Dry mouth, also known as xerostomia, is a frequent complaint among adults of all ages, particularly elderly people. The diagnosis of dry mouth, however, can be challenging because of a wide range of subjective complaints and objective salivary flow rates. For example, patients with xerostomic complaints may have normal salivary secretion (that is, unstimulated whole salivary flow rates of >0.2 milliliter/minute, as assessed by the patient’s drooling into a test

ABSTRACT

Background. Dry mouth is a frequent complaint of adults worldwide. In those who experience dry mouth, therapeutic options include the use of salivary substitutes and sialogogues.

Methods. The authors compared the efficacy and safety of mucoadhesive disks (OraMoist, Axiomedic, Zurich; distributed by Quantum Health, Eugene, Ore.) applied three times daily with those of placebo mucoadhesive disks in a double-masked, randomized, controlled crossover study. The primary end point of interest was within-participant differences in subjective (visual analog scale) ratings of dry mouth according to the New York University Bluestone Mouthfeel Questionnaire. The secondary end point was within-participant differences in salivary flow rates.

Results. Twenty-seven participants completed the single-site study. The results showed no significant difference between the two types of mucoadhesive disks, both of which were associated with a statistically significant improvement in the subjective experience of moistness across the 60-minute period after application and compared with baseline measures after two weeks of use. Furthermore, both disks were associated with a statistically significant improvement in salivary flow rates across the 60-minute period after application and compared with baseline measures after one and two weeks of use. The disks were well tolerated, and participants did not report any adverse events.

Conclusions. The mucoadhesive disks used in this study were safe and provided symptomatic relief from dry mouth.

Practice Implications. Patients with dry mouth may benefit from this novel delivery system.

Key Words. Xerostomia; dry mouth; salivary flow; randomized controlled trial; crossover trial; efficacy; safety; mucoadhesive; bioadhesive.
tube). Although less common, patients with flow rates of less than 0.2 mL/minute may have no xerostomic complaints. The prevalence of dry mouth is estimated to range from 6.2 to 46 percent of the population.\textsuperscript{2-4}

Dry mouth is caused by salivary gland hypofunction and can result from medical disorders (for example, Sjögren syndrome), head and neck radiation therapy and multiple medications.\textsuperscript{5} Medication use is a major cause of dry mouth—principally use of cardiovascular drugs, tranquilizers and sedatives, antihistamines, antidepressants and gastrointestinal drugs.\textsuperscript{6} The subjective symptoms of dry mouth can be functional or simply a sensation of a dry mouth. The functional symptoms include dysgeusia, swallowing difficulties, impaired use of removable prostheses, difficulty speaking because of oral dryness, increased dental caries and secondary infections such as candidiasis.\textsuperscript{7}

Most over-the-counter dry-mouth products are formulated as sprays, gels or rinses. OraMoist (Axiomedic, Zurich; distributed by Quantum Health, Eugene, Ore.) is a time-released disk approximately 1 centimeter in diameter that can adhere to any oral mucosal surface. It contains the following active ingredients: lubricating agents (carbomer homopolymer and triglycerides), gustatory and flavoring agents (lemon flavor and citric acid) and antimicrobial agents and enzymes (glucose oxidase, lysozyme and lactoferrin), along with inactive ingredients.\textsuperscript{8}

Aframian and colleagues\textsuperscript{9} conducted a pilot study involving 20 participants who complained of dry mouth. The authors assigned them to one of two treatment groups: a single application of a mucoadhesive disk (OraMoist) to the hard palate versus a 30-second swish and spit with a commercially available dry-mouth rinse. Participants in the disk group exhibited a statistically significant improvement in salivary flow rates, as well as subjective improvement in mouth dryness according to their responses to a questionnaire; however, the results showed no differences between the two treatment groups.\textsuperscript{9}

The purpose of our study was to compare the

\textbf{ABBREVIATION KEY: BMQ: Bluestone Mouthfeel Questionnaire. NYU: New York University. VAS: Visual analog scale.}
OraMoist mucoadhesive disks with placebo mucoadhesive disks in a double-masked, randomized, controlled crossover study to determine the safety and efficacy of OraMoist in alleviating symptoms of dry mouth.

