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Sialagogic Effect of a New Mouthwash for Relieving Oral Dryness

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Abstract

Background/purpose: Oral dryness is known to cause several oral disorders, including candidiasis, glossitis, atrophy of the oral mucosa, dysgeusia and multiple caries.

Recently, it has been noted that not only older people, but an increasing number of younger people are suffering from oral dryness as they become less able to accommodate to the range of emotional and physical environment changes, becoming over-stressed and developing symptoms of depression as a result.

Oral dryness is thus now a condition that affects people across the generations.

The authors have previously developed an agent that is both simple and capable of providing not only hydration, but also total oral dryness care, and they have reported its potential effect. In this study, whether this newly developed oral dryness care agent increased the amount of saliva produced and contributed to moisture retention was investigated in individuals of different generations.

Materials and methods: The young subjects (45 men) and the geriatric subjects (19 men, 27 women) washed their mouth with each mouthwash. Unstimulated salivary and stimulated salivary secretions were measured before mouth washing and immediately after (0 min) and 30 min and 60 min after mouth washing.

Results: The present results showed that, with the exception of saliva secreted by young subjects with stimulation, the test mouthwash significantly increased the amount of saliva secreted by all age groups, both at rest and with stimulation, compared with the control mouthwash, and this effect was persistent.

Conclusion: The present results suggest that the agent tested may be useful as a new mouthwash for relieving oral dryness, and it promoted saliva secretion in different age groups.

Keywords

Oral dryness; Mouthwash; Saliva secretion; Moisturizing effect

Introduction

Oral dryness is known to cause several oral disorders, including candidiasis, glossitis, atrophy of the oral mucosa, dysgeusia, and multiple caries [1]. Recent studies have also shown that the number of people suffering from oral dryness in Japan is increasing, both because the number of older people in the population is rising rapidly and because the social milieu is increasingly stressful [2].

The cause of oral dryness is generally believed to be reduced secretion of saliva, and the most important causes of this decrease in saliva production include diminished salivary gland tissue function due to drug side effects damage to salivary gland tissue by radiotherapy, Sjögren's syndrome, diabetes mellitus and aging [3-7]. In addition, depression may also reduce saliva production and loss of muscle strength in the perioral muscles and central salivary gland damage due to a cerebrovascular disorder may also be present; these may interact in a complex way to produce symptoms [8,9].

Many studies have reported that oral dryness is common in older people in whom several of these factors are present [10,11]. Recently, however, it has been noted that not only older people, but an increasing number of younger people is suffering from oral dryness as they become less able to accommodate to the range of emotional changes and changes in their physical environment, becoming over-stressed and developing symptoms of depression as a result [12,13]. Oral dryness is thus now a condition that affects people across generations.

Saliva normally contains a range of useful substances, including substances with antimicrobial and wound-healing properties, as well as growth factors and immunoglobulins, and is important for maintaining both oral and general health [14]. Oral dryness, in which these substances are not secreted in sufficient quantity, is thus a problem that dentists may not ignore. Patients with oral dryness should therefore be diagnosed and treated appropriately. However, at this juncture, it is difficult to deal with all the various causes of oral dryness and heal it completely. The use of symptomatic therapy in its treatment is thus comparatively common [1,15]. Such symptomatic therapies include the use of artificial saliva and moisturizers as well as other procedures such as salivary gland massage [16,17]. Artificial saliva and moisturizers are used to compensate for the lower amount of saliva secreted [16]. Salivary gland massage is performed with the aim of increasing saliva secretion [17]. A variety of different methods may thus be used in combination to treat patients with oral dryness [1,15].

These symptomatic therapies are widely used and can generally be said to be effective [1,15-17]. However, most such studies have described their use in older patients, and most reports of their use in younger patients are limited to statistical studies with few investigations having addressed the pathophysiology of oral dryness and its causes [12,13]. No conclusions can thus be drawn about the universal efficacy of conventional methods in all age groups. Older people may have difficulties in taking full responsibility for oral dryness self-care, and this naturally increases the burden on family members and caregivers. When considering measures to relieve oral dryness, the development of simple, effective methods that can be used by people of all generations and that are quick and easy to perform is desirable.

