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Dose- and Time-Related Effects of Pilocarpine Mouthwash on Salivation

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Purpose: Pilocarpine as a salivation stimulant in pill form has mostly been used to relieve oral dryness for xerostomic patients but its use may often be limited due to variable side effects from systemic absorption. Therefore, the purpose of this study was to investigate the effects of pilocarpine mouthwash on salivation according to the variable concentration and duration for healthy volunteers. Related adverse effects and subjective assessment on its effects on salivation were also examined.

Methods: This study was performed as placebo-controlled, double-blind, randomized clinical trial. Thirty healthy volunteers (male=23, mean age=22.2 years) were randomly allocated to 6 groups with the different concentration of pilocarpine mouthwash (placebo, 0.1%, 0.5%, 1.0%, 1.5%, and 2.0%). The whole experiment consisted of 3 sessions according to the duration of mouthwash, i.e., 1, 3, and 5 minutes with the mean wash-out period ≥2 days between the sessions. Unstimulated whole saliva was collected before and after gargling with a mouthwash.

Results: Salivation of the higher concentration groups ≥1% significantly increased than those of lower concentration group. The application period of mouthwash did not cause any changes of salivary flow rate at the higher concentrations ≥1.0%. The lower concentrations of 0.5% and 0.1% had no effects on salivation even after 5-minute mouthwash. There was no significant difference between blood pressure and pulse rate before and after use of mouthwash.

Conclusions: From the results of the current study, pilocarpine mouthwash with at least 1.0% concentration more than a minute might be clinically effective in salivation without any serious side effects. Dose of mouthwash rather than duration seems to be a critical factor to salivation.

Key Words: Dose; Mouthwash; Pilocarpine; Salivation; Time; Topical

INTRODUCTION

Though xerostomia is defined as the subjective perception of dry mouth,[1] it is commonly associated with salivary gland hypofunction, a condition in which unstimulated or stimulated salivary flow is significantly reduced, and can also result in changes of composition of saliva.[2-4]

It is generally accepted that aging per se has no significant clinical impact on salivary flow rates, yet the prevalence of xerostomia appears to increase with age, mainly affecting the middle-aged and elderly population. There is also evidence that medication use, and particularly polypharmacy may increase the risk of xerostomia.[3] As saliva is crucial in maintaining oral health, long-standing xerostomia have a major impact on a patient's oral health and quality of life.[3]

As saliva is difficult to reproduce and as yet an ideal replacement does not exist,[5] salivary stimulants, such as oral pilocarpine have mostly been used to relieve symptoms of oral dryness for patients with xerostomia. Unfortunately its

non-specific stimulation of muscarinic receptors[6,7] causes a number of unwanted side effects including nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, bladder tightness, urinary frequency, headache, syncope, sweating, tremor, flushing, hypotension, hypertension, bradycardia and arrhythmia.[8] Due to these adverse side effects, systemic use of pilocarpine may often be restricted in xerostomic patients who are predominantly middle-aged and elderly persons, possibly having 1 and more of systemic diseases.

In this regards, topical pilocarpine can be considered as a promising alternative. Though the rationale for topical administration of pilocarpine is to minimize adverse side effects of systemic pilocarpine, topical use is expected to offer some other benefits: there is mechanical salivary stimulation.[8-12]

There exist a few studies concerning about topical use of pilocarpine. In 1980, topical use of pilocarpine was mentioned in a United States patent document, reporting that the 0.025% to 1% pilocarpine mouthwash was effective for dry mouth relief.[13] Park[14] compared salivary flow rate with chewing tablets containing 5 mg pilocarpine but total amounts of saliva were not significantly different between pilocarpine and placebo chewing tablets. Salivary flow rate in healthy volunteers was evaluated between 2% pilocarpine solution, 5 mg pilocarpine tablet and placebo solution, and promising results were found that 2% pilocarpine solution has comparable effect compared with 5 mg tablets in the study of Park et al.[15]

Therefore, the purpose of this study was to investigate the effects of pilocarpine mouthwash on salivation according to the various concentration and duration for healthy volunteers prior to establishment of clinical usefulness of topical use in xerostomic patients. Related adverse effects and subjective assessment of its effects on salivation were also evaluated.

MATERIALS AND METHODS

1. Subjects

Thirty healthy adults voluntarily participated in this study (23 males and 7 females). Their mean age was 22.2 years old (ranging from 19 to 30 years) and mean weight of them was 65.4 kg (ranging from 48 to 100 kg). Excluded were those with history of allergy to pilocarpine; those with cardiovascular, renal and pulmonary diseases including asthma, chronic obstructive pulmonary diseases; those with acute iritis or narrow-angle (angle closure) glaucoma; those in pregnancy or lactation. All of the participants provided written informed consents before enrollment.

