The Influence of Xylitol on Some Salivary Parameters Involved in Saliva Remineralisation Capacity

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The aim of the study was to investigate the effect of xylitol, from some oral hygiene products and chewing gums, on salivary parameters variation in patients with carious disease. The study was performed on 30 patients with a medium level of carious disease, randomly divided in two groups as follows: group 1 (study group), using xylitol-based products for 30 days, and group 2 (control group), using products without xylitol. The way of administration, dose, and frequency of use were as follows: toothpaste (normal daily brushing, 3 times daily); mouthwashing (5 ml, twice daily); chewing gums (two tablets, 5 times daily), for 30 days. The assessment targeted the salivary parameters as follow: saliva microcrystallisation index (IMK), resting salivary flow rate (RSF), stimulated salivary flow rate(SSF). The results of our study confirm the improvement of salivary parameters due to the use of xylitol-based products, by the positive influence on the remineralisation capacity of saliva. The assessment method of saliva IMK represents a noninvasive, simple, informational indicator for the assessment of the remineralisation capacity of saliva.

Keywords: xylitol, remineralisation, saliva, microcrystallization index

The carious disease is a complex pathology influenced by genes, infectious factors, environment factors, and risk behaviour [1-4].

The dental caries is an infectious process defined by a cariogenic acid biofilm that produces the demineralisation of hard dental tissues [3-5]. Also the dental caries represent a dynamic, reversible, out-of-step phenomenon, that in the noncavitary stages can be healed by preventive-therapeutical measures [2, 6].

In 2010, the untreated dental caries were most prevalent pathological condition for posterior teeth, affecting 2.4 miliarde people, while untreated dental caries to primary teeth were 10th most prevalent condition, affecting 621 milions children [7].There is an increasing trend to 6 years children in various countries [7].

As carious process has a multifactorial ethiology and the disease has a dynamic character, the clinical and therapeutical management is a complex one, with numerous variables that can challenge the prediction and the therapeutical decisions [2, 3]. The fundamental research is requested for a better understanding of the carious disease phenomenon to the molecular level. The saliva plays an important role in the health status of the dental and soft oral tissues [2, 6].

The salivary flow varies between different individuals, but also at the same patient in relation to time, body position, light intensity and other factors. In 2008 M. Navazesh proved that the measurement of the unstimulated salivary flow is the most predictive method for the assessment of the caries risk [8]. The resting salivary flow rate is 0.3-0.4 mL/min and values lower than 0,1 mL/min are pathological. Some commercial salivary kits allow the accurate evaluation of the salivary flow rate [2-4, 6].

The hypothesis regarding the saliva supersaturation with nanohydroxiapatite cristals sustains that saliva don't contains free ions of calcium, phosphate and fluorine but rather microcrystals of hydroxiapatite and fluorapatite maintained in this structure by salivary glycoproteins. These crystals grows if oral *p*H is higher than the critical *p*H. The critical *p*H is not constant, it varies in relation to the levels of calcium and phosphate in dental biofilm. In hiposalivation, associated with lower levels of calcium and phosphate, the critical *p*H will be higher, and the demineralisation processes will begin from *p*H = 5.9 or even 6.00 [5]. The stimulated saliva has a *p*H of 6.75-7.25. If the oral *p*H decreases significantly on long term, the development of cariogenic bacteria will take place. If bacterial biofilm maintains a minimum *p*H 7, the exposure to glucose will not provoke acidogenicity. If *p*H of oral environment is neutral or alcaline, the composition of biofilm will not favourise the increase of acidogenic bacteria. The transformation of a cariogenic environment in a noncariogenic environment is performed by reducing the level of bacterial load, the change of community climax of cariogenic biofilm in a *healthy* biofilm, by facilitating the change of minerals and favourising the conditions for neutral *p*H. The saliva is an active biological fluid with complex composition and numerous possibilities for the saliva unlimited noninvasive assessment [6, 9, 10].

