Benzocaine:

Primary:

Chrubasik S, Beime B, Maora F. Efficacy of a benzocaine lozenge in the treatment of uncomplicated sore throat. Eur Arch Otorhinolaryngol 2012; 269:571-77.

Extended Abstract:

Study objectives: To compare uncomplicated sore throat outcomes in subjects receiving benzocaine lozenges or placebo lozenges.

Methods:

Design: randomized, double-blind, placebo-controlled study

Allocation: The inclusion criteria included patients who contacted their family doctor because of sore throat were eligible to participate. Patients were excluded based on (1) participation in another clinical trial within 30 days beforehand, (2) actual or possible pregnancy, or lactation, (3) any suspicion of drug or alcohol abuse, (4) history of allergy to the study medication, (5) any severe chronic disease, (6) any current pain treatment, (7) treatment with steroids, oro-pharyngeal therapeutics, anticonvulsants, psychotropic or immunosuppressant agents within 24 hours (or, prolonged action NSAIDs, within 10 days), or antibiotics within the 14 days up to enrollment, (8) known or suspected bacterial infection, (9) known or suspected NADH-diaphorase deficiency.

Blinding: double-blinded.

Follow-up period: Pain assessments were recorded at 15, 30, 45, 60, and 90 minutes. The study was scheduled to finish at 120 minutes.

Setting: in a multi outpatient clinic

Participants: 165 total patients were enrolled, where the benzocaine group contained 83 patients, while the placebo group contained 82 patients.

Intervention: treatment was benzocaine 8mg lozenge OR placebo lozenge. Patients received the study medication, and two stop-watches. The stop-watches were started simultaneously with administration of the study medication. Patients were instructed to stop one stop-watch as soon as he or she experienced what they was worthwhile pain relief. The other stop-watch was stopped if and when the pain returned to baseline level. Pain assessments were recorded at 15(±3), 30 (±3), 45(±3), 60 (±3), and 90 (±3) minutes. Each time patients reported pain, the patients were asked if they were experiencing any adverse effects, local or systemic.

Outcomes: The primary outcome was the sum of the pain intensity differences (SPID) over 2 hours. The secondary outcomes were change in pain intensity after 2 hours in comparison to baseline, the number of patients who reported a halving or more of their baseline pain (so-called responders), the number of patients who experienced worthwhile and complete within 60 minutes and 120 minutes and the time to worthwhile/complete pain relief and to recurrence of pain.

Patient follow-up: Patients were assessed for their well-being, the acceptability of the study medication, any adverse effects, and their vital signs at 120 minutes after receiving study medication.

Main results: A predefined interim analysis after including 50 patients revealed the superiority of benzocaine versus placebo in the SPID ($p = 0.0086$). In the full analysis set (FAS), median SPID had significantly more decreased in patients receiving benzocaine compared to placebo (-12 vs. -5, $p = 0.001$). There were significantly more responders and patients with worthwhile pain relief in group

benzocaine. The number of patients with complete pain relief was very small. Median time to worthwhile pain relief was 20 minutes (benzocaine) and greater than 45 minutes (placebo). Adverse events were not observed.
Conclusions: Benzocaine lozenges are superior to placebo lozenges and a useful, well-tolerated treatment option to reduce painful pharyngeal discomfort. Patients who are looking to gain temporary pain relief from uncomplicated sore throat can benefit from taking benzocaine 8 mg lozenges.
Comments/critical appraisal (including assessment of internal and external validity): This study was high quality since it met many of the internal validity criteria, including randomized controlled trial, double blinded, strict inclusion/exclusion criteria, and demographic characteristics and medication history were similar between groups. However, the relatively small sample size makes it difficult to derive population-based generalizations. In addition, the outcome measures were highly subjective and used soft endpoints. However, the outcomes were based on pain reduction, which is an important indicator of patient satisfaction for sore throat management. Although, outcomes were subjective in this study, significant pain reduction was seen in patients taking benzocaine. All in all, this study showed benzocaine lozenges can provide significantly faster pain relief compared to placebo.

McNally D, Shephard A, Field E. Randomised, double-blind, placebo-controlled study of a single dose of an amylmetacresol/2,4-dichlorobenzyl alcohol plus lidocaine lozenge or a hexylresorcinol lozenge for the treatment of acute sore throat due to upper respiratory tract infection. J Pharm Pharmaceut Sci 2012;15(2):281-94.

