

## ACIDITY OF UNSTIMULATED SALIVA AND DENTAL PLAQUE IN ASTHMATICS, TREATED WITH INHALED CORTICOSTEROIDS AND LONG-ACTING SYMPATHICOMIMETICS

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### SUMMARY:

The number of asthmatics is continuously increasing all over the world. The aim of the study is to study the effect of different combinations of inhaled corticosteroids and long-acting sympathicomimetics on salivary and plaque pH in asthmatics with mild persistent asthma. The effect of different quantities of lactose, as gustatory corrector in the inhalers, is traced out.

Thirty patients of both sexes, from 20 to 55 years old participated in the study. Salivary and plaque pH values are traced out in 30 minutes period after drug inhalation, at 6-months interval.

It is found out that inhaled drugs cause significant decrease of initial salivary pH values, the lowest ones reported on first and fifth minute after the inhalation. The average salivary pH levels on the 30th minute remain significantly lower than initial ones.

Most considerable changes in pH values are registered for patients treated with Fluticasone propionate and Salmeterol.

**Key words:** asthma, inhaled corticosteroids, inhaled long-acting sympathicomimetics, plaque pH, salivary pH

### INTRODUCTION:

Up-to-date treatment of bronchial asthma is connected with combinations of inhaled corticosteroids and long-acting sympathicomimetics, frequently containing gustatory correctors such as lactose. Their prolonged everyday use can lead to a reduction of unstimulated salivary flow rate because of the  $\beta$ -agonists and decrease in salivary and dental plaque pH.[4, 7, 15, 27]

Dental caries is a chronic disease involving localized destruction of specific sites of tooth surface. It is a multifactorial dynamic process that is modified by protective factors.[15, 27-29]

The enamel surface is in a state of dynamic equilibrium with its local oral environment (plaque fluid and saliva), involving constant movement of ions in and out. As plaque pH drops under 6.5 a process of demineralization begins,

followed by a concomitant process of remineralization till pH range of 5.5 is reached. pH range of 5.5 is known as critical of enamel because after reaching it only demineralization processes are taking place. Acid production in plaque depends on: type of carbohydrates (simple sugars and sucrose), microbial composition (acidogenic and aciduric microorganisms) and the level of diffusion of substrate in the plaque and the metabolic products out of it. When the plaque is with low thickness saliva can modify it with its buffering systems. As the plaque thickness grows saliva can't neutralize the acidity and pH levels remain low.[4, 6, 11, 14-16; 27-29]

There is little evidence in literature for the relation between saliva parameters and dental health in asthmatics and their treatment. Most of the studies are carried out on kids and the obtained results are contradictory. [1, 2, 8, 9, 12, 18, 25, 26, 30, 34, 35]

### MATERIAL AND METHODS:

Thirty asthmatics of both sexes, from 20 to 55 years old, participate in the study. They suffer from mild persistent asthma and are systematically treated with combinations of inhaled corticosteroids and long-acting sympathicomimetics. All patients with accompanying diseases and treatment, affecting saliva quantity and acidity are excluded from the investigation. Those with bad oral hygiene and parodontal diseases are excluded as well.

The asthmatic patients are divided in three groups, according to their medication (*Seretide* - Fluticasone propionate + Salmeterol, *Symbicort* - Budesonide + Formoterol and *Foster*- Beclometasone + Formoterol). The active component in all devices is inhaled in a dry powder form. The investigated medications have different quantity of gustatory correctors - 12,5 mg Lactose monohydrate in Fluticasone propionate + Salmeterol; 0.730 mg Lactose monohydrate in Budesonide + Formoterol and no correctors in Beclometasone + Formoterol.

All patients have made two visits in a period of six months. In each visit we followed up pH levels of unstimulated saliva in the course of 30<sup>th</sup> minutes after the inhalation of the medication. The patients expectorated in a

container before the inhalation and on the 1<sup>st</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 20<sup>th</sup> and 30<sup>th</sup> minute after it. pH levels are measured by pH test strips, placed into the saliva sample for 10 seconds. Strip colour is compared with the testing chart available in the package of GC Saliva-Check BUFFER, GC EUROPE N.V.

Dental plaque pH levels are measured in the course of 30<sup>th</sup> minutes after the inhalation of the medication as well - before the inhalation and on the 1<sup>st</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 20<sup>th</sup> and 30<sup>th</sup> minute after it. Measurements are made with Dental Beetrode NMPH3, WPI Germany GmbH i.G. and pH meter Hanna 211 at the distal surfaces of 14, 24, 34 и 44.

All patients have signed an informed consent.

