Gerodontology

Original article

Evaluation of the efficacy of two mouthrinses formulated for the relief of xerostomia of diverse origin in adult subjects

Irene Morales-Bozo[1], **Gonzalo Rojas**[2,3], **Ana Ortega-Pinto**[2], **Iris Espinoza**[2], **Lilian Soto**[4], **Anita Plaza**[1], **Carla Lozano**[1] and **Blanca Urzúa**[1]

[1]Oral Biology and Oral Biochemistry Laboratory, Department of Basic and Communitarian Sciences, Faculty of Dentistry, University of Chile, Chile; [2]Department of Pathology, Faculty of Dentistry, University of Chile, Chile; [3]Dento-Maxilo-Facial Service, Clinical Hospital, University of Chile, Chile; [4]Reumathology Division, Clinical Hospital, University of Chile, Santiago, Chile

doi: 10.1111/j.1741-2358.2012.00626.x

Evaluation of the efficacy of two mouthrinses formulated for the relief of xerostomia of diverse origin in adult subjects

Objective: To evaluate the efficacy of two new mouthrinses in the reduction of xerostomía-associated symptomatology.
Background: Xerostomia is a common chronic health condition that affects a great number of adults and significantly deteriorates quality of life, such that treatment is necessary.
Materials and methods: Sixty-seven adult subjects of both sexes presenting xerostomia of diverse origin were selected. Mouthrinses were tested using a double-blind, randomized, cross-over clinical trial with an intervining wash out period.
Results: The 100% of subjects presented sensation of dry mouth, and 86% stated sensation of thick saliva. Burning tongue sensation, need to drink liquids to swallow and the sensation of swallowing difficulty were recorded in more than 50% of the patients. The most frequent pathologies in the sample were depression, arthritis, and arterial hypertension. Results of the clinical tests showed that mouthrinse 1 relieves sensation of dry mouth, need to drink liquids, and swallowing difficulty. In contrast, mouthrinse 2 relieves only latter two symptoms. Both rinses were more effective in relieving xerostomía-associated symptomatology in patients taking 3 or more medicines simultaneously.
Conclusion: Both mouthrinses were effective in relieving various xerostomia symptoms, could be distributed at a low cost, thereby improving the quality of life of population affected.

Keywords: xerostomia, mouthwash, palliative management, clinical trial.

Accepted 4 September 2011

Introduction

Saliva is a complex fluid that is fundamental for adequate function of the oral system. It facilitates the digestion of food and speech articulation. It lubricates, cleans and maintains the integrity of the mucosa and teeth. It provides bactericidal and antifungal properties, as well as other systems of protection[1].

Xerostomia is the subjective sensation of dry mouth, a symptom that may or may not be accompanied by hyposalivation, described as a reduction in salivary flow (below 0.1–0.2 ml/min, for total unstimulated saliva, or below 0.7 ml/min, for total stimulated saliva)[2,3].

Diverse local or systemic pathologies may affect salivary secretion, producing the sensation of dry mouth. Among these pathologies are Sjögren syndrome, rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, primary biliary cirrhosis, diabetes mellitus, acquired immunodeficiency syndrome and depression[4–10]. An important causal factor among cancer patients is radiation therapy of the head and neck. Additionally, the consumption of diverse medicines, such as tricyclic antidepressants, sedatives and tranquilisers, anticonvulsants, antihistamines, antihypertensives, antispasmodics, and diuretics, provoke a sensation of dry mouth[11]. Reduced salivary flow and the sensation of dry mouth are significant determinants of quality of life in elderly people[12]. A substantial segment of these populations requires treatment for xerostomia for different reasons[6,10].

Once a diagnosis has been established, multidisciplinary step-based management of the condition must be implemented. This management consists in the relief of symptoms, treatment of oral conditions, improvement of salivary function if possible and management of underlying systemic conditions[8]. When there is residual salivary gland function, the stimulation of secretion may be obtained through masticatory and gustatory stimulation, with medications, and through acupuncture[13]. When glandular function is severely compromised, the management of symptoms may turn to the use of salivary substitutes (artificial saliva), oral mucosa moisturisers and lubricants in the form of gels, rinses, sprays or toothpastes[8,14,15].

At a national level in Chile, synthetic products aimed at reducing or relieving xerostomia are generally high in cost for the patient and can only be obtained from a compounding pharmacy, that is, a pharmacy where custom medications are compounded to meet unique patient needs. Today, low-cost mouthrinses for xerostomia of any origin, which are available without a medical prescription and which are distributed nation-widely within the specialised market, have yet to be formulated.