Oral hydration alone does not necessarily provide adequate oral dryness care, and other multifaceted measures that should also be

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taken include eliminating underlying factors, providing a variety of stimuli with the aim of restoring the amount of saliva secreted and oral cleaning [18]. However, no method currently integrates all these aspects.

The authors have previously developed an agent that is both simple and capable of providing not only hydration, but also total oral dryness care, and they have reported its potential effect [19]. In this study, whether this newly developed oral dryness care agent increased the amount of saliva produced and contributed to moisture retention was investigated in individuals of different generations.

Material and Methods

Subjects

The subjects were 90 individuals (63 men and 27 women, mean age 45.6 ± 22.22 years) who were classified as „young" or „geriatric" according to the Ministry of Health, Labour and Welfare age categories. The young subjects comprised 45 individuals who were either attending the Sleep Clinic at Nihon University School of Dentistry at Matsudo Hospital or were students in the Nihon University School of Dentistry at Matsudo (45 men, mean age 24.9 ± 4.7 years) and the geriatric subjects comprised 45 individuals resident in or regularly attending a geriatric care facility (18 men, 27 women, mean age 66.4 ± 9.8 years). In compliance with the Helsinki Declaration, subjects were informed of the nature of the study, and their consent was obtained (the Ethics Committee Nihon University School of Dentistry at Matsudo. approval number EC14-049). Some of the subjects did not necessarily complain of subjective symptoms of oral dryness. Individuals with oral soft tissue disorders requiring treatment at the time of oral examination were excluded, as were those who had undergone treatment for a salivary gland disorder within 6 months of the start of the study or who were currently undergoing such treatment.

Mouthwashes

The following three test solutions were used in this study.

Control mouthwash: The control mouthwash used was Mondahmin Nonalcoholic® Mouthwash (Earth Chemical Co., Ltd., Tokyo, Japan), a commercially available mouthwash. Commercially available mouthwashes are formulated with cetylpyridinium chloride (CPC) as an antiseptic and the cleaning agents disodium ethylenediaminetetraacetate (EDTA-2Na) and polyoxyethylene cetylether (CETETH-25). These ingredients are compounded in a ratio of 1:2:20 CPC:EDTA-2Na:CETETH-25.

Test mouthwash: The test mouthwash was formulated by adding a sialagogic ingredient (kelp extract) and moisturizing ingredients (betaine and sodium hyaluronate) to the control mouthwash. These ingredients were formulated in a ratio of 50:250:1 kelp extract:betaine:sodium hyaluronate.

Water: Commercially available mineral water (I LOHAS) [Coca Cola (Japan) Company, Limited, Tokyo, Japan] was used.

All test solutions were tasteless and odorless, and they were used at room temperature.

Experimental Procedure

Measurement conditions

The subjects were asked to finish meals by at least 1 h before the experiments were due to start and not to eat or drink thereafter when attending the hospital on the day measurements were made. After entering the test room, they were allowed to rest quietly for 15 min to accustom themselves to the environment, after which the measurements were made. The same procedure was followed at the geriatric care facility.

Measurements of the amount of saliva secreted were made between 1 p.m. and 3 p.m., a period during which saliva production is comparatively stable, on each day on which measurements were performed [20].

Measurement environment

Measurements were made in a conference room with little coming and going, at room temperature of 25°C and humidity ≤ 60%.

Measurement procedure of saliva secretion

The amount of saliva secreted was measured by the spitting test and the Saxon test [21].

The spitting test was performed by asking the subjects to spit out the mixture of saliva in their mouths into a measuring cup while seated at rest on a chair. The volume of saliva produced over a 10 min period (ml/10 min) was recorded.

