

Detailed analysis of relevant studies

| Author, date | Population (age, sex, location, representative of?) | Intervention, or Test treatment, numbers studied | Control treatment (number studied) | Outcome | Critical appraisal comments (see checklists) | Conclusion, strength of evidence and classification |
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| Pisanty, Rafaely, Polishuk 1975 The effect of steroid hormones on buccal mucosa of menopausal women | 22 post-menopausal women complaining of dry, burning sensation in the mouth. | Single-center, double blind, CCT Group A – estrone ointment, 50 000 U. per gram in base Group B – estrone, 10 000 U., and progesterone, 50mg. per gram in base Group C – placebo base ointment Patients instructed to massage ointment into oral mucosa 3 times daily for 30 days. | Group C – 6 patients. Received a placebo ointment and instructed to use the same as Group A and B. Patients instructed to massage ointment into oral mucosa 3 times daily for 30 days. | Findings on subjective complaints. | 1. The study was ethical as consent was received from all participants. 2. Study used a double blind case controlled trial. 3. Severity of symptoms was not measured on a standardized scale. Either patients had relief or they did not. 5. Results did not reveal significant differences between the 3 treatments. 6. The patients were randomized but all the patients in each group complained of dry burning sensation in the mouth and all the patients were post-menopausal. -The steroid treatment was used for only 30 days, which does not seem to be long enough to produce significant results. -Only 22 women were used in the study and not all the participants followed the ointment regime to the end date. -Care outside of the study was not identified. | There was no significant improvement of the complaints on dryness and burning sensation in either of the 3 groups. Level of Evidence: C |
| Gremeau-Richard et al 2004 Topical clonazepam in stomatodynia: randomized placebo-controlled study | 48 patients with BMS from 6 centres in France. 44 females and 4 males (mean age 65 years old, range 62.9-67.9) Duration of BMS: ≥ 4 months | 24 patients (23 female, 1 male) received tablets containing 1mg clonazepam to be used 3 times a day for 14 days (hold tablet on site of pain for 3 minutes, then spit). | 24 patients (21 female, 3 male) received placebo 3 times a day for 14 days. Same method as for treatment group. | Measured outcome as a decrease in pain on visual analog scale | 1. The study was approved by a local ethics committee and written consent was received from all participants. 2. Study used a double blind, randomized study. 3. Severity of symptoms was measured using a written numerical pain scale (1 to 10) 5. Results did reveal significant differences between the 2 treatments. 6. The patients were randomized, 3 participants did not complete the study due to side effects, 2 week duration, double blinded, the groups were similar at the start of the trial. | Significant differences were seen between the 2 treatment groups. (p=0.014) Level of Evidence: C |

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| <p>Tammialia-Salonen, T & Forssell, Heli 1999</p> <p>Trazodone in Burning Mouth Pain: A Placebo-Controlled, Double-Blind Study.</p> | <p>37 women in Finland referred to the University hospital as a result of mucosal burning pain (mean age: 58.6yr-range: 39-71 yrs).</p> <p>Strict criteria was used to narrow down from 146 pts. Criteria for inclusion were daily oral burning pain, lasting at least 6 months and moderate to severe pain intensity (30/100 on VAS scale).</p> | <p>18 received Trazodone 100mg for first 4 days, then increased to 200mg daily for a trial period of 8 weeks.</p> | <p>19 received placebo for 8 weeks.</p> | <p>Both groups were evaluated at 0, 2 4, and 8 weeks. Visual analogue scales (VAS) were used to measure intensity of BMS pain, pain upon eating, speaking and sleeping and suffering caused by pain.</p> | <ol style="list-style-type: none"> 1. Was ethical, approved by the Joint Commission on ethics of Turku University and University Central hospital. 2. Design was double blind, randomized, placebo controlled study. 3. Measure of pain done by visual analogue scales (adaptions of the McGill pain questionnaire). 5. Results: not clinically important, not beyond chance. There was no difference. 6. Study was randomized with careful pt selection. Follow up loss greater than 20%, in the end, persons that completed the trial were 4/18 in the tx group and 15/18 in the placebo group. 8 weeks is sufficient to see changes in pain. All personnel were blinded. And the groups were similar at the start of the trial. Pt's were allowed to keep a diary of other meds that they took (2 pt in both groups used NSAIDs). 7. No significant differences. No benefits (major side effect was dizziness). | <p>In this study, there was no difference observed in decrease in BMS pain between treatment and placebo groups.</p> <p>Level of Evidence: C</p> |
| <p>Petruzzi M, Lauritano D, De Benedittis M, Bladoni M & Sercipo R 2003</p> <p>Systemic capsaicin for burning mouth syndrome: short-term results of a pilot study.</p> | <p>50 patients (14 male & 36 female) were recruited from one centre.</p> | <p>25 patients received oral capsaicin 0.25% capsule 3 times a day for 1 month.</p> | <p>25 patients received placebo (same size/shape/color/smell) as treated pts for 1 month.</p> | <p>Pain outcomes (and baseline) were evaluated using a visual analogue scale (VAS)</p> | <ol style="list-style-type: none"> 1. Ethics committee approval plus written consent from all participants. 2. Strong design: triple blind (pt, investigators and outcome assessors). Treatment vs. placebo. Alternating assignment. 3. Pain outcomes (and baseline) were evaluated using a visual analogue scale (VAS). 4. Interventions of drug vs. placebo. 5. The data was significant statistically, can have a clinical importance, however, there was a side effect (adverse effect) of gastric pain. 6. The assignment of treatments was done in an alternating fashion, and the baseline VAS, duration of BMS, age and sex were matched well. There was no follow- up loss. Triple blinded but there was no mention of any care received outside of study. | <p>Significant evidence in treating pain from BMS (short term only). Concern with adverse effects.</p> <p>Level of Evidence: C</p> |

