Sage

Primary:

1. **Schapowal A, Berger D, Klein P, Suter A. Echinacea/sage or chlorhexidine/lidocaine for treating acute sore throats: A randomized double-blind trial. Eur J Med Res 2009; 14: 406-412.**

Extended Abstract:
Study Objectives: The aim of the trial was to assess the relative efficacy of a herbal Echinacea/sage spray to a chlorhexidine/lidocaine spray in the treatment of acute sore throats.

Methods:

- Design: Multicenter, randomized, double-blind, double-dummy controlled trial.
- Allocation: A total of 154 patients were screened, randomized and treated. A total of 80 patients were allocated to the echinacea/sage group and 74 to the chlorhexidine/lidocaine group. The baseline characteristics between treatment groups were comparable, with the only significant difference found for age were those patients allocated to the chlorhexidine/lidocaine group seemed to be younger. Furthermore, the throat score as determined by the tonsillopharyngitis severity score was found to be somewhat higher at baseline for patient allocated to the chlorhexidine/lidocaine treatment group.
- Blinding: double-blind, double-dummy controlled trial.
- Follow-up Period: 5 days following the onset of sore throat symptoms. The average study duration was 5.6 days for the echinacea/sage group and 6.4 days for the chlorhexidine/lidocaine group.
- Participants: A total of 154 patients were recruited from 11 different general physician practices in Switzerland. All patients were at least 12 years old with acute sore throat (i.e. acute pharyngitis or tonsillitis with symptoms of pain and inflammation of the pharynx and/or tonsils) present for not more than 72 hours prior to study inclusion with a tonsillopharyngitis severity score of 6 or greater. Patients were excluded from the study if they had recently used analgesics, antibiotics, topical throat pain medication or systemic corticosteroids. Additional exclusion criteria were symptoms of a bacterial pharyngitis infection, allergy to of the study herbs, pregnancy or lactation, hypersensitivity to ibuprofen or recent participation in a previous clinical trial.
- Intervention: Patients received either a 50 mL Echinacea/sage throat spray containing an aqueous alcohol fresh-plant extract of *Echinacea purpurea* (95% aerial parts and 5% root) and leaves tincture of *Salvia officinalis* or a commercial throat spray containing 1% chlorhexidine gluconate and 2% lidocaine hydrochloride. Regardless of which treatment group patients were assigned to, both sprays were administered as two sprays every 2 hours up to 10 times daily until they were symptom-free, for a maximum of 5 days. Owing to the fact it was a double-dummy blinded study, in addition to receiving a treatment spray each patient also received a placebo spray that was similar in appearance, taste and smell to other treatment spray they did not receive. The treatment and placebo sprays were issued to patients in a sealed box together with 20 tablets of ibuprofen 200 mg hat served as a rescue medication if the pain symptoms became too severe.
- Outcomes: The primary study outcome was to compare the patient response rates to the Echinacea/sage throat spray to those obtained for the chlorhexidine/lidocaine spray during the first 3 days of use. The patient response to the treatment was assessed at baseline and during treatment by the patient using a tonsillopharyngitis symptom severity score which consisted of ratings for symptoms of throat pain, difficulty swallowing, salivation, erythema and fever. A

response to treatment was defined as a decrease of at least 50% of the total baseline symptom score taken prior to treatment.

- Patient Follow-up: Treatment duration was until illness resolution or for a maximum of 5 consecutive days. Although 154 patient were screened, randomized and treatment, 21 patient were either excluded secondary to incorrect use of the study medications or were lost to follow-up. Therefore, a total of 133 patients were included as part of the study. To check blinding at the end of the treatment, patient were asked to guess which bottle contained the treatment. Compliance was checked by weighting the returned bottles and counting the number of rescue ibuprofen used and patients documented in a dairy how many times they had applied each spray daily.
- Setting: Outpatient, multicenter, general physician practice, community trial in Switzerland.