For these reasons, and because of the increase in the prevalence of symptoms related to the sensation of dry mouth, burning tongue and lack of lubrication, two rinses were formulated independently to relieve these symptoms. To relieve mucosa irritability in xerostomic patients, we created an innocuous formulation with a fluid consistency, non-irritating agents, a low level of flavourings, neutral pH and without sugar. To reduce the sensation of lack of lubrication in xerostomic patients, citric acid was added to the aforementioned formulation to serve as a salivary stimulation agent. Moisturising and lubricating agents were also added, which gave the solution a more viscous consistency. The objective of this study was to evaluate the efficacy of two new mouthrinses in the reduction in symptomatology associated with xerostomia of diverse origin, through the performance of a randomised clinical trial.

Materials and methods

Patients

A group of 67 volunteer adult patients with xerostomia of diverse origin was included, having been recruited from the diagnostic clinics of the school of dentistry and the dentomaxillofacial and rheumatological clinics of the Clinical Hospital of the University of Chile. Patients were selected according to the following inclusion criteria: (i) adults of either sex at the age of 40 and (ii) presenting with sensation of dry mouth of any origin, as determined by the xerostomia survey utilised by Fox *et al.*[3]. The criteria of exclusion were as follows: (i) lesions of the oral mucosa that were visible upon clinical inspection, (ii) history of hypersensitivity to mouthrinses, (iii) oral motor deficits and (iv) severe cognitive deterioration. The health history of the patients was taken and extra and intraoral examinations were performed. The intraoral exam included an inspection of the state of the mucosa and teeth, and the data were registered in clinical records. The study was approved by the Ethics Committee of the School of Dentistry at the University of Chile. All of the patients signed informed consent forms to participate in the study.

Study design

Figure 1 presents details of the study design, which corresponds to a randomised crossover clinical study, with progressive recruitment and a washout period. Patients, recruiters, event coordinators, technicians and data analysts were all blinded. Prior to the beginning of the study, the volunteers were assigned to one of the two groups by block randomisation (random allocation software). This was a simple randomisation that identified

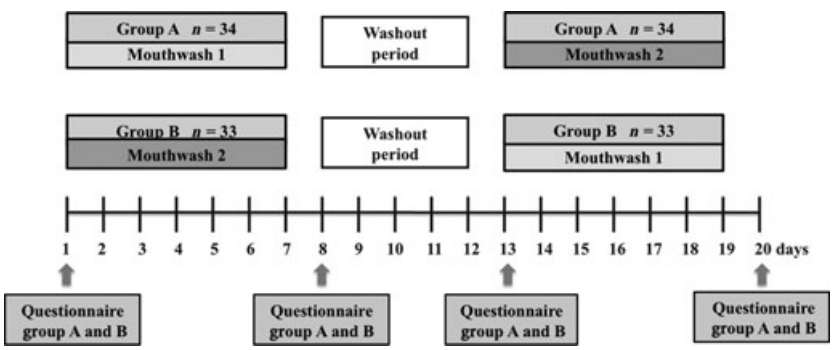

Figure 1 Experimental Design of Study.

sequentially the subjects assigned either to the intervening group or the control group. The randomisation sequence was concealed from the research team that was encharged of the clinical assessment. To conceal the randomisation sequence, the containers of both mouthrinses were labelled with a code number whose meaning was only known to the team member who generated the sequence. Subsequently, on day 1, half of the patients (n = 34, group A) started the study using rinse 1 and the other half (n = 33, group B) started the study using rinse 2. Patients used the appropriate solution for 7 days. Later, there was a 4-day washout period, in which the patients were instructed to suspend the use of the rinses. On day 13, the order of the mouthrinses administered to the patients was inverted, and the patients used the rinses for seven more days. At the beginning of days 1 and 13 of the study, a survey determining the xerostomia baseline was performed to evaluate the severity of xerostomia before the use of the rinse being tested. This survey corresponds to the transformation on the visual analogue scale (VAS) of the questions found in the survey proposed by Fox *et al.*[3]. At the beginning of days 8 and 20 of the study, this survey was again applied to evaluate xerostomia after use of the mouthrinses being tested. In the survey, the VAS has a scale of 1–10, in which '1' represents the absence of symptom and '10' represents the maximum imagined symptomatic perception. For all the survey items, the positive pole is located at 1, which represents a lower grade of perception.

By chance, both groups were equivalent in terms of the severity of xerostomia at the beginning of the study, because there was no statistic difference (p value >0.05) when comparing survey results for the sensations of dry mouth, thick saliva, burning tongue, need to drink liquids to swallow food and swallowing difficulty, before the patients used the rinses.

To calculate the sample size, we used a difference of proportions between the two groups of 0.4 ml/min, with an alpha error of 0.05, a power of 0.8 and a two-tailed hypothesis.

