Khaliq W, Alam S, Puri NK. Topical lidocaine for the treatment of post-herpetic neuralgia (Review). Cochrane Database of Systematic Reviews 2007, Issue 2, Art. No. CD004846.

Design: Meta-analysis

PICOS:

- **P**atient population: patients of any age who fulfill definition of post-herpetic neuralgia: pain persisting at the site of shingles at least one month after onset of acute rash
- **I**ntervention: all topical applications of lidocaine
- **C**omparison intervention: placebo or any other active treatment
- Outcome: mean improvement in pain relief on a 6 point scale reporting change in pain (0=much worse, 5=complete relief)
- **S**tudy type: all randomized or quasi-randomized trials

Study search and selection:

- Search databases included Cochrane Pain, Palliative, and Supportive Care Register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, LILACS (Latin American and Caribbean literature database), SIGLE (System for Information on Grey Literature in Europe) for conference proceedings, and Citation Index
- Quality assessment was done by all three authors, resolving disagreements through discussion; criteria were allocation concealment, blinding of patient and observer, inclusion/exclusion criteria, baseline differences, and completeness of follow-up
- Search revealed 800 titles, of which 9 were relevant to the review; 6 were excluded (lacking random allocation, for single blinding, for mixing post-herpetic neuralgia with other types of neuralgia, or for using enriched enrollment); 3 studies were included for the analysis

Results:

- The 3 eligible trials had 182 participants treated with lidocaine and 132 control participants; all 3 had the same first author
- 2 trials used lidocaine patches, and 1 used lidocaine gel
- Meta-analysis of primary outcome measure, mean improvement in pain on a 6 point scale, had a weighted mean difference in favor of lidocaine of 0.42 (95% CI, 0.14 to 0.69); only 2 studies reported this scale
- Highest lidocaine blood concentration reported was 431 ng/ml; lidocaine may have toxic systemic effects above 400 ng/ml, but no systemic toxic effects were reported
- Local skin reactions were reported in both groups and may have been due to use of the patch

Authors' conclusions:

- Very little data was available for estimating effectiveness of lidocaine; when different outcome measures are used, there is scant data for combining studies
- No studies compared lidocaine with other active treatments
- There is insufficient evidence to recommend lidocaine as a first-line treatment for post-herpetic neuralgia

Comments:

- The review looked at studies of post-herpetic neuralgia; this led to the exclusion of a study which mixed PHN with other kinds of neuropathic pain
- If neuropathic pain of other causes responds similarly to lidocaine, the inclusion of such studies could increase the data for combining in a meta-analysis
- With so few studies, there is no chance to apply tests for publication bias; since the authors conclude that there is insufficient evidence to recommend lidocaine, publication bias is not a major issue for their conclusions
- The study which was excluded for having a mixed neuropathic pain population (Meier 2003) does not report data in a way which would allow it to be combined with the included studies even if its inclusion were attempted
- Both included studies are by the same author (Rowbotham 1996a and 1996b), which may underestimate the heterogeneity of results
- Rowbotham 1996a is cited in Analysis 1.1 as having a mean pain improvement for lidocaine of 2.17 (SD 0.97) and 1.85 (SD 0.72) for placebo; the only one of these numbers reported by Rowbotham is the mean improvement of 2.17 for lidocaine
- Since Rowbotham 1996a is stated to be based on “published data only,” it is not apparent where the other data points came from; the pain relief scores are presented in a figure with no bars to indicate standard deviations, and no tabular data were presented

Assessment: Inadequate (no transparency as to the origin of the data used to pool results) with respect to the pooled effect size for lidocaine on pain relief