ORIGINAL ARTICLE

Efficacy Evaluation of Moisturising Spray Formulations in Xerostomia Patients – A Randomised Clinical Trial

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ABSTRACT

Introduction: Xerostomia is defined as a subjective sensation of oral dryness. This is a widespread problem in the elderly population with physiologically reduced salivation and with certain types of oral lesions. Oral7® is an immunologically active saliva substitute (IASS), formulated with natural enzymes like lactoperoxidase, lysozyme, glucose oxidase and lactoferrin that mimics natural saliva. This study aims to evaluate the efficacy of Oral7 Moisturising Spray with IASS formulation in treating xerostomia and patients' perception. **Materials and Methods:** In this randomized double-blind study involving 27 patients from Oral Medicine Clinic in Faculty of Dentistry, Universiti Kebangsaan Malaysia, and Oral Medicine Clinic at the Oral Maxillofacial Surgery Department, Hospital Canselor Tuanku Muhriz. The patients were allocated into two groups: Oral7® and Brand X. Initially, 35 patients involved in the first round of assessment, however, only 27 of the participants from both groups have completed the study phase involving demographical data, Clinical Oral Dryness Score (CODS), unstimulated and stimulated salivary flow test and Product Performance and Attribute Questionnaire (PPAQ). **Results:** There is an increase in stimulated and unstimulated saliva volume and flow rate in Oral7® group, whereas in Brand X group shows increase in unstimulated saliva volume, flow rate, decrease in stimulated saliva volume, and flow rate. The perception of patient in Oral7® group provided more positive feedback compared to Brand X group based on PPAQ. **Conclusion:** Oral7® provide positive effectiveness in treating xerostomia based on saliva production and patients' perception.

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INTRODUCTION

According to Millsop et al. and Tanasiewicz et al., xerostomia is classified into two; true xerostomia and pseudo xerostomia (1,2). True xerostomia is defined as mouth dryness caused by salivary gland malfunction, while pseudo xerostomia is when the patient experiences a subjective dry mouth even as the patient has normal salivary gland function. A meta-analysis from Agostini et al. (3), showed that the general estimated prevalence of xerostomia from the general population based in a range of 0.01 to 45%. The clinical signs and symptoms of xerostomia include increased incidence of dental caries, increased plaque accumulation and tooth hypersensitivity, gingivitis, mucositis, recurrent oral candidiasis, ulcerations of the oral mucosa, burning mouth sensation, angular cheilitis, and dry lips (1,2,4). It was also reported patients experience discomfort such as halitosis, difficulty in speech, chewing, and swallowing, and altered taste sensation (1,2,4).

In a study by Niklander et al. (5), xerostomia is more common in women and within the 6th decade of life. It is also associated with medical conditions such as autoimmune and inflammatory conditions like Sjogren Syndrome, amyloidosis, sarcoidosis; systemic infections such as AIDS and hepatitis C, salivary gland aplasia; endocrine diseases like diabetes mellitus and lymphoma (1,2,6,7). Xerostomia is also a symptom of chronic kidney disease due to medications such as diuretics

and suggested to be associated with reduction of bicarbonate and raised calcium in the saliva (8). It is also manifested as an adverse effect of prolonged medication intake such as anticholinergic drugs, antihistamines, antihypertensive agents, opioids, antidepressants, antipsychotics and skeletal muscle relaxants (1,2,4,5).

Radiotherapy to the head and neck region in cancer patients commonly causes salivary gland damage leading to decreased salivary production, eventually causing xerostomia (1,4,5,9). In a study conducted among nasopharyngeal carcinoma patients undergoing chemoradiotherapy in Universiti Kebangsaan Malaysia Medical Centre, the prevalence of xerostomia is at 96.8% of the sample population (10). The perception of dry mouth may be due to physiological or psychogenic factors such as dehydration, mouth breathing and psychological disorders (2,4,5,7).

The diagnosis of xerostomia is determinedstarts with a thorough medical and dental history to determine the presence of hyposalivation, conditions and treatments associated with reduced saliva, such as radiotherapy and salivary gland hypofunction (1,4,7). A questionnaire is needed to further assess xerostomia regarding patient comfortability and impressions of dry mouth. Xerostomia Inventory (XI) is an 11-item questionnaire that is validated to identify xerostomia targeted on the dry mouth experience aspects based on the category of frequency of incidence (1,11). The simpler version of this is the Summated Xerostomia Inventory (SXI) reduces the category into three ("Never," "Occasionally," "Ever") to ease older respondents to be able discriminate between frequencies better than the original XI (11).