PARTICIPANTS AND METHODS

Figure 1 summarizes the study methods. The institutional review board of New York University (NYU) School of Medicine, New York City, approved the investigation and informed consent form. We scheduled all visits for the morning to reduce the effects of diurnal variation.

Visit 1. At the first visit, participants provided written informed consent and we assessed eligibility criteria (Box), the most important of which was to include only people with dry mouth who had a standardized unstimulated whole salivary flow rate of 0.2 mL/minute or less. A hygienist performed baseline cleanings and gave standardized oral hygiene instructions to participants.

Visit 2. At visit 2, one of three investigators (A.R.K., P.M.C., S.S.S.) obtained subjective measurements of mouth dryness by using a 100-millimeter visual analog scale for a series of 11 items on the NYU Bluestone Mouthfeel Questionnaire (BMQ). Item 2 (dryness), “My mouth feels dry,” and item 4 (moistness), “My mouth feels moist,” have been validated as surrogates for salivary hypofunction. They also obtained baseline objective measurements of whole unstimulated salivary flow rates (in milliliter per minute), according to the technique described by Navazesh and colleagues. Participants then began a one-week no-treatment “washout” period during which they refrained from using any dry mouth products and used a standardized toothbrush, toothpaste and floss.

Visit 3. One week later, at visit 3, we randomly assigned participants in a double-masked fashion to one of two groups (OraMoist or placebo disks [that is, the OraMoist disks without the sweetener, enzymes and lubricating agent]) (Figure 2). We gave participants instructions and a sufficient supply of disks to use at home for one week, three times per day. The packaging was identical for both types of disks and we coded them with a link to a randomization list. Unmasking took place after the study was completed. Our intent was to determine whether the ingredients in the OraMoist disks had a meaningful effect.

At visit 3, the investigators obtained baseline subjective and objective measurements of mouth dryness, and the study coordinator (M.E.) gave participants instructions on how to place the disk on the hard palate. The investigators obtained subjective and objective measurements again at
five and 60 minutes after disk application.

**Visit 4.** One week later, at visit 4, the investigators recorded subjective and objective measurements of mouth dryness at baseline. They then gave participants the other type of disk and obtained measurements at five and 60 minutes after disk application.

**Visit 5.** One week later, at visit 5, the investigators recorded subjective and objective measurements of mouth dryness at baseline. Participants completed a short exit survey, which concluded their participation in the study. The investigators measured patients’ safety by conducting objective oral tissue examinations at study visits 3, 4 and 5 and recording any adverse events.

**Statistical analysis.** The primary end point was the participant’s subjective complaint of dry mouth, as assessed by the BMQ. We used a within-participant (owing to the wide variation in dry mouth measures in the general population) repeated-measures (RM) analysis of variance (ANOVA) for each of two BMQ measures (that is, item 2 [dryness] and item 4 [moistness]). The three predictor variables used in the analysis were treatment (OraMoist, placebo disks), visit number (2, 3, 4 and 5) and time within visit (baseline, five minutes, 60 minutes). Given the study design (RM ANOVA with three predictor variables) and constraint on sample size and assuming a type I error of 5 percent, a large effect size ($f^2 = 0.4$, which implies $h^2 = 0.8$) would be desirable to generate power of 75 percent or greater.

Our secondary end point was salivary flow (in milliliters per minute), which we also measured using a within-participant RM ANOVA and the same three predictor variables that we used for the primary end point.

**RESULTS**

Twenty-seven participants completed the study. The table provides participants’ demographic, baseline subjective and objective measurements and medical history profile. Regarding the causes of salivary hypofunction, most of the patients had medical conditions for which they were being treated with multiple xerogenic medications, three participants had a history of head and neck radiation therapy and one had a history of Sjögren syndrome.