The Saxon test was performed by inserting a piece of cotton gauze (30 cm × 30 cm Sterile Square Gauze Blister Pack, Hasegawa Menko Co., Ltd., Aichi, Japan) into each subject's mouth and asking the subjects to perform chewing movements approximately once a second for 2 min. The gauze was weighed on an electronic balance (BL-320S, Shimadzu Corporation, Kyoto, Japan) before use, and this weight was subtracted from the weight of the masticated gauze to calculate the weight of saliva. The results are expressed as weight of saliva per 2 min period (g/2 min).

On the other hand, the amount of saliva produced before mouth washing was measured as the baseline value. The subjects then washed their mouth with each mouthwash, and saliva secretion was measured immediately after (0 min) and 30 min and 60 min after mouth washing. Without knowing which solution was which, the subjects performed mouth washing by taking 20 ml of each individual test solution (test mouthwash, control mouthwash or water) into their mouth, swishing it around their mouth for 30 s and spitting it out. The experiment was performed three times at 1 week intervals.

Statistical analysis

The amounts of saliva secreted by the young and geriatric subjects before and after mouth washing with each test solution were analyzed. SPSS version 21 (IBM Japan, Tokyo, Japan) was used for statistical analysis, using repeated measure analysis of variance (ANOVA) followed by multiple comparisons using Bonferroni's method, with $p<0.05$ regarded as significant.

Results

Amount of saliva secreted by young subjects at rest

Analysis of the amount of saliva secreted at each time point after washing with each mouthwash showed that significantly more saliva was secreted immediately after mouth washing with the test mouthwash than with either water or the control mouthwash ($p<0.001$). At 30 min after mouth washing, significantly more saliva

was secreted after mouth washing with the test mouthwash than with either water or the control mouthwash. Similarly, at 60 min after mouth washing, significantly more saliva was secreted after mouth washing with the test mouthwash than with either water or the control mouthwash (p0.001) (Table 1).

Analysis of the amount of saliva secreted at each time point for each mouthwash showed that there was no significant difference between the amount of saliva secreted immediately after mouth washing with water and the baseline value. At 30 and 60 min after mouth washing with water, however, the amount of saliva secreted decreased significantly compared with the baseline value (p<0.001) (Table 1).

For the control mouthwash, there was no significant difference between the amount of saliva secreted immediately after mouth washing and the baseline value. At 30 and 60 min after mouth washing, however, the amount of saliva decreased significantly compared with the baseline value. For the test mouthwash, the amount of saliva secreted increased significantly immediately after mouth washing and at 30 min and 60 min after mouth washing compared with the baseline value (Table 1).

Amount of saliva secreted by geriatric subjects at rest

Analysis of the amount of saliva secreted at each time point for each mouthwash showed that significantly more saliva was secreted immediately after mouth washing with the test mouthwash than with either water or the control mouthwash (p<0.01). At 30 min after mouth washing, significantly more saliva was secreted after mouth washing with the test mouthwash than with either water or the control mouthwash. Similarly, at 60 min after mouth washing, significantly more saliva was secreted after mouth washing with the test mouthwash than with either water or the control mouthwash (p<0.01) (Table 1).

Analysis of the amount of saliva secreted at each time point for each mouthwash showed that the amount of saliva secreted immediately after mouth washing with water increased significantly compared with the baseline value after 30 min, but there was no significant difference after 60 min (Table 1).

For the control mouthwash, the amount of saliva increased significantly compared with the baseline value up to 60 min after mouth washing. Similarly, for the test mouthwash, the amount of saliva also increased significantly compared with the baseline value up to 60 min after mouth washing (Table 1).

Amount of saliva secreted by young subjects with stimulation

Analysis of the amount of saliva secreted at each time point after washing with each mouthwash showed that there was no significant difference in the amount of saliva secreted immediately after mouth washing with the test mouthwash, water or the control mouthwash. The amount of saliva secreted 30 min after mouth washing was significantly greater for the control mouthwash than for water, but for the test mouthwash, the amount of saliva was not significantly different from those for either water or the control mouthwash. The amount of saliva secreted 60 min after mouth washing was significantly greater for both the test and control mouthwashes than for water, but there was no significant difference between the control mouthwash and the test mouthwash (Table 2).

