Management of patients suffering from xerostomia with a combined mouthrinse containing sea salt, xylitol and lysozyme

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Dry mouth, including xerostomia, is a common symptom especially in older adults. The causes of dry mouth include medication, autoimmune disease (Sjögren's Syndrome), radiotherapy or chemotherapy for cancer, hormone disorders and infections (1-3). There is a huge variety of therapeutic approaches for relieving dry mouth symptoms such as chewing-gum, sugar-free lozenges, moisturizers and toothpastes, but most of them are are frequently restricted to palliative treatment. A Cochrane review concluded that there is no strong evidence that any topical therapy is effective in relieving the symptom of dry mouth, and more studies are required to provide evidence to guide clinical care (4-7).

The inclusion of antimicrobial agents, such as lysozyme, lactoferrin, lacoperoxidase, or xylitol in xerostomia healthcare products, was proposed as early as the 1990s, and appears to be a promising approach for the prevention of microbial-related diseases in xerostomic patients (8, 9). Despite the significant prevalence of xerostomia in the general population, however, no standard treatment guidelines exist. Successful treatments are typically individualized for the specific patient and should be targeted at the underlying pathophysiology of the disease (10-12).

The aim of the present study was to evaluate the efficiency of a combined mouthrinse containing purified water, sea salt, xylitol, lysozyme, and menthol (H2Ocean Sea Salt Mouthwash) in the management of patients suffering from xerostomia and hyposalivation.

MATERIALS AND METHODS

Study subjects

The present study was conducted at a dental community cabinet in collaboration with the University of Bari Aldo Moro, Italy. A total of 30 patients between the ages of 40 and 70 years (mean age 57±1) were enrolled and divided into two categories. In order to have the unbiased and accurate clinical data, a double-blind protocol was followed for enrolment of the patients in terms of treatment plan and further categorization into a study group. All eligible

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subjects were given oral information about the products and the purpose of the study and signed an informed consent, in accordance with the ethical principles originating in the Declaration of Helsinki and consistent with good clinical practices.

Participants with dry mouth symptoms, regardless of their salivary flow, were included in the study, while patients having major systemic diseases, patients who had taken pilocarpine or cevimeline in the 7 days preceding the study and who refused to participate during the follow-up were excluded from the study group. The two groups of patients were called for follow-up after treatment on the 90th day to check the overall response on the mouthwash or placebo treatment.

A randomized double-blind, placebo-controlled, parallel group design was used for this study. A computer-generated double randomization sequence was carried out by an investigator who was not directly involved in the treatment and the assessment of the subjects. After completing baseline measures, participants were stratified by gender and randomized into one of two groups. The subjects were then categorized into two treatment regimes in groups I and II (15 in each group). Both the mouthrinses were made to look identical:

Group I (n = 15): H2Ocean Sea Salt Mouth rinse (H2Ocean, Inc. FL. USA);

Group II (n = 15): Placebo mouth rinse (physiologic saline solution with no mouthwash dilution added).

Participants were asked to rinse twice a day after brushing - once in the morning and once at night before going to bed - for 12 weeks. Patients were instructed to rinse with 15 mL of the solution for at least 1 min followed by expectoration of the residual mouthrinse and to avoid eating and drinking for 30 min afterwards. To avoid the effect of new variables, subjects were asked to continue their usual daily brushing method during the study period using a toothbrush with extra soft bristles and non-medicated fluoride free dentifrice. Written instructions were provided explaining how to use the mouthwash. Rinsing was performed at home without supervision. To check for

Table I. *Variations reported between baseline (T_0) and after a cycle of treatments (T_1) with the 2 proposed protocols in the 2 different groups.*

Unstimulated whole salivary flow	**T_0**	**T_1**
Group 1(Test)	0.21	0.56
Group 2(CTRL)	0.34	0.62
Stimulated whole salivary flow		
Group 1 (Test)	0.99	1.20
Group 2(CTRL)	1.12	1.31
Salivary pH		
Group 1(Test)	6.82	7.06
Group 2(CTRL)	6.44	6.60

compliance, subjects were asked to note the times of day when they rinsed.

Signs of oral dryness were registered clinically by clinical observation of lip and oral mucosa dryness. Oral mucosa dryness was recorded when the investigator noticed the absence of a saliva coating over most of the dorsum of the tongue, buccal and labial mucosa as well as the absence of pooled saliva in the floor of the mouth.