Rinses tested

In this study, two new mouthrinses, which are registered in Chile by the Public Health Institute (ISP), were tested as to their ability to reduce symptomatology of patients with xerostomia of diverse origin. Rinse 1 was composed principally of an aqueous solution containing xylitol, sodium fluoride, cetylpyridinium chloride, sodium chloride and spearmint flavouring. Rinse 2 was composed of the same components as rinse 1, with the addition of propylene glycol, aloe vera, glycerine and citric acid.

Measurement of total unstimulated salivary flow

After a fasting period of at least 2 h, measurements were performed between 9 and 11 AM using the expectoration method. Before the collection of saliva, patients rinsed their mouths with water and waited for 5 min. Patients were then asked to deposit the saliva produced during a 5-min period into a container. The total volume of collected saliva was determined gravimetrically, and the salivary flow, expressed in ml/min, was determined by assigning a density of 1.0 g/ml to the salivary fluid. Those patients presenting salivary flows less than or equal to 0.2 ml/min were considered hyposialic.

Determination of main results

The principal parameter was the relief of xerostomia, as determined by the comparison of the score values of the responses in the survey conducted both before and after use of the test rinses.

Determination of secondary results

The secondary results were hyposialia and severity of xerostomia, as determined by the responses in the survey conducted before the patients used the test rinses.

Statistical analysis

Relief of xerostomia and severity of xerostomia were measured using VAS (ordinal scale). Hyposialia was expressed as a dichotomous variable. The variable salivary flow was measured in ml/min, and the median and range were determined. To compare differences between groups, the Student's t-test or the Wilcoxon test was used, according to the case. Data were analysed using STATA 8.1 software (Stata Corporation LP, College Station, TX, USA). Statistically significant differences were accepted with an alpha error ≤0.05% and a confidence interval of 95%.

Results

Age and gender composition of the sample

The population under analysis comprised 67 volunteer subjects with xerostomia of diverse origin, with average age of 60.10 ± 13.47 years. Among

Table 1 Frequency and percentage of subjects affected by symptomatology associated with xerostomia based on the survey described by Fox *et al.*[3].

Symptomatology	*n*	%
Sensation of dry mouth	67	100
Sensation of thick saliva	54	80.6
Sensation of burning tongue	35	52.2
Need to drink liquids to swallow	39	58.2
Sensation of difficulty in swallowing food	34	50.8

these individuals, 60 were women and seven were men.

Symptomatology associated with xerostomia in the sample

Table 1 presents the parameters of xerostomia symptoms, based on the survey described by Fox *et al.*[3]. All of the patients reported the sensation of dry mouth, this being the principal criterion of inclusion in the study. The sensation of thick saliva was present in 80.6% of the patients; the other parameters included in the survey proposed by Fox *et al.*[3] affected more than 50% of the individuals (Table 1). In the study sample, only 6% of the individuals ($n = 4$) presented with only the sensation of dry mouth. In contrast, 94% of the patients ($n = 61$) presented with the association of two or more of the five symptoms defined in the survey by Fox *et al.*[3]. Upon detailed analysis of the frequencies of these symptoms, it was observed that 12 individuals (17.9%) presented two associated symptoms; 17 patients (25.4%) presented three symptoms simultaneously; 21 individuals (31.3%) reported the presence of four symptoms simultaneously; and 13 subjects (19.4%) displayed all of the symptoms.

Pathologies, factors and consumption of medicines associated with xerostomia in the sample

Considering that the xerostomia in the analysed sample was of diverse origin, the pathologies and factors associated with this condition were also varied (Table 2). The most frequent associated pathologies were depressive symptoms, arthritis, arterial hypertension and Sjögren syndrome. It was observed that 48 of the patients presented two or more pathologies simultaneously; 11 patients presented only one pathology, and eight were not affected by any pathology. Only 4.6% of the analysed individuals ($n = 3$) had been subjected to therapeutic radiation of the maxillofacial area, and 25.4%

Table 2 Frequency and percentage of subjects with pathologies, factors and consumption of medicines associated with xerostomia in the studied sample.

Pathology or associated factor	*n*	%
Depressive symptoms	43	64.1
Arthritis	24	35.8
Arterial hypertension	23	34.3
Sjögren syndrome	18	27.7
Diabetes	13	19.4
Heart disease	3	4.5
Lupus	2	2.3
Radiation therapy	3	4.6
Smoking	17	25.4
Consumption of medicines		
Antidepressants	27	40.3
Antihypertensives	23	34.3
Diuretics	10	14.9
Immunosuppresive therapy	5	7.5
Anti-Parkinsonism	1	1.5

($n = 17$) of them reported being smokers. As shown in the same table, the medicines most often consumed were antidepressants and antihypertensives. Concerning the number of medicines consumed by each individual, the study revealed that four subjects (6%) consumed 9–14 medicines simultaneously; 17 individuals (25.4%) consumed 5–8 medicines simultaneously; 32 subjects (47.8%) consumed 2–4 medicines at the same time; and 8 individuals (11.9%) consumed only one medicine. Only 6 people (8.9%) did not consume any medicine.