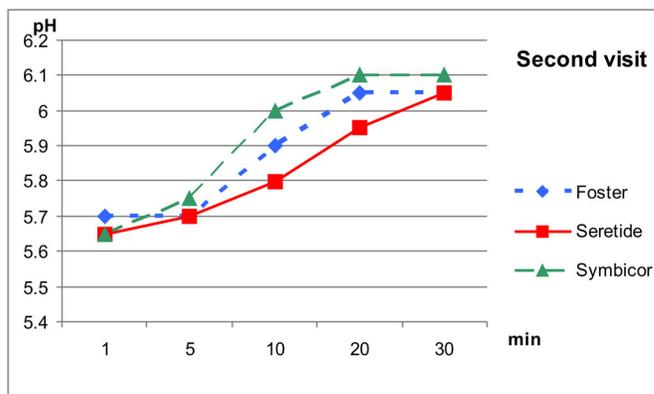
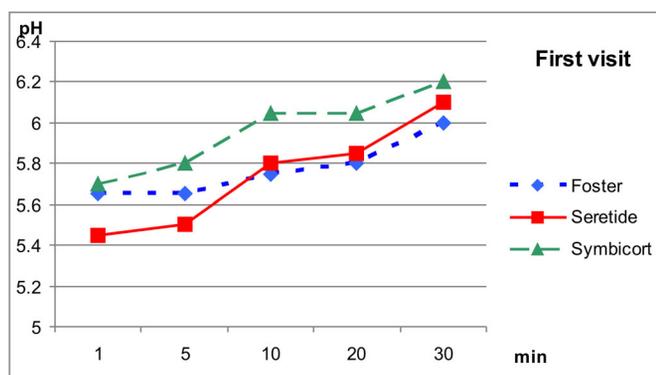
Data analyses are conducted using statistical software program SPSS 15.0 and paired simple t-test.

### RESULTS:

Inhalation of corticosteroids and long-acting sympathicomimetics reduces salivary pH, especially on the first and fifth minute. Lowest pH levels are founded after the inhalation of Fluticasone propionate + Salmeterol (*Seretide*) on the first visit - on the 1<sup>st</sup> minute 5.45 and on the 5<sup>th</sup> minute - 5.5. Higher pH levels are reported for the other two medications on both visits - Beclometasone + Formoterol (*Foster*)- first and second visit - 5.65, Budesonide + Formoterol (*Symbicort*) - first visit - 5.7, second visit - 5.8. Only after inhalation of Fluticasone propionate + Salmeterol salivary pH levels remain under 6.00 for a period of 20 minutes in both visits.

Salivary pH levels grow up till the 30<sup>th</sup> minute after the inhalation in both visits but the oral environment remains moderately acidic because pH doesn't exceed 6.2. Fig.1, Fig.2

**Fig. 1 and Fig. 2.** Comparison of salivary pH levels after the drug inhalation for each visit



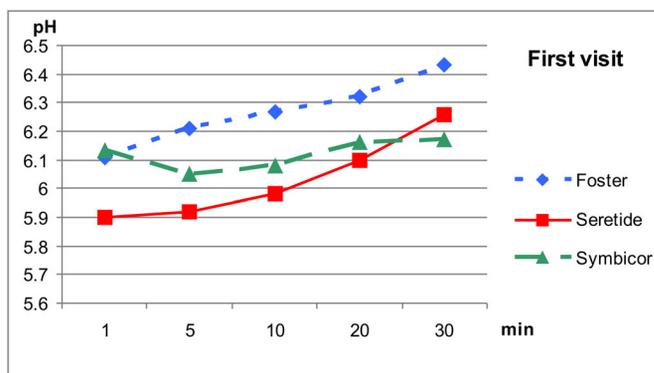
Comparison of initial salivary pH levels and these on the first and fifth minute indicates a significant decrease in both visits for each medication (paired simple t-test,  $p < 0.001$ ).

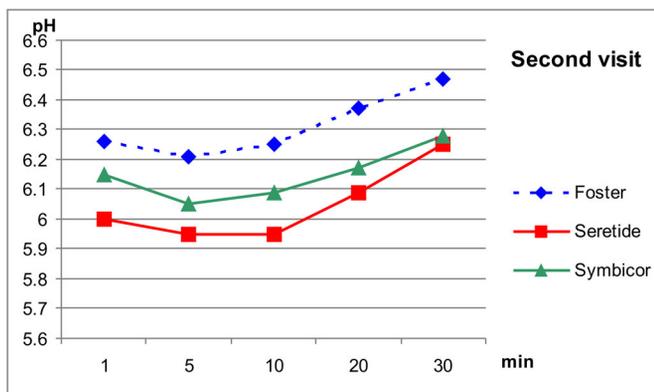
Despite the observed tendency of increase of salivary pH levels till 30<sup>th</sup> minute after drug inhalation, the results from the last measurements remain significantly lower when compared with the initial ones for each medicine on both visits (paired simple t-test,  $p < 0.05$ ).

We followed up the effect of each drug on plaque pH as well. Once again, drug inhalation decreases plaque pH, especially on the first and fifth minute. Lowest levels are registered after the inhalation of Fluticasone propionate + Salmeterol (*Seretide*) in all measurement of both visits, with the exception of that on the 30<sup>th</sup> minute at the first visit. Highest plaque pH levels are found out after the inhalation of Beclometasone + Formoterol (*Foster*), but the differences are not statistically significant (paired simple t-test,  $p > 0.05$ ).

