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Salivary pH After a Glucose Rinse: Effect of a New Mucoadhesive Spray (Cariex®) Based on Sodium Bicarbonate and Xylitol

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Abstract

- **Objective:** This study evaluated whether sodium bicarbonate applied on the oral mucosa through a new mucoadhesive spray (Cariex®) could control a drop of salivary pH after a glucose rinse, and therefore enhance the buffering potential of saliva.
- **Methods:** A sample of 50 healthy adults was selected. At day 1, the measurement of salivary pH was performed in the lower fornix in correspondence with the lower molars. Each subject rinsed with 10 ml of a 10% glucose solution and then pH was monitored continually for 40 minutes. At day 2, the same experimental procedure was repeated and three shots of the spray were administered on the oral mucosa. The tested spray is composed of sodium bicarbonate, xylitol, and excipients.
- **Results:** Without the mucoadhesive spray, salivary pH became significantly lower following the glucose rinse ($p < 0.01$). Following the spray, the time in which the pH remained lower than 6.0 was reduced statistically significantly ($p < 0.01$). A continual rise of salivary pH was observed for the 40 minutes in which the pH recording was performed.
- **Conclusions:** The use of a sodium bicarbonate spray on the mucosa was shown to control the lowering of salivary pH following carbohydrate consumption, and might therefore add to the prevention of caries and dental erosion.

(J Clin Dent 2014;25:71–75)

Introduction

Saliva plays an essential role in the maintenance of oral health.[1] The salivary secretion rate and the buffering capacity of saliva protects the teeth against the effects of acids.[2] The three major salivary components contributing to this buffering capacity are bicarbonate, the phosphate, and the protein buffer systems. Of these, the bicarbonate component is the most important,[3] as it increases the stimulated saliva up to ten times the usual status of the regular buffer systems. This effect helps to inhibit the harmful effects of acids to dental enamel.[2] Imfeld[4] found that rinsing with sodium bicarbonate increases the pH of human plaque previously lowered by the presence of fermentable carbohydrates. For instance, a sorbitol-containing chewing gum supplemented with sodium bicarbonate was found to enhance the ability of plaque pH to be maintained at an elevated level after a cariogenic challenge.[5] Additionally, sucking on a sugar-free tablet containing bicarbonate and phosphate buffers elevated the pH of human plaque and saliva after a sucrose rinse.[6] More recently, the addition of baking soda to a fluoridated dentifrice was demonstrated to be effective in reducing plaque acidity, with its neutralizing effects lasting up to 60 minutes after treatment.[7] Further, a low concentration of bicarbonate ions was found to have a pronounced effect in elevating the pH in subsurface enamel lesions and enhancing remineralization.[8]

Caries still represents one of the most common diseases in the general population.[9-11] The development of dental caries is the result of the interaction between a cariogenic microflora, a diet rich in fermentable carbohydrates, and host factors.[12] Among the host-related factors, the buffering capacity of saliva has a protective effect against enamel demineralization.[13,14] Tanzer and coworkers[15] reported that both sodium bicarbonate-based dental powder and dentifrices inhibit tooth decay in rats. Anderson and Orchardson[16] suggest that increasing salivary pH with a bicarbonate gum may have implications for the prevention of human dental caries. However, and surprisingly, the research support in the dental literature for the buffering capacity to be a caries prevention opportunity is not very apparent.

Recent studies have confirmed that the prevalence of erosive dental wear is increasing and that erosive lesions can progress rapidly.[17] Dental erosion occurs as a result of acidic attacks during simultaneous unsaturation of both hydroxyl- and fluorapatite in saliva, causing loss of dental hard tissue, layer by layer.[17] Lussi and coworkers[18] reported that patients with erosion showed significantly greater decreases in pH of the dental surface after drinking orange juice compared to subjects exhibiting no dental erosion, and that the pH stayed lower for a longer period of time. The support of the buffering capacity of the saliva could therefore represent a protective factor against dental erosion.

Dentin hypersensitivity represents another disorder of the dental tissues with a growing prevalence in the general population.[19,20] It has been treated successfully with many different approaches, one of which involved the use of arginine, a basic amino acid that promotes the buffering potential of saliva.[21]

The study reported here was designed to evaluate the effects of sodium bicarbonate applied on the oral mucosa through a

new mucoadhesive spray (Cariex®, Brux S.r.l, Cislago, Varese, Italy). This spray has the ability to control the drop of the pH of the saliva after a glucose rinse, and therefore act as an enhancing agent for the buffering potential of the saliva.

Materials and Methods

Criteria for Patient Recruitment

From the students of the University of Insubria, Varese, Italy, 50 young adults (mean age 25.2; standard deviation 4.1) were selected. The subjects were healthy, free from caries or periodontitis. Participants signed an agreement form explaining the aim and the characteristics of the study. An identifying code was assigned to each subject according to the Italian legislation on privacy. The research was ethically conducted in accordance with the Declaration of Helsinki.

Measurement of pH

Assessment of the salivary pH was performed with a portable device used in gastroenterology for 24-hour monitoring of pH of the esophagus and stomach (pH-day 2®, Menfis bioMedica S.r.l., Bologna, Italy). This device has been previously used in the oral cavity.[22-24] The active part of the probe is a unique disposable unit consisting of an antimonium electrode with a reference electrode covered by resin (2.0 mm diameter), connected to the pH-meter with a thin, flexible cable that can be easily brought through the mouth-angle of the subject. The device records pH continuously, with a sampling period of 1–6 seconds, a resolution of 0.1 pH, and a range of 0.1–14 pH. The pH measurement was performed in the lower fornix in the area of the first molar.

Experimental Procedure

Tests were performed at least two hours after the last food intake and regular oral hygiene procedures. Since salivary secretion has a circadian rhythm,[25] all tests were carried out in the morning. At day 1, participants rinsed with a 10% glucose solution for one minute, and then pH was monitored continually for 40 minutes. At day 2, the same participants rinsed with a 10% glucose solution for one minute, then the mucoadhesive was sprayed on to the oral mucosa and the pH was monitored continually for 40 minutes (Figure 1). The spray was used three times; one shot on each side of the mucosa of the cheek and one shot on the tongue. No measure of the quantity of spray dispensed by the device was done. One week after the experimental procedure, the patients answered a questionnaire regarding the taste of the spray and the occurrence of any side effects.

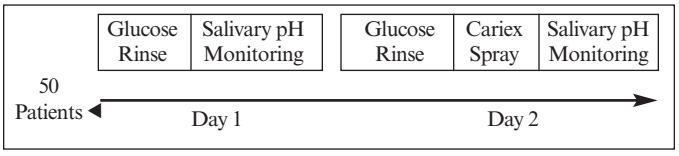

Figure 1. *Flow chart of the experimental procedure.*

Mucoadhesive Spray

Cariex is an oral spray, composed of sodium bicarbonate, xylitol, and excipients that assist flowability and flavor. The mucoadhesive capacity is due to a calibrated mixture of polyoils and ialuronic acid. According to the producer, this unique combination allows a slow release of bicarbonate for at least 40 minutes.

Statistical Analysis

The software of the pH meter showed pH values in a graphic form and displayed their mean value, as well as the minutes of consistent pH < 6 and the percentage of time the pH was < 6, with each experimental procedure.

Descriptive statistical analyses were performed to summarize the main characteristics of the subjects in the two conditions under comparison. Paired t-tests were used to study whether the means of pH and of time below the value of 6.0 differed for the subjects in the experimental conditions. The non-parametric version of the paired samples t-test, the Wilcoxon signed rank test, was also used with equivalent results (data not shown). The level of significance was set at $p < 0.05$. All analyses were performed using the Stata statistical package, version 12 (StatsCorp, LP, College Station, TX, USA).

Results

The experimental study was completed without complications. None of the patients exhibited any side effects; 86% classified the taste of the oral spray as pleasurable.

After rinsing with glucose and using Cariex, the mean salivary pH for each subject increased when compared to the corresponding test after rinsing with glucose but without the Cariex spray (Figure 2). For only two patients, the pH remained unchanged in the two tests (Figure 3). In no subjects who used the mucoadhesive spray was there a reduction of the salivary pH.