2. Experimental Design

This study was designed as placebo-controlled, double-blind, randomized clinical trial. Its flowchart was represented in Fig. 1. The whole experimental protocol was reviewed and approved by Institute Review Board of Dankook University Dental Hospital, Cheonan, Republic of Korea (IRB No. H-1309/009/006).

3. Preparation of Experimental Solutions for Mouth Rinse

Six different concentrations of pilocarpine mouthwash including placebo were prepared by mixing 2% pilocarpine ophthalmic solution (Isoptocarpine; Alcon Korea Ltd., Seoul, Korea) and commercially-available mouth gargle (Care Gargle; Hanmi Pharmaceutical Co., Ltd., Seoul, Korea) according to mixing protocol in Table 1. Care Gargle were used as placebo solution and to mask bitter taste of pilocarpine solution, which contained benzethonium HCl 10 mL/100 mL. Four milliliters of mouthwash with various

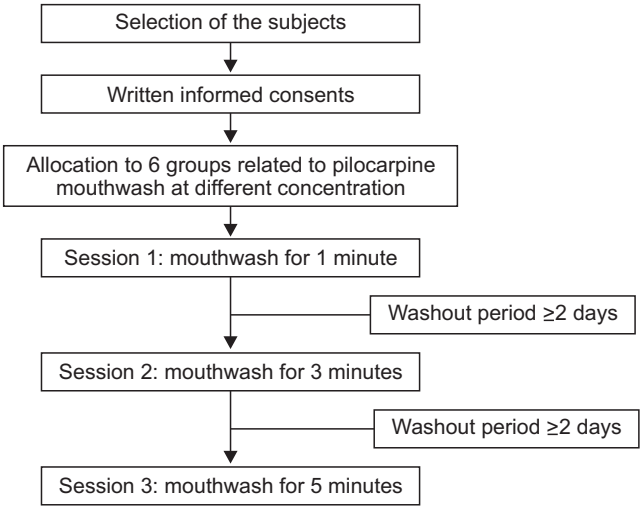

Fig. 1. Flow of the experiment (each session comprises measurement of vital sign and unstimulated salivary flow rate and questionnaires).

Table 1. Mixing protocol of experimental solutions

Variable	2% Isoptocarpine (mL)	Care Gargle (mL)
Placebo	0.0	4.0
0.1% pilocarpine mouthwash	0.2	3.8
0.5% pilocarpine mouthwash	1.0	3.0
1.0% pilocarpine mouthwash	2.0	2.0
1.5% pilocarpine mouthwash	3.0	1.0
2.0% pilocarpine mouthwash	4.0	0.0

concentration was prepared in the morning of each experimental day and given to the subjects without any information about its concentration. The examiners were not given such information, either.

4. Procedure

Thirty volunteers were randomly allocated to 6 groups according to the different concentration of pilocarpine mouthwash. Fig. 1 represents our experiment flow. The whole experiment consisted of 3 experimental sessions according to application time of mouthwash (1, 3, and 5 minutes) with wash-out period of at least 2 days between the sessions. Prior to experiments, all subjects underwent baseline medical history taking and physical examination.

All experimental sessions were conducted between 9:00 to 12:00 in the morning to minimize the effects of diurnal variation. The subjects were instructed not to eat, drink, smoke, or perform oral hygiene, which may cause the chemical or mechanical salivary stimulation, for at least 1 hour before a saliva collection.

The subjects were instructed to maintain the solution in the mouth for a given period of time, without swallowing and being very careful to spit the entire volume of the solution. To evaluate salivary flow rate, unstimulated whole saliva was collected 6 times—before treatment (baseline) and at 20, 40, 60, 90, 120 minutes after gargling. Whole saliva was collected by having the subjects swallow to empty the mouth of saliva, then refraining from swallowing for 1-minute and expectorating into a tube. The collection volumes were determined gravimetrically: the saliva-filled tube was weighed and then the weight of the tube measured previously was subtracted.

After finishing a session of 120 minutes, the subjects were asked to complete a self-administrated questionnaire about subjective effects on salivation and potential side effects, such as facial flushing, sweating, palpitation, nausea, dizziness, headache, increased urinary frequency and gastrointestinal irritation. Subjective assessment on salivation was obtained using 10-cm visual analogue scales (VAS) ranging from 0 to 10: 0, no effect at all and 10, highly effective salivation. Blood pressure and pulse rate were measured and recorded before and after each session.