Salivary flow and hyposialia in the patients included in the study

The median unstimulated salivary flow in the study sample was 0.230 ml/min with a range from 0.04 to 0.982 ml/min. Forty per cent of the patients presented with hyposialia, with a salivary flow less than or equal to 0.2 ml/min. In these patients, the salivary flow presented an average of 0.09 ml/min with a range from 0.04 to 0.184 ml/min. Therefore, 60% of the patients with xerostomia presented with normal salivary flow. In this group, the average salivary flow was 0.426 ml/min, with a range from 0.205 to 0.982 ml/min.

Efficacy of rinse 1 in relieving the symptomatology associated with xerostomia

The values corresponding to the magnitudes of the sensation of dry mouth, burning tongue, thick saliva, need to drink liquids to swallow and difficulty in swallowing food were assessed both before

Table 3 Values corresponding to the magnitudes of symptomatology associated with xerostomia before and after the use of two mouthrinses tested.

	Mouthrinse 1			*Mouthrinse 2*		
	Before	*After*		*Before*	*After*	
Symptomatology associated with xerostomia	*Mean ± SD*	*Mean ± SD*	*p value*	*Mean ± SD*	*Mean ± SD*	*p value*
Sensation of dry mouth	6.03 ± 2.07	5.33 ± 2.59	0.048*	6.30 ± 2.18	5.83 ± 2.38	0.126
Sensation of thick saliva	5.35 ± 2.83	4.36 ± 2.98	0.190	4.84 ± 2.85	4.87 ± 2.88	0.882
Sensation of burning tongue	3.17 ± 2.95	3.60 ± 3.25	0.324	3.03 ± 3.07	3.40 ± 3.33	0.582
Need to drink liquids to swallow	4.14 ± 3.32	3.03 ± 2.86	0.006*	4.63 ± 3.53	3.37 ± 2.89	0.032*
Sensation of difficulty in swallowing food	4.03 ± 3.47	2.73 ± 2.55	0.011*	4.14 ± 3.34	3.32 ± 2.34	0.014*

*Statistical significances.

and after the use of the rinse. Results and statistical analysis of the comparisons are shown in Table 3 and indicate that this rinse effectively relieves the sensation of dry mouth, the need to drink liquids to swallow and the difficulty in swallowing food. Rinse 1 does not relieve symptoms of sensation of thick saliva and burning tongue (Table 3).

Efficacy of rinse 2 in the relief of the symptomatology associated with xerostomia

The same analysis of the previous section, but with rinse 2, showed that this rinse effectively relieves the patients both from the need to drink liquids to swallow, as well as the difficulty in swallowing food. In contrast, this rinse does not have significant effects on the relief of other symptoms associated with xerostomia (Table 3).

Efficacy of mouthrinses in relieving the symptomatology associated with xerostomia in relation with the number of medicines taken simultaneously

The patients included in the study were distributed into two groups according to the number of medicines they take every day. Both groups of patients were compared with each other with regard to the magnitudes of sensation of dry mouth, sensation of thick saliva, burning tongue, need to drink liquids to swallow and difficulty in swallowing food, both before and after the use of the rinses. Both results and statistical analysis are shown in Tables 4 and 5 and demonstrate that in patients having more than three medicines ($n = 41$), rinse 1 is effective in relieving the sensation of dry mouth, the sensation of thick saliva, the need to drink liquids to swallow and the difficulty in swallowing food. By contrast, rinse 1 did not relieve any of the xerostomia-associated symptoms in patients having 2 or less medicines ($n = 26$) (Table 4). Rinse 2 was found to be effective in relieving the sensation of dry mouth, the need to drink liquids to swallow and the difficulty in swallowing food in patients taking 3 or more medicines. By contrast, rinse 2 did not relieve any of the xerostomia-associated symptoms in patients taking 2 or less medicines (Table 5). None of the rinses was found to be effective in relieving the burning tongue sensation in either group of patients (Tables 4 and 5).

Table 4 Effect of mouthrinse 1 on the xerostomia-associated symptomatology in patients taking different numbers of medicines.

