

Derry S, Lloyd R, et al Topical capsaicin for chronic neuropathic pain in adults (Review). Cochrane Database of Systematic Reviews 2009; Issue 4, Art # CD007393.

Design: Meta-analysis of randomized trials

PICOS:

- **Population:** Adults with neuropathic pain of at least 3 months duration
- **Intervention:** Topical capsaicin; at least 3-4 times a day for low dose (<0.1%); single dose acceptable for high dose (8%)
- **Comparison intervention:** Placebo or other active treatment
- **Outcome:** Clinical improvement defined as 50% pain reduction, or “very good” or “excellent” global assessment of outcome
- **Study types:** Randomized double blind controlled trials of at least 6 weeks duration comparing topical capsaicin with placebo or other active treatment, with at least 10 patients per study arm; studies published only as abstracts or studying experimental pain were excluded

Study search and selection:

- Electronic searches of MEDLINE, EMBASE, Cochrane Central, and Oxford Pain Relief Database
- Two authors independently selected studies for inclusion, assessed methodological quality and study validity, resolving disagreements through discussion
- Quality assessed by a 5 point Oxford Quality Score (randomization, double blinding, withdrawals/dropouts), and validity assessed by a 16 point Oxford Pain Validity Scale (OPVS) (blinding, size of groups, study sensitivity to detect a treatment effect, data analysis)

Results:

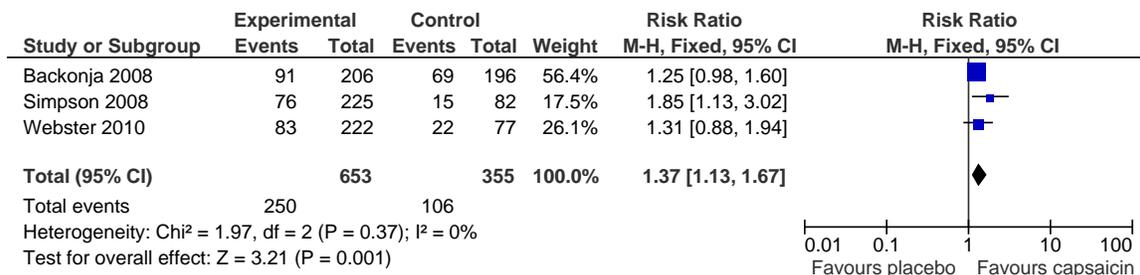
- 9 studies, with 1600 participants in total, met the entry criteria
- 7 studies used low-dose (0.075%) capsaicin qid for 6-12 weeks
- Patient populations included postherpetic neuralgia, diabetic neuropathy, peripheral polyneuropathy, postsurgical neuropathic pain, HIV neuropathy, and postmastectomy pain syndrome
- For low dose capsaicin, the success rate for capsaicin was 41%, with a success rate for placebo of 26%, for a relative benefit of 1.6 in favor of capsaicin
- 2 studies used a single high-dose (8%) capsaicin, with the treatment area pre-treated with topical anesthetic cream due to the high potency of 8% cream
- For high dose capsaicin, the success rate was 39%, with a 30% success rate for placebo, for a relative benefit of 1.4 in favor of capsaicin
- Reporting of adverse effects was inconsistent and incomplete; local skin reactions were the most common adverse effect, and occurred more commonly with capsaicin (63%) than with placebo (24%) for a relative risk of 2.6

Authors' conclusions:

- Capsaicin at either low concentration for several weeks, or at high concentration for one dose, appears to provide some improvement in a range of neuropathic pain conditions
- A new large study (of 300 participants with no treatment effect) could significantly change the estimates of the effectiveness of capsaicin; therefore, the results cannot be regarded as robust
- Overall the quality of studies was adequate, but blinding was problematic, even though several studies used a skin irritant in the control group to mimic the effect of capsaicin
- The use of very low dose (0.04%) capsaicin in the control arm of the high dose capsaicin may have underestimated its efficacy
- Capsaicin may be worth trying as an add-on treatment for patients with poor response to other interventions, if the adverse effects are tolerable

Comments:

- Many of the strengths of the Cochrane Review methods are apparent: the search strategy, the pooled estimates of treatment effect, and the reporting of the lack of robustness of the results, collectively give a realistic assessment of capsaicin's effectiveness
- Publication bias is not explicitly addressed, except for the calculation that a single large study of 300 patients with null results would make the treatment effect appear not great enough to be clinically useful
- The wide variety of clinical conditions in the included studies is useful for the external validity of the study
- Figure 4 is a forest plot of 8% capsaicin vs. placebo for >30% pain relief; when Cochrane's RevMan software is used to add in the effect observed in Webster et al, J Pain 2010, the pooled risk ratio is very close to the result in Figure 4 (Risk ratio=1.37, 95% CI [1.13, 1.67])



Assessment: For evidence that low dose capsaicin provides moderate relief of neuropathic pain: good

For evidence that high concentration capsaicin provides moderate relief of neuropathic pain: good

Because the results are not robust (a large study could weaken the estimate of the effectiveness of capsaicin), a stronger evidence statement is not warranted. Overall adequate.