Local Oral Pilocarpine Drops for Relieving Xerostomia (Dry Mouth) in the Elderly: A Pilot Study

JAMDA 22 (2021) 185–186

JAMDA

journal homepage: www.jamda.com

Research Letter

Local Oral Pilocarpine Drops for Relieving Xerostomia (Dry Mouth) in the Elderly: A Pilot Study

To the Editor:

Xerostomia is the feeling of dry mouth, a symptom frequently occurring in older people. Xerostomia is associated with alterations in the quality and quantity of saliva and leads to functional alterations such as halitosis, burning sensations, altered taste perception, malnutrition, and difficulties with chewing. As a result, xerostomia can have disabling social consequences and reduces quality of life.[1] Xerostomia increases with age because of a decrease in the acinar cells of salivary glands and is a common side effect of chronic drug treatment.[2] Among community-dwelling older people, the prevalence is up to 40%.[3]

When withdrawal from or substitution of xerostomia-inducing drugs is no option, it is important to evaluate whether other treatment options are effective in reducing xerostomia and improving quality of life for these patients. Pharmacologic and nonpharmacologic treatments were reviewed by Gil-Montoya et al.[4] Local treatments such as very short-acting mucinous artificial saliva or slightly longer active mouthwashes are available.[4] Chewing gum belongs to the group of nonpharmacologic salivary stimulants and appeared to be equally effective in relieving the complaint of xerostomia compared with artificial saliva.[5] The effects of both, however, are short-lived.[4,6] In the group of pharmacologic treatment options, pilocarpine is registered for the treatment of xerostomia in Sjögren syndrome and following radiotherapy in the head-and-neck region, and considered the best performing drug for these indications.[4] Peak plasma concentrations are reached 75 minutes after ingestion of 5 mg tablets 3 times a day. Pilocarpine is eliminated mainly in the urine with an elimination half-life of about 45 minutes for 5 mg doses,[7] depending on the individual pilocarpine esterase activity.[8] However, systemic pilocarpine has frequent side effects. To avoid rapid elimination and maximize exposure at the site of action, absorption of pilocarpine into the systemic system should be minimized (eg, by local administration of lower doses direct to the undamaged salivary glands). Unfortunately, research on the efficacy of locally administered pilocarpine drops is scarce, especially in older people. Therefore, we aimed to evaluate the effect size of 2 different dosages of locally administered pilocarpine drops in older patients with xerostomia complaints by means of a pilot study.

An open-label, randomized control pilot trial was conducted. Patients aged ≥70 years were recruited if they had a clinical diagnosis of chronic (>3 months) xerostomia defined as a score ≥5 at the Numeric Rating Scale (NRS 0–10). Patients were randomized to a low-dose group (ie, pilocarpine nitrate 3 × 2 mg/day) or a high-dose group (ie, pilocarpine nitrate 3 × 5 mg/day) [Pilocarpine Minims (nitrate), eye drops, Bausch & Lomb, Schiphol-Rijk, the Netherlands]. All patients were treated for 14 days; measurements were performed at baseline and at day 7, 14, and 21. The study was approved by the Medical Ethics Committee and registered at *EudraCT/2018-004352-38*.

Seventy-nine patients were screened for eligibility, 14 patients gave informed consent, and 10 were suitable for evaluation. In all patients, both the low- and high-dose group together, NRS xerostomia scores dropped significantly from day 0 to day 14 (NRS last week: $P = .028$, NRS now: $P = .017$). High dose pilocarpine seemed more effective than low dose; however, this was not significant (Figure 1).

After 1 week, 100% of the high-dose group and 57% of the low-dose group rated their xerostomia complaints as better than before. One patient experienced new onset of dizziness. All 3 domains of the oral health-related quality of life index (GOHAI) showed a small but nonsignificant improvement.

Local formulations of pilocarpine (drops, lozenges, and mouthwashes) are reported to have no or minor local side effects.[9–11] Our pilot study is in line with these findings. The positive outcome in effectiveness in our study is in line with the studies of Taweechaisupapong et al and Watanabe et al. The first showed that a 5 mg locally applied pilocarpine lozenge produced better clinical results, decreased feeling of oral dryness, less sore mouth or speaking difficulties, than a 5 mg pilocarpine oral tablet in 33 relatively young head-and-neck cancer patients.[11,12] The second showed a significant increase in salivary flow in 24 patients with Sjögren syndrome with a new local formulation containing 0.96 mg/dose.[11] The effect reported in other studies varied from no effect[9] to a reasonable effect[10] of different local formulations.

An important lesson of this pilot study is the low recruitment rate despite high symptom burden in the older population, mainly because of gatekeeping by relatives. This has implications for the power calculation of a future study.

We have chosen for a parallel-group design instead of a crossover design because of a possible “switch-on” effect by pilocarpine drops (ie, the salivary glands are triggered to keep producing higher levels of saliva). Although both NRS last week and NRS now were higher on day 21 than on day 14, a significant switch-on effect cannot be ruled out.

We conclude that pilocarpine oral drops seem to alleviate xerostomia in older people without important side-effects or costs. A larger placebo-controlled randomized control trial is needed.