5. Statistical Analysis

Statistical analysis was performed by PASW Statistics ver. 18.0 software (IBM Co., Armonk, NY, USA). Dose- and time-related effects on salivation were investigated by repeated measures two-way analysis of variance (ANOVA) and multiple comparison tests. VAS for subjective assessment on salivation and change of vital signs, such as blood pressure and pulse rate before and after the experimental session was also analyzed by the same statistical methods. Statistical significance was defined as $p<0.05$.

RESULTS

All of 30 subjects completed the whole experiments with no drop-out. Mean wash-out period between experimental sessions was 4.1 days, ranging from 2 to 15 days.

1. Dose-Effect of Pilocarpine Mouthwash

Fig. 2A represents salivary flow rates by topical use of pilocarpine solutions at different concentrations for 5 minutes. Repeated measures two-way ANOVA revealed significant difference between different concentrations ($p<0.001$) and between elapsed time ($p=0.014$). The 2.0% and 1.5% pilocarpine mouthwash significantly increased salivation compared to other lower concentration solutions ($p<0.05$, multiple comparison tests). Salivary flow rates between 1.5% and 2.0% of mouthwash did not differ statistically. There was no significant difference between placebo, 0.1% and 0.5% groups. Like placebo solution, effects of 0.1% and 0.5% of pilocarpine mouthwash on salivation appear to be negligible. Overall, increase of salivation was noticeable from 40 minutes after mouthwash and increased salivary flow rate persisted up to 120 minutes. The 2.0% solution had peak of salivation between 40 and 60 minutes after mouthwash

