**Critically Appraised Topic (CAT)**

|  |
| --- |
| **Project Team:**  |
| **6B-1** |
| **Project Team Participants:**  |
| **Joe Maciejewski (D3, me), Janae Momchilovich (D4), Lauren Hogan (D2), Jack Birch (D1)** |
| **Clinical Question:** |
| **What are the most effective interventions for xerostomia?** |
| **PICO Format:** |
| **P:** |
| **Patients with xerstomia** |
| **I:** |
| **Pharmacotherapy** |
| **C:** |
| **Patients receiving no treatment for xerostomia** |
| **O:** |
| **Improvement in treatment outcome** |
| **PICO Formatted Question:** |
| **In patients with xerostomia, is there a difference in treatment prognosis with pharmaceutical interventions?** |
| **Clinical Bottom Line:** |
| **The patient has xerotomia and we want to provide her with the most successful treatment, but don’t want her xerostomia to impinge on the success of her treatment.** |
| **Date(s) of Search:**  |
| **10/11/2020** |
| **Database(s) Used:** |
| **PubMed** |
| **Search Strategy/Keywords:** |
| **I visited PubMed and found a list of MESH terms relevant to my topic. After doing some initial research, I found that pilocarpine was a new and popular pharmacotherapeutic used to treat xerostomia. I inputed my MESH terms, set the results to within 5 years to get the most recent research, and looked for articles with the highest level of evidence and reliability.** |
| **MESH terms used:** |
| **Xerostomia, therapeutics, pilocarpine, drug therapy** |
| **Article(s) Cited:** |
| 1. Gil-Montoya, J-A et al. “Treatment of xerostomia and hyposalivation in the elderly: A systematic review.” *Medicina oral, patologia oral y cirugia bucal* vol. 21,3 e355-66. 1 May. 2016, doi:10.4317/medoral.20969
2. Riley, Philip et al. “Pharmacological interventions for preventing dry mouth and salivary gland dysfunction following radiotherapy.” *The Cochrane database of systematic reviews* vol. 7,7 CD012744. 31 Jul. 2017, doi:10.1002/14651858.CD012744
3. Li KX, Loshak H. “Pilocarpine for Medication-induced Dry Mouth and Dry Eyes: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines [Internet].” *Ottawa (ON): Canadian Agency for Drugs and Technologies in Health*; 2019 Dec 11.
4. Tanasiewicz M, Hildebrandt T, Obersztyn I. Xerostomia of Various Etiologies: A Review of the Literature. Adv Clin Exp Med. 2016 Jan-Feb;25(1):199-206. doi: 10.17219/acem/29375. PMID: 26935515.
 |
| **Study Design(s):** |
| **All were systematic reviews of RCT except #4 which was a a narrative review.** |
| **Reason for Article Selection:** |
| The systematic reviews of RCT were chosen because of high levels of evidence and they were recently published. The narrative review was a fairly comprehensive paper from authors in the field of dentistry. Although not a high level of evidence, it gives the etiology, clinical manifestations, evaluation, and treatment of xerostomia. Pharmacotherapy used to treat xerostomia is a relatively new phenomenon, so high levels of evidence advocating for its clinical effectiveness are limited. |
| **Article(s) Synopsis:** |
| 1. The goal of this study was to investigate the latest pharmacological and non-pharmacological treatments for dry mouth in older individuals, regardless of the cause of the problem. The literature was searched in March 2015 using Medline and Embase databases. Clinical trials from 2006 to March 2015 were included in the filtering process. MeSH terms xerostomia or Dry Mouth Syndrome, and Elderly Aged were used. Assessment of article quality and criteria for inclusion were based on PRISMA and the “Oxford Quality Scale.” The studies were then divided into 3 categories. The categories were clinical trials testing pilocarpine or cevimeline, clinical trials using non-pharmacological intervention or artificial saliva, and clinical trials using alternatives like acupuncture or elector-stimulation. The initial search yielded a total of 9,275 references and using the selection and quality criteria, 26 trials were deemed acceptable to be used in this review. 14 were related to pharmacological drug treatments, 10 were non-pharmacological, and 2 were alternative treatment. Based on the results of the randomized control trials used in the review, the effectiveness of different therapeutic interventions used to treat xerostomia aren’t effective enough to recommend one treatment over the other, whether pharmacological or not. In xerostomia caused by irradiation or Sjogren’s Syndrome, pilocarpine seemed to give the best results whether swallowed, dissolved in the mouth or in mouth rinses. None of the studies examined the adverse effects of pilocarpine probably due to the short follow-up period. In xerostomia caused by medications alone, there were some positive indications for the use of malic acid with fluoride and xylitol to counteract the harmful effects on dental enamel. However, studies with larger sample sizes must be carried out. Lubrication of the oral membrane can reduce symptoms, but is often short acting. Intraoral devices and electrostimulation were also analyzed in this systematic review, but were not effective enough to recommend them as solid treatment. Moving forward, more trials must be carried out, with crossover designs, larger sample sizes and long-term monitoring. The limitations of this study were just lack of studies showing clinical effectiveness of pharmacotherapeutics.