Clinical parameters

Plaque Index (PI) was taken from all participants by the same blinded trained examiner at baseline and at the end of the sudy. The PI was recorded by assigning a score to each surface (5 for great amount of plaque present, 0 for totally absent) and calculating the percentage of total tooth surfaces that revealed the presence of plaque.

Salivary flow rate and pH

In order to measure salivary flow rate, unstimulated saliva was collected by direct emission into a sterile plastic glass. Measurements were performed between 8 and 10 a.m. using the expectoration method. Saliva was weighed with high precision scales. Patients did not drink, perform oral hygiene, or smoke for at least 60 min beforehand. Salivary flow above 0.25 ml/min was considered normal.

The pH value of the saliva is lower in unstimulated than in stimulated saliva. The pH value of saliva cited in literature is in the range of 6-7, making it slightly acidic, but when stimulated it may increase to about 7.8. Evaluations were made before and after 12 weeks of product/placebo application.

Statistical analysis

Outcome measures of the exploratory study were analyzed with a *t*-test for paired samples for pre/post differences with time as the factor using Statistical Package for Social Sciences (SPSS for Windows, Version 11.5, Chicago, Ill) software, to detect significant differences between pre-test and post-test scores.

RESULTS

All subjects (N = 30) completed the trial, and there were no missing values. No adverse events or

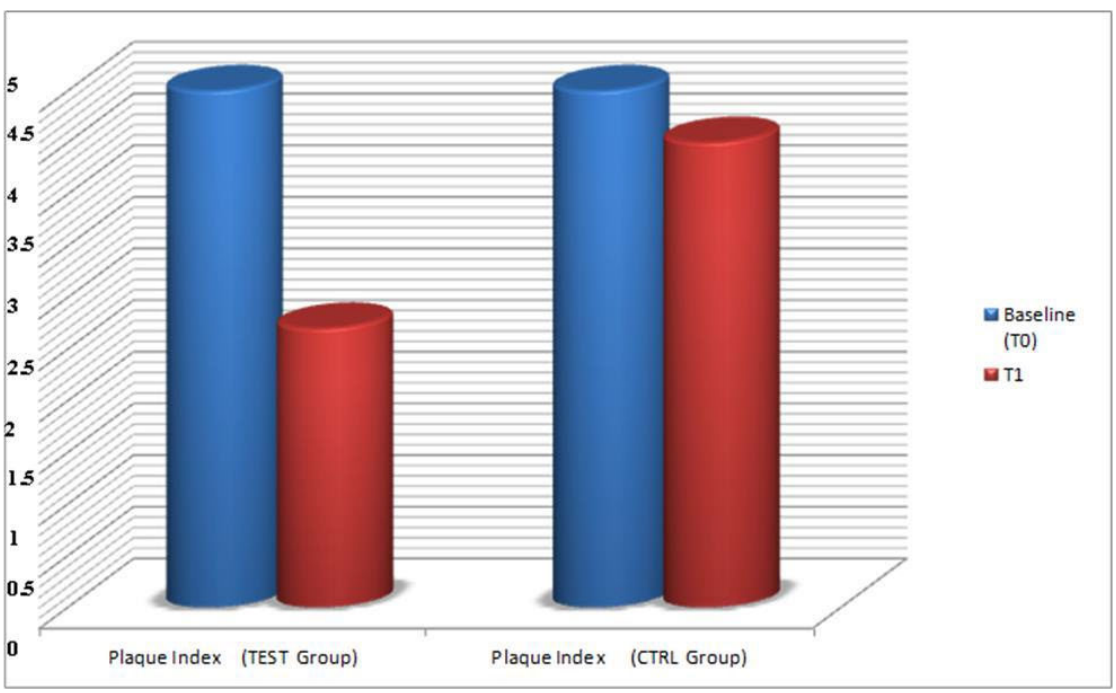

Fig. 1. *Clinical Index results before and after the study period.*

side effects were reported or observed. All the clinical parameters were recorded for both groups during the study at baseline (TO) and at the end of study, i.e. at 90 days (T1). The amounts of mouthwash used indicated good compliance with the instructions. No adverse events or side effects were reported or observed. A sample of 18 women and 12 men with xerostomia underwent treatment with H2Ocean Sea Salt Mouthrinse or a similar placebo-mouthrinse.