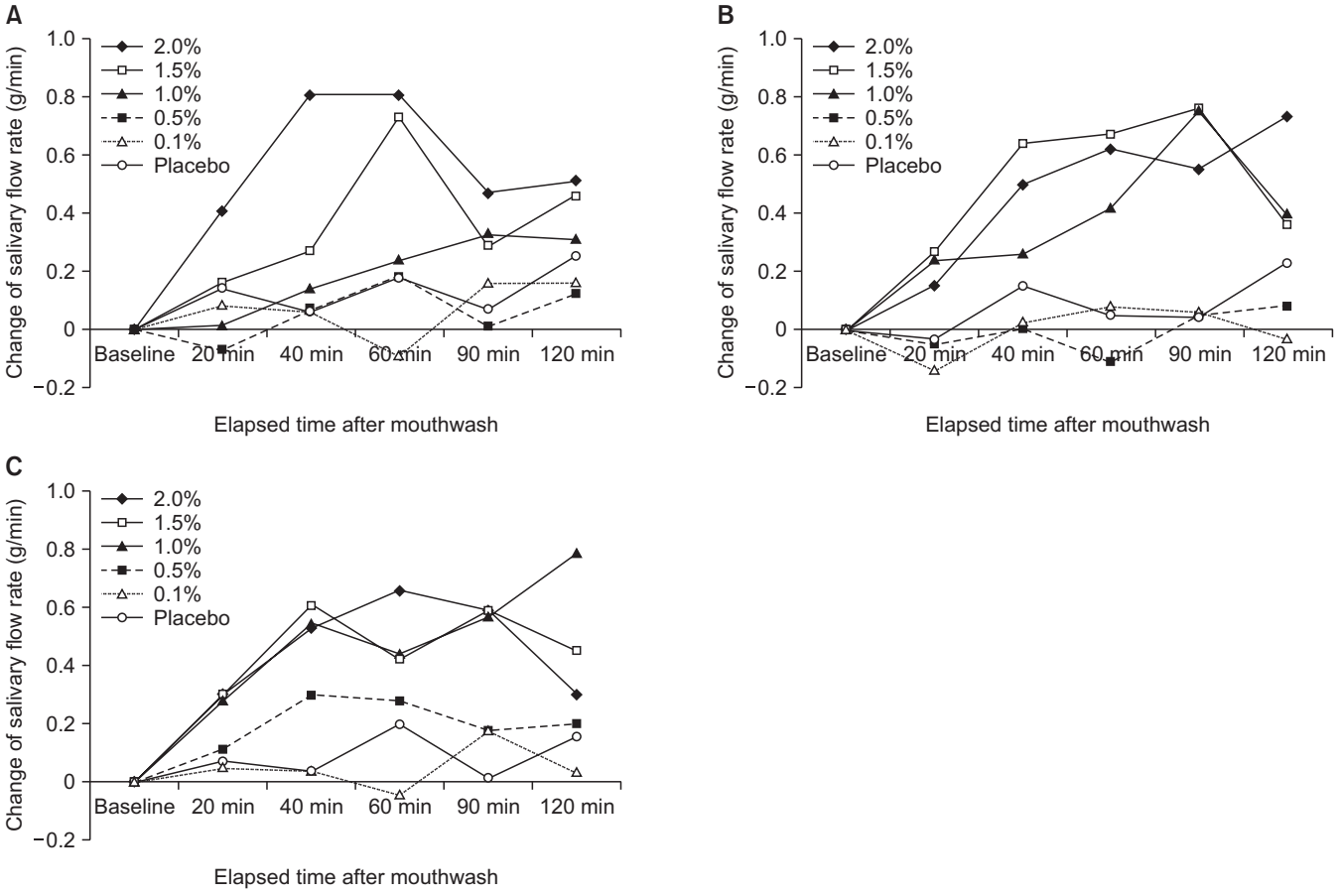

Fig. 2. Dose-effect of pilocarpine mouthwash. (A) Change of salivary flow rate following pilocarpine mouthwash at different concentrations for 5 minutes. Significant difference between pilocarpine mouthwash at different concentrations and between elapsed time ($p<0.001$ and $p=0.014$, respectively; Repeated measures two-way analysis of variance [ANOVA]). Significant increase of salivation at 2.0% compared to placebo, 0.1%, 0.5%, and 1.0%, significant increase of salivation at 1.5% compared to 0.1% and 0.5% ($p<0.05$, multiple comparison tests); significant increase of salivation at 40, 60, 90, 120 minutes after mouthwash compared to baseline ($p<0.05$, multiple comparison tests). (B) Change of salivary flow rate following pilocarpine mouthwash at different concentrations for 3 minutes. Significant difference between pilocarpine solutions at different concentrations and between elapsed time ($p<0.001$ and $p=0.001$, respectively, Repeated measures two-way ANOVA). Significant increase of salivation at 2.0%, 1.5%, and 1.0% compared to placebo, 0.1% and 0.5% ($p<0.05$, multiple comparison tests); significant increase of salivation at 40, 60, 90, 120 minutes after mouthwash compared to baseline ($p<0.05$, multiple comparison tests). (C) Change of salivary flow rate following pilocarpine mouthwash at different concentrations for a minute. Significant difference between pilocarpine mouthwash at different concentrations and between elapsed time ($p<0.001$ and $p<0.001$, respectively; Repeated measures two-way ANOVA). Significant increase of salivation at 2.0%, 1.5%, and 1.0% compared to placebo, 0.1% and 0.5% ($p<0.05$, multiple comparison tests); significant increase of salivation at 20, 40, 60, 90, 120 minutes after mouthwash compared to baseline ($p<0.05$, multiple comparison tests). Change of salivary flow rate indicates the difference between the salivary flow rates at baseline and 20, 40, 60, 90, and 120 min.

and peak time of 1.5% was at 60 minutes and then slow decrease was observed in both of the solutions, while 1% solution increased steadily salivary flow rate until 90 minutes after mouthwash and then decreased ($p<0.05$, multiple comparison tests). Changes of salivary flow rate in placebo, 0.1% and 0.5% solutions groups appear to be inconsistent with elapsed time.

After pilocarpine mouthwash at different concentrations for 3 minutes, there was dose-dependent effect on salivary flow rate ($p<0.001$, two-way ANOVA) as shown in Fig. 2B. Salivation was significantly greater in 1.0%, 1.5% and 2.0% groups than placebo, 0.1% and 0.5% groups ($p<0.05$, multiple comparison tests). There was no significant difference between placebo, 0.1% and 0.5% groups. There was significant increase of salivation at 40, 60, 90 and even 120 minutes after mouthwash compared to baseline ($p<0.05$, multiple comparison tests).

Fig. 2C presents with salivary flow rate after mouthwash

with different concentrations for a minute. Like the results of mouthwash for 3 or 5 minutes, significant differences were observed among the different concentrations of pilocarpine mouthwash ($p<0.00$) and among elapsed time ($p<0.001$). The 2.0%, 1.5% and 1.0% of pilocarpine mouthwash significantly increased salivation compared to those of placebo, 0.1% and 0.5% ($p<0.05$, multiple comparison tests). There was also no significant difference between placebo, 0.1% and 0.5%. Compared to baseline salivary flow rate, salivation increased significantly from at 20 minutes and decreased after 90 minutes, although salivation at 120 minutes was yet higher than baseline ($p<0.05$, multiple comparison tests).