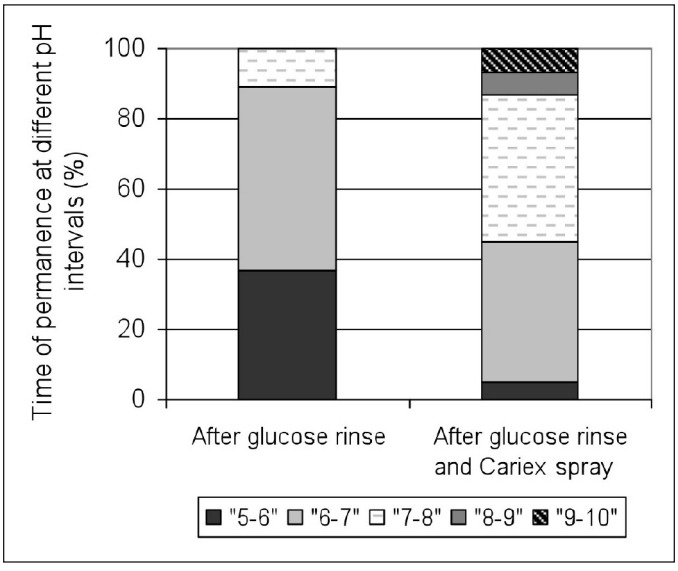

Figure 2. *Percentage of time of permanence at different pH intervals after glucose rinse with and without Cariex spray.*

In all subjects, the rinse with glucose resulted in a period of pH lower than 6.0, and the use of the spray annulled or substantially reduced the period of time the pH stayed lower than 6.0 (Figure 4). The mean time period that the pH remained lower than 6.0 after the glucose rinse was 7.1 minutes. When the spray was also used, the time for the elevation of pH was 0.7 minutes (Figure 2).

The mean values of the salivary pH of patients after rinsing with glucose were statistically different ($p < 0.01$), with (6.9) and without (6.5) the use of the mucoadhesive spray (Table I).

Discussion

In this study, the use of a spray based on sodium bicarbonate was effective in raising the salivary pH after a cariogenic challenge and in reducing the time of the pH remaining below the critical threshold of 6.0. The individual variability of the pH values recorded in this study is a well-known phenomenon since baseline values range between 6.0 and 7.4, with considerable differences found relative to the location of the sites in the oral cavity used to obtain the measurement.[26] This variability can be attributed to the variability of the baseline pH values among subjects in general, and thus different individual responses to a glucose challenge in relation to the acidophilic bacterial count and the buffering capacity of a subject's saliva.[27]

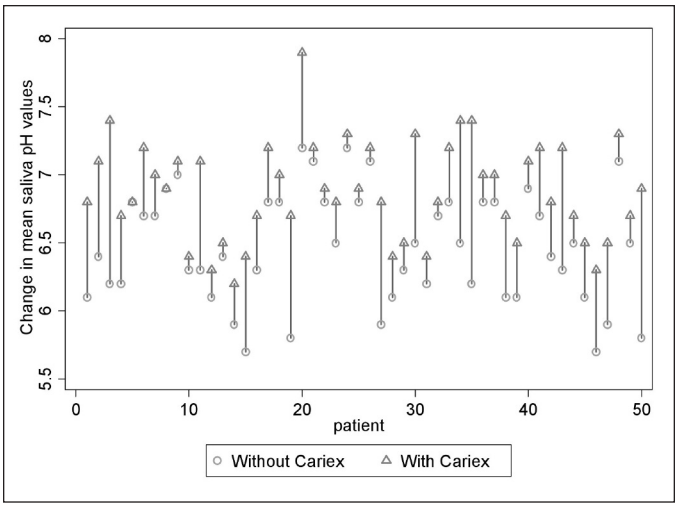

Figure 3. *Change in mean salivary pH values, shown by vertical line segments with patient number on the x-axis, after a glucose rinse with and without Cariex spray*.

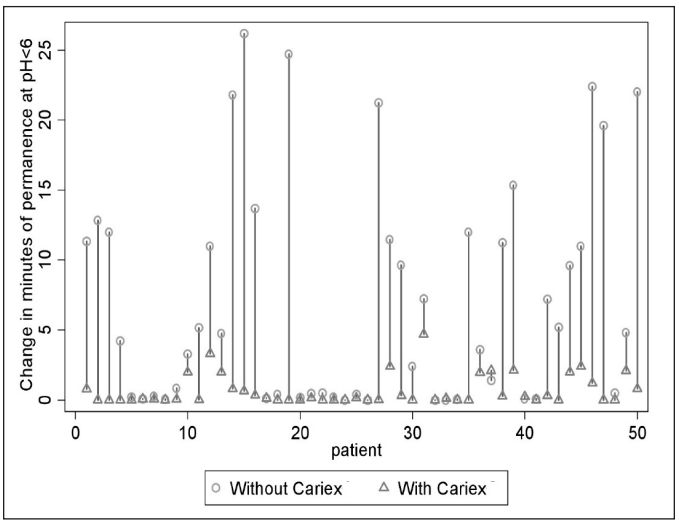

Figure 4. *Change in minutes of permanence at pH < 6, shown by vertical line segments with patient number on the x-axis, after a glucose rinse with and without Cariex spray.*

These are clinically relevant variations as demineralization of the dental enamel occurs when the pH value nears 5.7. It is reported that the critical pH of dental enamel does not have a fixed value and varies for each individual in relation to the different ions in the saliva, such as the calcium and phosphate ions which make up the hydroxyapatite of dental enamel.[28] Fluoride transforms hydroxyapatite in fluorapatite which, being less soluble than hydroxyapatite, has the effect of reducing the critical pH. Despite exposure to fluorides, there are still large segments of the population in which this is not enough to equilibrate the acidogenic challenge of the diet.[29,30] Basically, the therapeutic approach to patients with an acidogenic diet must first be addressed to control the pathogenic biofilm, otherwise fluorides or agents supporting the buffering capacity of saliva could not be sufficient to prevent the mineral loss from the tooth surface. The combined use of both bicarbonate ions for favorable alteration of the pH in subsurface lesions and aggressive application of fluorides could be effective in making early caries lesions, so-called enamel white spots, acid-resistant through remineralizing therapy, as suggested by Tanaka and Iijima.[8]

Since the salivary secretion rate and the buffering capacity of saliva already protect the teeth against acids, one way to further inhibit the acids is to add buffering agents, like bicarbonate and phosphate, to the oral cavity.[2] In the study reported here, an increase in salivary pH values was observed when the buccal mucosa of the cheek was sprayed with the mucoadhesive spray. This was noticeable in the mean pH values over the 40-minute measurement period ($p < 0.01$) and also in the time spans that the pH was < 6 ($p < 0.01$). The spray evaluated in this study kept the pH above the values considered to be harmful for dental enamel for the entire 40 minutes in which the pH was monitored. The mean percentage of time in which the pH values were below 6.0 changed from 16.6% to 2.9% when the mucoadhesive spray was applied. The mucoadhesive effect of the spray seems to permit a gradual release of sodium bicarbonate and a prolonged increase in the buffering capacity of saliva. In this study, pH values were continuously monitored via the software of the pH meter, in addition to a record of the time that the pH remained lower than 6.0.

Patients with manifest erosive lesions have a greater risk for increased tooth substance loss by erosive tooth wear than healthy individuals because of lower pH levels on tooth surfaces and lower salivary clearance capacity.[18] Gudmunsson and coworkers[22] found that salivary buffer capacity was significantly lower among erosion patients, and suggested that the consumption of acidic foods, especially soft drinks in this patient group, may be the causative

Table I
Comparison of Mean Salivary pH Values and Time in Minutes of Permanence at pH < 6
After a Glucose Rinse With and Without Cariex Spray

	pH				Minutes of Permanence at pH < 6			
	Without Cariex Spray	With Cariex Spray	t-test	p-value	Without Cariex Spray	With Cariex Spray	t-test	p-value
Whole Sample	6.5 (0.4)	6.9 (0.4)	-9.30	< 0.00	7.1 (7.8)	0.7 (1.1)	5.82	< 0.00

factor of erosion in subjects predisposed to enamel dissolution because of a low buffering capacity. According to the results reported in the present study, in these sorts of patients a device supporting the buffering capacity of the saliva could be particularly beneficial in preventing permanence of pH at levels at which tooth mineral loss is possible. Messias and coworkers[31] reported that rinsing with a sodium bicarbonate solution after a simulated endogenous erosive challenge controlled enamel surface loss, but did not remain available in the oral cavity for acting against future acidic challenges. The mucoadhesive effect of the spray tested here could represent a solution to this problem, together with the portability that permits patients to use the product at any time an acidic attack occurs in the oral cavity.