Salivary flow rate and pH analysis, at 12 weeks of treatment application in the test group, showed an improvement of approximately 19.9% and 9.52%, respectively, for unstimulated vs stimulated whole salivary flow, and 33.33% of pH parameters compared to the control group (Table I). The clinical scores for the test and control groups at baseline and at the end of the experimental study period are shown in Fig. 1, showing a reduction of 50% from baseline in the test group compared to the control group (16% from baseline). These results support that H2Ocean Sea Salt Mouthwash worked significantly to improve all the clinical parameters and to promote salivary flow activity in patients affected by Xerostomia.

DISCUSSION

Xerostomia, the main causes of which are the use of drugs and hormonal disorders, is a condition that affects 1-29% of the population, especially adults and the elderly (4-8). This condition is on the rise and negatively affects the quality of life of patients, causing problems with swallowing, chewing and speech, therefore leading to social and psychological problems. There are no products or drugs that can cure all the symptoms of this condition, however various topical products such as gels, sprays, mouthwashes and toothpastes which can improve the patient's quality of life have been tested (2, 6). This is, of course, also possible through timely diagnosis and appropriate treatment for each patient.

There is a lack studies in the literature that have tested the effectiveness and effects of a sea salt and xylitol rinse on dry mouth and xerostomia patients. The results reported in this pilot study after H2Ocean Sea Salt Mouthwash treatment are significantly positive in all aspects and symptoms of xerostomia. Obviously, further clinical studies should be carried involving a larger cohort of subjects, and perhaps a longer trial period.

This approach may provide a valuable addition or alternative to the armamentarium of treatment options for oral hygiene procedures in xerostomia and dry mouth syndrome, preventing dental plaque formation, with the additional benefit of no alcohol presence in the solution. It could be concluded that H2Ocean Sea Salt Mouthrinse contains excellent daily oral hygiene agents, and its use should be promoted based on the present and previous scientific knowledge of its benefits and proper use.

REFERENCES

1. Inchingolo F, Dipalma G, Cirulli N, et al. Microbiological results of improvement in periodontal condition by administration of oral probiotics. J Biol Regul Homeost Agents 2018; 32:1323-28.
2. Cantore S, Ballini A, Mori G, et al. Anti-plaque and antimicrobial efficiency of different oral rinses in a 3-day plaque accumulation model. J Biol Regul Homeost Agents 2016; 30:1173-78.
3. Ballini A, Scacco S, Coletti D, Pluchino S, Tatullo M. Mesenchymal stem cells as promoters, enhancers, and playmakers of the translational regenerative medicine. Stem Cells Int 2017; 2017:3292810.
4. Ballini A, Cantore S, Farronato D, et al. Periodontal disease and bone pathogenesis: the crosstalk between cytokines and porphyromonas gingivalis. J Biol Regul Homeost Agents 2015; 29:273-81.
5. Ballini A, Gnoni A, De Vito D, et al. Effect of probiotics on the occurrence of nutrition absorption capacities in healthy children: a randomized double-blinded placebo-controlled pilot study. Eur Rev Med Pharmacol Sci 2019; 23:8645-57.
6. Foti C, Romita P, Rigano L, et al. Isobornyl acrylate: an impurity in alkyl glucosides. Cutan Ocul Toxicol 2016; 35:115-9
7. Grassi FR, Pappalettere C, Di Comite M, et al. Effect of different irrigating solutions and endodontic sealers on bond strength of the dentin-post interface with and without defects. Int J Med Sci 2012; 9:642-54.

8. Cicinelli E, Ballini A, Marinaccio M, Poliseno A, Coscia MF, Monno R, De Vito D. Microbiological findings in endometrial specimen: our experience. Arch Gynecol Obstet 2012; 285:1325-29.
9. Ballini A, Santacroce L, Cantore S, et al. Probiotics efficacy on oxidative stress values in inflammatory bowel disease: a randomized double-blinded placebo-controlled pilot study. Endocr Metab Immune Disord Drug Targets 2019; 19:373-381.
10. Ballini A, Santacroce L, Cantore S, et al. Probiotics improve urogenital health in women. Open Access Maced J Med Sci 2018; 6:1845-50.
11. Cantore S, Mirgaldi R, Ballini A, et al. Cytokine gene polymorphisms associate with microbiogical agents in periodontal disease: our experience. Int J Med Sci 2014; 11:674-79.
12. Cantore S, Ballini A, Farronato D, et al. Evaluation of an oral appliance in patients with mild to moderate obstructive sleep apnea syndrome intolerant to continuous positive airway pressure use: Preliminary results. Int J Immunopathol Pharmacol. 2016 Jun;29(2):267-73.