Analysis of the amount of saliva secreted at each time point for each mouthwash showed that the amount of saliva secreted after mouth washing with water increased significantly compared with the baseline value for up to 30 min (Table 2).

The amount of saliva secreted after mouth washing with the control mouthwash increased significantly compared with the baseline value for up to 60 min. However, the amount of saliva secreted after 60 min decreased significantly compared with both immediately after and 30 min after mouth washing. For the test mouthwash, the amount of saliva increased significantly compared with the baseline value for up to 60 min (Table 2).

The amount of saliva secreted 30 min after mouth washing decreased significantly compared with immediately after, but there was no significant difference between the amounts of saliva secreted after 30 min and after 60 min (Table 2).

Table 1: Amount of saliva secreted at rest.

Age group	Measurement method	Mouthwash	Control		0 min		30 min		60 min		Multiple comparisons
			M	SD	M	SD	M	SD	M	SD	
Young	Spitting method	Test mouthwash			6.20	2.24	6.02	2.01	5.78	1.85	Control<0 min=30 min=60 min
		Control mouthwash	3.91	1.18	4.32	0.96	3.10	0.99	2.40	1.19	Control=0 min>30 min=60 min
		Water			3.19	1.12	2.72	1.44	2.06	0.56	Control>30 min=60 min, 0 min>60 min
		Multiple comparison			Water<Control<Test		Water, Control<Test		Water, Control<Test		
		Mouth washing solution	Control		0 min		30 min		60 min		Multiple comparisons
			M	SD	M	SD	M	SD	M	SD	
Geriatric	Spitting method	Test mouthwash			3.98	1.23	3.18	1.00	3.08	0.73	Resting<0 min, Resting<30 min, Resting<60 min, 0 min>30 min=60 min
		Control mouthwash	1.13	0.57	2.58	0.81	2.33	0.66	1.62	0.57	Resting<0 min=30 min, Resting<60 min, 0 min=30 min>60 min
		Water			1.61	0.74	1.63	0.56	1.30	0.56	Resting<0 min=30 min
		Multiple comparison			Water<Control<Test		Water<Control<Test		Water, Control<Test		

Table 2: Amount of saliva secreted with stimulation.

Age group	Measurement method	Mouthwash	Control		0 min		30 min		60 min		Multiple comparisons
			M	SD	M	SD	M	SD	M	SD	
Young	Saxon test	Test mouthwash	4.52	1.17	5.53	1.21	5.27	1.30	5.49	1.55	Resting<0 min, Resting<30 min, Resting<60 min, 0 min>30 min=60 min
		Control mouthwash			5.04	0.91	5.32	0.84	5.25	1.10	Resting<0 min=30 min, Resting<60 min, 0 min=30 min>60 min
		Water			5.09	0.85	4.79	1.04	4.19	0.73	Resting<0 min=30 min
		Multiple comparisons					Water<Control		Water<Control, Test		
			Control		0min		30min		60min		Multiple comparisons
			M	SD	M	SD	M	SD	M	SD	
Geriatric	Saxon test	Test mouthwash	1.53	0.42	4.26	1.17	4.76	0.86	4.11	0.82	Resting<0 min=60 min<30 min
		Control mouthwash			2.39	1.19	1.97	0.50	1.42	0.60	Resting<0 min=30 min, 0 min=30 min>60 min
		Water			1.93	0.84	1.84	0.70	1.64	0.85	
		Multiple comparisons			Water<Control<Test		Water, Control<Test		Water, Control<Test		

Amount of saliva secreted by geriatric subjects with stimulation

Analysis of the amount of saliva secreted at each time point after washing with each mouthwash showed that significantly more saliva was secreted immediately after mouth washing with the test mouthwash than with either water or the control mouthwash. At 30 min after mouth washing, significantly more saliva was secreted after mouth washing with the test mouthwash than with either water or the control mouthwash. Similarly, at 60 min after mouth washing, significantly more saliva was secreted after mouth washing with the test mouthwash than with either water or the control mouthwash (Table 2).