The Clinical Oral Dryness Score (CODS) assesses the degree of mouth dryness by using a scoring system consisting of a 10-point scale with each point portraying a characteristic of mouth dryness (12). The features are mirror sticks to buccal mucosa, mouth mirror sticks to the tongue, frothy saliva, no pooling of saliva on floor of mouth, loss of papillae of tongue, altered gingival structure, glassy appearance on other oral mucosa, lobulated or fissured tongue, recently restored cervical caries on more than two teeth in the last six months and debris on the palate. The COD score is interpreted into severity levels of mild dryness (score 1- 3), moderate dryness (score 4-6) and severe dryness (score 7-10). Salivary tests are done to assess the function of the salivary gland and production of saliva. Unstimulated salivary flow rate, stimulated salivary flow rate, palatal secretion and parotid secretion are among tests to assess function of the secretory glands (2).

Blood tests and biopsies are taken to assess suspected systemic disease that causes xerostomia. Full blood count (FBC) may be used in case of suspected systemic-disease-related xerostomia. Antibody analysis may be beneficial to link xerostomia to xerophthalmia and as a feature of Sjogren's Syndrome (4). Biopsy of the salivary gland, on the other hand can be used to find underlying associated systemic diseases (4). The histologic changes are one of the criteria in diagnosing Sjogren's Syndrome, amyloidosis, and sarcoidosis, among other related diseases.

Themanagementofxerostomiaincludespatienteducation with information about causes and complications of dry mouth, oral hygiene education, consultation with primary care providers regarding change of dose or drug for systemic medications (1,2,4,13). Sialagogues such as pilocarpine and cevimeline are prescribed to stimulate saliva production as a method to manage xerostomia (1,2,4,13). Pilocarpine acts on wide spectrum of cholinergic parasympathomimetic activity on M1 and M3 receptors thus its adverse effect is greater while cevimeline targets both receptors but with more affinity on M3 receptor, resulting lesser adverse effects (14). A study by Farag et al (14) compared the effectiveness between pilocarpine and cevimeline in hyposalivation cases yield a result of similar effectiveness among the two sialagogues. The adverse effects of the sialagogues are increased sweating, flushing, nausea, diarrhoea, dizziness, tachycardia and increased urination (14). Acupuncture, an alternative medicine, also has beenalso used in the management of xerostomia related to head and neck cancer irradiation (2,13). It helps in reducing mouth dryness, sticky saliva and frequency to drink water to swallow food at night (15). A study suggested that acupuncture provide direct stimulation of residual salivary gland tissue or increasing the gland's blood supply. (15)

Topical saliva substitutes such as mouthwash, mouth spray, toothpaste, chewing gum, gel, and lozenges help in alleviating dry mouth sensations. They are developed to mimic the physical properties of salivary glycoproteins, antimicrobial components of saliva, and inorganic components of salivary functions (13). The route of administration and duration effect of these formulations are factors affecting patient's preferences regarding saliva substitutes. The ideal product characteristics include rapid relief, long effect duration, simulates saliva, non-irritating, aseptic, no side effects, convenience, accessibility and high patient compliance (13). Different formulations also affect the efficacy of the saliva substitutes. According to Plemons et al. (4), there is no definite conclusion on the most efficacious formulations or products in managing xerostomia.

Mouth spray is one of the saliva substitute products (13). Tanasiewicz al. (7) stated patients highly prefer aerosol saliva substitutes. Sialagogue spray containing 1% malic acid is beneficial in antihypertensive and antidepressant induced xerostomia but has a risk for loss of enamel (2). The product, however, is not without its downside. Villa et al. (2015) stated the efficacy of mouth spay is controversial, with sprays containing several active

components did not improve xerostomia symptoms.

Immunologically active saliva substitute (IASS) is formulated with natural enzymes like lactoperoxidase, lysozyme, glucose oxidase, and lactoferrin mimics natural saliva (9). A study by Montaldo L, et al. (6) concluded that IASS product in therapy can be beneficial in reducing plaque, gingivitis and positive yeast counts. The product in mouthwash form significantly decreases subjective xerostomia scores in the Summated Xerostomia Inventory and improves salivary flow measurement in xerostomia among nasopharyngeal cancer patients due to the product is safe and has good side effect profiles (9).

This study focuses on evaluating the efficacy of Oral7® Moisturizing Spray with IASS formulation in treating xerostomia. It is also the first to be done in the Malaysian population as there is yet a study that compares the mouth spray to other products with the same formulations or even with other formulations. Furthermore, in terms of mode of application, mouth spray has the potential to be more favoured due to its convenience and increased patient compliance. Hence, this study aims to evaluate the efficacy of Oral7® spray formulation in treatment of xerostomia and to evaluate patient's perception towards Oral7® Moisturizing Spray formulation.