	Two or less medicines (n = 26)			*Three or more medicines (n = 41)*		
	Before	*After*		*Before*	*After*	
Symptomatology associated with xerostomia	*Mean ± SD*	*Mean ± SD*	*p value*	*Mean ± SD*	*Mean ± SD*	*p value*
Sensation of dry mouth	5.81 ± 2.09	5.84 ± 2.55	0.949	6.12 ± 2.08	4.89 ± 2.54	0.018*
Sensation of thick saliva	5.08 ± 2.48	5.23 ± 3.18	0.805	4.81 ± 3.01	3.63 ± 2.58	0.014*
Sensation of burning tongue	3.16 ± 3.19	3.80 ± 3.41	0.390	3.19 ± 2.87	3.37 ± 3.17	0.748
Need to drink liquids to swallow	3.87 ± 3.42	3.65 ± 3.37	0.746	4.18 ± 3.25	2.50 ± 2.29	0.024*
Sensation of difficulty in swallowing food	3.95 ± 3.22	2.91 ± 3.04	0.220	3.97 ± 3.66	2.42 ± 1.89	0.009*

*Statistical significances.

Table 5 Effect of mouthrinse 2 on the xerostomia-associated symptomatology in patients taking different numbers of medicines.

	Two or less medicines (n = 26)			*Three or more medicines (n = 41)*		
	Before	*After*		*Before*	*After*	
Symptomatology associated with xerostomia	*Mean ± SD*	*Mean ± SD*	*p value*	*Mean ± SD*	*Mean ± SD*	*p value*
Sensation of dry mouth	6.07 ± 2.23	6.46 ± 2.45	0.531	6.45 ± 2.17	5.43 ± 2.27	0.030*
Sensation of thick saliva	4.85 ± 2.54	5.46 ± 2.84	0.407	4.84 ± 3.07	4.49 ± 2.88	0.571
Sensation of burning tongue	3.26 ± 2.95	4.17 ± 3.52	0.249	2.89 ± 3.17	2.94 ± 3.17	0.920
Need to drink liquids to swallow	3.78 ± 3.30	3.60 ± 2.99	0.834	5.15 ± 3.61	3.23 ± 2.86	0.003*
Sensation of difficulty in swallowing food	4.08 ± 3.03	3.29 ± 2.62	0.295	4.18 ± 3.55	2.82 ± 2.63	0.009*

*Statistical significances.

Table 6 Effect of mouthrinse 1 on the xerostomia-associated symptomatology in patients displaying different numbers of pathologies.

	One pathology (n = 19)			*Two or more pathologies (n = 48)*		
	Before	*After*		*Before*	*After*	
Symptomatology associated with xerostomia	*Mean ± SD*	*Mean ± SD*	*p value*	*Mean ± SD*	*Mean ± SD*	*p value*
Sensation of dry mouth	6.13 ± 2.07	5.44 ± 2.51	0.043*	5.72 ± 2.09	4.95 ± 2.71	0.337
Sensation of thick saliva	5.07 ± 2.87	4.38 ± 2.98	0.148	4.63 ± 2.66	4.09 ± 2.86	0.491
Sensation of burning tongue	3.29 ± 2.91	3.17 ± 3.08	0.815	2.95 ± 3.17	4.28 ± 3.52	0.137
Need to drink liquids to swallow	3.78 ± 3.40	2.98 ± 2.85	0.128	4.65 ± 3.04	2.85 ± 2.72	0.018*
Sensation of difficulty in swallowing food	3.79 ± 3.38	2.67 ± 2.59	0.032*	4.37 ± 3.71	2.47 ± 1.95	0.029*

*Statistical significances.

Efficacy of mouthrinses in relieving the symptomatology associated with xerostomia in relation with the number of associated pathologies

The patients included in the study were distributed into two groups according to the number of their xerostomia-associated pathologies. Again, both groups of patients were compared with each other with regard to the magnitudes of sensation of dry mouth, sensation of thick saliva, burning tongue, need to drink liquids to swallow and difficulty in swallowing food, both before and after the use of the rinse. Both results and statistical analysis are shown in Tables 6 and 7. In the group of patients displaying one xerostomia-associated pathology ($n = 48$), rinse 1 relieved only the sensation of dry mouth, in contrast to its effect among patients displaying 2 or more xerostomia-associated pathologies ($n = 19$) among which it relieved the need to drink liquids to swallow and the difficulty in swallowing food (Table 6). Rinse 2 relieved the need to drink liquids to swallow and the difficulty in swallowing food only among patients displaying 2 or more associated pathologies (Table 7). None of the rinses was found to be effective in relieving the sensation of thick saliva or the burning tongue sensation in either group of patients (Tables 6 and 7).

Discussion

Xerostomia is an often chronic condition that affects a great number of adults and significantly deteriorates the quality of life, such that treatment is necessary[12,16]. When the associated glandular damage is severe, palliative treatment, such as salivary substitutes, moisturisers and oral mucosa lubricants, should be used. Although formulations of gels, sprays, mouthrinses and toothpastes exist in the European and North American markets, these products are not accessible to the entire affected world population[8,14]. In Chile, patients obtain these products through importation or by obtaining other formulations from a compounding pharmacy. It is worthy of note that usually these formulations are not clinically tested. In both cases,

Table 7 Effect of mouthrinse 2 on the xerostomia-associated symptomatology in patients displaying different numbers of pathologies.