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| <p>Sardella A, Uglietti D, Demarosi F, Lodi G, Bez C & Carrassi 1999</p> <p>Benzydamine hydrochloride oral rinses in management of burning mouth syndrome</p> | <p>30 patients with BMS referred to the Dept of Oral Path & Med at the University of Milan. 26 females and 4 males (mean age 69 years old, range 54-85) Mean duration of BMS: 18 months</p> | <p>10 patients (9 female, 1 male) received an oral rinse solution containing benzydamine hydrochloride 0.15% to be used 3 times a day for 4 weeks (15mL for 1 minute).</p> | <p>10 patients (9 female, 1 male) received placebo 3 times a day for 4 weeks.</p> <p>Another 10 patients (8 female, 2 male) received no treatment for 4 weeks.</p> | <p>Severity of symptoms was measured using a visual analogue scale (VAS). Score was said to be not effective, partially effective or effective.</p> | <ol style="list-style-type: none"> 1. The study was approved by the University ethics committee and written consent was received from all participants. 2. Double blind, block randomized longitudinal study. 3. Severity of symptoms was measured using a visual analogue scale (VAS). 5. Results did not reveal any significant differences between the 3 treatments. 6. The patients were randomized, all participants completed the study, 4 week duration, double blinded only within the first 2 groups (not the group who received no treatment), the groups were similar at the start of the trial and no indication of whether outside care was received. | <p>No significant differences were seen between the 3 treatment groups.</p> <p>Level of Evidence: C</p> |
| <p>Bergdahl et al. 1995</p> <p>Cognitive therapy in the treatment of patients with resistant burning mouth syndrome: a controlled study</p> | <p>Mean age 54 years (range 38 to 69), male/female ratio is 6/24</p> | <p>Cognitive therapy 1 hour, weekly sessions for 12 to 15 visits (n = 15)</p> | <p>Attention placebo 3 visits over 12 to 15 weeks (n = 15)</p> | <p>Severity of symptoms was measured using a visual analogue scale (VAS).</p> | <ol style="list-style-type: none"> 2. Single-centre RCT 3. Not clear whether the visual analogue scale (VAS) used was validated 5. A statistically significant difference in reduction in pain intensity 6. Groups were comparable at baseline, Mean duration of BMS not stated. No further information regarding randomization, allocation concealment or blinding <p>Did not indicate what constituted clinically significant burning intensity</p> | <p>Authors report a statistically significant difference in reduction in pain intensity.</p> |
| <p>Femiano F, Scully C. 2002</p> <p>Burning Mouth Syndrome (BMS): double blind controlled study of alpha-lipoic acid (thioctic acid) therapy</p> | <p>60 of 96 patients, examined for the clinical symptoms of burning discomfort of the anterior region of the tongue with an unknown cause, were diagnosed with having BMS. The 60 patients were made up of 42 females and 18 males (median age 45, range 22-68)</p> | <p>Group 1: received alpha-lipoic acid in 200mg oral pills, three times a day for a 2 month duration (note: if improvement in symptoms was observed at 2 months, patients were given an additional months treatment and followed for one year)</p> | <p>Group 2: received cellulose starch 100mg/day, three times a day for a 2 month duration</p> | <p>Changes in symptomatology were scored as worsening, unchanged, slight improvement, decided improvement, resolution</p> | <ol style="list-style-type: none"> 1. The study received consent from all participants and offer no health risk to those participating 2. The study used double blind randomized control trial 3. Severity of symptoms was measured using a visual analogue scale (VAS) 4. Intervention: alpha-lipoic acid or placebo 5. The results showed significant improvement in the group taking alpha-lipoic acid as compared to the placebo 6. The patients were randomized, the study was double blinded, there was no loss to follow up, the groups were similar to begin the trial with no indication of outside care during the study. | <p>There was a significant symptomatic improvement of the testing group over the control group. This gives support to the hypothesis that BMS is of neuropathic aetiology.</p> <p>Level of Evidence: C</p> |

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| <p>Femiano F, Gombos F, Scully C. 2004</p> <p>Burning Mouth Syndrome: open trial of psychotherapy alone, medication with alpha-lipoic acid (thioctic acid), and combination therapy.</p> | <p>The open study consisted of 192 BMS patients that were otherwise healthy. Of the 192 patients 104 were females and 88 males (median age 48, range 24-67)</p> | <p>Group 1: received cognitive psychotherapy for 1 hour daily</p> <p>Group 2: received Alpha-lipoic acid 600mg/day</p> <p>Group 3: received Alpha-lipoic acid 600mg/day + Cognitive psychotherapy for 1 hour daily</p> <p>The duration for each group was 2 months (note: Patients in groups 1, 2 and 3 were followed for six months after treatments to show maintenance of the beneficial effects)</p> | <p>Group 4: received cellulose starch 100mg/day for a 2 month duration</p> | <p>Changes in symptomatology were scored as worsening, unchanged, slight improvement, decided improvement, resolution.</p> | <ol style="list-style-type: none"> 1. The study received local ethical approval. 2. Double blind randomized control trial. 3. Severity of symptoms was measured using a visual analogue scale (VAS). 5. Combination therapy (group 3) showed the largest improvement followed by ALA treatment (group 2) and lastly cognitive psychotherapy (group 1). 6. The patients were randomized, the study was double blinded, the loss to follow up was less than 20%, the groups were similar to begin the trial with in the beginning, no indication of outside care during the study was given. | <p>This study suggests that alpha-lipoic acid can be used in combination or as an alternative to psychotherapy.</p> <p>Level of Evidence: C</p> |
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