A tendency of normalizing dental plaque acidity is observed. Highest pH levels are registered on the 30<sup>th</sup> minute for all inhaled drugs. There is an insignificant increase of pH on the second visit when compared with the first one. Fig. 3, Fig. 4

**Fig. 3 and Fig. 4.** Comparison of plaque pH levels after the drug inhalation for each visit





Drug inhalation decreases plaque pH levels on the first and fifth minute when compared with the initial measurements. We registered considerable differences in almost all comparisons ( $p < 0.05$ ). Table 1.

**Table 1.** Comparison of initial plaque pH levels and pH on the 1<sup>st</sup> and 5<sup>th</sup> minute after drug inhalation

Inhaled drug			Group differences			Level of importance
			Mean	Std. Dev.	Std. Error Mean	
Foster	I visit	Initial pH - pH 1st minute	0,48	0,21	0,07	< 0.001
		Initial pH - pH 5th minute	0,39	0,31	0,10	0.003
	II visit	Initial pH - pH 1st minute	0,40	0,31	0,10	0.002
		Initial pH - pH 5th minute	0,45	0,23	0,07	< 0.001
Seretide	I visit	Initial pH - pH 1st minute	0,44	0,52	0,17	0.026
		Initial pH - pH 5th minute	0,41	0,66	0,21	0.080
	II visit	Initial pH - pH 1st minute	0,45	0,27	0,08	< 0.001
		Initial pH - pH 5th minute	0,49	0,33	0,10	0.001
Symbicort	I visit	Initial pH - pH 1st minute	0,29	0,44	0,14	0.064
		Initial pH - pH 5th minute	0,36	0,52	0,16	0.053
	II visit	Initial pH - pH 1st minute	0,32	0,20	0,06	0.001
		Initial pH - pH 5th minute	0,43	0,26	0,08	0.001

The average plaque pH levels registered on the 30<sup>th</sup> minute are lower than initial ones on both visits for each drug. Significant differences are found out only after inhalation of Fluticasone propionate + Salmeterol (*Seretide*) on the second visit (paired simple t-test,  $p = 0.039$ ).

#### DISCUSSION:

Combinations of inhaled corticosteroids and long-acting sympathicomimetics cause similar changes in salivary and plaque pH. Initial pH values sharply drop on the first and fifth minute after the inhalation and in almost all comparisons we found out significant differences. This process is followed by a tendency of gradual increase of pH up to the 30<sup>th</sup> minute. Nevertheless, oral environment remains moderately acidic and

doesn't reach initial pH levels. Statistically important differences are registered when the first and last pH measurements are compared.

We assume that the changes in acidity can be explained with the local effect of inhaled long-acting sympathicomimetics on salivary glands secretion. The reduced salivary flow rate influences negatively its buffering and clearing abilities.[1, 2, 5, 21-24] Drug gustatory correctors, such as sucrose, additionally decrease salivary and plaque pH.

At the same time lower pH values are expected in asthmatics with gastro-esophageal reflux. [19]

As we expected, drugs with greatest quantity of lactose as gustatory correctors decrease most sharply salivary and plaque pH values. On the other hand, the active ingredient in

the examined drugs is in a powder form and is easily adhered and kept on the tooth surface after the inhalation. The combination of these two factors and the necessity of everyday treatment in asthmatics will increase caries risk for these patients.[7, 19, 33]

Kargul et al. achieve similar results. They find out significant decrease in salivary and plaque pH after inhalation of different drugs ( $p < 0,001$ ). They attribute these findings to the drug composition and not to the disease itself. [10]

Tootla et al. study the effect of 14 inhaler drugs on plaque pH but don't find lower pH values than 6.0. The DPI inhaler devices containing lactose decrease at greatest degree and for longest time the pH levels ( $p < 0,05$ ) which increases the risk for hard dental tissues.[33]

The same team establishes significant decrease of salivary quantity and pH, measured in the course of 30 minutes after drugs' inhalation.[32, 33]

Other scientists [5, 23] state greater salivary acidity with the prolonged drug intake.

C. Sag et al. trace out the effect of fluticasone propionate 100 mcg and salmeterol 50 mcg in asthmatic children under the age of 7-17 years. They consider that these children need special dental care because of their continuous treatment.[23]

Information about increased caries risk and the

influence of gustatory correctors in inhaler drugs on plaque pH can be found in the study of I. Roberts and S. Sunitha as well. [20, 31]

Other scientists, such as M. Lenander-Lumikari et al. [13] don't find out critical pH levels after drug inhalation in any patients' group. However, they presume increased caries risk in asthmatics treated with inhaled corticosteroids, containing lactose.

At the same time we find articles in accordance of which prescribed inhaler drugs do not affect substantially oral environment. [3, 8, 17]

## CONCLUSIONS:

- Inhalation of different combinations of corticosteroids and long-acting sympathicomimetics decreases initial salivary and plaque pH, especially on first and fifth minute. It is followed by a tendency of increase of pH values up to the 30<sup>th</sup> minute without reaching the initial levels.

- The average salivary pH levels on the 30<sup>th</sup> minute remain significantly lower than initial ones.

- Combination of Fluticasone propionate and Salmeterol decreases salivary and plaque pH most substantially and for longest time. Prolonged use of drugs with greater quantities of lactose as gustatory correctors increases caries risk for asthmatics.

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