	One pathology (n = 19)			*Two or more pathologies (n = 48)*		
	Before	*After*		*Before*	*After*	
Symptomatology associated with xerostomia	*Mean ± SD*	*Mean ± SD*	*p value*	*Mean ± SD*	*Mean ± SD*	*p value*
Sensation of dry mouth	6.11 ± 2.25	5.78 ± 2.47	0.494	7.05 ± 2.06	5.94 ± 2.39	0.215
Sensation of thick saliva	4.63 ± 2.91	4.92 ± 2.81	0.606	5.47 ± 2.81	5.10 ± 3.03	0.712
Sensation of burning tongue	3.10 ± 3.00	3.55 ± 3.17	0.409	2.94 ± 3.50	3.44 ± 3.52	0.596
Need to drink liquids to swallow	3.89 ± 3.42	3.34 ± 2.93	0.417	6.27 ± 3.42	3.77 ± 3.02	0.010*
Sensation of difficulty in swallowing food	3.26 ± 2.89	2.87 ± 2.71	0.467	6.50 ± 3.36	3.38 ± 2.65	0.001*

*Statistical significances.

the availability of the product is not immediate, it is usually more expensive than common medicines, and its acquisition demands an additional effort and time from the patient.

In this study, a randomised clinical test was performed to evaluate the efficacy of two palliative inexpensive products for xerostomia (mouthrinses), which could be widely distributed in the Chilean national market (40% off compared to the average prize of conventional mouthrinses). The individuals included in the study were patients of either the diagnostic clinic of the School of Dentistry or the Clinical Hospital of the University of Chile. The sample mainly consisted of female and elderly subjects. In this study, 66% (44/67) of the patients presented autoimmune pathologies, such as Sjögren syndrome, rheumatoid arthritis and systemic lupus erythematosus, which are associated with xerostomia and are found more frequently among women. Additionally, a high percentage of the patients in the sample presented systemic diseases associated with xerostomia, such as depression, diabetes and hypertension, or consumed a high amount of xerostomia-causing medicines (usual among elderly patients). In general, the pathologies and consumption of medicines found within the study sample matched those described in the literature as causing xerostomia[1–4,6–11].

All of the patients presented with the sensation of dry mouth, because this was the criterion for inclusion in the study. The rest of the symptoms considered in the survey of Fox *et al.*[3] were present in more than 50% of the patients (Table 1). Also, 94% of the patients presented an association of two or more of the symptoms listed in the study. Only 40% of the patients presented hyposialia, which coincides with results reported in other studies and emphasises the need to record the patient's perception as part of the exam and health history[8,13]. Therefore, in any clinical study that aims to test the formulation of a palliative agent for xerostomia, it is necessary to create objective standards for the related symptomatology. That is why, in this study, unstimulated salivary flow and associated symptoms were quantified, according to the criteria proposed by Fox *et al.*[3], which involve the use of a VAS.

In an effort to evaluate the degree of discomfort that the tested rinses could cause, a small pilot study with a small number of healthy participants, performed prior to the clinical test, determined that the principal discomfort perceived was the sensation of burning oral mucosa. Both formulations were then adjusted by reducing the amount of flavouring (mint) until the sensation was completely eliminated among all subjects (data not shown). As a result, the adjusted formulations of rinses 1 and 2 were tested among xerostomic patients.

When patients were distributed in two groups according to the number of medicines they consume every day, we observed that both rinses were more effective in relieving xerostomia-associated symptomatology in patients taking 3 or more medicines, as compared to the whole group of patients. In the group of patients taking 3 or more medicines, rinse 1 also relieved the sensation of thick saliva and rinse 2 relieved additionally the dry mouth sensation, at variance of the effect in the whole group of patients (Tables 3, 4 and 5). On the other hand, none of the rinses was found to be effective in relieving any of the symptoms in the patients taking 2 or less medicines (Tables 3, 4 and 5). These observations suggest that the xerostomia-associated symptomatology displayed by the patients in the study may well be influenced by polypharmacy.

Patient distribution according to the number of simultaneous pathologies showed no significant differences in the observed effect of either rinse as compared to their respective effect on the whole group of patients (Tables 3, 6 and 7).

According to the results of the clinical study, rinse 1, which had a more fluid consistency, more effectively relieved the sensation of dry mouth, the principal symptom of the xerostomic patients (Table 3). Additionally, it relieved the need to drink liquids and the difficulty in swallowing foods. Therefore, this rinse was effective in relieving three of the five symptoms associated with xerostomia. On the other hand, rinse 2, which had a more viscous consistency and included oral mucosa-lubricating additives as well as a salivary secretion stimulant, relieved two of the symptoms of xerostomia: the need to drink liquids and the difficulty in swallowing foods (Table 3). Burning tongue and the sensation of thick saliva were not relieved by either of the two tested rinses. The observed differences in this clinical study were significant despite the relatively small number of patients and short follow-up time considered in the study. In addition, the study was designed to ensure the control of placebo effect, but we have not definitely discarded the possibility that the improvement in symptoms after the use of these mouthrinses is in some way associated to a Hawthorne effect.

