

Meier T, Wasner G, et al. Efficacy of lidocaine patch 5% in the treatment of focal peripheral neuropathic pain syndromes: a randomized, double-blind placebo-controlled study. Pain 2003;106:151-158

Design: Randomized crossover trial

Population/sample size/setting:

- 58 patients (30 women, 28 men, mean age 63) treated for painful peripheral focal neuropathic syndromes (PNPS) at universities in Germany and Switzerland
- PNPS was defined as mechanical allodynia in the territory of peripheral nerves, evoked by repetitive gentle movement of a cotton swab over the affected skin
- Most had postherpetic neuralgia (n=32) or postsurgical neuralgia (n=10); trunk (n=28) and arm (n=10) were most commonly affected sites
- Eligibility criteria were age over 21, average VAS pain score of 40 or more on a 100 mm scale, stable consumption of analgesic and antidepressant drugs for at least 4 weeks
- Exclusion criteria were the presence of another form of pain with similar intensity, previous nerve blockade or neurosurgery, inflammation or insufficient wound healing of skin in the treated area

Main outcome measures:

- Study was done in 4 phases: run-in phase (4 days), treatment phase 1 (7 days), washout period (variable), and treatment phase 2 (7 days)
- Washout period was begun at 7 days; if at the end of 7 days, the pain had returned to pre-treatment values ($\pm 20\%$), the patient advanced to phase 2; if the pain had not returned to pre-treatment levels, the washout period was extended for 7 days; then, if the pain had not returned to pre-treatment levels, the patient was withdrawn from the study; otherwise, the patient went on to phase 2
- Patients received both 5% lidocaine patch and identical-appearing placebo patch in random order; 28 patients were randomized to lidocaine first, with 30 randomized to placebo first
- Patches were to be applied for at most 12 hours per day to the area of maximal pain; up to 4 patches were to be applied
- Large attrition occurred in both groups; of 28 patients who started with lidocaine patch, 8 withdrew; of 30 patients who started with placebo patch, 10 withdrew
- In each group, 5 withdrawals occurred because of the design of the study (they did not return to pre-treatment levels of pain at the end of the second washout week)
- Primary efficacy parameter was the area under the curve between baseline and 8 hours, with VAS pain scores taken at 0, 2, 4, 6, and 8 hours, with an additional score 1 hour after patch removal; this was done for every day

during the 7 day patch application period, using data recorded by the patients using a diary

- Both placebo and lidocaine patches showed improvements in pain intensity from day 1 to day 7 during the two treatment periods
- The lidocaine patch data revealed significant differences between it and placebo patches (p values alone are reported; actual values are displayed graphically, without tabular values)
- Pain reduction of 50% was achieved in 31% of lidocaine patch treatment periods, and in 8.1% of placebo periods; for 30% reduction, the response rates were 41% and 8.6% respectively
- Carryover and sequence effects were not apparent using a non-parametric test
- Allodynia was measured separately, also by the patients, using the same diaries and at the same time intervals
- Allodynia results were approximately the same as pain VAS results, with statistically significant improvement in lidocaine compared to placebo
- Adverse effects were mostly skin irritation related to the patch itself, with no difference between groups in frequency of skin symptoms; 41 such adverse effects were noted in 29 of the 58 patients; only 1 case withdrew from the study due to an eczematous folliculitis

Authors' conclusions:

- Lidocaine patch is acutely effective and remains effective throughout a 7 day period
- The lidocaine patch has advantages over systemic drug treatment, and can be used as a first line treatment or as an add-on therapy

Comments:

- There was high attrition due to pain score not coming back to within 20% of the pre-treatment level in both groups, even after a 14 day extended washout period
- The attrition was equal between placebo and lidocaine patches
- If there is a carryover effect, it would be partly manifested as pain scores remaining below their pre-treatment level for more than 7 days; however, the equal frequency in the treatment groups suggested that the comparison is not likely to be biased by this carryover
- Since the 5 patients in each group who were withdrawn after the first treatment period did not complete the study, the comparison of the completers may somewhat overestimate the difference between lidocaine and placebo
- The lack of tabular displays of numerical data reduces the usefulness of the study data; means and standard deviations are important parameters which cannot be inferred from graphs alone
- However, the comparison of frequency of 30% and 50% reduction is helpful; even though fewer than half of lidocaine patch users had a 50% reduction in pain scores, the comparison does show an advantage over placebo

- Allodynia was recorded at the same intervals as pain score by the patients themselves; since the patch was covering the skin during the treatment, it is not clear just how this was accomplished
- Lidocaine blood levels were not measured; past studies have done this to ensure that the levels remain below those associated with toxic effects
- The effects of indefinite lidocaine patch use cannot be estimated from its use for 12 hours/day for 7 days

Assessment: Adequate for evidence that 5% lidocaine patch may be an option for neuropathic pain; inadequate for evidence that it is a first line treatment