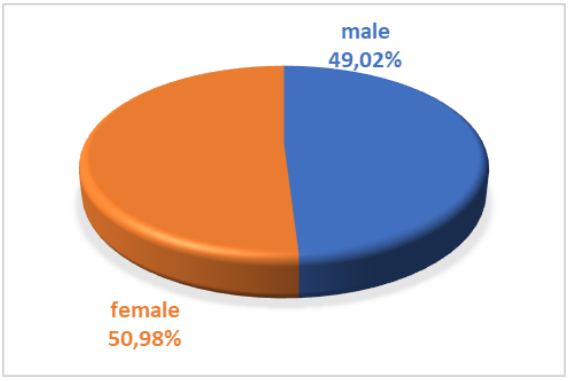

Figure 2. Distribution of cases according to gender

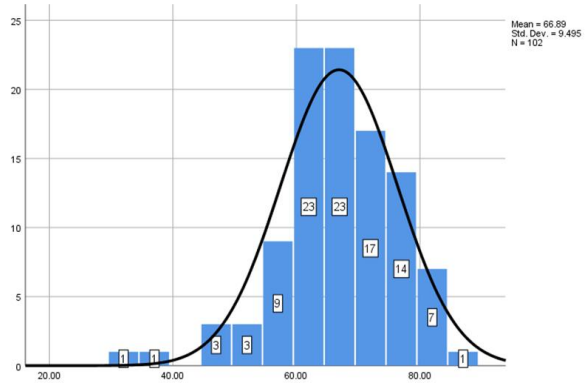

Figure 3. Variation of the number of cases in relation to the age of the patients

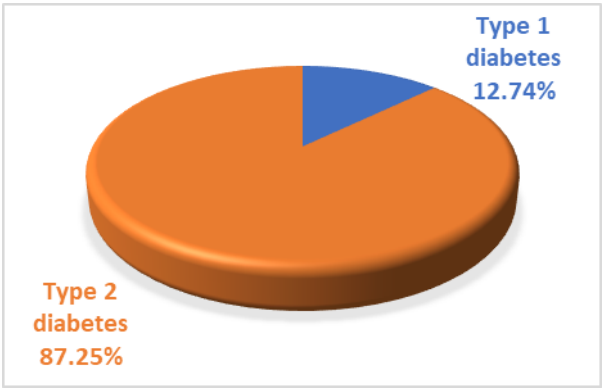

Figure 4. Distribution of cases according to type of diabetes

Arterial hypertension was part of the clinical picture of 78.4% of patients, while ischemic heart disease (30.4%), angina pectoris (12.7%) and atrial fibrillation (19.6%) were objectified in low percentages in the statistically analyzed batch. Among the valvular diseases, special attention was directed to the presence of aortic or mitral insufficiency which were present as comorbidities in 23.5% (24 cases) of the patients (Figure 5, Table 3).

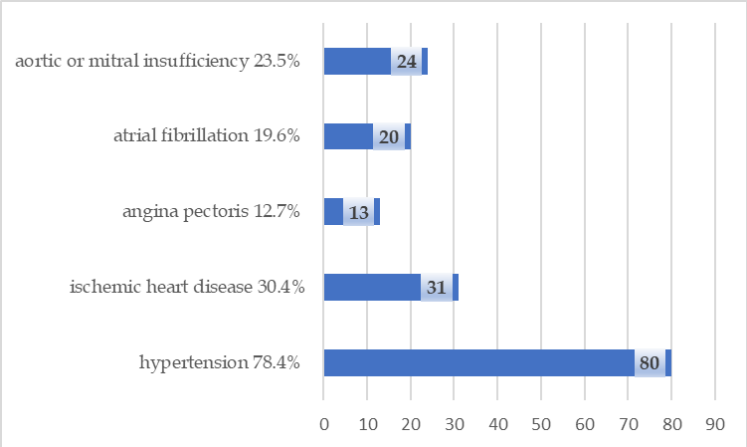

Figure 5. Distribution of cases according to the association of cardiac conditions

Table 3. The share of comorbidities according to the type of diabetes

		DIABETES MELLITUS				P value
		Type 1		Type 2		
		Number of cases	Percentage (%)	Number of cases	Percentage (%)	
GENDER	Female	8	61.5%	44	49.4%	0,415
	Male	5	38.5%	45	50.6%	
HYPERTENSION	Yes	10	76.9%	70	78.7%	0,887
	No	3	23.1%	19	21.3%	
ANTICOAGULANT TREATMENT	Yes	6	46.2%	44	49.4%	0,825
	No	7	53.8%	45	50.6%	
ISCHEMIC HEART DISEASE	Yes	4	30.8%	27	30.3%	0,975
	No	9	69.2%	62	69.7%	
ANGINA PECTORIS	Yes	1	7.7%	12	13.5%	0,559
	No	12	92.3%	77	86.5%	
ATRIAL FIBRILLATION	Yes	4	30.8%	16	18.0%	0,278
	No	9	69.2%	73	82.0%	
AORTIC OR MITRAL INSUFFICIENCY	Yes	2	15.4%	22	24.7%	0,459
	No	11	84.6%	67	75.3%	

Statistical analysis of post-extraction complications

The post-extraction complications manifested by the patients included in the study are: post-extraction hemorrhage, abscess, alveolitis and osteitis (Table 4).