Main Results: The Echinacea/sage treatment spray exhibited similar efficacy to the chlorhexidine/lidocaine treatment spray in reducing sore throat symptoms during the first 3 days following use and for each day of use. Response rates after 3 days were reported as 63.8% in the echinacea/sage group and 57.8% in the chlorhexidine/lidocaine group. The response rates for day 4 were 69.6% for echinacea/sage and 70.3% for chlorhexidine/lidocaine, respectively, and for day 5, they were 73.9% and 79.7. The time point at which 50% of patients in the Echinacea/sage treatment group were symptom-free (total tonsillopharyngitis symptom severity score ≤ 2) was the evening of day 4, while 50% of patients in the chlorhexidine/lidocaine group achieved symptom-free status the morning of day 5. At day 5, 50.7% of the patients allocated to the Echinacea/sage treatment group and 56.7% of patients allocated to the chlorhexidine/lidocaine treatment group were assessed to be symptom-free. Both treatments were very well tolerated by study participants. Investigators rated the efficacy as very good or good in 88.4% of patients using the echinacea/sage spray and in 89.1% of all patients using the chlorhexidine/lidocaine spray. Patients' efficacy ratings were similar, with "very good" or "good" in 89.9% of the echinacea/sage and 89.1% of the chlorhexidine/lidocaine cases.

Conclusions: An echinacea/sage spray preparation is as efficacious and well tolerated as chlorhexidine/lidocaine spray in the treatment of acute sore throats.

Comments/Critical Appraisal (including assessment of internal and external validity):

A major limitation of this study was its small sample size and that despite randomization, there was some variability in term baseline throat symptom severity between treatment groups as study patients allocated to the chlorhexidine/lidocaine treatment group reported has having a higher throat score compared to those allocated to the echinacea/sage treatment group. Furthermore, given that Echinacea and sage were administered and studied together, it is difficult to elucidate whether the efficacy demonstrated by this study was attributed to the Echinacea, the sage or the combination of both being administered together. The internal validity of the study is strong since investigators randomized, double-blinded and double-dummied the study, assessed for blinding during the study, accounted for compliance as well as performed objective physician assessments at baseline and following treatment completion. The subjective nature of the patient throat symptom severity scoring system used by the study investigators to assess efficacy supports the study's internal validity although it is unknown whether the scoring system itself is validated. The strict inclusion and exclusion criterion strengthens the study's internal validity but weakens its external validity. The study is externally valid only for patients who meet the inclusion/exclusion criteria limiting the number of patient eligible to use an echinacea/sage throat spray. One last thing that may call into question the internal and external validity of the study is the fact that it was sponsored by A. Vogel Bioforce AG, the manufacturers of the

echinacea/sage herbal throat spray utilized as part of this study. Considering this, results obtained may be bias and further investigation is required in order to confirm or refute this. However, subsequent investigations of sage throat sprays and its efficacy are limited. In terms of external validity, the fact that A. Vogel Bioforce AG sponsored the investigation does strength its external validity since a very similar herbal throat spray to the one utilized in the study, specifically the A.Vogel Sore Throat Spray, is readily available in Canada for patients to use.

2. Hubber M, Sievers H, Lehnfeld R, Kehrl W. Efficacy and Tolerability of a Spray with *Salvia Officinalis* in the Treatment of Acute Pharyngitis – A Randomized, Double-Blinded, Placebo-Controlled Study with Adaptive Design and Interim Analysis. *Eur J Med Res*. 2006;11:20-6.

Extended Abstract:

Study objectives: To determine the efficacy and tolerability of sage (*Salvia officinalis*) for treating patients with acute viral pharyngitis.

Methods:

- Design: randomized, double-blinded, parallel control group phase II/III study with two stage design and interim analysis.
- Allocation: in part 1 of the study, patients were equally randomized to 5%, 15%, 30% sage spray or placebo, in part 2 of the study patients were equally randomized to 15% sage spray or placebo.
- Blinding: patients and providers were unaware which spray they were receiving.
- Follow-up period: December 2001 – February 2002 (study part 1), April 2002 – June 2002 (study part 2).
- Setting: 16 doctor's offices (first part of study), 21 doctor's offices (second part of study).
- Participants: 286 patients with acute pharyngitis randomized in two parts of study (122 in first part and 164 in second part). *Inclusion criteria:* > 18 years old, sore throat symptoms within 48 hours with spontaneous throat pain or inflammation, visual analog scale (VAS) score > 40 mm/100 mm, pharyngitis confirmed by a physician, completed written consent. *Exclusion criteria:* group A β-hemolytic *streptococci* , rhinosinusitis, laryngitis, tracheitis, bronchitis, fever, wounds, changes in oral cave, unallowed medications, dental or trauma pain requiring analgesics, oropharyngeal surgery < 4 weeks, seizures, any hypersensitivity to product ingredients, pregnant, lactating, women of childbearing age without contraception.
- Intervention: 5%, 15%, 30% (first part of study) and 15% (second part of study) sage extract throat spray, administered 9 puffs on day 1, 9 puffs on day 2 and 3 puffs on day 3.
- Outcomes: primary outcome was sore throat pain intensity (spontaneous pain) assessed by patient using VAS (100 mm), determined area under curve and pain intensity differences, secondary outcomes included meaningful pain relief, complete pain reduction after first application, change in throat pain intensity, number of patients discontinuing therapy due to lack of efficacy, overall efficacy and safety assessment by physician and patient, adverse effects.
- Patient follow-up: baseline and follow-up visit in 3 days, symptoms were recorded by patient every 15 minutes for 2 hours using a VAS and pain diary.
- Main results: In study part 1, sage extract spray 15% showed superior reduction in VAS over placebo (p=0.093), in study part 2, sage extract spray 15% showed a statistically significant reduction in VAS over placebo (p=0.002) with an 11-12 mm reduction in pain. Overall sage spray 15% showed a reduction in pain within the first 2 hours (p=0.0002) and sustained up to 3 days

when treatment was stopped. There was no significant difference in tolerability and safety of using the sage product.

Conclusion: The use of sage fluid extract spray 15% showed a significant reduction in sore throat pain scores on VAS by 11 points (p=0.002) with no difference in safety or tolerability.

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

Hubbert *et. al.* provided the highest quality study design and evidence supporting the use of sage for sore throat to date. The internal validity was strong due to the randomized, double blinded, placebo controlled study design. The internal and external inclusion criteria were clearly defined. One weakness was that the baseline characteristics were very vague by only comparing gender and age without any other health information. A medium patient population size was included and equally randomized into treatment groups. The use of a two stage study design strengthened the internal validity by pre-screening the most effective dose early, then further studying the treatment effect with more patients. The treatment effect was monitored closely using a validated pain assessment of VAS. A second weakness was that there was a high placebo effect and the product contained alcohol which may have contributed to the analgesic effect. All patients were monitored closely, followed up and accounted for. The external validity is high since the study may be reproduced in patients. However, the external validity may be reduced by only assessing spontaneous pain which was very specific instead of including all other clinically relevant pain sources such as pain of swallowing which would be of concern for patients with a sore throat. Overall, it is clear that sage is a treatment option for patients with sore throat by providing an effective and safe treatment option.

Tertiary/Secondary:

3. **Adams J.D. *et. al.* Sage (*Salvia officinalis, Salvia lavandulaefolia, Salvia lavandulifolia*). Natural Standard Professional Monograph. accessed at: www.naturalstandard.com on Mar 26, 2013.**

Source description: Natural Standard is a database containing systematic review of scientific evidence on complementary and alternative medicine. Its editorial board contains MDs, NDs, PharmDs, PhDs, DC, Administrator of Ayurveda Institute, Director of the research group for Mind-Body dynamics at the Institute for Nonlinear Science and Ayurveda Physician, and Executive Director of Ayurvedic Institute of India. The database is generally updated every 3-18 months. However, it does not mention when each individual monograph was updated. Based on the evidence, the Natural Standard provides evidence grade and they are as follows: A – Strong positive scientific evidence, B – Positive scientific evidence , C – Unclear scientific evidence, D – Negative scientific evidence, F – Strong negative scientific evidence.

Summary: evidence grade C (unclear), sage is a popular treatment option for inflammation of the mouth and throat especially in Europe. Sage mouth washes and gargles have been approved in Germany by the German Commission E for many years with good clinical evidence for use in sore throats. A high quality randomized controlled trial by Hubbert *et. al.* showed that sage spray significantly reduced pain intensity of a sore throat. Product recommendation is a 15% spray containing 140 µL of *Salvia officinalis* per dose used 6-9 times daily for three days.

Comments/critical appraisal: The information provided on Natural Standard is internally valid since it considered primary literature to support a recommendation of grade C for use in sore throats. Natural

standard clearly defines its grading criteria for recommendations based on quality of evidence. There is one high quality clinical trial supporting the use of sage for reducing sore throat pain symptoms. Therefore, the external validity is limited since there is not a large body of evidence supporting the use of sage.