According to the ecological plaque hypothesis, caries can be prevented by interfering with the key factors moving the ecological changes in the oral cavity; Marsh[32] has underlined that a low pH represents one of these key factors. The support of the buffering capacity of the saliva can, in this context, assume an important role in the prevention of caries disease. Moreover, the mucoadhesive spray tested in this study contains xylitol and, as suggested by Campus and coworkers,[33] xylitol can affect the oral ecology by decreasing plaque acidogenicity, producing a modification in the microbial composition of the oral biofilm.

This study has some strengths and limitations. One strength is the device used for monitoring pH. The thin and flexible cable of the pH meter used in this study could easily be brought through the mouth-angle of the subjects, causing less disturbance of the salivary clearance of the oral cavity. This approach permits the subjects to breath and swallow normally, and salivary pH to be monitored continually.[22-24] Other authors have stated the importance of considering salivary clearance when studying the pH of the oral cavity, showing that pH tended to become more acidic when a surface of the oral cavity became dehydrated.[34,35] Another strength lies in the continuous recording of the salivary pH and in the possibility to easily observe the total time of the level of pH < 6 through the use of the pH meter software.

A limitation of the study was that the quantity of spray dispensed by the device during the experimental tests was not measured. However, from a research perspective this became less of a factor because the device delivers the same quantity of active ingredients with each spray. In this study, 50 young adults were assessed, and further studies should be conducted on a larger sample if this new approach to the prevention of tooth mineral loss were to be proposed as a method of prevention on a large scale. Furthermore, the beneficial effect of containing the lowering of the salivary pH needs to be verified on the tooth surface, and also in patients in whom the acidic diet challenge is particularly strong, such as in the case of xerostomia, gastroesophageal reflux, or alimentary disorders.

Conclusions

Supporting the buffering capacity of saliva represents an approach to the prevention of caries and dental erosion, and to the treatment of xerostomia and dentin hypersensitivity that has still not been sufficiently studied. The product tested in this study significantly increased the salivary pH after a glucose rinse, keeping it above the threshold values for dental enamel demineralization. We therefore believe it can be used as a preventive tool that could be useful in reducing the amount of mineral tissue loss following acid attacks on tooth surfaces. Cariex represents a versatile device that is portable and can be used after consuming snacks, beverages, or foods, or after acid attacks occurring in case of vomiting, regurgitation, or gastroesophageal reflux.

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Original article

Impact of a sodium carbonate spray combined with professional oral hygiene procedures in patients with Sjögren's syndrome: an explorative study

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Impact of a sodium carbonate spray combined with professional oral hygiene procedures in patients with Sjögren's syndrome: an explorative study

Objectives: The aim of this study was to make an initial estimation on the effects of a sodium bicarbonate and xylitol spray (Cariex®), associated with non-surgical periodontal therapy, in participants with primary Sjögren's syndrome.
Background: Sjögren's syndrome (SS) is a multisystem autoimmune disease that predominantly involves salivary and lachrymal glands, with the clinical effect of dry eyes and mouth.
Materials and methods: A prospective cohort of 22 women and two men has been evaluated. They were randomized into three groups (eight patients each): Group A) those treated once with non-surgical periodontal therapy, education and motivation to oral hygiene, associated with the use of Cariex®; Group B) treated only with Cariex®; Group C) treated only with non-surgical periodontal therapy, education and motivation to oral hygiene. Clinical variables described after treatment were unstimulated whole salivary flow, stimulated whole salivary flow, salivary pH, reported pain (using Visual Analogue Scale) and the Periodontal Screening and Recording index.
Results: Salivary flow rate improved in all groups, but the difference was statistically significant only in those treated with Cariex®, alone or in combination with periodontal therapy. Gingival status improved in participants who underwent periodontal non-surgical therapy while remained unchanged in those only treated with Cariex®. Reported pain decreased in all groups, showing the best result in participants treated with periodontal therapy together with Cariex®.
Conclusions: We propose a practical approach for improving gingival conditions and alleviating oral symptoms in patients with SS. Future randomized and controlled trials are however required to confirm these results as well as larger population, and also assessing other parameters due to oral dryness, possible oral infections and more comprehensive periodontal indices.

Keywords: sodium carbonate spray, oral hygiene, salivary flow, Sjögren.

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Introduction

Sjögren's syndrome (SS) is a multisystem autoimmune disease characterised by hypofunction of the salivary and lacrimal glands[1]. SS may occur alone and is defined as primary SS, or in association with other autoimmune diseases; therefore, it is defined as secondary SS[2]. Dysfunction and destruction of the exocrine glands (relating also to alterations in secretory products) are associated with lymphocytic infiltration and immunological hyperactivity, with 88% of SS subjects having a reduced salivary flow rate, followed by complaints of xerostomia in the 75–92% range.

The distinctive reduction in saliva production (hyposalivation) is often associated with meaningful consequences for oral health. A feeling of a dry mouth (xerostomia), difficulty to talk, swallow and eat, difficulty in controlling dentures, taste disturbances and burning sensation are among the most frequent subjective symptoms reported[3,4]. These symptoms have a typically

negative impact on the oral health-related quality of life of patients[5,6].

Patients with SS may also have a significantly higher dental plaque accumulation if compared to healthy controls[7], leading to many dental and gingival problems.

Glandular manifestations of SS are mostly alleviated with symptomatic treatments – such as saliva substitutes and eye lubricants – and/or cholinergic stimulators; the latter however, in association with other different systemic therapy usually prescribed, are related to many potential adverse effects[8,9].

The aim of this study was to make a preliminary estimate on the effects of a sodium bicarbonate and xylitol spray (Cariex®), associated with non-surgical periodontal therapy, on oral discomfort and gingival status of people with primary SS.

Materials and methods

Participants enrolled

Consecutive Caucasian participants, attending the Oral Medicine Section of the CIR – Dental School, University of Turin, Italy, from January to October 2014, were selected.

The inclusion criteria were (i) diagnosis of primary SS on the basis of AECG criteria[10], (ii) presence of reported complaint of xerostomia; (iii) ability to complete the present clinical trial. The exclusion criteria were (i) earlier head and neck radiotherapy, (ii) diagnosed lymphoma, (iii) hepatitis C infection, (iv) pregnant or breastfeeding subjects, (v) to have <20 natural teeth.

Different treatment options were discussed with the participants, and they all submitted written informed consent before enrolment, which was carried out in accordance with the Helsinki Declaration. The ethics review board of the CIR – Dental School approved the study.

Clinical recordings

All participants had their unstimulated whole salivary flow (UWS) measured mid-morning, at least 2 h after the last food intake; they were asked to allow all saliva to drain into a beaker by drooling or gentle spitting; they were instructed not to chew, swallow or speak. Saliva was collected for a period of 15 min and the flow expressed in ml/min. Ten minutes later, stimulated whole salivary flow (SWS) was measured by dropping citric acid on the dorsum of the tongue every 60 s[11].

Permanent dentitions were studied for decayed, missing and filled teeth (DMFT): all teeth with a realistic suspicion of or definitely showing a cavity in the dentin layer were assigned to the D component; filled and crowned teeth were evaluated as component F; missing teeth were assigned to the M component.