METHODS AND MATERIALS

Study type and design

The efficacy of the moisturising spray was assessed in a randomized control trial that was double-blind and parallel designed. The method of sampling used was convenient sampling.

Study population and size

The study was conducted on patients registered in Oral Maxillofacial Department, Hospital Canselor Tuanku Mukhriz and Oral Medicine Clinic in the Faculty of Dentistry Universiti Kebangsaan Malaysia (UKM) who were diagnosed with xerostomia. The patients were chosen based on inclusion criteria that has met and did not land on the exclusion criteria. The inclusion criteria include patients aged 18 years old and above, patients diagnosed with xerostomia (moderate to severe) with an additive score of 4-10 using The Clinical Oral Dryness Score (CODS) (12).

The exclusion criteria were as follows: patients who do not have xerostomia or mild xerostomia (score of 1-3 after being assessed with CODS); patients who use mouthwash or mouth spray within one week before the first week of intervention; patients who have oral motor function deficits; patients unable to utilise chewing gum for stimulated saliva flow rate test; patients with deteriorating cognitive function; patients who are unable to provide saliva samples and patients who are pregnant.

The sample size is calculated by using a sample calculator available in https://riskcalc.org/samplesize/#. The website is dedicated to calculating sample size according to the type of study design. In this study, it is a randomised controlled trial with superiority design (16). At a margin error estimated at 5% and a confidence interval of 95% (a=0.05), at power of 0.9 and drop rate of 5%, a total sample of 40 patients is necessitated, and will be divided into two groups with 20 patients in each group.

The sample size is achieved by a formula for random controlled trial, superior design based on proportion difference as follows:

$$n_c = \left(\frac{Z_{1-\alpha} + Z_{1-\beta}}{d-\delta}\right)^2 \left[\frac{P_T(1-P_T)}{k} + P_C\right];\ n_T = kn_c$$

Where k is the ratio of sample size of treatment group (nT) to sample size to control group (nC). 1-α denotes as confidence interval whereas 1-β denotes as power, or probability of detecting a real effect. PC is the expected proportion of the outcome of interest in control group. PT is the expected proportion of the outcome of interest in the treatment group and PC is the expected proportion of the outcome of interest in control group. In this research, PT is 0.8 while PC is 0.5, respectively. The total sample size for controlled group and treatment group are 19 each. The number is rounded to 20 in controlled group, 20 in treatment group.
Study procedures

Patients diagnosed with moderate or severe xerostomia in Oral Maxillofacial department, Hospital Canselor Tuanku Mukhriz and the Oral Medicine Clinic in Faculty of Dentistry, Universiti Kebangsaan Malaysia were recruited after assessing their fitness into the inclusion criteria of the study. The study method was adapted from Marimuthu et al. (9). The patients were screened with CODS for xerostomia. The selected participants had been briefed, and their consent was obtained verbally and in written consent form. On the first visit, the patients' demographic information such as age, gender, ethnicity, and disease diagnosed related to xerostomia was taken. Baseline salivary function assessment will bewas taken with 1) unstimulated salivary flow test in which patient's saliva wais collected when at rest for 5 minutes, and 2) Stimulated salivary flow test in which patient's saliva will bewas collected after chewing-on-chewing gum for 5 minutes.

The patients were randomised into two groups which are using: 1) Sample A: Oral7® Moisturizing Spray, and 2) Sample B: Brand X Moisturizing Spray. Brand X active ingredients containing saliactive formulation. The ratio of allocation of patients in each group was 1:1.

The samples were repackaged and dispensed into non-pressurised pumps, labelled Sample A and Sample B respectively, 90g equally. These pumps were the same in dimension as to blind the patients to the intervention they will be obtaining. The patients who have started treatment for xerostomia before the study is conducted were instructed to halt the current treatment for a week before the first visit. During the period of intervention, patients were reminded to not use other products or medications for xerostomia unless required to continue. Patients were instructed to spray 3 puffs 4 times per day. The follow up of the patients was done via phone calls or clinic visits to ensure compliance and to report any side effects following the intervention. The estimated intervention period was four weeks to observe marked resolution of the dry mouth symptoms. On the final day of intervention, the patients were called for clinical follow-up. Unstimulated and stimulated salivary flow test were reassessed to compare with the baseline assessment. The patients were given a questionnaire, Product Performance and Attribute Questionnaire, adopted from a study made by Jose et al. (17) to compare the efficacy and preference between the two samples in treatment of xerostomia. Flowchart of procedure was as shown in Figure 1.