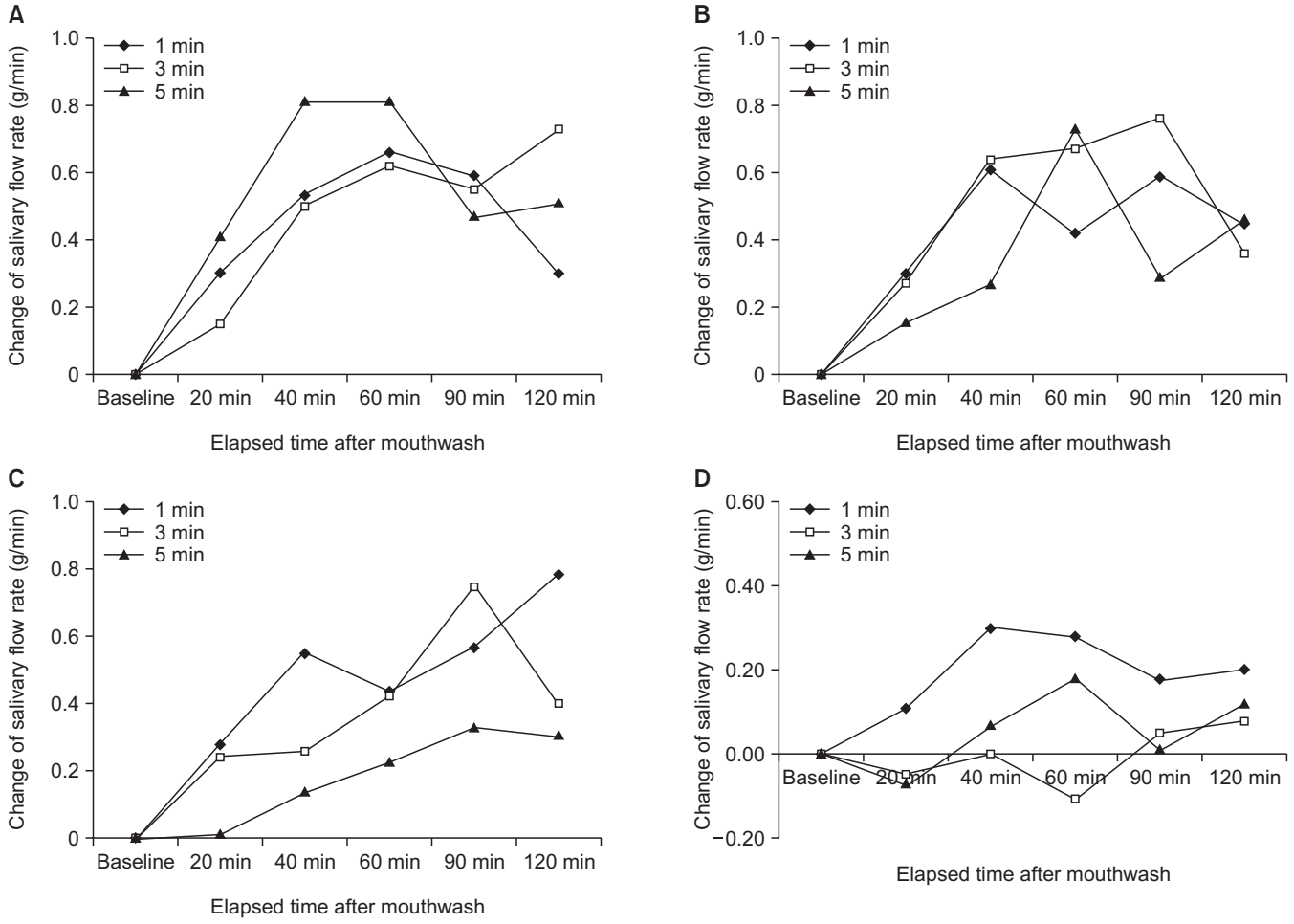

Fig. 3. Time-effect of pilocarpine mouthwash. (A) Change of salivary flow rates at 2.0% pilocarpine mouthwash. No significant difference between duration of mouthwash but significant increase of salivation with elapsed time ($p<0.001$; Repeated measures two-way analysis of variance [ANOVA]); Significant increase of salivation at 20, 40, 60, 90, 120 minutes compared to baseline ($p<0.05$, multiple comparison tests). (B) Change of salivary flow rates at 1.5% pilocarpine mouthwash. No significant difference between duration of mouthwash but significant increase of salivation with elapsed time ($p=0.013$; Repeated measures two-way ANOVA); Significant increase of salivation at 40, 60, 90, 120 minutes compared to baseline ($p<0.05$, multiple comparison tests). (C) Change of salivary flow rates at 1.0% pilocarpine mouthwash. Significant difference between duration of mouthwash and between elapsed time ($p=0.028$ and $p=0.02$, respectively; Repeated measures two-way ANOVA); Significant difference of salivation between 1 and 5 minutes ($p=0.009$, multiple comparison t-tests). Significant increase of salivation at 40, 60, 90, 120 minutes compared to baseline ($p<0.05$, multiple comparison tests). (D) Change of salivary flow rates at 0.5% pilocarpine mouthwash. No significant difference between application time of mouthwash and between elapsed time (Repeated measures two-way ANOVA). (E) Change of salivary flow rates at 0.1% mouthwash. No significant difference between application time of mouthwash and between elapsed time (Repeated measures two-way ANOVA). (F) Change of salivary flow rates for placebo solution as mouthwash. No significant difference between application time of mouthwash but significant difference between elapsed time ($p=0.001$; Repeated measures two-way ANOVA); Significant increase of salivation at 60 minutes compared to baseline and at 90 minutes, significant increase of salivation at 120 minutes compared to baseline, at 20, 40, 90 minutes after mouthwash ($p<0.05$, multiple comparison tests).