The periodontal condition was assessed with the use of the Periodontal Screening and Recording (PSR) index. The examination was performed with the World Health Organization probe at six points per tooth, and the PSR score was recorded using the following criteria: '0' if probing depth (PD) < 3.5 mm, no bleeding on probing (BOP) and no calculus; '1' if PD < 3.5 mm, BOP and no calculus; '2' if PD < 3.5 mm, BOP and calculus is present; '3' if PD is 3.5–5.5 mm; and '4' if PD is >5.5 mm. The highest score was determined for each sextant of the dentition. Using the PSR scores, the periodontal classification was categorised as follows: (i) healthy: maximum one sextant score 1 or 2, (ii) gingivitis: score 0–2, maximum one sextant score 3, (iii) moderate periodontitis: >1 sextant score 3, maximum one sextant score 4, and (iv) severe periodontitis: >1 sextant score 4.

The subjective oral discomfort was assessed by the xerostomia questionnaire (XQ-I), a self-administered tool with eight questions, the sum of which is transformed linearly to produce the final summary score ranging from 0 to 100, with higher scores representing greater levels of xerostomia[12].

Moreover, the reported pain due to xerostomia was assessed by Visual Analogue Scale (VAS), consisting of a 100-mm vertical line marked with 0 (=no pain) to 100 (=most severe pain experienced)[13].

Levels of USW pH were measured using an Oakton ph5/6® pH meter (Eutech Instruments Europe B.V., Landsmeer, the Netherlands) with an Hamilton Minitrode® electrode.

The EULAR Sjögren's Syndrome Disease Activity Index (ESS-DAI) was also used to score disease activity at baseline[14].

Experimental design

The product tested (Cariex®, Brux srl, Cislago, Italy) is a novel mucoadhesive spray that contains sodium bicarbonate, xylitol, polyols, hyaluronic acid and various excipients. It was used for 89 days.

The participants were randomized into three groups: Group A) treated once with non-surgical periodontal therapy, education and motivation to oral hygiene, associated with the use of Cariex®; Group B) treated only with Cariex®; Group C)

treated only with non-surgical periodontal therapy, education and motivation to oral hygiene.

Allocation to the three different groups was performed by non-clinical staff via a permuted random block approach and was concealed in opaque envelopes, which were opened on the first visit data collection (T0).

After every meal (three times daily), the Cariex® had to be applied three times in correspondence with the buccal mucosa of the cheek; then participants had to wait 20 min before performing standard oral hygiene procedures.

Group A and C received non-surgical periodontal therapy (once at baseline), consisting of supra- and subgingival scaling with removal of all deposits and staining. They were also instructed about oral hygiene maintenance at home. Instructions included modified Bass technique with medium brushes always associated with interdental brushes. Patients were advised to change brushes every 4 weeks and to change interdental brushes every 2 weeks.

The study was single blinded; a skilled single examiner (A.C.) visited participants and performed the follow-up visits or clinical measurements at baseline (T0), after 30 and 90 days from the procedure (T1–T2) (Table 1).

Table 1 Clinical protocol and indexes evaluation.

Pro-operative time (during the 2 months prior to T0):
Clinical evaluation
Investigation to detail inclusion and exclusion criteria
Randomization
Baseline _Day 0 (T0):
Clinical evaluation
Pain and symptoms reported evaluation
Unstimulated whole salivary flow (UWS) record
Stimulated whole salivary flow (SWS) record
pH analysis
Dental (DMFT index) and periodontal (PSR index) evaluation
Oral hygiene instruction and periodontal therapy (Group A and C)
Start therapy with Cariex® (Group A and B)
Time 1_Day 30 (T1):
Clinical evaluation
Adverse effects evaluation
Time 2_Day 90 (T2):
Clinical evaluation
Pain evaluation
Unstimulated whole salivary flow (UWS) record
Stimulated whole salivary flow (SWS) record
pH analysis
Periodontal (PSR index) evaluation
Adverse effects evaluation
Stop therapy with Cariex® (Group A and B) (at day 89)

Statistical design

This is a descriptive exploratory study. Sample size was not estimated on the lack of any previously reported changes in alleviating xerostomia in patients with SS using a sodium bicarbonate and xylitol spray with non-surgical periodontal therapy. However, a possible sample size was calculated on a supposed overall efficacy of 85% and 35% for both treatments and only one, respectively; with a power of 80% and a type I error of 0.05, at least 24 patients had to be recruited.

The statistical analysis was performed using the Kruskal–Wallis test to assess the variability between samples at baseline, the Wilcoxon signed-ranks test to assess the difference in each group before and after treatment proposed and the Mann–Whitney test for comparison between the three groups at the end of therapy. Statistical significance level was set at 0.05. SPSS (SPSS for Windows, version 19, SPSS Inc, Chicago, IL, USA) statistical software was utilised.

Results

A total of 22 women and two men were selected; the average age at presentation was 64.58 years. Of the 24 patients with SS, eight were treated in each of the three different protocols.

At baseline, demographical and clinical parameters showed no statistical differences in the study population (Table 2). Saliva substitutes were used in 15 patients (62.5%) (five patients in each group; $p = 1$). Specific medications for SS above all taken by our cohort study population were hydroxychloroquine (25%), systemic steroids (20.8%) and methotrexate (4.1%), with no differences between groups (data not shown).

Changing of clinical parameters, before (T0) and after (T2) the proposed protocols, is reported in Table 3. Salivary production improved in every groups; the differences, however, were statistically significant only in Group A and Group B if considering UWS. pH values increased in all groups, but in a statistically manner only for those participants not treated with Cariex® ($p = 0.03$). Gingival status statistically improved in participants who underwent periodontal non-surgical therapy while remained almost unchanged in those only treated with Cariex®. Reported pain decreased in all groups, showing the best result in participants treated with periodontal therapy together with Cariex® ($p = 0.03$).

Table 2 Demographical and clinical parameters analysed at baseline for each group.

	Group A	*Group B*	*Group C*	p^a
Variables[b]				
Age [years]	61.25 (±4.73)	68.88 (±2.88)	63.63 (±3.75)	0.49
Unstimulated whole salivary flow	0.21 (±0.06)	0.34 (±0.13)	0.61 (±0.25)	0.82
Stimulated whole salivary flow	0.99 (±0.32)	1.12 (±0.34)	1.21 (±0.47)	0.83
Salivary pH recording	6.82 (±0.13)	6.44 (±0.16)	6.62 (±0.21)	0.25
Periodontal evaluation (PSR)	3.25 (±0.31)	3.13 (±0.23)	3.00 (±0.27)	0.77
Date of diagnosis of SS				
From 2003 to 2008 (n° of pts)	3	2	2	0.89
After 2009 to 2013 (n° of pts)	5	6	6	0.93
Xerostomia questionnaire	82.5 (±12.51)	79.4 (±10.51)	78.9 (±9.59)	0.79
EULAR Sjogren's Syndrome Diseases Activity Index	17.71 (±5.49)	12 (±7.03)	18.56 (±11.98)	0.37
Underlying disease:				
Hypertension (n° of pts)	1	2	2	ns
Diabetes (n° of pts)	0	0	0	ns
Previous cancer (n° of pts)	1	0	0	ns
Thyroiditis (n° of pts)	1	1	0	ns
Pain evaluation (VAS)	7.88 (±0.51)	6.38 (±0.70)	6.75 (±0.56)	0.17
Dental evaluation (DMFT)	13.87 (±1.66)	19.12 (±1.69)	18.87 (±2.95)	0.16

[a]Kruskal–Wallis test.
[b]Variables: the Periodontal Screening and Recording index (PSR); Visual Analogue Scale (VAS); decayed, missing and filled teeth (DMFT).

Table 3 Changing of clinical parameters before (T0) and after (T2) the proposed protocol for the three different groups.