The literature data [11-18] confirm the use of xylitol as a method for the reducing of the dental caries prevalence. Xylitol, an important saccharine replacement, was used as nutritional agent from sixties [19]. Some observations were made about the reducing of the *S.mutans* transmission from mothers to children [20-23]. The saliva that contains xylitol is more alkaline than saliva containing other types of sugar [24-25]. Xylitol has a bacteriostatic effect on *Streptococcus Mutans,* and the regular consume of xylitol can reduce the consistency and adhesion of the cariogenic biofilm. Also on long term xylitol inhibates the development of *Lactobacillus acidophilus* and increases the remineralisation capacity of saliva.

Xylitol is a carbohydrate found in many vegetables and fruits, with a crystallized structure, composed by five carbon atoms. The anticariogenic effect of xylitol was found in the fourties, when xylitol replaced sugar in Scandinavian

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countries. In the fifties these countries had less children affected by dental caries compared with countries where sugar was not replaced by xylitol [26]. Some literature data demonstrate that xylitol promotes the remineralisation by the increase of salivary flow rate and by the inhibition of the bacteria matabolism in the dental biofilm [17, 26, 27] and other studies sustain that the arguments for the clinical effectiveness of xylitol are controversial [13, 28-31].

The aim of the study is to assess the effect of xylitol, from some oral hygiene products, as toothpaste, mouthwash, chewing gums, on the remineralisation capacity of saliva for patients with carious disease.

Experimental part

The study was performed on 30 patients treated in Clinical Base *M. Kogalniceanu* UMF Ia'i with medium cariogenic risk. The patients were randomly divided in two groups: group 1(S) - study group (for 30 days patients used xylitol-based toothpaste, mouthwash, chewing gum); group 2 (C) – control (for 30 days patients used oral hygiene products without xylitol) (fig. 1).

The protocol consisted in the use of toothpaste with xylitol (3 times daily toothbrushing, 3 weeks), mouthwash with xylitol (oral rinses, 5 mL, 2 times daily, 3 weeks), chewing gums with xylitol (2 tablets, 5 times daily, 3 weeks). The assessment targeted the salivary parameters as follow: saliva microcrystallisation index (IMK), resting salivary flow rate (RSF), stimulated salivary flow rate (SSF).

The saliva microcrystallisation index (IMK) was measured by Leus method, modified after Belischaia [32]. The results were framed in three categories of microcrystallisation: type I (high), type II (medium), type III (low), in relation to the score:

IMK = 0.6÷1 (high level of microcrystallisation);
IMK = 0.4÷0.6 (medium level of microcrystallisation);
IMK = 0÷0.4 (low level of microcrystallisation).

The determination of resting salivary flow rate (RSF) was performed as follows: patients is asked to eliminate the saliva at every two minutes in a sialometer; after 5 minutes the volume of saliva is measured.

The determination of the stimulated salivary flow rate (SSF) was performed as follows: patients is asked to eliminate the saliva in a sialometer for 5 min after he chewed a parafine piece for 30-60 s and swallowed the saliva.

The normal values of rest saliva flow and stimulated saliva flow are presented in table 1.

The statistical analysis of the results was performed using SPSS v.17.

Results and discussions

Accordingly to the results, the values of RSF, SSF and IMK increased 30 days from baseline. The values of RSF are presented in table 2.

The mean values and standard deviations of RSF between groups are presented in table 3.

RSF mean values recorded in the study group and control group increased after treatment from 0.49 to 0.69 in group I (S), from 0.46 to 0.62 in group II (C), with higher increase in group I(S) (table 3).

Data were statistically analysed using Wilcoxon test. The levels of significance for comparison between groups are presented in table 4. The values were considered significantly statistical different when $p < 0.05$. The comparison of groups at baseline and after treatment recorded significantly statistical differences.

SSF values at baseline and after treatment for study group and control group are presented in table 5.

The mean values and standard deviations for SSF between groups are presented in table 6.