### Table

**Characteristics of study participants.**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>NO. (%) OF PARTICIPANTS* (N = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
</tr>
<tr>
<td>Mean (± SD) Age in Years</td>
<td>61 ± 14</td>
</tr>
<tr>
<td>Mean (± SD) Baseline Salivary Flow at Visit 2 (mL/minute)</td>
<td>0.062 ± 0.079</td>
</tr>
<tr>
<td>Mean (± SD) Baseline Oral Dryness§ at Visit 2 (100-mm VAS)</td>
<td>70.2 ± 24.98</td>
</tr>
<tr>
<td>Mean (± SD) Baseline Oral Moistness§ at Visit 2 (100-mm VAS)</td>
<td>30.9 ± 26.75</td>
</tr>
<tr>
<td>Medical Conditions</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>12 (44)</td>
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<tr>
<td>Hypothyroidism</td>
<td>9 (33)</td>
</tr>
<tr>
<td>Psychiatric diagnosis</td>
<td>7 (26)</td>
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<tr>
<td>Hypercholesterolemia</td>
<td>5 (19)</td>
</tr>
<tr>
<td>Acid reflux/gastroesophageal reflux disease</td>
<td>5 (19)</td>
</tr>
<tr>
<td>History of head and neck radiation therapy</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Asthma</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Hepatitis C infection</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Sjögren syndrome</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Human immunodeficiency virus infection</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

* Unless otherwise specified.
† SD: Standard deviation.
‡ mL: Milliliter.
§ Assessed according to participants’ responses to the New York University Bluestone Mouthfeel Questionnaire.10
¶ mm: Millimeter.
# VAS: Visual analog scale.

**Subjective complaints of dry mouth.** Compared with both of the subjective baseline measures at visit 2, there were no significant within-participant effects during the no-treatment washout week, as measured at visit 3. During visit 3, the investigators found within-participant effects across time (baseline to 60 minutes) for “moistness” ($P < .005$) but not for “dryness” ($P > .05$) (Figures 3 and 4). The results showed no differences between the group treated with the OraMoist disks and the group treated with the placebo disks for either of these two measures.

Results from the visit 4 analysis indicated statistically nonsignificant within-participant effects across time for both disk groups (baseline to 60 minutes) and no significant differences between the group treated with OraMoist disks and the group treated with placebo disks for either of these two subjective measures. The investigators found no differences in baseline subjective measures between visit 3 and visit 4 and no significant differences in baseline measures between the OraMoist and
placebo disk groups between visit 3 and visit 4. Compared with baseline primary subjective measures at visit 3, participants perceived a significant ($P = .007$) increase in moistness at visit 4 (Figure 3). The results also show a nonsignificant decrease in participants’ perception of dryness at visits 4 and 5 (Figure 6). In addition, the investigators found no significant differences between OraMoist and placebo disks with regard to the primary subjective outcome measures from visit 3 to visit 5.

**Salivary flow rate.** Compared with baseline measures at visit 2, there were no significant within-participant effects in salivary flow during the no-treatment washout week, as measured at
visit 3. During visit 3, the investigators found within-participant effects across time (baseline to 60 minutes), and the salivary flow rate increased significantly ($P < .001$) (Figure 7). They found no differences in salivary flow between the group treated with OraMoist disks and the group treated with placebo disks at visit 3.

The visit 4 results demonstrated statistically nonsignificant within-participant effects across time (baseline to 60 minutes) for salivary flow and no significant differences between the OraMoist disk group and the placebo disk group. The investigators found a statistically significant ($P = .047$) increase in the salivary flow rate from baseline at visit 3 to baseline at visit 4 for both groups (Figure 8) but no significant differences between the OraMoist and placebo disk groups from visit 3 to visit 4. In addition, compared with participants’ baseline objective measure at visit 3, the results showed a significant ($P = .015$) increase in the salivary flow rate at visit 5. However, the investigators found no significant differences between the OraMoist and placebo disk groups from visit 3 to visit 5.