	T0	*T2*	*Z*	p^a
Unstimulated whole salivary flow				
Group A	0.21 (±0.06)	0.56 (±0.20)	−2.214[b]	**0.03**
Group B	0.34 (±0.13)	0.62 (±0.24)	−2.032[b]	**0.04**
Group C	0.61 (±0.25)	0.92 (±0.36)	−1.604[b]	0.11
Stimulated whole salivary flow				
Group A	0.99 (±0.32)	1.20 (±0.31)	−0.674[b]	0.50
Group B	1.12 (±0.34)	1.31 (±0.31)	−0.365[b]	0.71
Group C	1.21 (±0.47)	1.72 (±0.59)	−1.841[b]	0.07
Salivary pH				
Group A	6.82 (±0.13)	7.06 (±0.15)	−1.378[b]	0.17
Group B	6.44 (±0.16)	6.60 (±0.19)	−1.633[b]	0.10
Group C	6.62 (±0.21)	7.09 (±0.14)	−2.207[b]	**0.03**
Periodontal evaluation (PSR)				
Group A	3.25 (±0.31)	2.25 (±0.25)	−2.530[c]	**0.01**
Group B	3.13 (±0.23)	3.00 (±0.19)	−1.000[c]	0.32
Group C	3.00 (±0.27)	1.88 (±0.23)	−2.460[c]	**0.01**
Reported pain (VAS)				
Group A	7.88 (±0.51)	6.00 (±0.80)	−2.214[c]	**0.03**
Group B	6.38 (±0.70)	6.13 (±0.69)	−0.447[c]	0.65
Group C	6.75 (±0.56)	6.25 (±0.45)	−1.633[c]	0.10

[a]Wilcoxon signed-ranks test.
[b]Based on negative ranks.
[c]Based on positive ranks.
The bold values are statistically significant.

Finally, a comparison of gained results between the three protocols was made (Table 4), reporting few differences. The only statistical data were obtained between Group B and Group C: participants treated only with Cariex® did not show a better gingival status after the end of the follow-up period.

None of the patients treated with Cariex® reported any adverse effects.

Discussion

In this study, we preliminarily showed the outcome that the combined use of a sodium bicarbonate and xylitol spray (Cariex®), associated with non-surgical periodontal therapy, had in patients with SS. Salivary flow rate statistically improved only in participants treated with Cariex®, alone or in combination with periodontal therapy. Gingival status improved only in those who underwent periodontal non-surgical therapy. Reported pain decreased in all groups, showing the best result if treated with periodontal therapy together with Cariex®.

Oral symptoms reported are very common among patients with SS: feeling of dry mouth, difficulty to talk, swallow and eat, difficulty in controlling dentures, taste disturbances and burning

Table 4 Comparison of obtained results, between the three different groups, at the end of the protocol (T2).

T2		*p*[a] *(A vs. B)*	*p (B vs. C)*	*p (C vs. A)*
Unstimulated whole salivary flow				
Group A	0.56 (±0.20)	1.00		
Group B	0.62 (±0.24)		0.80	
Group C	0.92 (±0.36)			0.72
Stimulated whole salivary flow				
Group A	1.20 (±0.31)	0.88		
Group B	1.31 (±0.31)		0.72	
Group C	1.72 (±0.59)			0.72
Salivary pH				
Group A	7.06 (±0.15)	0.06		
Group B	6.60 (±0.19)		0.06	
Group C	7.09 (±0.14)			0.80
Periodontal evaluation (PSR)				
Group A	2.25 (±0.25)	0.06		
Group B	3.00 (±0.19)		**0.00**	
Group C	1.88 (±0.23)			0.33
Reported pain (VAS)				
Group A	6.00 (±0.80)	0.96		
Group B	6.13 (±0.69)		0.89	
Group C	6.25 (±0.45)			0.96

[a]Mann–Whitney test.

sensation are among the most frequent. These symptoms may have a negative impact on the oral health-related quality of life[9]. In this study, we only assessed reported pain, but future study must be directed to analyse all other parameters. The VAS for symptoms showed a statistically significant difference at T0 and T2 only for participants treated with both protocols (Group A). This may suggest that the synergistic action of the sessions of oral hygiene and sodium bicarbonate, applied on the oral mucosa, could decrease subjective reported oral pain in patients with SS.

To date, there are few data focused on the possible correlation between SS and periodontal disease, although with some contradiction. One analysis of the relative risk of periodontitis showed that the SS group developed periodontal disease twice often if compared to the control group[7], but other authors did not find any correlations[15]. In our study, it is also possible to assume that patients with SS had a poor gingival and periodontal status. All patients in groups A and C were subjected to non-surgical periodontal therapy and showed an improvement of PSR at the end of treatment. We also have a significant difference of PSR ($p = 0.005$) between the second and the third group; this difference was predictable because in group C, non-surgical periodontal was performed, unlike group B. No significant difference was found between group A and group B; this could be due to the limits of the PSR index: one single site may affect the assessment assigned to the whole sextant and could not represent the complete periodontal status of the patients[12].

It has been known for a long time that patients with SS have greater susceptibility to develop caries and susceptibility to infections[16–18]. Particularly, root and incisal caries, which are occasionally detected among the general population, are of greater apprehension for those with SS[19]. In healthy people with suitable salivary output, bacteria are dislocated from the teeth by the mechanical process of chewing, tongue movement and salivary flow; however, for those suffering from SS, impaired salivary flow does not permit the oral self-cleansing which buffers, lubricates and performs essential antimicrobial duties[19,20]. Despite the small sample of this study, the data obtained are in agreement with these studies.

To date, sodium bicarbonate has never been tested in patients with SS; few reports on its use are present in literature but in healthy subjects and for a limited period. It has been reported that a chewing bicarbonate-containing gum could have a positive effect on salivary flow rate and in pH[21]. More recently, the Cariex® spray has been positively tested, showing to control the lowering of salivary pH following carbohydrate consumption[22].

Our exploratory results showed that the sodium bicarbonate spray could have a partial effect and could not affect salivary acidity for a long period; however, in combination with periodontal non-surgical therapy, it could be useful in controlling oral discomfort for patients with SS; moreover, even if the average age of participants was in the mid-sixties, it has to be said that this protocol could also be useful for younger patients with SS. Patients' related outcome, measured with VAS, appeared to be the main indicator supporting the use of Cariex® in those patients.

Subjects who underwent both protocols showed statistically significant differences for the salivary flow values, gingival parameters and symptoms reported. In terms of clinical evaluation, a change in salivary pH was observed in patients after they had been instructed to correct oral hygiene at home and were able to maintain a good compliance, as PSR indexes of all groups show the following: in fact, lowering the oral bacteria has contributed to a change in the pH of saliva to basic values observed over a period of 3 months.

Treatment for SS is symptomatic and supportive; with no adequate amount of saliva to give proper oral pH and regulate microbial populations, the mouth can rapidly be colonised with more pathogenic microorganisms. A personalised treatment plan must be developed, and a preventive oral health plan should include meticulous oral hygiene instructions to improve the quality of life, and avoid further complications[19].

Conclusion

To the best of our knowledge, similar data have never been reported.

This exploratory study found possible beneficial effects of a sodium bicarbonate and xylitol spray (Cariex®) when combined with non-surgical periodontal therapy on oral discomfort and gingival status of people with primary SS. However, it seems that the effectiveness of the offered treatment had a limited range of action. For this reason, it is essential that patients with SS undergo regular oral and dental examinations.

We propose a practical approach for managing the problematic oral health conditions in patients with SS, providing possibly measurements that can be used to fully test the effectiveness of this or other preventive agents in subjects with dry mouth. Future randomized and controlled trials are actually required to confirm these results as well as larger population, and also assessing other parameters (such as talking, swallowing and eating, controlling dentures, taste disturbances and burning sensations), oral infections and more comprehensive periodontal indices.

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RIASSUNTO

Scopo del lavoro Valutare se l'aggiunta di bicarbonato alla saliva attraverso un nuovo spray mucoadesivo applicato sulle mucose orali è in grado di contrastare la discesa del pH e quindi di sostenere la capacità tampone della saliva dopo uno sciacquo con soluzione glucosata.
Materiali e metodi È stato selezionato un campione di 30 soggetti adulti in buone condizioni di salute orale e generale. La misurazione del pH è stata effettuata al giorno 1 nel fornice inferiore nella zona dei primi molari, i soggetti hanno sciacquato la bocca con 10 ml di soluzione glucosata al 10% e il pH è stato monitorato per 40 minuti. Al giorno 2 è stata ripetuta la stessa procedura sperimentale con l'aggiunta di 3 spruzzi di spray mucoadesivo in corrispondenza della mucosa geniena. Il prodotto applicato è a base di bicarbonato di sodio, xilitolo ed eccipienti.
Risultati È stata riportata una certa variabilità individuale nei valori di pH registrati. Senza l'utilizzo del prodotto testato il pH è risultato significativamente inferiore ($p=0,0016$). Il tempo di permanenza a valori di $pH<6$ è significativamente diminuito applicando lo spray mucoadesivo ($p=0,001$), il prodotto testato inoltre ha esplicato la propria azione per tutti i 40 minuti in cui il pH salivare è stato monitorato.
Conclusioni Lo spray mucoadesivo è stato in grado di contrastare la discesa del pH dopo risciacquo con soluzione glucosata. Il sostegno della capacità tampone salivare attraverso questo nuovo approccio potrebbe avere un ruolo importante nella prevenzione della carie e dell'erosione dentale.