SSF mean values between groups increased after treatment from 1.06 to 1.88 in group I (S) and from 0.94 to 1.17 in group II (C), with higher increase for group I(C) (table 6).

Xylitol-based products (Spry Dental Defence, Xlear Inc., USA)	Ingredients:
	**Wintergreen Natural Oral Rinse** Purified Water, Xylitol, Ethanol (Grain Alchohol, Natural Wintergreen Flavor, Vegetable Gliceryn, Cassia Extract, Calcium Glycerophosphate, Aloe Vera, Calendula officialis flower extract, Chamomilla recutita extract, Echinacea purpurea extract, Oleo europea leaf extract, Thymus vulgaris extract.
	**Anti-Cavity Peppermint Xylitol Toothpaste** Sodium Fluoride, Water, Glycerin, Silica, Xylitol, Erythritol, Lauryl Glucoside, Sodium Methyl, Cocoyl Taurate, Zinc Citrate, Cranberry Extract, Aloe Vera, Xanthan Gum, Cellulose Gum, Stevia, Natural Peppermint Flavor, Sodium Benzoate, Titanium Dioxide.
	**Natural Peppermint Xylitol Gum** Xylitol, Gum Base, Natural Peppermint Oil, Vegetable Glycerin, Gum Arabic, Soy Lecithin, Calcium Carbonate, Carnauba Wax.

Fig. 1. Xylitol-based products used in study group

	RSF – unstimulated salivary flow (ml/min)	SSF – stimulated salivary flow (ml/min)
Normal	0.25 – 0.35	1 - 3
Hiposalivation	<0.1	<0.7

Table 1
NORMAL VALUES
RSF AND SSF

RFR assessment				
Groups/ Number	**Group I (S)**		**Group II (M)**	
	baseline	**post-treatment**	**baseline**	**post-treatment**
1	0.4	0.6	0.4	0.6
2	0.5	0.7	0.5	0.6
3	0.3	0.6	0.3	0.6
4	0.4	0.6	0.6	0.8
5	0.5	0.7	0.5	0.6
6	0.6	0.8	0.5	0.6
7	0.4	0.7	0.3	0.5
8	0.5	0.8	0.5	0.7
9	0.5	0.6	0.3	0.4
10	0.5	0.8	0.6	0.7
11	0.4	0.6	0.4	0.6
12	0.7	0.8	0.5	0.7
13	0.6	0.7	0.5	0.6
14	0.5	0.7	0.4	0.6
15	0.6	0.7	0.6	0.7

Table 2
RSF VALUES

Statistics					
		Group I (S) baseline	Group I (S) post	Group II (C) baseline	Group II (C) post
N	Valid	15	15	15	15
	Missing	30	30	30	30
Mean		**.4933**	**.6933**	**.4600**	**.6200**
Std. Error of Mean		.03754	.02737	.03207	.02482
Std. Deviation		.10328	.079881	.10556	.094112

Table 3
RSF MEAN VALUES AND STANDARD DEVIATIONS AT BASELINE AND POST-TREATMENT

RFR	Group I(S) baseline	Group II(C) Baseline	Group I(S) final	Group II(C) final
Group I(S) baseline	-		0.35	-
Group II(C) baseline		-	-	0.01
Group I(S) final	0.35	-	-	-
Group II(C) final	-	0.01		-

Table 4
WILCOXON TEST. COMPARISON OF RSF RESULTS BETWEEN GROUPS I (S) AND II (C) AT BASELINE AND AT THE END OF TREATMENT.

Data were statistically analysed using Wilcoxon test. The levels of significance for comparison between groups are presented in table 7. The values were considered significantly statistical different when $p < 0.05$. The comparison of groups at baseline and after treatment recorded significantly statistical differences.

IMK values at baseline and after treatment are presented in table 8.

IMK mean values and standard deviations in the groups are presented in table 9.

IMK mean values in groups increased after treatment, from 0.59 to 0.92 in group I (S) and from 0.56 to 0.68 in group II (C), with higher increase in group I (S) (table 9).

