Webster LR, Malan TP, et al. A Multicenter, Randomized, Double-Blind, Controlled Dose Finding Study of NGX-4010, a High-Concentration Capsaicin Patch, for the Treatment of Postherpetic Neuralgia. J Pain 2010

Design: Randomized clinical trial

Population/sample size/setting:

- 299 patients (112 men, 110 women, mean age 71.6) treated for postherpetic neuralgia (PHN) at pain clinics in Utah, Arizona, and Florida
- Inclusion criteria were Numeric Pain Rating Scale (NPRS) between 3 and 9, if at least 6 months had elapsed since vesicles had crusted, and if other chronic pain medications had been used at a stable dose for at least 21 days
- Exclusion criteria were use of any topical medication at the affected site within 21 days of starting treatment, uncontrolled diabetes or hypertension, PHN areas only on the face above the scalp hairline

Main outcome measures:

- Randomized to capsaicin (n=222) or control (n=77)
- Capsaicin was an 8% patch administered randomly for either 30 minutes (n=72), 60 minutes (n=77), or 90 min (n=73)
- Control was very low dose capsaicin (0.04%) patch for 30, 60, or 90 minutes to induce some local erythema and burning sensation to attempt blinding
- Lidocaine 4% patch was applied to the treatment area for 60 minutes just prior to placing the experimental patch; lidocaine was used to reduce the burning pain of the high-dose capsaicin patch
- Primary endpoint was percent reduction in NPRS from baseline to weeks 2 through 8; the scores in week 1 were not used in the primary analysis
- The percentage of patients with >30% and >50% NPRS reduction was also recorded and used in the efficacy analysis
- 91% of the patients completed the study (90% of the capsaicin and 95% of the control patient)
- Mean reduction in NPRS from weeks 2 to 8 for capsaicin was 26.5% compared with 17.3% for placebo; the reductions were similar for patch placement of 30, 60, and 90 minutes
- Mean reduction in NPRS from weeks 2 to 12 was 25% for capsaicin and 14.7% for control, again with similar reductions for 30, 60, and 90 minute patch placement
- Percent of patients with a reduction of NPRS of 30-50% 37% of capsaicin and 29% of control (non-significant), but percent of NPRS with 50% reduction or more was 25% of capsaicin and 10% of control (p=.0049)
- Post-hoc analyses showed that men had a smaller response to capsaicin than women, and the analyses of the percentages of patients with 30 and 50% reductions in pain were adjusted for gender
- 3 capsaicin patients requested early removal of the patch due to pain during the patch application

- Oxycodone was used on the day of treatment by 51% of the capsaicin and by 4% of the control patients; the duration of patch application was correlated with the use of oxycodone (40% of the 30 minute patch group and 66% of the 90 minute group)
- Blood pressure increases of <10 mm Hg systolic and < 6 mm diastolic were observed during patch application, but returned to baseline values within 60 minutes

Authors' conclusions:

- A single application of 8% capsaicin provided pain reduction that was maintained for up to 3 months in patients with postherpetic neuralgia
- Post-hoc analyses found that treatment duration of 60 minutes was the lowest effective dose
- The effects of gender should be taken into account when analyzing pain studies

Comments:

- Some aspects of randomization are unclear: the sequence generation and the concealment of allocation are not described
- Blinding is difficult when an irritant treatment is used; it was attempted by using a low dose capsaicin irritant in the control application, which may tend to attenuate the observed difference between the 8% concentration and the control treatment
- Attrition was low and the flow of patients was well documented
- Risk of bias: intermediate
- This study is consistent with the Cochrane Review of the same intervention

Assessment: Adequate for evidence that a single application of 8% capsaicin may reduce neuropathic pain for up to 3 months