Extended Abstract:
Study objectives: to determine the analgesic efficacy of two lozenges – one containing amylmetacresol (AMC)/2,4-dichlorobenzyl alcohol (DCBA) and lidocaine and one containing hexylresorcinol – versus placebo in patients with acute sore throat due to upper respiratory tract infection (URTI).
Methods:
Design: randomized controlled trial
Allocation: patients were randomly allocated to one of three groups. Group 1 received one lozenge containing AMC 0.6 mg, 2,4-DCBA 1.2 mg and lidocaine hydrochloride 10 mg; Group 2 received one lozenge containing hexylresorcinol 2.4 mg; and Group 3 received a non-medicated sugar-based placebo lozenge.
Inclusion criteria: Adults (male or female, aged 18-75 years inclusive) were included if they had a sore throat with onset within the previous 4 days due to URTI. Patients had to have at least one out of 40 symptoms of URTI on the URTI questionnaire, and baseline score of greater or equal to 6 on the throat soreness scale, >50 mm on the difficulty swallowing scale, and >33 mm on the swollen throat scale. Objective confirmation by a physician for the presence of tonsillopharyngitis was required, with a TPA score of > or equal to 5 on a 21-point scale.
Exclusion criteria: included a sore throat that had been present for more than 4 days, evidence of mouth breathing or severe coughing, existence of other distracting pain (such as mouth ulcer), or concomitant disease with the potential to compromise breathing (e.g. asthma, bronchopneumonia). It also included patients who had used any sore throat medication containing a local anesthetic within the previous 4 hours; analgesic, antipyretic, or cold medication (e.g. decongestant, antihistamine, antitussive, or throat

lozenge/spray) within the previous 8 hours; a longer acting or slow-release analgesic during the previous 24 hours (e.g. piroxicam, naproxen); any medicated confectionary, throat pastille, spray, or any product with demulcent properties (e.g. boiled sweets) in the previous 2 hours; or antibiotics in the previous 14 days. Women of childbearing potential who were not taking contraceptive methods, or who were pregnant or lactating, were excluded, as well as patients with known allergy to the active ingredients or intolerance to fructose.

Blinding: double blinded. Patients and investigators were unaware of which lozenge the patient had received.

Follow-up period: The study was conducted between February 2 to March 31, 2011 (approximately 2 months).

Participants: 190 patients.

Intervention: Group 1 received one lozenge containing AMC 0.6 mg, 2,4-DCBA 1.2 mg and lidocaine hydrochloride 10 mg; Group 2 received one lozenge containing hexylresorcinol 2.4 mg; and Group 3 received a non-medicated sugar-based placebo lozenge.

Outcomes: Subjective ratings of throat soreness, difficulty swallowing, swollen throat, numbing, and sore throat relief were obtained up to 2 hours post dose. Patient and investigator global ratings and a consumer questionnaire were also collected.

Patient follow-up: Patients received a follow-up telephone call 1-3 days after being assessed.

Setting: research centre

Main results: The hexylresorcinol lozenge demonstrated superiority over placebo from primary and secondary efficacy variables including those related to throat soreness, sore throat relief, and difficulty swallowing. The AMC/DCBA + lidocaine lozenge was also superior to placebo fro secondary endpoints at various time points, but did not reach significance for the primary efficacy variable. Both lozenges had a rapid onset of action from 1-10 minutes post dose for the AMC/DCBA + lidocaine lozenge and 1-5 minutes post dose for the hexylresorcinol lozenge. Numbness was reported from 1 minute post dose with the AMC/DCBA + lidocaine lozenge and was greatest at 15 minutes. Numbness was reported from 5 minutes post dose with the hexylresorcinol lozenge and was greatest at 10 minutes. Both lozenges were well-tolerated.

Conclusions: Both AMC/DCBA + lidocaine and hexylresorcinol lozenges provided rapid and effective sore throat relief in patients with URTI.