Data were statistically analysed using Wilcoxon test. The levels of significance for comparison between groups are presented in table 10. The values were considered

SSF assessment				
Groups/ Number	Group I(S)		Group II(C)	
	baseline	post-treatment	baseline	post-treatment
1	1.1	1.8	0.9	1.2
2	0.9	1.6	0.8	0.9
3	0.8	2.1	0.8	1.1
4	0.9	1.9	0.8	1.3
5	1.4	2.3	1.1	1.4
6	0.9	1.6	0.9	1.2
7	1.1	1.7	1.3	1.4
8	0.8	1.6	0.7	0.9
9	1.3	1.8	1.2	1.5
10	0.8	1.4	0.9	1.3
11	1.3	1.8	0.8	0.9
12	1.2	2.2	1.3	1.3
13	1.5	2.3	0.8	0.9
14	1.2	2.6	0.7	0.9
15	0.8	1.6	1.1	1.4

Table 5
SSF VALUES

Statistics					
		Group I (S) baseline	Group I (S) post	Group II (C) baseline	Group II (C) post
N	Valid	15	15	15	15
	Missing	30	30	30	30
Mean		**1.0666**	**1.8866**	**0.94**	**1.1733**
Std. Error of Mean		.03754	.02737	.03207	.02482
Std. Deviation		.24103	.339888	.206328	.221897

Table 6
SSF MEAN VALUES AND STANDARD DEVIATIONS AT BASELINE AND POST-TREATMENT

RFR	Group I(S) baseline	Group II(C) baseline	Group I(S) final	Group II(C) final
Group I(S) baseline	-		0.24	-
Group II(C) baseline		-	-	0.041
Group I(S) final	0.24	-	-	-
Group II(C) final	-	0.41		-

Table 7
WILCOXON TEST. COMPARISON OF RSF RESULTS BETWEEN GROUPS I (S) AND II (C) AT BASELINE AND AT THE END OF TREATMENT.

significantly statistical different when $p < 0.05$. The comparison of groups at baseline and after treatment recorded significantly statistical differences.

The microscopic analysis found various types of saliva microcrystallisation: arborescent, fern, snow flake, multiple points, micronetwork, oval or cube structures, lamellas with various forms and contrasts, various combinations (figs. 2 and 3).

High IMK (0.7-1) is associated with high volume crystals, arborescent, fern type aspect, with distribution of crystals from center to periphery (fig. 2b). Medium IMK (0.6-0.4) is associated with less organized medium volume crystals, moderate arborescent type aspect, associated with cube or disparate crystals (fig. 2a, 3b). Low IMK (0.3-0.1) is associated with diffuse, low volume or cube crystals, disparate or organized randomly or in groups of crystals to periphery of saliva drop (fig. 3a).

The role of saliva in the neutralizing the acids from dental biofilm is controversial [1, 3, 5-7]. Some clinical studies show the role of the stimulated saliva flow [10]. The use of chewing gum without saccharose after tables reduces the initiation of dental caries, but this effect is due rather to the increase of the saliva flow [13, 15, 16, 30]. One study demonstrated the effectiveness of xylitol pills in the prevention of active caries on adults [33]. A research demonstrated that consume of xylitol daily (3-5 grams) is

RFS assessment				
Groups/ Number	Group I(S)		Group II(C)	
	baseline	post-treatment	baseline	post-treatment
1	0.5	0.7	0.4	0.8
2	0.7	1.0	0.7	0.6
3	0.4	0.8	0.5	0.8
4	0.3	1.7	0.6	0.7
5	0.5	0.9	0.4	0.6
6	0.7	1.0	0.6	0.8
7	0.6	0.7	0.3	0.5
8	0.4	0.6	0.7	0.8
9	0.3	0.6	0.5	0.6
10	0.7	1.0	0.7	0.8
11	0.8	1.0	0.6	0.6
12	0.9	1.0	0.3	0.4
13	0.6	0.9	0.8	0.9
14	0.7	1.0	0.7	0.8
15	0.8	1.0	0.6	0.6