During the exit interview, the investigators collected information about the participants’ experiences after the second week of disk use. More than 70 percent of participants reported that the disks dissolved completely after more than two hours (two participants reported that the disks lasted less than one hour and four reported that they lasted more than four hours). All but one participant reported that the disks were easy to use, and 18 participants (67 percent) reported that they would use the disks in the future (71 percent and 62 percent who used the OraMoist and placebo disks, respectively). Twenty-two participants (81 percent) reported that they experienced no interference in their ability to eat or talk while using the disks, and 20 participants (74 percent) reported that the disk flavor was pleasant.

No serious adverse events occurred during this study, and no adverse events were attributed directly to use of the disks.

**DISCUSSION**

Overall, the study results show that the mucoadhesive disks had a positive effect on both subjective and objective end points in this population of people with dry mouth. Similar to the results of the previous study, we were not surprised to find a positive effect during the first hour after disk application, because we would expect a stimulation in salivary flow and commensurate improvement in xerostomic complaints after placing an object in the mouth. Although the improved measurements are relatively small, one needs to bear in mind that any augmentation in salivary flow in a population of people with dry mouth can be helpful.
The limitations of the study design did not allow us to evaluate objectively the length of time these effects lasted, although on the basis of the exit interviews, they seemed to last for the life of each disk, which was more than two hours for the majority of participants. However, we were surprised that participants demonstrated a sustained effect (that is, lasting after the disk had dissolved), as measured after one and two weeks of disk use (regardless of which disk was used). Baseline salivary flow rates at visit 4 and visit 5 were significantly higher than those at visit 3; when we measured baseline flow rates, participants had not placed a disk in their mouths since the night before and had neither eaten nor consumed beverages for at least 90 minutes before the visit. Subjective symptoms of moistness mirrored this improvement after two weeks of disk use (an improvement occurred after one week, but it was not significant). We did not predict such a sustained effect and, consequently, the differences in both subjective and objective measures between visits 4 and 5 were smaller than the differences between visits 3 and 4 because of the elevated baseline measures before the crossover at visit 4.

According to our study design, we decided not to use a washout period in the middle of the study (at the crossover) as clinical researchers generally do in a drug study in which several half-lives are required for the study drug to be excreted. We believed that a one-week period at the beginning of the study was needed to wash out the variable effects of different oral hygiene products and to normalize the population after a prophylaxis; moreover, it would simulate a no-treatment arm. In retrospect, this was a study limitation, and a preferable design would have included a one-week washout period in the middle of the study, allowing us to recalibrate baseline measures. Nevertheless, the sustained effect appears real, although the mechanism by which it occurs is unclear. One hypothesis is that repeated stimulation of the salivary glands results in an increase in unstimulated salivary flow.

Participants tolerated this formulation well, and because of its adherence to mucosal surfaces, it follows that the effect would last longer than that of other commercially available topical dry mouth products that require frequent dosing owing to quick clearance from the oral cavity. OraMoist is classified as an over-the-counter agent because it does not contain any prescription medications. However, similar mucoadhesive systems have been developed that deliver active therapeutic agents for a number of oral and systemic diseases.

CONCLUSION

Although the study results showed no significant differences between the OraMoist and placebo disks, disk use led to a statistically significant improvement in both subjective and objective measures of dry mouth for up to 60 minutes—and possibly longer—after application. After two weeks of daily use, participants experienced a statistically significant improvement in baseline subjective (experience of dryness and moistness) and objective (salivary flow) measures, suggesting a sustained effect. Larger studies of longer duration are warranted to explore this delivery system further.

Disclosure. Bluestone Center for Clinical Research, New York University, New York City, received funding from Axismedic, Zurich, the developer of OraMoist. The company also provided the mucoadhesive disks used in this study.

The authors acknowledge Dr. Jonathan A. Ship’s leadership in initiating this study and his contribution to protocol development.

8. OraMoist Time Released Dry Mouth Patch (product packaging).