2. The purpose of this systematic review of RCT was to assess the effects of pharmacological interventions for the prevention of radiation-induced xerostomia. Cochrane Oral Health’s Information Specialist searched a large number of databases. Randomized controlled studies were included in the selection process. Participants of all ages, ethnic origins, and genders were included in the evaluation. Pharmacological therapy prescribed prophylactically or during treatment were included. A total of 39 studies were included. Based on this study, low quality evidence was shown for effective treatment with amifostine compared to placebo or no treatment. Insufficient evidence was shown for effective treatment of pilocarpine compared to placebo or no treatment. Some low-quality evidence suggested that pilocarpine might be associated with an increase in sweating. There is some low-quality evidence to suggest that amifostine can lessen the feeling of dry mouth in radiotherapy patients in the short and medium term. More research needs to be done with these pharmacotherapeutics in the long term. There was little evidence to suggest any of these pharmacotherapeutics are beneficial in treating the effects of xerostomia. Again, this article lacked analysis of many studies showing clinical effectiveness of pharmacotherapeutics.
3. The purpose of this study was to examine recent literature regarding clinical effectiveness and cost effectiveness of pilocarpine in treating psychoactive medication induced dry mouth and dry eyes. A literature search was carried out by an information specialist on databases including Embase, Cochrane Library, and Medline among others. Literature was limited to publication between January 1, 2009 and November 25, 2019. MeSH terms included xerostomia, pilocarpine, and dry eyes. Studies had to meet a list of inclusion criteria. The authors of this study were not able to find any studies regarding the clinical effectiveness or cost effectiveness of pilocarpine in treatment of psychoactive medication induced dry mouth and dry eyes. More studies must be carried out in order to gain knowledge on clinical and cost effectiveness of pilocarpine. This study was limited by the number of studies out there suggesting the clinical effectiveness of pharmacotherapeutics in treating xerostomia.
4. This paper gave some of the main causes, clinical manifestations, evaluation methods, and treatments of xerostomia. In terms of treatment of medication based xerostomia, focus is on eliminating the medications that are the cause. Amifostine has been found to be useful in patients with xerostomia caused by radiation therapy. However, different studies have found conflicting evidence. Some have found very high clinical effectiveness while others have only found placebo type effects depending on the patient. Pilocarpine has been shown to induce saliva secretion through parasympathetic influences. It has an affinity for muscarinic receptors M1 and M3, which lead to increased saliva secretion in peripheral tissues. Pilocarpine is contraindicated in some patients with drug induced xerostomia. Cevimeline is another agent used to treat xerostomia with high affinity for muscarinic receptors M1 and M3. It is effective in treating head and neck radiation patients. This paper concluded that the treatment of xerostomia whether from head and neck radiation, Sjogren’s syndrome, medication, or aging, is long term and demanding. Treatment requires a high level of patient motivation. Although very informational, this paper did not have a very high level of evidence.
 |
| **Levels of Evidence:** (For Therapy/Prevention, Etiology/Harm) See <http://www.cebm.net/index.aspx?o=1025>[x]  **1a** – Clinical Practice Guideline, Meta-Analysis, Systematic Review of Randomized Control Trials (RCTs)[ ]  **1b** – Individual RCT[ ]  **2a** – Systematic Review of Cohort Studies[ ]  **2b** – Individual Cohort Study[ ]  **3** – Cross-sectional Studies, Ecologic Studies, “Outcomes” Research[ ]  **4a** – Systematic Review of Case Control Studies[ ]  **4b** – Individual Case Control Study[ ]  **5** – Case Series, Case Reports[x]  **6** – Expert Opinion without explicit critical appraisal, Narrative Review[ ]  **7** – Animal Research[ ]  **8** – In Vitro Research |
| **Strength of Recommendation Taxonomy (SORT) For Guidelines and Systematic Reviews**See article **J Evid Base Dent Pract 2007;147-150**[x]  **A** – Consistent, good quality patient oriented evidence[ ]  **B** – Inconsistent or limited quality patient oriented evidence[x]  **C** – Consensus, disease oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening |
| **Conclusion(s):** |
| The available evidence to support the use of pharmacotherapeutics for the treatment of xerostomia as a result of multiple causes is weak at best. All four of the studies came to a similar basic conclusion that pharmacotherapeutics could possibly be beneficial in treating xerostomia, but more extensive research needs to be carried out before definitive recommendations can be given to patients. I would recommend the use of more traditional palliative treatment for this case. Examples of such treatment could include gels, aerosols/sprays, oral rinses, or chewing gums. |