Table 8
IMK VALUES

Statistics					
		Group I (S) baseline	Group I (S) post	Group II (M) baseline	Group II (M) post
N	Valid	15	15	15	15
	Missing	30	30	30	30
Mean		**.5933**	**.9266**	**.5602**	**.6866**
Std. Error of Mean		.03754	.02737	.03207	.02482
Std. Deviation		.18695	.26313	.15491	.14074

Table 9
IMK MEAN VALUES AND STANDARD DEVIATIONS AT BASELINE AND POST-TREATMENT

RFR	Group I(S) baseline	Group II(C) baseline	Group I(S) final	Group II(C) final
Group I(S) baseline	-		0.39	-
Group II(C) baseline		-	-	0.43
Group I(S) final	0.39	-	-	-
Group II(C) final	-	0.43		-

Table 10
WILCOXON TEST. COMPARISON OF RSF RESULTS BETWEEN GROUPS I (S) AND II (C) AT BASELINE AND AT THE END OF TREATMENT.

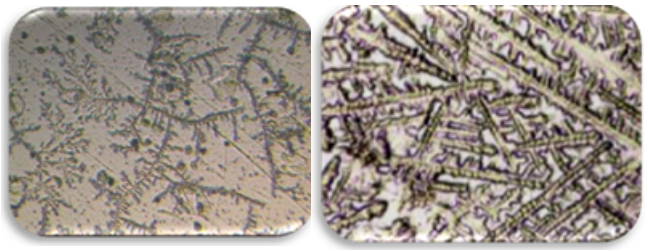

Fig. 2. Aspects of saliva microcrystallization Group I
a).baseline, b). post-treatment

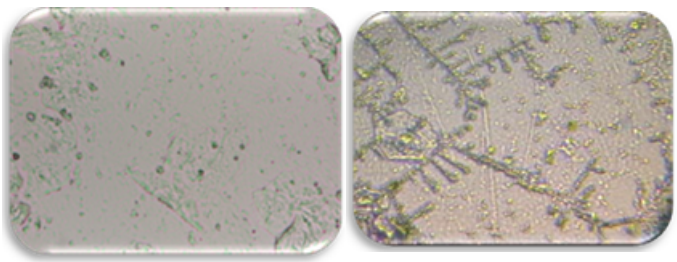

Fig. 3. Aspects of saliva microcrystallization Group II
a). baseline, b). post-treatment

associated with a significant decrease of dental caries incidence, comparing with placebo [34].

In 2007, American Academy of Pediatric Dentistry (AAPD) confirmed the existence of numerous studies regarding the role of xylitol in the oral health of children and young adults with disabilities [35]. AAPD supports the use of xylitol and other polyols, but recognizes that might not be possible to use in daily life the high dose of xylitol used in clinical researches [35]. AAPD supports the initiative for additional researches regarding the most effective ways of yadministration, optimal dose and frequency [35].

Xylitol is not indicated only for children and young adults. In an article published in Journal of American Gerontology Society, the researchers found on a group of 111 adults with age over 60 years, that study group (consuming chewing gums with xylitol) had a lower risk of oral aphthous ulceration or fungus infections [34]. The chewing gums with xylitol offer a real clinical benefit to the aged people with weak immune system [36].

The results of our study support the literature data [11, 31, 37-42] that confirm the association between the products for oral hygiene with xylitol and the improvement of salivary parameters and the remineralisation capacity of saliva. Dental practitioners should include xylitol-based products as preventive and non-operative therapeutic measures to successfully improve the saliva quantity and quality.

Conclusions

The results of our study confirm the improvement of salivary parameters due to the use of xylitol-based products, by positive influence on the remineralisation capacity of saliva. The assessment method of saliva IMK represents a noninvasive, simple, informational indicator for the assessment of the remineralisation capacity of saliva.

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