D.J.A.J. has received lectures fees from Novartis, AstraZeneca and Boehringer Ingelheim. The other authors declare no conflicts of interest.

https://doi.org/10.1016/j.jamda.2020.06.036

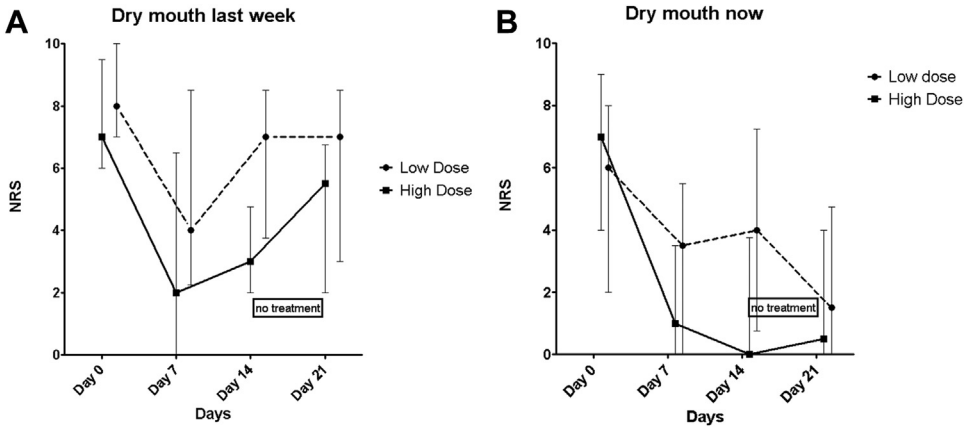

Fig. 1. NRS xerostomia score. a, Dry mouth last week; b, Dry mouth now. NRS median (interquartile range). Baseline measurement: day 0; treatment period: day 0–14; post-treatment measurement: day 21.

Acknowledgments

We thank CZ fonds (CZ Zorgverzekeraar, the Netherlands) for subsidizing this study.

References

1. Enoki K, Matsuda KI, Ikebe K, et al. Influence of xerostomia on oral health-related quality of life in the elderly: A 5-year longitudinal study. Oral Surg Oral Med Oral Pathol Oral Radiol 2014;117:716–721.
2. van Eijk J, van Campen JP, van der Jagt H, et al. Prevalence of xerostomia and its relationship with underlying diseases, medication, and nutrition: A descriptive observational study. J Am Geriatr Soc 2013;61:1836–1837.
3. Liu B, Dion MR, Jurasic MM, et al. Xerostomia and salivary hypofunction in vulnerable elders: Prevalence and etiology. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;114:52–60.
4. Gil-Montoya JA, Silvestre FJ, Barrios R, Silvestre-Rangil J. Treatment of xerostomia and hyposalivation in the elderly: A systematic review. Med Oral Patol Oral Cir Bucal 2016;21:e355–e366.
5. Davies AN. A comparison of artificial saliva and chewing gum in the management of xerostomia in patients with advanced cancer. Palliat Med 2000;14:197–203.
6. Dost F, Farah CS. Stimulating the discussion on saliva substitutes: A clinical perspective. Aust Dent J 2013;58:11–17.
7. Malallah OS, Garcia CMA, Proctor GB, et al. Buccal drug delivery technologies for patient-centred treatment of radiation-induced xerostomia (dry mouth). Int J Pharm 2018;541:157–166.
8. Aromdee C, Fawcett JP, Ferguson MM, Ledger R. Serum pilocarpine esterase activity and response to oral pilocarpine. Biochem Mol Med 1996;59:57–61.
9. Kim JH, Ahn HJ, Choi JH, et al. Effect of 0.1% pilocarpine mouthwash on xerostomia: double-blind, randomised controlled trial. J Oral Rehabil 2014;41:226–235.
10. Tanigawa T, Yamashita J, Sato T, et al. Efficacy and safety of pilocarpine mouthwash in elderly patients with xerostomia. Spec Care Dentist 2015;35:164–169.
11. Watanabe M, Yamada C, Komagata Y, et al. New low-dose liquid pilocarpine formulation for treating dry mouth in Sjogren's syndrome: Clinical efficacy, symptom relief, and improvement in quality of life. J Pharm Health Care Sci 2018;4:4.
12. Taweechaisupapong S, Pesee M, Aromdee C, et al. Efficacy of pilocarpine lozenge for post-radiation xerostomia in patients with head and neck cancer. Aust Dent J 2006;51:333–337.

Maurice Theunissen, PhD
Center of Expertise for Palliative Care
Maastricht University Medical Center+ (MUMC+)
Maastricht, the Netherlands

Shanly Rideaux-Seferina, MD, PhD
Department of Internal Medicine
Maastricht University Medical Center+
Maastricht University
Maastricht, the Netherlands

Fabienne J. Magdelijns, MD, PhD
Division of General Medicine
Department of Internal Medicine
Maastricht University Medical Center+
Maastricht University
Maastricht, the Netherlands

Daisy J.A. Janssen, MD, PhD
Department of Health Services Research
Care and Public Health Research Institute Maastricht University
Maastricht, the Netherlands

Department of Research and Development
CIRO
Horn, the Netherlands

Marieke H.J. van den Beuken-van Everdingen, MD, PhD
Center of Expertise for Palliative Care
Maastricht University Medical Center+ (MUMC+)
Maastricht, the Netherlands