PAROLE CHIAVE pH salivare, capacità tampone, glucosio, bicarbonato di sodio, spray mucoadesivo.

ABSTRACT

Aim of the work The aim of this research was to evaluate if sodium bicarbonate, applied on the oral mucosa through a new mucoadhesive spray, can counteract the drop of saliva pH after a glucosal rinse and support the buffering capacity of saliva. The mucoadhesive spray contains sodium bicarbonate, xylitol and excipients.
Materials and methods A sample of 30 healthy adults was selected. The measurement of the salivary pH was performed at day 1 in the lower fornix in correspondence of the lower molars. Each subject rinsed with 10 ml of a 10% glucosal solution and then pH was monitored for 40 minutes. At day 2 the same experimental procedure was repeated, but the mucoadhesive spray was applied three times in correspondence of the buccal mucosa of the cheek.
Results The subjects showed individual variability in the pH values recorded. Without the bioadhesive spray salivary pH resulted significantly lower (p 0,0016). The time span during which pH values were lower than 6 was significantly shortened when the product tested was applied on the oral mucosa (p 0,001). This effect was observed for all the 40 minutes during which pH was recorded.
Conclusion The mucoadhesive spray tested resulted able to contrast the drop of the salivary pH after a glucosal rinse. The support of the buffering capacity of the saliva with this new approach could play an important role in the prevention of caries and dental erosion.

KEYWORDS salivary pH, buffering capacity, glucose, sodium bicarbonate, mucoadhesive spray.

INTRODUZIONE

La patologia cariosa è in stretta correlazione con le caratteristiche della dieta, della salivazione e del biofilm batterico presente sulle superfici dentali. Un frequente consumo di carboidrati e la conseguente variazione del pH generata dalla fermentazione degli zuccheri da parte dei batteri presenti nella placca batterica dentale inducono alterazioni microbiologiche all'interno del biofilm in cui i batteri stessi sono organizzati (1-3). L'abbassamento del pH crea infatti un ambiente che favorisce la crescita di microrganismi acidofili tra i quali troviamo lo Streptococcus mutans e i Lattobacilli che vengono a trovarsi in condizioni ideali per promuovere ulteriori abbassamenti del pH ed eventuali aree di demineralizzazione dello smalto. Tra gli zuccheri presenti nella dieta il saccarosio è considerato il più cariogeno per la facilità con cui può essere metabolizzato dai batteri con il conseguente rilascio di acidi e riduzione del pH (4-6).
Il pH della placca riveste pertanto un ruolo fondamentale nell'equilibrio della flora del biofilm presente sulle superfici dentali e il suo abbassamento costituisce una spinta selettiva a favore di specie batteriche acidofile in grado di mantenere, se adeguatamente nutrite, condizioni di persistente acidità nell'ambito del biofilm stesso. Quando vengono introdotti alimenti nel cavo orale e si verifica un abbassamento del pH, questo è seguito da una risalita verso valori più basici grazie all'azione compiuta dalla saliva che esplica una funzione tampone calmierante del pH che permette, in condizioni di salute, una restituzione del tessuto minerale andato perso in seguito all'attacco acido dello smalto (7, 8). In questo equilibrio tra fenomeni di demineralizzazione e remineralizzazione la capacità tampone della saliva gioca quindi un ruolo fondamentale (9). La capacità tampone della saliva mostra inoltre una correlazione inversamente proporzionale con l'indice di prevalenza di carie ed è dovuta soprattutto al bicarbonato presente nella saliva stessa (10). L'idrogenocarbonato di sodio o bicarbonato di sodio è un sale di sodio dell'acido carbonico usato in diverse preparazioni farmaceutiche come antiacido. In campo odontoiatrico è stato studiato l'effetto del bicarbonato sul pH orale veicolato in gomme da masticare, in gel e in compresse, col risultato di ottenere un considerevole effetto di sostegno della capacità tampone della saliva (11, 12).
Nella letteratura scientifica vi è inoltre evidenza sui rapporti tra capacità tampone della saliva e fenomeni di erosione dentale; è stata infatti riscontrata una insufficiente capacità di contrastare la discesa del pH in soggetti affetti da erosione, sottolineando l'importanza di sostenere in questi casi la capacità tampone della saliva (13-16). Quest'ultima capacità sembra quindi avere un ruolo fondamentale nei casi di erosione, ancor maggiore rispetto ai casi di pazienti con carie (17). È noto inoltre che i pazienti che soffrono di xerostomia possono presentare una riduzione della capacità tampone della saliva ed è pertanto ipotizzabile che anche pazienti di questo tipo possano trarre beneficio da un prodotto che consenta di rendere più efficaci i sistemi di controllo salivare del pH (11,12,16). Diversi autori sottolineano inoltre che esistono ancora gruppi di pazienti in cui l'esposizione al fluoro è insufficiente per bilanciare l'effetto acidogeno dei carboidrati introdotti con la dieta (18, 19) e che pertanto è necessario mettere a punto nuove e più mirate strategie di prevenzione.
Lo scopo di questa sperimentazione è studiare il comportamento del pH della saliva dopo sciacquo con una soluzione glucosata e la successiva applicazione di un nuovo spray mucoadesivo (Cariex; Brux s.r.l, Cislago - VA). Il prodotto testato è composto da bicarbonato di sodio, xilitolo, polioli, acido ialuronico ed eccipienti.
Si vuole osservare se l'aggiunta di bicarbonato alla saliva attraverso lo spray mucoadesivo sia in grado di contrastare la discesa del pH e quindi di sostenere la capacità tampone della saliva e se l'adesività del prodotto consenta un'azione prolungata per un tempo sufficiente a evitare abbassamenti clinicamente rilevanti del pH salivare.

MATERIALI E METODI

Selezione del gruppo sperimentale

È stato selezionato un campione di 30 soggetti adulti tra i pazienti della Clinica Odontoiatrica dell'Università degli Studi dell'Insubria. Il campione di popolazione selezionato presentava buone condizioni di salute orale (assenza di carie, parodontite, lesioni delle mucose orali) e anamnesi negativa per qualsiasi tipo di patologia sistemica ed è stato pertanto sottoposto a visita odontoiatrica e alla compilazione di un questionario anamnestico, acquisendo anche il consenso informato sulla raccolta dei dati personali e sulle caratteristiche dell'esame a scopo di ricerca. Ad ogni paziente esaminato è stato assegnato un codice identificativo (una lettera e un numero) nel rispetto della legge n. 675 del 31/12/1996 e successive modifiche sulla privacy. Le procedure seguite sono conformi alle norme etiche proposte dal comitato responsabile della sperimentazione umana e alla Dichiarazione di Helsinki del 1975.

Analisi del pH

L'analisi del pH salivare è stata effettuata con un pH-metro (pH-day 2; Menfis bioMedica s.r.l.) portatile a due canali, impiegato per registrazioni esofagee di 24 ore, dotato di una sonda all'antimonio monouso, già impiegato in altri studi sul pH salivare (20). L'apparecchio registra in continuo il valore del pH con un periodo di campionamento da 1 a 6 secondi, con una risoluzione di 0,1 pH e un range da 0,1 a 14 pH. La sonda impiegata prima di ogni esame è calibrata con una soluzione tampone pH 1 e pH 7 secondo le istruzioni fornite dalla ditta produttrice. Il filo che connette la

sonda con il pH-metro è sottile e flessibile essendo studiato per l'utilizzo naso-gastrico, e può essere comodamente usato nel cavo orale anche per monitoraggi lunghi facendo fuoriuscire il filo nella zona dell'angolo della bocca senza provocare alterazioni dell'omeostasi salivare.
Tutti i rilievi sono stati eseguiti durante le ore mattutine: i soggetti si sono presentati a digiuno e senza aver effettuato manovre di igiene orale da almeno due ore. La misurazione del pH è stata fatta al giorno 1 nel fornice inferiore nella zona dei primi molari, i soggetti hanno sciacquato la bocca con 10 ml di soluzione glucosata al 10% e il pH è stato monitorato per 40 minuti. Al giorno 2 è stata ripetuta la stessa procedura sperimentale con l'aggiunta di 3 spruzzi di spray mucoadesivo in corrispondenza della mucosa geniena.