Comments/critical appraisal (including assessment of internal and external validity):

The study was internally valid since it was a high quality randomized, placebo-controlled trial, where patients were randomized to one of the 3 groups (AMC/DCBA + lidocaine vs. hexylresorcinol vs. placebo group). The patients were double-blinded, where the patients and investigators were unaware of which lozenge the patient had received. However, limitations of the study included the relatively small sample size, which may have limited the statistical power. This played a large role in the failure of the AMC/DCBA + lidocaine lozenge data to reach statistical significance on the primary endpoint. It may also have explained some of the inconsistencies seen, for example, the difference in the efficacy of the AMC/DCBA + lidocaine lozenge at 60 minutes on the swollen throat scale. However, significantly greater improvements in severity of throat soreness, difficulty swallowing, swollen throat symptoms, and greater sore throat relief, were reported with both lozenges compared with placebo. In addition, this trial clearly showed that anesthetic effect of both lozenges, as evidenced by the significantly greater

numbness scores achieved vs. placebo. The study is externally valid only for patients who meet the inclusion/exclusion criteria so not all patients may use this medication, as mentioned above. The patient needs to be at least 18 years of age with a sore throat onset within the previous 4 days due to URTI. Although, both AMC/DCBA + lidocaine and hexylresorcinol lozenges provided rapid and effective sore throat relief in patients with URTI, it is difficult to extrapolate lidocaine's efficacy as an individual agent to our EBSCR patient, as it was studied as a combination with other agents. This study did not show the effect of the individual agent, lidocaine versus placebo. Therefore, conclusion cannot be made to recommend lidocaine as an effective treatment for sore throat, but may considered as a combination agent.

Tertiary/Secondary:

Stead W. Patient information: Sore throat in adults (Beyond the Basics). UpToDate. 2013.

Source description: UpToDate® is a trusted evidence-based clinical decision support tool for clinicians. The articles are written by doctors, editors and peer reviewers without any funding from private companies or drug manufacturers. The publications are continuously monitored, in order to ensure articles reflect the most accurate information supported by recent evidence.

Summary: the author states that sprays containing topical anesthetics (e.g. benzocaine) are available to treat sore throat. However, such sprays are no more effective than sucking on hard candy. In terms of throat lozenges, it may persist longer in the throat than sprays or gargles, and thus, may be more effective for symptom relief.

Comments/critical appraisal (including assessment of internal and external validity): the author's claim is based on a paper showing lozenges or tablets are the most effective delivery method of sore throat formulations. Both lozenges and tablets offered greater advantages over sprays or gargles, both in terms of proportion of the dose delivered to the mouth and throat, combined, and clearance from these regions. These delivery formats provide fast, effective, and prolonged delivery of active ingredients, highlighting their potential benefits for sore throat medication (Limb et al).

Drutz JE. Symptomatic relief of sore throat in children and adolescents. UpToDate. 2013.

Source description: UpToDate® is a trusted evidence-based clinical decision support tool for clinicians. The articles are written by doctors, editors and peer reviewers without any funding from private companies or drug manufacturers. The publications are continuously monitored, in order to ensure articles reflect the most accurate information supported by recent evidence.

Summary: the author claims an oral rinse composed of equal parts of lidocaine, diphenhydramine, and Maalox may be helpful. When using this oral rinse, care must be taken to avoid overdosing the lidocaine component. Sprays containing topical anesthetics (e.g. benzocaine) are available to treat sore throat. However, such sprays are no more effective than sucking on hard candy. In addition, it may cause an allergic reaction, and topical benzocaine has been associated with methemoglobinemia and should not be used in children younger than two years. The author suggests not using such sprays for symptomatic

relief of throat pain in children. In addition, medicated throat lozenges containing benzocaine may provide symptomatic relief, but it is not clear that they work any better than other forms of hard candy. Similar to throat sprays, lozenges have the potential to cause an allergic reaction, and those that contain benzocaine may cause methemoglobinemia. Once again, the author does not suggest using medicated throat lozenges for symptomatic relief of throat pain in children. Lozenges are a chocking hazard for young children and should not be offered to those who are younger than three to four years of age.

Comments/critical appraisal (including assessment of internal and external validity): In the children and adolescent population, it is not recommended to use medicated throat sprays or medicated lozenges for the treatment of sore throat. The results from this article fit with other available evidence, however, more studies have to be completed. The authors do not describe the search strategies used to select references used to support opinions, and therefore, there may a selection bias in the literature used to guide therapeutic options. The article fails to provide specific detailed information about individual treatment options (dose, duration, etc.). Also, preferred agents for treatment are not systematically ranked. Overall, this article provides fundamental information about acute sore throat treatment in children, but should not be used to guide therapeutic decisions.