Analysis of the amount of saliva secreted at each time point for each mouthwash showed that there was no significant increase compared with the baseline value at any time point after mouth washing with water (Table 2).

For the control mouthwash, the amount of saliva secreted increased significantly compared with the baseline value for up to 30 min after mouth washing, but the amount of saliva secreted after 60 min decreased significantly compared with the amounts of saliva secreted immediately after and 30 min after mouth washing. For the test mouthwash, the amount of saliva increased significantly compared with the baseline value for up to 60 min (Table 2).

The amount of saliva secreted 30 min after mouth washing was significantly greater than the amounts of saliva secreted immediately after and 60 min after mouth washing (Table 2).

Discussion

The present results showed that, with the exception of saliva secreted by young subjects with stimulation, the test mouthwash significantly increased the amount of saliva secreted by all age groups, both at rest and with stimulation, compared with the control mouthwash, and this effect was persistent.

The amounts of saliva secreted by young subjects at rest and by geriatric subjects at rest and with stimulation after mouth washing with the test mouthwash may have increased significantly compared with the control mouthwash because of the effect of kelp extract, a flavoring used to add *umami,* that was one of the ingredients of the test mouthwash. Several studies have found that among various flavorings, stimulation with *umami* in particular promotes the secretion of saliva, and Hodson et al. showed that stimulation with, among the basic five tastes, *umami* encourages the greatest secretion of saliva, especially by the parotid gland [22]. Sasano et al. and Satoh-Kuriwada et al. reported that stimulation with *umami* acts to encourage saliva production by minor salivary glands, as well as the major salivary glands [23,24]. The kelp extract, *umami* flavoring, included in our product may thus have stimulated all of the salivary glands and encouraged the secretion of saliva.

Ekstrom found that stimulation by sour, salty, sweet, and bitter tastes, the four of the five basic tastes other than *umami*, causes taste information to be sent from the taste buds on the tongue to the salivary nucleus in the medulla oblongata, after which the major and minor salivary glands are stimulated, encouraging the secretion of saliva [25]. Although *umami* has not been closely studied, it is conceivable that our product may also have encouraged saliva production in a way similar to these other tastes. Studies to ascertain the mechanism whereby *umami* stimulation promotes the secretion of saliva may be required in the future.

The amount of saliva secreted by young subjects at rest and by geriatric subjects at rest and with stimulation 30 min after mouth washing with the test mouthwash was significantly greater than after mouth washing with the control mouthwash, and this increase was maintained until 60 min after mouth washing. Ship et al. [26] and López-Jornet et al. [27] reported that a mouthwash formulation containing betaine was effective in moisturizing the mouth, and they reported that it improved oral dryness. Söderling et al. also found that toothpaste formulated with betaine moisturized the mouth and

they also concluded that this improved oral dryness [28]. Yuan et al. reported that a moisturizer containing sodium hyaluronate improved poor saliva production and dry mouth, suggesting that sodium hyaluronate may be effective for this purpose [29]. These findings suggest that the betaine and sodium hyaluronate contained in our product may have moisturized the mouth and maintained the long-term level of saliva after its secretion. However, the possibility that the moisturizing ingredients in our product may also have acted as stimulants encouraging saliva production cannot be ruled out.

All three of our added ingredients are natural substances that are very safe and have few side effects**.** Artificial saliva is one existing agent that is widely used to treat patients with oral dryness [1,30,31]. However, although it is somewhat effective, in many cases its properties and form render its continued use problematic and it must be used with caution [32]. The side effects of the sialagogic agent cevimeline hydrochloride hemihydrate include abdominal pain, diarrhea, and vomiting, and its use in treatment must frequently be discontinued [33]. Our product, however, adds three very safe natural ingredients to an existing commercially available mouthwash to create a new mouthwash, and its safety is thus thoroughly assured. Although the present study involved only short-term use, no subject complained of discomfort or feeling unwell.