The data analysis was done by using the Statistical Package for Social Science (SPSS) version 26 (18). Descriptive data will be expressed as mean ± standard deviation (SD) unless otherwise stated. The salivary flow rate will be analysed against normal value before and after intervention period.

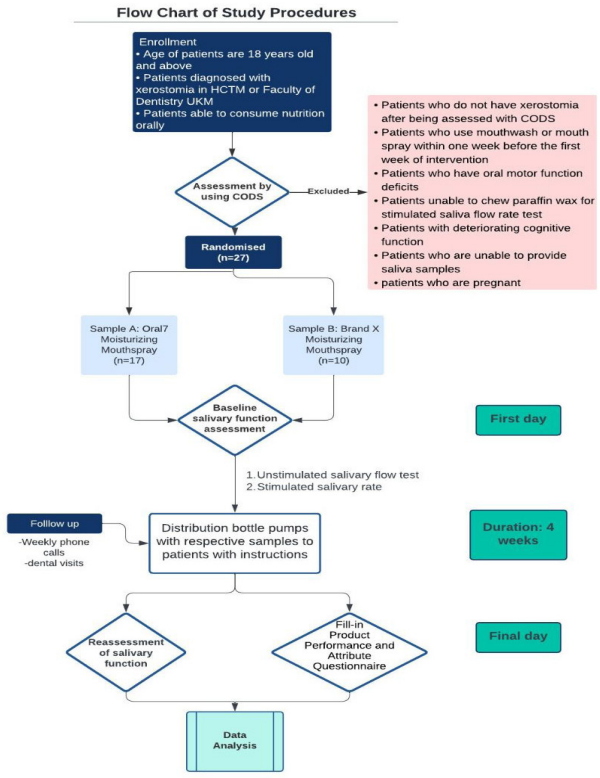

Figure 1: Flowchart of Study Procedure

RESULTS

Demographic data

A total of 35 patients from Oral Maxillofacial department, Hospital Canselor Tuanku Mukhriz and Oral Medicine Clinic in Faculty of Dentistry Universiti Kebangsaan Malaysia (UKM) had participated in the study. 27 of the patients had successfully completed the study procedure. Three (3) patients have yet to complete the study procedure at the time of data collection period ended. Five (5) patients were excluded from the study due to loss of interest, and two (2) did not complete the intervention period instruction, due to having mild xerostomia (n=2), and a repeated sample (n=1). In this report, the result analysed was based on the 27 patients that had completed the study procedures.

The patients of the study consisted of 5 male (18.5%) and 22 female patients (81.5%). The age range of participants are between 25 years old to 91 years old. The average age among the patients is 62.07±16.41 years old.

Based on Table I, the ethnicity most distributed is Malay with 12 patient (44.4%), Chinese with 10 patients (37%), Indian with two patients (7.4%) and three patients of other ethnicities (11.1%).

Table I: Patients' Demographic and Health Conditions

		Number (n)	Percentage (%)
Ethnicity	Malay	12	44.4
	Chinese	10	37
	Indian	2	7.4
	Others	3	11.1
Health status/ condition related to xerostomia	Smoker	0	0
	Undergo radiotherapy or chemotherapy	3	11.1
	Autoimmune disease	2	7.4
	Systemic condition	16	59.3
	Consume xerostomia-inducing medication	19	70.4
	Denture wearer	8	26.6
	Fixed prostheses or implant	1	3.7
	No illness	4	14.8

Based on Table I, the patient's health condition which is relevant to xerostomia was also recorded. Most patients had a combination of health factors, most being systemic conditions and on medications. None of the patients were current smokers. Four patients were fit and healthy. Most of the patients were on medication-causing xerostomia (n=19) such as diuretics, anticholinergics, antihistamines, antihypertensive and antipsychotics. 16 patients have existing systemic conditions such as hypertension, diabetes and hypercholesterolemia. Three patients have undergone radiotherapy and/or chemotherapy; two of them with history of radiotherapy

on the head and neck region and one had a history of chemotherapy for breast cancer.

A total of four of these patients smoke or were former smokers. There were three patients who consumed alcohol. Majority patients had dry mouth during meals [n=20], perceive small amounts of saliva in their mouth most of the time [n=20] and feel dry mouth at night or upon waking up [n=23]. Some patients [n=14] complain of having difficulty swallowing food.

Clinical Oral Dryness Score (CODS)

Based on Table II, majority of the patients had clinical signs of xerostomia such as mirror stick to buccal mucosa (n=25), mirror stick to tongue (n=23), no saliva pooling in floor of mouth (n=21) and lobulated or fissured tongue (n=18). Based on Table II, most of the patients (n=24) had CODS score between 4-6 and categorised as moderate xerostomia while three patients scored between 7-10 in CODS and categorised as severe xerostomia.