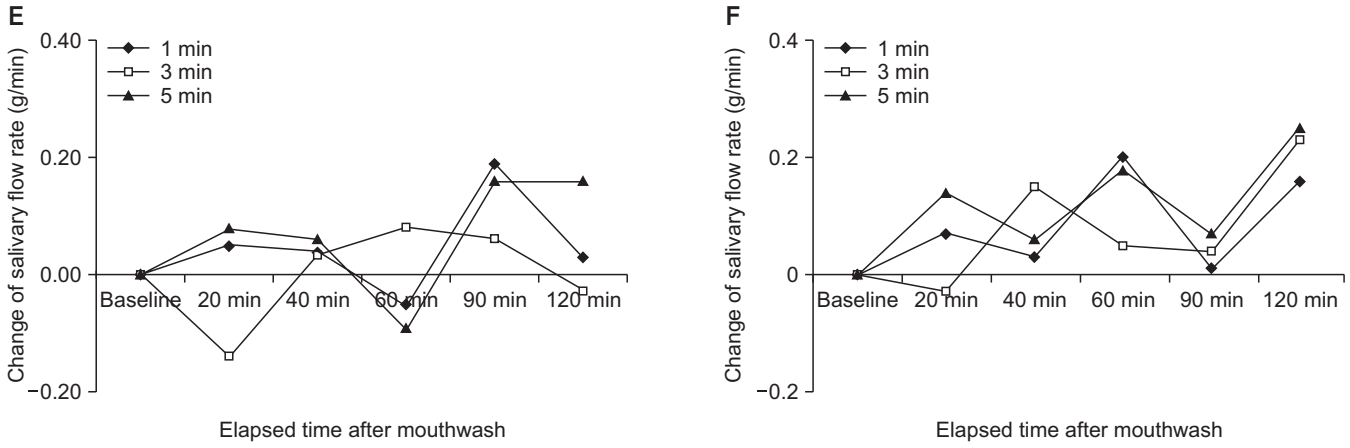

Fig. 3. Continued.

2. Time-Effect of Pilocarpine Mouthwash

Changes of salivary flow rate in relation to application time of mouthwash were shown in Fig. 3A to 3B. Although salivary flow rate after mouthwash with 1.5% and 2.0% concentration increased with elapsed time ($p<0.05$, Fig. 3A, B), application time of mouthwash didn't affect salivation at 1.5% and 2.0% of pilocarpine solutions (Fig. 3A, B). Significant difference between application time was found at 1% solution but, strangely, 1-minute gargle increased salivation greater than 5-minute gargle ($p=0.009$, Fig. 3C). Changes of salivary flow rate were significantly greater from 20 minutes after 2.0% mouthwash than baseline while 1.5% and 1.0% produced significant changes from 40 minutes after mouthwash ($p<0.05$).

When 0.1% and 0.5% pilocarpine solutions were given, there were no significant differences between duration of mouthwash and between elapsed time (Fig. 3D, E). Neither placebo produced noticeable increase of salivation with time. Interestingly, 5-minute gargle with placebo increased salivation, particularly at 120 minutes after mouthwash ($p<0.05$, Fig. 3F).

3. Subjective and Systemic Effect of Pilocarpine Mouthwash

Effectiveness on salivation all the subjects felt subjectively were examined by VAS. There was no significant difference on subjective evaluation for salivation with the use of mouthwash at different concentrations and duration.

To evaluate adverse side effects of pilocarpine mouthwash, vital signs, such as blood pressure and pulse rate were measured before and after each experiment. Significant difference was not observed in blood pressures and pulse rates (Table 2). Two of all subjects reported adverse effects during the whole experiments. One of them belonged to the 0.1% group, presenting with dizziness and palpitation after mouthwash for 1-minute and dizziness after mouth rinse for 3 minutes (Table 3). The other in 2.0% group reported sweating and chill after 1-minute mouthwash and sweating after 3- and 5-minute mouthwash (Table 3).