The mouthwash tested in this study also contained hydroxyethyl cellulose as a thickener. This ingredient is used to add viscosity to some cosmetics, and it was also added to our product for this purpose. Alves et al. compared an oral moisturizing gel with a placebo for the treatment of oral dryness in patients with Sjögren's syndrome and they found that the oral moisturizing gel not only improved oral dryness symptoms to a greater extent than the placebo, but it also adhered better to the oral mucosa [34]. We therefore added hydroxyethyl cellulose to our product to make it more viscous, and this may have helped retain the ingredients in our product within the mouth for a longer time. This would have helped its antiseptic and cleansing actions and also its sialagogic and moisturizing effects to last longer.

However, although the amount of saliva secreted by young subjects with stimulation at 0, 30 and 60 min after mouth washing with both the control mouthwash and the test mouthwash was significantly greater than after mouth washing with water, there was no significant difference between the control and test mouthwashes at any point. For both the control and test mouthwashes, the amount of saliva secreted 60 min after mouth washing was significantly greater than the baseline value. For water, however, no such significant change was apparent. The possibility cannot be ruled out that, in young subjects, both the control mouthwash and the test mouthwash, unlike water, may have stimulated the increased secretion of saliva. Ono et al. reported that young men produced significantly more saliva during masticatory stimulation than in the absence of stimulation, and it is possible that the stimulation imparted by chewing a piece of gauze may have had a greater effect than the stimulation provided by the mouthwash [35]. None of the present experimental subjects had any salivary gland complaints, and it is unlikely that there were any abnormal variations in the amount of saliva secreted. It is entirely possible that no significant difference between the increases in saliva caused by the control and test mouthwashes was apparent in this experiment because the masticatory stimulation also promoted saliva production. However, there was a significant difference between water and the control mouthwash. Yu et al. compared the amount of saliva secreted by patients with oral dryness after mouthwash stimulation alone and without such stimulation, and they found that it increased significantly [36]. Mouthwash stimulation may thus also promote saliva production. Fukunaga et al. reported that members of younger age groups showed higher sensitivity to taste, and the possibility cannot be excluded that the young subjects may have responded sensitively to the faint difference in taste compared with water, despite the fact that all the mouthwashes were tasteless and odorless [37]. Compared with geriatric individuals, there have been few detailed studies of saliva secretion by young people from a pathological perspective and there is little awareness of the issue. More in-depth studies of saliva secretion by young people may be required in the future.

A comparison of the baseline amounts of saliva secreted by the geriatric participants in this study at rest and with stimulation with the reference values for Sjögren's syndrome of 1 ml/10 min at rest (spitting method) and 2 g/2 min with stimulation (Saxon test) showed that the amount of saliva secreted at rest was approximately the same as the reference value, whereas the amount of saliva secreted with stimulation was below the reference value [38]. This suggested that the geriatric subjects may have normally experienced low saliva production, particularly while eating. Low saliva production may cause masticatory problems and aspiration pneumonia, and, most importantly, make eating less enjoyable. The authors gave the study subjects feedback following the experiments, but they should perhaps have paid attention to their course. Both the control and test mouthwashes increased the amount of saliva secreted after mouth washing compared with the baseline value. Although this effect was maintained for 30 min after mouth washing with the control mouthwash, no significant increase in saliva production was evident after 60 min. For the test mouthwash, however, a significant increase was maintained for 60 min. This also suggested that the kelp extract, betaine and sodium hyaluronate in the test mouthwash may have promoted the secretion of saliva, and that this effect was long-lasting as a result of its moisturizing effect. This finding, that the effect persists for longer, may offer an effective new strategy for not just older oral dryness patients, but also for younger oral dryness patients, and in settings where assistance and long-term care are required, it may help to relieve the burden on caregivers in particular. Our product may thus be useful as a mouthwash for relieving oral dryness.

This study had some limitations. It was carried out over a single, brief time span, with no observations of long-term use. We intend to investigate matters such as the timing, amount, and duration of use of this mouthwash in order to identify more effective methods of use.