Table II: Clinical Oral Dryness Score (CODS) and Xerostomia Severity

Criteria		Number (n)
Mirror sticks to buccal mucosa	Yes	25
	No	2
Mirror sticks to tongue	Yes	23
	No	4
Frothy saliva	Yes	9
	No	18
No saliva pooling in floor of mouth	Yes	21
	No	6
Tongue shows loss of papillae	Yes	9
	No	18
Altered/ smooth gingival architecture	Yes	7
	No	20
Glassy appearances to other oral mucosa especially palate	Yes	8
	No	19
Tongue lobulated/fissured	Yes	18
	No	9
Active or recently restored (in the last 6 months) cervical caries (more than 2 teeth)	Yes	3
	No	24
Debris on palate (excluding under dentures)	Yes	2
	No	25
CODS score	4	18
	5	5
	6	1
	7	3
Xerostomia severity based on CODS	Mild	0
	Moderate (4-6)	24
	Severe (7-10)	3
Had started treatment for xerostomia	No	16
	Yes	11

Saliva Flow Test

Based on Table III, there is an increase in mean of unstimulated saliva volume for both Oral7® sample group [(1.12±1.03) mL to (1.77±1.28) mL] and Brand X sample group [(1.58±0.99) mL to (1.71±0.94) mL]. There is an increase in the mean of unstimulated saliva flow both the Oral7® sample group [(0.22±0.21) mL/min to (0.35±0.26) mL/min] and Brand X sample group [(0.32±0.20) mL/min to (0.38±0.20) mL/min]. The result is presented as bar chart in Figure 2.

Table III: Baseline Unstimulated/Stimulated Salivary Volume And Unstimulated Salivary Flow Test And After Intervention

	Sample type			
	ORAL7		BRAND X	
	Mean	Standard Deviation	Mean	Standard Deviation
Baseline Unstimulated saliva volume (mL)	1.12	1.03	1.58	.99
Unstimulated saliva volume after intervention(mL)	1.77	1.28	1.71	.94
Baseline Unstimulated salivary flow test (mL/min)	.22	.21	.32	.20
Unstimulated salivary flow test after intervention (mL/min)	.35	.26	.38	.20
Baseline stimulated saliva volume (mL)	4.04	2.28	3.65	2.03
Stimulated saliva volume after intervention (mL)	4.92	2.75	3.42	1.50
Baseline stimulated salivary flow test (mL/min)	.73	.46	.73	.41
Stimulated salivary flow test after (mL/min)	.91	.58	.68	.30

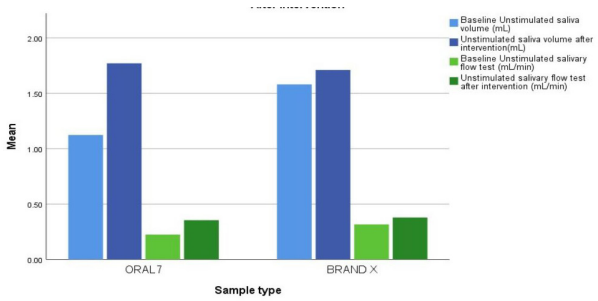

Figure 2: Bar Chart Mean of Unstimulated Saliva Volume (mL) and Salivary Flow Test (mL/min)- Before and After Intervention. In Figure 2, the bar chart shows that there is a greater unstimulated saliva volume increase in the Oral7® sample group compared to Brand X sample group after intervention

In Table III, there is an increase of mean of stimulated saliva volume for Oral7® sample group [(4.04±2.28) mL to (4.92±2.75) mL], while there is a decrease in Brand X sample group [(3.65±2.03) mL to (3.42±1.50) mL]. There is an increase in mean of stimulated saliva flow for the Oral7® sample group [(0.73±0.46) mL/min to (0.91±0.58) mL/min] while there is a decrease in Brand X sample group [(0.73±0.41) mL/min to (0.68±0.30) mL/min]. The result is presented as bar chart in Figure 3.

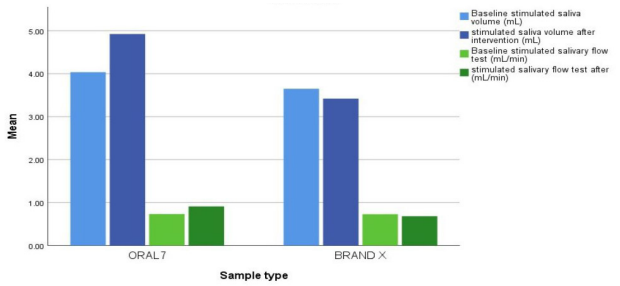

Figure 3: Bar Chart Mean of Stimulated Saliva Volume (mL) and Salivary Flow Test (mL/min)- Before and After Intervention. In Figure 3, the bar chart shows the increase in stimulated saliva volume and flow rate in Oral7® sample group, whereas in Brand X sample group, there is a decrease in saliva volume and flow rate after intervention.

