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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Abstract

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 females and 2 males has been evaluated. They were randomized into three groups (8 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.

Introduction

Sjögren's syndrome (SS) is a multisystem autoimmune disease characterized 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 to 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: a) diagnosis of primary SS on the basis of AECG criteria (10); b) presence of reported complaint of xerostomia; c) ability to complete the present clinical trial. The exclusion criteria were: a) earlier head and neck radiotherapy; b) diagnosed lymphoma; c) hepatitis C infection; d) pregnant or breast-feeding subjects; e) to have less than 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 two hours 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 minutes 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 seconds (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 to 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 categorized as follows: 1) healthy: maximum one sextant score 1 or 2; 2) gingivitis: score 0 to 2, maximum one sextant score 3; 3) moderate periodontitis: >1 sextant score 3, maximum one sextant score 4; and 4) severe periodontitis: >1 sextant score 4.

The subjective oral discomfort was assessed by the xerostomia questionnaire (XQ-I), a self-administered tool with 8 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 (3 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 minutes before performing standard oral hygiene procedures.

Group A and C received non-surgical periodontal therapy (once at baseline), consisting of supra- and sub-gingival 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).

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 SS patients by 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 3 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 utilized.

Results

A total of 22 females and 2 males were selected; the average age at presentation was 64.58 years. Of the 24 patients with SS, 8 were treated in each of the 3 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%) (5 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, are 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® ($p=0.03$).

Finally, a comparison of gained results between the 3 protocols was made (Table 4), reporting few differences. The only statistical data was 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 preliminary 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 SS patients: feeling of dry mouth, difficulty to talk, swallow and eat, difficulty in controlling dentures, taste disturbances and burning 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 scale 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 SS patients 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 SS patients have greater susceptibility to develop caries and susceptibility to infections (16-18). Particularly, root and incisal caries, which are occasionally detected amongst 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 SS patients; 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 SS patients. 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: in fact, lowering the oral bacteria has contributed to a change of the pH of saliva to basic values observed over a period of three 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 colonized with more pathogenic microorganisms. A personalized 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 SS patients 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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