Conclusion

The present results suggest that the new mouthwash tested in this study, which contained kelp extract as a sialagogic agent, as well as betaine and sodium hyaluronate as moisturizers, added to a commercially available mouthwash that is highly safe and has a cleansing effect, may be useful as a new mouthwash for relieving oral dryness, and it promoted saliva secretion in members of different age groups.

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Conflicts of Interest

All authors certify that have no affiliations with or involvement in any organization or entity with any financial interest.

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References

1. Altamimi AM (2014) Update knowledge of dry mouth: A guideline for dentists. Afr Health Sci 14: 736-742.
2. Plemons JM, Al-Hashimi L, Marek CL (2014) Managing xerostomia and salivary gland hypofunction: executive summary of a report from the American Dental Association Council on Scientific Affairs. J Am Dent Assoc 145: 867-873.
3. Nguyen CT, MacEntee MI, Mintzes B, Perry TL (2014) Information for physicians and pharmacists about drugs that might cause dry mouth: a study of monographs and published literature. Drugs Aging 31: 55-65.
4. Kakudate N, Muramatsu T, Endoh M, Satomura K, Koseki T, et al. (2014) Factors associated with dry mouth in dependent Japanese elderly. Gerodontology 31: 11-18.
5. Hutchinson CT, Suntharalingam M, Strome SE (2104) What are the best management strategies for radiation-induced xerostomia? Laryngoscope 124: 359-360.
6. Kerr GD, Sellars C, Bowie L, Bagg J, Sweeney MP, et al. (2009) Xerostomia after acute stroke. Cerebrovasc Dis 28: 624-626.
7. Malicka B, Kaczmarek U, Skośkiewicz-Malinowska K (2014) Prevalence of oral dryness and the salivary flow rate in diabetic patients. Adv Clin Exp Med 23: 225-233.
8. Grover SS, Rhodus NL (2016) Xerostomia and depression. Northwest Dent 95: 33-35.
9. Desoutter A, Soudain-Pineau M, Munsch F, Mauprivez C, Dufour T, et al. (2012) Xerostomia and medication: a cross-sectional study in long-term geriatric wards. J Nutr Health Aging 16: 575-579.
10. Mavragani CP, Moutsopoulos HM (2014) Sjögren's syndrome. Annu Rev Pathol 9: 273-285.
11. Gerdin EW, Einarson S, Jonsson M, Aronsson K, Johansson I (2005) Impact of dry mouth conditions on oral health-related quality of life in older people. Gerodontology 22: 219-226.
12. Benn AM, Broadbent JM, Thomson WM (2015) Occurrence and impact of xerostomia among dentate adult New Zealanders: findings from a national survey. Aust Dent J 60: 362-367.
13. Veerabhadrappa SK, Chandrappa PR, Patil S, Roodmal SY, Kumarswamy A, et al. (2016) Evaluation of xerostomia in different psychological disorders: an observational study. J Clin Diagn Res 10: ZC24-ZC27.
14. Dawes C, Pedersen AM, Villa A, Ekström J, Proctor GB, et al. (2015) The functions of human saliva: A review sponsored by the World Workshop on Oral Medicine VI. Arch Oral Biol 60: 863-874.
15. Lopez-Lopez J, Salas JE, Kustner CE (2014) [Prognosis and treatment of dry mouth. Systematic review. Med Clin (Barc) 142: 119-124.
16. Dalodom S, Lam-Ubol A, Jeanmaneechotechai S, Takamfoo L, Intachai W, et al. (2016) Influence of oral moisturizing jelly as a saliva substitute for the relief of oral dryness in elderly patients with hypertension and diabetes mellitus. Geriatr Nurs 37: 101-109.
17. Hakuta C, Mori C, Ueno M, Shinada K, Kawaguchi Y (2009) Evaluation of an oral function promotion programme for the independent elderly in Japan. Gerodontology 26: 250-258.
18. Han P, Suarez-Durall P, Mulligan R (2015) Dry mouth: A critical topic for older adult patients. J Prosthodont Res 59: 6-19.