Product Performance and Attribute Questionnaire

From Table IV, the responses between 24 participants showed positive feedback ranging from "Fair" to "Excellent" across the items list. Both Oral7® sample and Brand X sample participants' response range between "Fair", "Good", "Very Good" and "Excellent".

Table IV: Product Performance and Attribute Questionnaire

		Sample type			
		ORAL7		BRAND X	
		Count	Sample percentage %	Count	Sample percentage %
Relieving the discomfort of dry mouth	Poor	0	0.0%	0	0.0%
	Fair	3	17.6%	5	50.0%
	Good	10	58.8%	3	30.0%
	Very good	4	23.5%	1	10.0%
	Excellent	0	0.0%	1	10.0%
Feeling comfortable in the mouth	Poor	0	0.0%	0	0.0%
	Fair	3	17.6%	4	40.0%
	Good	7	41.2%	2	20.0%
	Very good	6	35.3%	2	20.0%
	Excellent	1	5.9%	2	20.0%
Soothing your mouth	Poor	0	0.0%	0	0.0%
	Fair	2	11.8%	5	50.0%
	Good	9	52.9%	2	20.0%
	Very good	6	35.3%	2	20.0%
	Excellent	0	0.0%	1	10.0%
Allowing you to speak without difficulty	Poor	0	0.0%	0	0.0%
	Fair	3	17.6%	6	60.0%
	Good	8	47.1%	1	10.0%
	Very good	3	17.6%	2	20.0%
	Excellent	3	17.6%	1	10.0%
Effectively moistens your mouth	Poor	0	0.0%	0	0.0%
	Fair	2	11.8%	5	50.0%
	Good	10	58.8%	2	20.0%
	Very good	3	17.6%	2	20.0%
	Excellent	2	11.8%	1	10.0%

CONTINUE

Table IV: Product Performance and Attribute Questionnaire (CONT.)

		Sample type			
		ORAL7		BRAND X	
		Count	Sample percentage %	Count	Sample percentage %
Effectively lubricates your mouth	Poor	0	0.0%	0	0.0%
	Fair	3	17.6%	5	50.0%
	Good	8	47.1%	2	20.0%
	Very good	5	29.4%	2	20.0%
	Excellent	1	5.9%	1	10.0%
Helping to freshen your breath	Poor	0	0.0%	0	0.0%
	Fair	4	23.5%	5	50.0%
	Good	8	47.1%	2	20.0%
	Very good	2	11.8%	3	30.0%
	Excellent	3	17.6%	0	0.0%
Protecting your mouth from drying out	Poor	0	0.0%	0	0.0%
	Fair	2	11.8%	5	50.0%
	Good	11	64.7%	2	20.0%
	Very good	3	17.6%	2	20.0%
	Excellent	1	5.9%	1	10.0%
Providing whole mouth comfort	Poor	0	0.0%	0	0.0%
	Fair	3	17.6%	6	60.0%
	Good	10	58.8%	2	20.0%
	Very good	3	17.6%	1	10.0%
	Excellent	1	5.9%	1	10.0%
Helping you to swallow without difficulty	Poor	0	0.0%	0	0.0%
	Fair	4	23.5%	5	50.0%
	Good	8	47.1%	2	20.0%
	Very good	3	17.6%	1	10.0%
	Excellent	2	11.8%	2	20.0%
Helping mouth feel "normal"	Poor	0	0.0%	0	0.0%
	Fair	2	11.8%	5	50.0%
	Good	9	52.9%	4	40.0%
	Very good	6	35.3%	1	10.0%
	Excellent	0	0.0%	0	0.0%
Having a long-lasting dry mouth relief	Poor	0	0.0%	0	0.0%
	Fair	5	29.4%	8	80.0%
	Good	8	47.1%	1	10.0%
	Very good	4	23.5%	0	0.0%
	Excellent	0	0.0%	1	10.0%
Having a long-lasting lubricating effect	Poor	0	0.0%	0	0.0%
	Fair	5	29.4%	8	80.0%
	Good	7	41.2%	1	10.0%
	Very good	5	29.4%	1	10.0%
	Excellent	0	0.0%	0	0.0%
Having a long-lasting moisturizing effect	Poor	0	0.0%	0	0.0%
	Fair	5	29.4%	8	80.0%
	Good	6	35.3%	1	10.0%
	Very good	5	29.4%	0	0.0%
	Excellent	1	5.9%	1	10.0%

Majority of the Oral7® sample patients responded "Good" across the table while in majority of Brand X sample patients responded "Fair" in most of the questions. Oral7® sample has significant positive respond more than in Brand X in terms of "allowing to speak without difficulty", " effectively moist the mouth", " protecting the mouth from drying out", " providing whole mouth comfort", " helping to swallow without difficulty", " helping mouth feel normal", and " having long lasting dry mouth relieve", "having long lasting lubricating effect" and "having a long-lasting moisturizing effect."