In our study, the most effective rinse was the one with the simpler mix of components (rinse 1). The components of this rinse are part of the base formulation for the majority of rinses that are currently available on the market. Rinse 2, which was made of the same components as rinse 1, but with the addition of moisturising agents and oral mucosa lubricants (such as propylene glycol, glycerine, aloe vera) and a salivary secretion stimulant (such as citric acid) did not reduce the sensation of dry mouth, burning tongue or thick saliva. The moisturising and lubricating components added to this rinse were not effective in reversing this symptomatology.

The problem regarding which additives to include in tested formulations for relief of xerostomia is a relevant topic within the current literature[17–21]. An analysis of some of the clinical studies performed to test certain products revealed that a variety of formulations and active ingredients are used to relieve various symptoms of xerostomia. Additionally, it was observed that a wide range of forms of these tested products exist; for example, sprays, gels, mouthrinses and toothpaste. There is also a diverse array of parameters utilised to evaluate xerostomia, which makes it difficult to compare the results between studies. For example, Momm *et al.*[19] performed a crossed study that evaluated a spray salivary substitute containing swine mucin, an aloe vera-based gel, a spray with carboxymethylcellulose, and rapeseed oil-based sprays. All of the products significantly improved xerostomia. However, burning tongue was not included as a symptom of xerostomia in that study. On the other hand, in the single-blind study by Alpöz *et al.*[21], which evaluated the efficacy of a salivary substitute (Sialine®) containing the polysaccharide xanthan gum as a viscoelastic component and water-diluted tea as placebo, it was shown that both completely relieved the symptoms under analysis (oral dryness, difficulty in swallowing, the need to drink liquids in order to swallow and difficulty in talking), although the patients preferred the administration of the tested product. Additionally, Silvestre *et al.*[17] evaluated the efficacy of a spray salivary substitute, with a base of aqueous mineral salts, xylitol and citric acid and reported that 20 of 37 patients reported feeling a reduction in the sensation of dry mouth, this being the only symptom of xerostomia under analysis. In the crossed, blinded, randomised study by McMillan *et al.*[20], the efficacy of the Oral Balance® gel administered through an intraoral slow-release device was compared with administration using an intraoral gel tab. It was observed that the gel tab reduced difficulty with chewing hard foods but not soft foods, although it did not reduce difficulty associated with speaking or swallowing food. A crossed, blinded, randomised study by Ship *et al.*[18] investigated the use of Xerostom® paste, gel, spray and mouthrinse, all of which contain olive oil as a lubricating agent. The study also evaluated the efficacy of betaine, xylitol, and vitamins E and B5. The results showed that use of these products relieved the difficulty with speaking, difficulty in swallowing food and oral dryness. The Ship *et al.* study did not include the evaluation of burning tongue or the sensation of thick saliva, as symptoms related to xerostomia. This analysis reveals that burning tongue and the sensation of thick saliva are symptoms that are rarely considered as indicators of xerostomia in clinical tests. Our results reveal that effective mouthrinses afford patients relief from the sensation of dry mouth, the need to drink liquids in order to swallow food and difficulty in swallowing food. However, 50% of the patients presented the sensation of thick saliva and burning tongue, symptoms which were not relieved by the tested products. This suggests that it would be fitting to group the patients according to the symptomatology associated with xerostomia to evaluate different palliative products geared towards relieving the symptoms most fre-

quently found in each group. Our study as well as that of Alpöz *et al.*[21] showed that the use of relatively simple formulated solutions is effective in relieving the symptoms associated with xerostomia. These solutions could serve as base formulations, to which different active ingredients could be added differentially, depending on the particular symptom being treated by a given formulation in randomised clinical studies.

Conclusion

In conclusion, this clinical test established that both tested rinses were effective in relieving various symptoms of xerostomia and could be distributed in the national market without medical prescription, at a relatively low cost, to improve the quality of life of the population affected by this condition. Modification of these base formulations, through the addition of specific active ingredients, could allow for the development of new palliatives for xerostomia, based on considerations of the aetiology and symptomatology of the group being studied.

Acknowledgements

This study was supported in part by University of Chile Grants: Domeyko, Multidisciplinary, Elderly Health Area and U-Apoya, VID. Dr. Remigio López Solís is acknowledged for helpful discussion and correction of the manuscript.