DISCUSSION

It is well known that 15 to 30 mg pilocarpine given by the oral route daily is safe and effective in stimulating salivary flow in patients with mild to severe hyposalivation.[16] The mechanisms responsible for the effects of pilocarpine on salivary flow involve local and direct cellular stimulation.[17] The parasympathetic action of pilocarpine induces water and electrolyte flow in saliva. Evidence indicates that pilocarpine also stimulates the production of mucin and of several other salivary constituents.[18,19] Even a small increase in salivary flow may induce symptomatic improvement for xerostomic patients.[16,18,20]

However, due to increased risk for adverse side effects, systemic pilocarpine has limitation to prescribe in the xerostomic patients, predominantly middle-aged and elderly persons who may have greater opportunities of systemic diseases and taking polypharmacy. Although topical use of pilocarpine as an alternative of systemic administration has been paid attention of dentistry, there are only small

Table 2. Change of blood pressure and pulse rate after pilocarpine mouthwash

Pilocarpine mouthwash	Systolic blood pressure			Diastolic blood pressure			Pulse rate		
	1 min	3 min	5 min	1 min	3 min	5 min	1 min	3 min	5 min
2.0%	2.6 (15.2)	2.8 (7.3)	−3.2 (4.7)	0.8 (11.5)	−3.2 (4.7)	0.2 (5.6)	12.6 (6.1)	10.8 (6.3)	1.0 (23.9)
1.5%	1.0 (9.6)	3.0 (10.1)	8.2 (11.4)	0.6 (8.8)	6.2 (9.7)	4.4 (7.3)	4.8 (8.3)	11.6 (13.4)	15.6 (12.8)
1.0%	5.8 (14.3)	6.2 (17.3)	5.8 (14.7)	6.6 (8.8)	−4.2 (10.9)	4.0 (4.5)	8.4 (5.0)	13.8 (7.0)	16.8 (14.2)
0.5%	3.4 (11.1)	−3.0 (4.5)	5.4 (14.4)	0.0 (14.5)	1.6 (7.9)	−2.4 (9.0)	9.4 (6.2)	8.2 (6.4)	4.8 (5.8)
0.1%	1.4 (13.4)	−4.2 (9.5)	2.4 (11.9)	−4.0 (8.6)	−2.4 (11.9)	1.0 (6.4)	0.2 (4.7)	3.2 (4.1)	1.0 (8.6)
Placebo	4.6 (14.4)	−0.2 (6.8)	3.2 (15.3)	2.8 (7.7)	−1.6 (6.5)	0.6 (9.8)	12.4 (9.1)	6.4 (9.4)	1.6 (13.3)

Values are the difference before and after mouthwash. The numbers in parenthesis indicate standard deviation.
No significant difference between solutions at different concentrations and between duration of mouthwash for systolic blood pressure, diastolic blood pressure and pulse rate, respectively (repeated measures two-way analysis of variance.

Table 3. Adverse effects reported after pilocarpine mouthwash

Pilocarpine mouthwash	Duration	Sweating	Palpitation	Nausea	Dizziness	Warmth	GI tract irritation	Frequent urination	Chill
2.0% (n=5)	1 min	1							1
	3 min	1							
	5 min	1							
0.1% (n=5)	1 min		1		1				
	3 min				1				
	5 min								

GI, gastrointestinal.
Two subjects reported side effects as above during the whole experiment; 1 from 2.0% group, the other from 0.1% group. There was no adverse side effect reported in other concentration groups and placebo group.
Number of total subjects=30.

numbers of related studies performed. Even some of them revealed lack of objective positive results.

Pilocarpine produces the best effects when the dose is titrated to suit individual needs.[7] This study aimed to investigate pilocarpine mouthwash with various conditions concerning different concentrations (placebo, 0.1%, 0.5%, 1.0%, 1.5%, and 2.0%) and duration (1, 3, and 5 minutes) of the mouthwashes and performed the experiments on healthy volunteers prior to test xerostomic patients.