DISCUSSION

Xerostomia is a condition when a patient experience a subjective sensation of mouth dryness (4,5,7). The prevalence of xerostomia range between 5.5% to 46% as it is based on the procedure and population studied (19). Xerostomia patient can present with increased incidents of dental caries, periodontal disease, ulcerations of the oral cavity tissues and other oral pathologies due to insufficient saliva present in the oral cavity.
One of the managements is topical saliva substitutes such as mouthwash, mouth spray, toothpaste, chewing gum, gel, and lozenges. Their formulations are developed to mimic the components of saliva and alleviate xerostomia symptoms (13). Immunologically active saliva substitute (IASS) is formulated with natural enzymes like lactoperoxidase, lysozyme, glucose oxidase and lactoferrin mimics natural saliva (9). Oral7® has released a new product in form of a mouth spray containing IASS formulations. This study aimed to evaluate the efficacy of Oral7 Moisturizing Spray in xerostomia management.

Demographic data

Participant recruitment via active recruitment strategy resulted in 35 participants. The recruitment was limited to patients having moderate to severe xerostomia based on CODS scoring system. The number of participants completing the procedures is further reduced when five participants were excluded before study completion and additional three has not completed the course in the data collection period. It can be factored to the patients' lack of knowledge regarding their oral dryness status and unwillingness to commit to the research. Clinical trial requires excellent communication between the researcher, participant and involved personnel to ensure the study is carried out without issues and complications. The study was carried out in two phases which are baseline phase and after intervention phase within a month of interval time. Childs et al. (20) believed that time commitment is a determining factor for patients to participate or withdraw from a study. Patel M, et al. (21) also mentioned that the number of research instruments should be reduced to reduce the extra participant burden. In the current study, the research instruments used were CODS, salivary flow test and questionnaire.

Clinical Oral Dryness Score (CODS)

For the CODS, Osailan et al. (202) integrated several clinical criteria resulting in 10 features of dryness in mouth. The study aimed to differentiate between mild (score 1-3), moderate (score 4-6), and severe (score 7-10) hyposalivation during routine assessment. In this study, majority of patients had positive criteria on "mirror stick to buccal mucosa," "mirror stick to tongue," "no saliva pooling in floor of mouth" and "lobulated or fissured tongue." The first two criteria stated are consistent with a study by Zainab Assy, et al. (213) where majority of the patients with perceived oral dryness selected these criteria in CODS. The validity of the CODS is sound as many studies have utilized them. Derk et al. (224) stated CODS was only significantly related to unstimulated whole saliva volume in the hyposalivation group. In addition to that, our study concludes that CODS can only be used to differentiate between hyposalivation and normal salivation.

Salivary Flow Test

Based on the results obtained from the 27 participants, there is a significant increase in unstimulated salivary volume and flow rate in both sample groups, with Oral7 sample group being higher than in Brand X sample group. Theis shows the effectiveness of Oral7® Moisturizing Mouthspray in treatment of xerostomia through IASS formulation. Similar formulation was used in other Oral7® products such as the mouthwash form. A study by Marimuthu, D, et al. (9) stated that Oral7® mouthwash improves the salivary flow among nasopharyngeal cancer patients with xerostomia. finding suggests that Oral7® Moisturizing Mouthspray significantly improves unstimulated salivary volume and flow rate, with a greater effect compared to Brand X. This is particularly relevant given that most patients in the study population suffer from xerostomia due to medications, systemic conditions, or past cancer treatments.

The increase in salivary flow observed with Oral7® aligns with its IASS formulation, which likely mimics natural saliva composition, providing relief for those experiencing dry mouth. Since many of the patients are on xerogenic medications (e.g., diuretics, antihypertensives, and antipsychotics) or have systemic conditions like diabetes and hypertension, their baseline salivary flow is reduced. The ability of Oral7® to enhance salivary flow suggests it could be particularly beneficial in counteracting medication-induced xerostomia.
Additionally, the study by Marimuthu et al. (9) supports the effectiveness of Oral7® mouthwash in nasopharyngeal cancer patients with xerostomia, further reinforcing its potential in patients who have undergone radiotherapy or chemotherapy, as seen in the study population. Since two patients had radiotherapy to the head and neck, and one underwent chemotherapy for breast cancer,

the improvement in salivary flow observed with Oral7® could be particularly meaningful for these individuals, as they are at high risk of severe and long-term salivary gland dysfunction.