References

1. **Sreebny LM.** Saliva in health and disease: an appraisal and update. *Int Dent J* 2000; **50:** 140–161.
2. **von Bultzingslowen I**, **Sollecito TP**, **Fox PC** ***et al.*** Salivary dysfunction associated with systemic diseases: systematic review and clinical management recommendations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; **103**(Suppl)**:** S57 e1–15.
3. **Fox PC**, **Busch KA**, **Baum BJ.** Subjective reports of xerostomia and objective measures of salivary gland performance. *J Am Dent Assoc* 1987; **115:** 581–584.
4. **Pijpe J**, **Kalk WW**, **Bootsma H** ***et al.*** Progression of salivary gland dysfunction in patients with Sjogren's syndrome. *Ann Rheum Dis* 2007; **66:** 107–112.
5. **Pedersen AM**, **Bardow A**, **Nauntofte B.** Salivary changes and dental caries as potential oral markers of autoimmune salivary gland dysfunction in primary Sjogren's syndrome. *BMC Clin Pathol* 2005; **5:** 4.
6. **Pajukoski H**, **Meurman JH**, **Halonen P** ***et al.*** Prevalence of subjective dry mouth and burning mouth in hospitalized elderly patients and outpatients in relation to saliva, medication, and systemic diseases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; **92:** 641–649.
7. **Orellana MF**, **Lagravere MO**, **Boychuk DG** ***et al.*** Prevalence of xerostomia in population-based samples: a systematic review. *J Public Health Dent* 2006; **66:** 152–158.
8. **Napeñas JJ**, **Brennan MT**, **Fox PC.** Diagnosis and treatment of xerostomia (dry mouth). *Odontology* 2009; **97:** 76–83.
9. **Brosky ME.** The role of saliva in oral health: strategies for prevention and management of xerostomia. *J Support Oncol* 2007; **5:** 215–225.
10. **Atkinson JC**, **Grisius M**, **Massey W.** Salivary hypofunction and xerostomia: diagnosis and treatment. *Dent Clin North Am* 2005; **49:** 309–326.
11. **Greenspan D.** Xerostomia: diagnosis and management. *Oncology (Williston Park)* 1996; **10**(Suppl 3)**:** 7–11.
12. **Gerdin EW**, **Einarson S**, **Jonsson M** ***et al.*** Impact of dry mouth conditions on oral health-related quality of life in older people. *Gerodontology* 2005; **22:** 219–226.
13. **Nieuw Amerongen AV**, **Veerman EC.** Current therapies for xerostomia and salivary gland hypofunction associated with cancer therapies. *Support Care Cancer* 2003; **11:** 226–231.
14. **Shiboski CH**, **Hodgson TA**, **Ship JA** ***et al.*** Management of salivary hypofunction during and after radiotherapy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; **103**(Suppl)**:** S66 e1–19.
15. **Jensen SB**, **Pedersen AM**, **Vissink A** ***et al.*** A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: management strategies and economic impact. *Support Care Cancer* 2010; **18:** 1061–1079.
16. **Turner MD**, **Ship JA.** Dry mouth and its effects on the oral health of elderly people. *J Am Dent Assoc* 2007; **138**(Suppl)**:** 15S–20S.
17. **Silvestre FJ**, **Minguez MP**, **Sune-Negre JM.** Clinical evaluation of a new artificial saliva in spray form for patients with dry mouth. *Med Oral Patol Oral Cir Bucal* 2009; **14:** E8–E11.
18. **Ship JA**, **McCutcheon JA**, **Spivakovsky S** ***et al.*** Safety and effectiveness of topical dry mouth products containing olive oil, betaine, and xylitol in reducing xerostomia for polypharmacy-induced dry mouth. *J Oral Rehabil* 2007; **34:** 724–732.
19. **Momm F**, **Volegova-Neher NJ**, **Schulte-Monting J** ***et al.*** Different saliva substitutes for treatment of xerostomia following radiotherapy**.** A prospective crossover study. *Strahlenther Onkol* 2005; **181:** 231–236.
20. **McMillan AS**, **Tsang CS**, **Wong MC** ***et al.*** Efficacy of a novel lubricating system in the management of radiotherapy-related xerostomia. *Oral Oncol* 2006; **42:** 842–848.
21. **Alpoz E**, **Guneri P**, **Onder G** ***et al.*** The efficacy of Xialine in patients with Sjogren's syndrome: a single-blind, cross-over study. *Clin Oral Investig* 2008; **12:** 165–172.

Correspondence to:
Prof Irene Morales-Bozo, Oral Biology and Oral Biochemistry Laboratory, Department of Basic and Communitarian Sciences, Faculty of Dentistry, University of Chile, Chile.
Tel.: +56-2-9781794
Fax: +56-2-9781708
E-mails: imorales@uchile.cl, irenemoralesbozo@gmail.com