Analisi statistica

Sono state elaborate le medie e le mediane dei valori di pH ottenuti con le relative deviazioni standard nei soggetti nei due tempi del test. È stato calcolato il tempo di permanenza del pH a valori inferiori a 6 e la percentuale corrispondente sui 40 minuti in cui il pH è stato monitorato. I risultati sono stati confrontati con il test di Wilcoxon-Mann-Whitney per valutare la significatività delle differenze riscontrate.

RISULTATI

La procedura sperimentale è stata condotta senza complicazioni, nessuno dei pazienti testati ha riferito effetti collaterali. Alla domanda se l'applicazione del prodotto

	Monitoraggio pH salivare per 40 minuti dopo sciacquo con soluzione glucosata senza applicazione di spray mucoadesivo bicarbonato				Monitoraggio pH salivare per 40 minuti dopo sciacquo con soluzione glucosata e applicazione di spray mucoadesivo bicarbonato			
	Media	Mediana	Tempo di permanenza a pH<6		Media	Mediana	Tempo di permanenza a pH<6	
			min	%			min	%
1	6,1	6,1	11,3	28,3	6,8	6,6	0,8	2,0
2	6,4	6,2	12,8	32,1	7,1	7,0	0,0	0,0
3	6,2	6,1	12,0	29,0	7,4	7,4	0,0	0,0
4	6,2	6,1	4,2	10,5	6,7	6,6	0,0	0,0
5	6,8	6,9	0,2	0,6	6,8	6,9	0,0	0,0
6	6,7	6,6	0,1	0,2	7,2	7,1	0,1	0,2
7	6,7	6,6	0,3	0,7	7,0	7,0	0,1	0,1
8	6,9	6,7	0,1	0,1	6,9	6,8	0,0	0,0
9	7,0	7,1	0,8	2,1	7,1	7,0	0,1	0,1
10	6,3	6,4	3,3	8,2	6,4	6,4	2,0	5,0
11	6,3	6,2	5,2	12,8	7,1	7,0	0,0	0,0
12	6,1	6,0	11,0	27,3	6,3	6,2	6,1	15,1
13	6,4	6,4	4,7	11,8	6,5	6,4	2,0	4,9
14	5,9	5,9	21,8	53,2	6,2	6,0	11,5	28,7
15	5,7	5,7	26,2	65,3	6,4	6,5	0,6	1,5
16	6,3	6,2	13,7	34,0	6,7	6,5	0,3	0,8
17	6,8	6,9	0,1	0,3	7,2	7,2	0,1	0,3
18	6,8	6,7	0,4	1,0	7,0	6,9	0,0	0,0
19	5,8	5,7	24,7	61,7	6,7	6,5	0,0	0,0
20	7,5	7,5	0,2	0,4	7,9	7,9	0,2	0,4
21	7,1	7,0	0,5	1,2	7,2	7,2	0,2	0,3
22	6,8	6,6	0,5	0,1	6,8	6,6	0,0	0,0
23	6,5	6,5	0,2	0,4	6,8	6,6	0,0	0,0
24	7,2	7,2	0,0	0,0	7,3	7,4	0,0	0,0
25	6,8	6,7	0,4	1,0	6,9	6,6	0,1	0,3
26	7,1	7,1	0,0	0,0	7,1	6,9	0,0	0,0
27	5,9	5,9	21,2	55,2	6,8	6,5	0,0	0,0
28	6,3	6,0	11,5	29,0	6,4	6,4	10,9	27,7
29	6,3	6,0	9,6	24,4	6,5	6,5	0,3	0,8
30	6,5	6,5	2,4	6,2	7,3	7,2	0,0	0,0
media	6,5	6,5	6,6	16,6	6,9	6,8	1,2	2,9

TAB. 1 *Media, mediana, tempo e percentuale di tempo di permanenza a pH<6 del pH salivare, nei 40 minuti di monitoraggio con e senza applicazione di spray mucoadesivo nei 30 soggetti testati.*

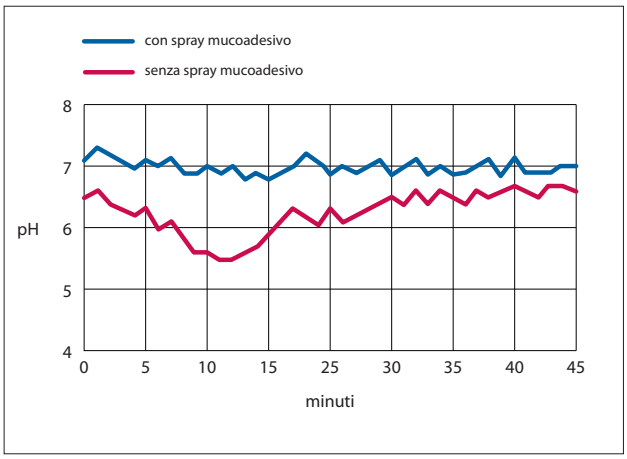

FIG. 1 *Grafico di andamento delle medie di pH salivare con e senza spray mucoadesivo a base di bicarbonato nei 40 minuti di monitoraggio.*

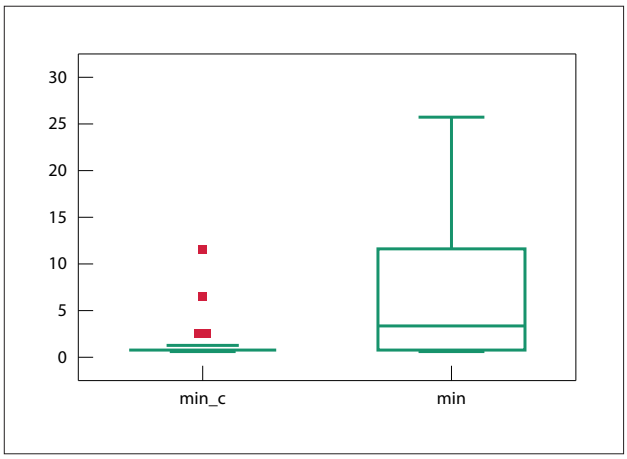

FIG. 2 *Distribuzione dei valori medi dei tempi di permanenza a pH<6 con (min_c) e senza il prodotto testato (min).*

pH medio senza spray mucoadesivo	pH medio con spray mucoadesivo	Significatività
6,5	6,9	P=0,0016

TAB. 2 *Confronto dei valori medi di pH ottenuti nei 40 minuti di monitoraggio con e senza il prodotto testato.*

pH<6 senza spray mucoadesivo	pH<6 con spray mucoadesivo	significatività
6,6 minuti	1,2 minuti	P=0,0001

TAB. 3 *Confronto dei tempi medi, espressi in minuti, di permanenza a pH<6, sui 40 minuti di monitoraggio, con e senza il prodotto testato.*

causasse una sensazione di gusto sgradevole, nullo o piacevole, il 100% dei soggetti ha risposto piacevole. Dopo ogni monitoraggio del pH il software del pH-metro ha permesso di ottenere un grafico dell'andamento dei valori di pH, un'elaborazione dei valori medi registrati, del tempo di permanenza a valori di pH<6 e della percentuale di tempo in minuti, sui 40 testati, in cui il pH risultava a valori <6.