Overall, the findings suggest that Oral7® products, including the moisturizing mouth spray and mouthwash, could serve as effective interventions for managing xerostomia in patients experiencing low salivary flow due to medications, systemic conditions, or cancer treatments.

However, tTher result of this study, is not sufficient to determine whether the Oral7 sample is superior to the Brand X sample in treating xerostomia due to insufficient patients and imbalanced distribution to achieve better association. In this study, unstimulated salivary flow test and stimulated flow test has shown to be the best method to measure changes of salivary production among patients with xerostomia undergoing saliva substitute treatment in addition to potentially be strongly associated to xerostomia and its risk factors as well.

Saliva flow rate test can be done via draining, spitting, swab and suction method. Draining method is accepted globally as a standard investigative tool in measuring unstimulated saliva flow rate in diagnosing Sjogren's syndrome (19). In a study by Hoseini et al (235), salivary flow rate was used to examine the salivary changes in diabetic patients with a statement that its findings showed significant reduction of salivary flow rate in both Type 1 and Type II diabetes. The study also stated the several factors that influence the outcome of the salivary flow tests such as methods of collecting, the time of collection, health conditions of the patients and diversity of patients of all ages and gender.

The validity of the salivary flow test is sound as many studies have carried it out to evaluate the methods of saliva collecting. In a study conducted by Hayashida et al (246), its purpose was to explain the effectiveness of non-invasive investigation tools in distinguishing neurogenic/neuropsychiatric disorders and drugs (DND) and Sjogren Syndrome (SS). The results found that the decrease of stimulated and unstimulated salivary flow rate in SS patients were due to salivary gland dysfunction whereas in DND patients were caused by suppression of central nervous system and innervation of salivary glands. Reduction in both tests caused chronic symptoms such as xerostomia and hyposalivation.

Lee et al (257) also had used investigative tools to obtain clinically optimal procedure to assess salivary flow rate and oral dryness. The downside of salivary flow tests is that they may give discomfort to the patients and need lengthy period of five minutes to complete this procedure. This may affect patient's compliance and cause errors in obtaining samples as accurately as possible. For a measuring tool to be valuable to both patient and the practitioner, it should be the most convenient, economical and reproducible to obtain more accurate data (267).

Product Performance and Attribute Questionnaire (PPAQ)

This study utilises the Product Performance and Attribute Questionnaire (PPAQ) to evaluate patients' perception towards the effectiveness of the sample that were given to them in reducing their xerostomia symptoms. It was adapted from a study by Jose et al (17) which uses the PPAQ to observe the differences of efficacy between test sample (experimental mouthwash) and the controlled sample (water). Statistical analysis was done by calculating the area-under-the-curve. From the results, there was a significant difference between the two groups, with the mouthwash group being the superior sample over water sample. The measurement of significance could not be calculated in this study to distinguish the association between the questionnaire items and the efficacy of both mouth spray samples in management of xerostomia due to the limited number of data obtained.

Limitation

In this study, the number of participants recruited is low due to time constraint among the researchers and patients, and patient's knowledge about xerostomia as well as compliance issues to complete the study phase. Due to these circumstances, the data collected were limited. Hence, obtaining a strong significance between variables became difficult.

However, this study achieved its aim to show the efficacy of Oral7® mouthspray in treating xerostomia. The study also validates the measuring tool that are suitable in measuring the efficacy of the mouth spray samples. Although the number of participants were limited, their perception of xerostomia, and its treatment are very much relevant.

CONCLUSION

Oral7® Moisturizing mouth spray is efficient in improving the unstimulated and stimulated salivary flow of patients with xerostomia as well as obtained positive feedback from the Product Performance and Attribute Questionnaire. Future studies should be conducted in consideration of the selection of population sample such as specifying type of condition of patients with xerostomia and expanding outside dental related department such as hospital-based patients of various disciplines. Oral7® Moisturizing Mouthspray is a new product released commercially in Malaysian market, further research should be done covering bigger population to obtain more significant results.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

ETHICAL CLEARANCE

The study was conducted in compliance with ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guideline. Detailed protocol and ethical approach were approved by the UKM Research Ethics Committee, with ethical reference number JEP-2022-310.

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