In this study, when comparing difference from baseline among different concentrations, irrespective of duration of mouthwash, the higher concentration groups ≥1% significantly increased salivation compared to the lower concentration group of 0.1% and 0.5% and placebo group (Fig. 2). There was no significant difference between the higher groups except significant difference between 2.0% and 1.0% mouthwash with duration of 5 minutes. Duration did not produce significant difference of salivary flow rate at these higher concentrations of ≥1.0% (Fig. 3A-C). The lower concentrations of 0.5% and 0.1% and placebo resulted in lack of effects on salivation even after 5-minute mouthwash (Fig. 3D, E). It seems that dose affected salivation more than duration of mouthwash. Overall, increase of salivary flow rate was noticeable at 40 minutes after mouthwash with a peak between 40-60 minutes and persisted even at 120 minutes compared to baseline (Fig. 2). The latency to increase salivation when pilocarpine is administered by the oral route is 15 minutes, with a peak at 60 minutes and a duration of 2 or 3 hours.[21,22]

Bernardi et al.[11] investigated pilocarpine mouthwash in various doses (0.5%, 1% or 2%) for healthy volunteers and they tested 1 minute-gargle only and kept track of salivary flow rate until 75 minutes after mouthwash. The result showed that pilocarpine mouthwash at concentrations of 1% to 2% induced a significant objective and subjective dose-dependent increase in salivary flow, similar to the previous studies that studied the effect of oral 5 mg pilocarpine. No adverse effects were reported.

Within the limit of our knowledge, there was no human data about buccal permucosal absorption of pilocarpine.

Weaver et al.[23] investigated the absorption rate of pilocarpine solution in anesthetized beagle dogs by determining plasma pilocarpine levels while pilocarpine solution (pKa 6.6 at 37°C) was applying to the buccal mucosa (2.8 cm^2) of the dogs at a rate of 0.2 mL/min. According to their study, the buccal absorption rate was 156.7 μg/kg/h (2.6 μg/kg/min). The maximum total surface area of the adult human mouth was reported as 227.6 cm^2 with the mean of 214.7±12.9 cm^2 and teeth, keratinized epithelium and non-keratinized epithelium occupied about 20%, 50%, and 30% of the total area.[24] To put these together, the maximum absorption amount of pilocarpine after holding 4 mL of 2% pilocarpine mouthwash is expected 0.91 mg/min in case of an adult weighed 65.4 kg, the mean weight of our subjects in this study. Extension of duration to 5 minutes for mouthwash increases up to 4.5 mg, which is the maximum absorption dose used in this study. Bernardi et al.[11] used 10 mL of 1 or 2% pilocarpine mouthwash for a minute. That is, the maximum absorption amount of pilocarpine for a minute is considered to be 2.3 mg for 2% and 1.2 mg for 1% (for a person with 65.4 kg).

Compared to the study of Bernardi et al.[11] the current study did not produce clear-cut results related to concentration and duration of pilocarpine mouthwash. That can be partly explained by small-sized sample (each group consisting of 5 subjects) and heterogeneity of subjects between different concentration groups.

However, this study demonstrated quite noticeable result of dose-dependent effects on salivation by pilocarpine mouthwash. Duration of pilocarpine mouthwash appears to be, at a degree, associated with increase salivary flow in most cases but the difference was not significant.

The rationale for topical administration of pilocarpine is to minimize adverse side effects of systemic pilocarpine. Rosas et al.[25] used 5 mg of pilocarpine in a 5% solution in patients with primary Sjögren syndrome and reported that the adverse side effects appeared to be negligible, in accord with the previous studies using topical pilocarpine.[11] From the study of Park et al.,[15] 4 mL of 2% pilocarpine mouthwash for a minute decreased frequency of side effects compared to oral administration of 5 mg pilocarpine tablet. In the same study, 2 of 30 volunteers reported some side effects including dizziness and palpitation from 0.1% group and sweating and chill from 2.0% group, which does not appear to be related to dose and duration of the mouthwash. There was no finding indicating adverse change of blood pressure and pulse rate even when using the highest concentration (2.0%) of pilocarpine mouthwash in this study. Administration of pilocarpine as mouthwash appears to be safe. However, it should be kept in mind that some adverse effects are frequently reported after chronic use of oral pilocarpine and are dose-dependent.[18,20] Frequent use of topical pilocarpine for long-term may result in adverse effects.

Positive effects of pilocarpine mouthwash ≥1.0% for young healthy volunteers obtained in this study may not guarantee the same results in the xerostomic patients. There were 2 randomized double-blind clinical trials that investigated the effect of topical oral pilocarpine on postradiation xerostomia and salivary hypofunction.[7,8] Topically administered pilocarpine did not yield a significant improvement in xerostomia-related symptoms in either study. Pilocarpine pastilles did not increase saliva production in postradiation patients with salivary hypofunction,[8] while the pilocarpine spray increased salivation only among patients with baseline salivary flow rate >0 mL/min.[7]

In conclusion, based on the results of this study, pilocarpine mouthwash with at least 1% concentration during at least 1-minute might be effective for topical use to obtain clinical effects on salivation without any serious side effects. Further studies on the usefulness of pilocarpine mouthwash deserve to be performed in xerostomic patients.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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