I risultati hanno mostrato valori di pH instabili, con continue oscillazioni rispetto ai valori basali. Nella tabella riassuntiva (tab. 1) sono riportati i dati registrati durante i 40 minuti di monitoraggio del pH salivare con e senza applicazione dello spray mucoadesivo. È stata riportata una certa variabilità individuale nei valori di pH registrati, i valori iniziali sono infatti compresi in un range tra 5,9 e 7,5. Le variazioni di pH verso il basso o verso l'alto hanno mostrato in ogni paziente ampiezze diverse; sebbene utilizzando i risultati calcolati come media, minuto per minuto nei 40 monitorati, è stato possibile ottenere un grafico dell'andamento del pH salivare medio di tutti i soggetti analizzati con e senza il prodotto testato (fig. 1). Le tabelle 2 e 3 riportano i dati relativi al confronto tra i dati medi ottenuti con e senza l'applicazione del prodotto testato. Nella figura 2 è possibile osservare la distribuzione delle medie dei tempi di permanenza a pH<6 durante i 40 minuti di monitoraggio del pH.

DISCUSSIONE

La secrezione salivare presenta un ritmo circadiano al quale pare contribuire l'ormone antidiuretico; è noto che durante il sonno il flusso salivare si riduce notevolmente (21). Per questa ragione è stato deciso di condurre i test durante le ore mattutine e tutti i soggetti testati erano a digiuno da almeno 2 ore, in modo da uniformare per quanto possibile la situazione di partenza prima della stimolazione con lo sciacquo di soluzione glucosata.

Il cavo sottile e flessibile collegante la punta attiva della sonda al pH-metro veniva fatto uscire in corrispondenza dell'angolo della bocca ed è stato così possibile effettuare una registrazione in continuo dei valori salivari di pH con il minimo disturbo dell'omeostasi e della clearance salivare del cavo orale. Altri autori hanno sottolineato l'importanza del rispetto della clearance salivare negli studi sul pH, mostrando come, quando una superficie della bocca va incontro a disidratazione, il pH tenda a scendere risultando più acido (22-24).

La variabilità individuale riscontrata nei valori di pH salivare è un fenomeno già conosciuto nella letteratura. Il pH del cavo orale mostra infatti valori basali medi compresi tra 6,0 e 7,4 con nessuna differenza significativa tra i due sessi ma con notevoli differenze rispetto ai siti di prelievo (25). I dati da noi riportati sono in accordo con queste osservazioni, il monitoraggio del pH è iniziato su-

bito dopo lo sciacquo con soluzione glucosata e i valori iniziali variavano tra 5,9 e 7,5 senza l'applicazione del prodotto testato. Questo risultato può essere interpretato considerando i valori di pH basali diversi tra un soggetto e l'altro e la risposta individuale diversa alla sfida glucogena in relazione alla carica batterica acidofila presente e alla capacità tampone salivare del soggetto (2).
Applicando 3 spruzzi dello spray mucoadesivo testato sulla mucosa geniena è stato osservato un innalzamento dei valori di pH salivare (tabb. 2 e 3), riscontrabile sia nei valori medi sui 40 minuti ($p=0,0016$) ma anche nei tempi di permanenza a $pH<6$ ($p=0,0001$). Si tratta di variazioni clinicamente rilevanti essendo indicato a 5,7 il valore di pH vicino al quale si possono osservare fenomeni di demineralizzazione dello smalto. Sappiamo in realtà che il pH critico per lo smalto non è costante, varia da soggetto a soggetto in relazione anche al contenuto salivare di diversi ioni, tra i quali troviamo ioni calcio e fosfato che compongono l'idrossiapatite dello smalto (26). Il fluoro trasforma l'idrossiapatite in fluoridrossiapatite, che essendo meno solubile ha l'effetto di abbassare il pH critico. Sappiamo però che nonostante l'esposizione al fluoro esistono ancora importanti parti della popolazione del mondo occidentale in cui questo non è sufficiente a bilanciare la sfida acidogena della dieta (18, 19). Fenomeni come l'erosione dentale e la xerostomia mostrano infatti una prevalenza in deciso aumento (17), inoltre indagini epidemiologiche recenti effettuate sul territorio nazionale hanno evidenziato una prevalenza di circa il 44% di bambini con esperienza di carie all'età di 12 anni (27). Molto vi è pertanto ancora da fare perché queste manifestazioni patologiche del cavo orale possano essere prevenute in maniera efficace. In quest'ottica il sostegno alla capacità tampone della saliva rappresenta un approccio ancora poco studiato. Per esempio Anderson e collaboratori (8) e Igarashi e collaboratori (11) hanno messo in luce l'utilità dell'aggiunta di bicarbonato alla saliva attraverso la gomma da masticare allo scopo di controllare la discesa del pH della placca dopo somministrazione di glucosio. I risultati dello studio da noi condotto sono in accordo con i dati riportati dagli autori precedentemente citati. Lo spray mucoadesivo da noi testato ha mantenuto il pH al di sopra dei valori considerati dannosi per lo smalto per tutti i 40 minuti in cui il pH è stato monitorato. La percentuale media di tempo in cui i valori di pH risultavano inferiori a 6 sono passati da 16,6% a 2,9% applicando lo spray mucoadesivo (tab. 1, fig. 2). Sembra pertanto che l'effetto mucoadesivo consenta un rilascio progressivo del bicarbonato e un aumento della capacità tampone della saliva prolungato nel tempo. Ulteriori studi, già in corso, dovranno confermare se l'aumento del pH salivare ottenuto si rifletta effettivamente in un beneficio per quanto concerne la quota di tessuto duro perso dallo smalto quando questo subisce un attacco acido. Da sottolineare inoltre è che il campione oggetto dello studio è rappresentato da giovani adulti privi di carie e di erosione dentale, è ipotizzabile che l'effetto benefico di sostegno della capacità tampone della saliva possa risultare ancora più marcato nei pazienti affetti da queste condizioni patologiche.
La praticità dello spray mucoadesivo lo rende uno strumento versatile, utilizzabile dal paziente in diversi momenti della giornata, per un suo utilizzo dopo assunzione di snack, bevande o alimenti; particolarmente utile potrebbe essere riportare i valori di pH a livelli in cui i fenomeni di demineralizzazione sono stati controllati prima di effettuare manovre meccaniche d'igiene orale. Lo smalto infatti subisce uno stress per l'attacco acido e una certa quota di tessuto minerale viene spesa per neutralizzare l'acidità della placca. Quest'osservazione è in accordo con quanto sostenuto da Wiegand e collaboratori (28) che hanno sostenuto l'utilità di attendere la fine dell'attacco acido sullo smalto prima di effettuare lo spazzolamento dei denti per minimizzare i fenomeni di erosione. Osservazioni sul pH sono state fatte anche per l'ipersensibilità dentinale, sono state proposte infatti soluzioni terapeutiche risultate efficaci basate sull'aumento del pH con dentifrici, soluzioni e gel a base di arginina, un amminoacido fortemente basico (29). È ipotizzabile pertanto un effetto benefico del prodotto testato in questo studio nei confronti dell'ipersensibilità dentinale, ricerche sono in corso per verificare queste osservazioni.
Si pongono pertanto basi concrete per ritenere il bicarbonato un principio attivo efficace nel gestire la prevenzione della carie anche su larga scala; in tal senso potrebbe essere utilizzato come sostanza nelle gomme da masticare o nelle caramelle nella grande distribuzione (30).

CONCLUSIONI

Il sostegno della capacità tampone salivare rappresenta un approccio alla prevenzione della carie e dell'erosione dentale e al trattamento della xerostomia e dell'ipersensibilità dentinale ancora poco studiato. Il prodotto da noi testato in questo studio preliminare è stato in grado di innalzare in maniera significativa il pH della saliva dopo applicazione di glucosio, portandolo al di sopra dei valori soglia di demineralizzazione dello smalto. Si pensa pertanto che possa rappresentare uno strumento di prevenzione utile per ridurre la quota di tessuto minerale che va persa in seguito all'attività degli acidi sulle superfici dentarie. Ulteriori studi sono in corso per verificare gli effetti del prodotto sul pH della saliva e dello smalto anche nei pazienti affetti da carie e da erosione dentale.

CONFLITTI D'INTERESSE

Nessuno degli autori dichiara conflitti d'interesse economico, lo studio presentato è indipendente e non è stato sostenuto da fonti di finanziamento.

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