Bleeding: 93.1% of patients did not have bleeding complications after dental extractions, but if these episodes were present, their frequency was associated with type 2 diabetes (prolonged and late form).

Abscess (5.9%) and alveolitis (2.0%) complete the list of complications, being objectified in low percentages of patients. Maxillary osteitis (18.8%), mandibular (14.7%) and bimaxillary (53.9%) completed the list of parameters included in the statistical analysis presented in the present paper, being entities more frequently associated with type 2 diabetes.

Table 3. The proportion of complications associated with dental extractions according to the type of diabetes

		DIABETES MELLITUS				P value
		Type 1		Type 2		
		Number of cases	Percentage (%)	Number of cases	Percentage (%)	
BLEEDING	ABSENCE	10	76.9%	85	95.5%	0,836
	PRECOCIOUS	1	7.7%	0	0.0%	
	EXTENDED	1	7.7%	2	2.2%	
	DELAYED	1	7.7%	2	2.2%	
ABSCESS	YES	2	15.4%	4	4.5%	0,119
	NO	11	84.6%	85	95.5%	
ALVEOLITIS	YES	1	7.7%	1	1.1%	0,600
	NO	12	92.3%	88	98.9%	
MAXILLARY OSTEITIS	YES	1	7.7%	18	20.2%	0,278
	NO	12	92.3%	71	79.8%	
MANDIBULAR OSTEITIS	YES	1	7.7%	14	15.7%	0,445
	NO	12	92.3%	75	84.3%	
BIMAXILLARY OSTITIS	YES	5	38.5%	50	56.2%	0,231
	NO	8	61.5%	39	43.8%	

DISCUSSIONS

Several studies have been conducted to investigate the relationship between severe multi space infections of the oral maxillofacial region and diabetes mellitus. Infection is a risk factor for patients with untreated diabetes because there is an increase in blood glucose levels.

When the body tries to fight an infection, stress hormones such as cortisol and glucagon are produced, which trigger the release of glucose, causing blood glucose levels to rise significantly [14]. A study conducted by Zheng et al showed that uncontrolled diabetics had more serious infections, complications and longer hospital stays than patients without diabetes [15].

Patients with diabetes suffer from dehydration, which affects the body in general and the salivary glands in particular. Thus, the decrease in flow and salivary pH favoring the increase in the colonization of Candida species in the oral cavity [16,17]. Dental extractions can create a gateway for fungal infection in patients with uncontrolled diabetes. Mucormycosis of maxillary sinuses, also known as black fungus, a rare and acute fungal infection which is frequently lethal, were detected after dental extraction in poorly controlled diabetic patients [18,19].

Some studies [20,21] indicated that several factors might be associated with dental caries in patients with diabetes, such as daily eating habits, salivary glucose, and low salivary flow, others [22] reported no association. Therefore, tooth extraction due to tooth decay may not be associated with diabetes. Diabetes mellitus was significantly associated with tooth extraction due to periodontal disease [23].

International studies on post-surgical complications after tooth extraction in patients with diabetes are divided. A study in an oral surgery unit shows no statistically significant difference between post-extraction complications in diabetic and non-diabetic patients [24]. Another study showed that smoking showed no significant relationship with the intensity of pain, edema and trismus after extraction [25]. Another study shows that patients with type 1 diabetes and insulin-dependent diabetes type 2, if well controlled, tend to heal well after tooth extraction, with no statistically significant rate of post-extraction complications, including infection [26].

Khan et al. showed that complication rates among patients with comorbidities are four times higher than in healthy subjects [27].

Some studies have concluded that the use of anticoagulant drugs does not have a significant impact on postoperative healing after tooth extraction, provided the INR is maintained <3.0 and effective local hemostasis measures are administered [28,29].

Patients with diabetes and hypertension are at significantly high risk for premature microvascular and macrovascular complications [30,31]. Glycemic control improves microvascular disease. Blood pressure control as well as dyslipidemia are extremely important in the prevention of macrovascular diseases, in addition to glycemic control [32].

The association of the increased percentage of patients with type 2 diabetes with the presence of various comorbidities, especially hypertension, is explained by the literature by the fact that some of the risk factors involved in the etiopathogenesis of type 2 diabetes are cardiovascular diseases and hypertension. Thus, the diagnosis of type 2 diabetes of the patients included in our study may be secondary to another systemic condition.

Although it is generally agreed that diabetic patients are at increased risk of infection and delayed post-extraction wound healing, there is little published evidence to support this claim [3,26,33].

CONCLUSIONS

Management of extractions in diabetic patients is often a difficult task for dentists.

The higher the blood glucose level, the greater the chance that predisposing conditions for post-extraction complications in diabetics will increase sharply.

Dentists must take great care in managing insulin-dependent diabetic patients compared to non-insulin-dependent diabetics or non-diabetic patients.

Surgical treatment of diabetic patients highlights the need to implement early detection, screening and awareness programs to alleviate the burden of managing complications.

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