19. Asakawa R, Suzuki H, Yagi T, Sakanashi K, Iwasaki S, Shimada T, et al. (2017) Pilot study to assess the potential of new moisturizing agents for oral dryness. Int J Oral Med Sci (in press).
20. Dawes C (1972) Circadian rhythms in human salivary flow rate and composition. J Physiol 220: 529-545.
21. Villa A, Connell CL, Abati S (2014) Diagnosis and management of xerostomia and hyposalivation. Ther Clin Risk Manag 11: 45-51.
22. Hodson NA, Linden RW (2006) The effect of monosodium glutamate on parotid salivary flow in comparison to the response to representatives of the other four basic tastes. Physiol Behav 89: 711-717.
23. Sasano T, Satoh-Kuriwada S, Shoji N, Iikubo M, Kawai M, et al. (2014) Important role of umami taste sensitivity in oral and overall health. Curr Pharm Des 20: 2750-2754.
24. Satoh-Kuriwada S, Sasano T (2105) A remedy for dry mouth using taste stimulation. Nihon Yakurigaku Zasshi 145: 288-292.
25. Ekstrom J (1989) Autonomic control of salivary secretion. Proc Finn Dent Soc 85: 323-331.
26. Ship JA, McCutcheon JA, Spivakovsky S, Kerr AR (2007) 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 34: 724-732.
27. Lopez-Jornet P, Camacho-Alonso F, Rodriguez-Aguado C (2012) Evaluation of the clinical efficacy of a betaine-containing mouthwash and an intraoral device for the treatment of dry mouth. J Oral Pathol Med 41: 201-206.
28. Söderling E, Le Bell A, Kirstilä V, Tenovuo J (1998) Betaine-containing toothpaste relieves subjective symptoms of dry mouth. Acta Odontol Scand 56: 65-69.
29. Yuan J, Tohara H, Mikushi S, Hoshino T, Yue B, et al. (2005) The effect of „Oral Wet" for elderly people with xerostomia - the effect of oral rinse containing hialuronan. Kokubyo Gakkai Zasshi 72: 106-110.
30. Porter SR, Scully C, Hegarty AM (2004) An update on the etiology and management of xerostomia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 97: 28-46.
31. Salom M, Hachulla E, Bertolus C, Deschaumes C, Simoneau G, et al. (2015) Efficacy and safety of a new oral saliva equivalent in the management of xerostomia: A national, multicenter, randomized study. Oral Surg Oral Med Oral Pathol Oral Radiol 119: 301-309.
32. Fayaz A, Attar M (2003) Comparing the clinical effects of saliva substitute (artificial saliva) and natural mucinogen in patients with xerostomia. J Dent Sch Shahid Beheshti Univ Med Sci 21: 755-765.
33. Noaiseh G, Baker JF, Vivino FB (2014) Comparison of the discontinuation rates and side-effect profiles of pilocarpine and cevimeline for xerostomia in primary Sjögren's syndrome. Clin Exp Rheumatol 32: 575-757.
34. Alves MB, Motta AC, Messina WC, Migliari DA (2004) Saliva substitute in xerostomic patients with primary Sjögren's syndrome: A single-blind trial. Quintessence Int 35: 392-396.
35. Ono K, Inoue H, Masuda W, Morimoto Y, Tanaka T, et al. (2007) Relationship of chewing-stimulated whole saliva flow rate and salivary gland size. Arch Oral Biol 52: 427-431.
36. Fukunaga A, Uematsu H, Sugimoto K (2005) Influences of aging on taste perception and oral somatic sensation. J Gerontol A Biol Sci Med Sci 60: 109-113.
37. Yu IC, Tsai YF, Fang JT, Yeh MM, Fang JY, et al. (2016) Effects of mouthwash interventions on xerostomia and unstimulated whole saliva flow rate among hemodialysis patients: A randomized controlled study. Int J Nurs Stud 63: 9-17.
38. Fujibayashi T, Sugai S, Miyasaka N, Hayashi Y, Tsubota K (2004) Revised Japanese criteria for Sjogren's syndrome (1999): Availability and validity. Mod Rheumatol 14: 425-434.

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