

Khoromi S, Patsalides A, et al. Topiramate in Chronic Lumbar Radicular Pain. J Pain 2005;6(12):829-36.

Design: Randomized crossover trial

Population/sample size/setting:

- 43 patients (23 men, 20 women, mean age not reported) treated for chronic lumbar radicular pain at the NIH in Bethesda, MD
- Eligibility criteria were lumbar radiculopathy manifested as pain in one or both buttocks or legs lasting at least 3 months with a frequency of at least 5 days per week, having an average intensity of at least 4 on a scale from 0-10, and willing to refrain from making changes in non-study medications being taken for sciatica
- Exclusion criteria were a number of coexisting medical conditions (hepatic, renal, pregnancy, seizures, fibromyalgia, nephrolithiasis, polyneuropathy, narrow angle glaucoma), concurrent pain of greater intensity in any other location than the low back and leg, and narcotic or alcohol abuse in the past year

Main outcome measures:

- Basic study design involved a crossover comparison of topiramate and diphenhydramine as active placebo, with two 8 week study periods consisting of 4 weeks of drug dose titration, 2 weeks of dose maintenance, and 2 weeks of drug tapering and washout
- Starting dose of topiramate was 50 mg at hs; this was escalated by 50 mg increments over 4 weeks to a maximum of 400 mg in 2 divided doses
- Starting dose of diphenhydramine was 6.25 mg at hs, titrated to a maximum of 50 mg in 2 divided doses
- Principal efficacy measure was a comparison of the mean scores for average leg pain during the 2 week maintenance phase of the 2 study drugs
- Secondary efficacy measures included global pain relief (leg and back combined), Oswestry disability score, Beck Depression Inventory, and SF-36
- 10 patients dropped out due to adverse effects while taking topiramate, and 1 dropped out for the same reason while taking placebo
- The mean final dose of topiramate was 208 mg and the mean final dose of diphenhydramine placebo was 40 mg
- Carryover and period effects were not significant in the crossover analysis
- Leg pain was reduced by 19% in the topiramate group compared to placebo; this was not statistically significant
- However, the global pain relief scores favored topiramate over placebo; 9 patients reported a lot or complete pain relief while taking topiramate, compared to only 1 while taking placebo
- Some secondary outcomes (back pain and average overall pain) did have statistically significant advantages for topiramate over placebo
- Beck Depression, SF-36, and Oswestry disability scores did not differ between treatment groups

- A post hoc subgroup analysis showed that 11 patients with neural foraminal stenosis had a small increase in pain with topiramate; patients with other MRI diagnoses had a decrease in pain with topiramate
- Number needed to treat (NNT) for moderate or better pain relief with topiramate was 5.3
- Number needed to harm (NNH) for adverse effects leading to withdrawal with topiramate was 4.4; these included sedation, rash, paresthesias, and GI upset

Authors' conclusions:

- The primary outcome of reduction in leg pain with topiramate just missed statistical significance, but several other pain scores (overall pain and global relief) showed statistically significant pain relief with topiramate
- Although the apparent pain reduction may have been due to chance or to dropout bias, it is more likely that topiramate has a small but real analgesic effect
- However, because of troublesome side effects, topiramate is at best marginally effective for the treatment of chronic lumbar radiculopathy pain, and is at best a second line treatment whose dose needs to be titrated slowly

Comments:

- Authors' assessment of the marginal benefits of topiramate are appropriate given the near equality of NNT and NNH, suggesting that the benefits and harms of the drug are not greatly different
- The sample size was calculated using an assumption about the standard deviation of the expected difference between topiramate and placebo (2.9); the mean difference between them is given in Table 2, but not the standard deviation; this makes it difficult to know whether the variation in this sample was larger than anticipated for the power calculation (study may have been underpowered)

Assessment: Adequate for evidence that topiramate may have a marginal benefit in the treatment of chronic lumbar radiculopathy