

Grosskopf GJ, Mazzola J, et al. A randomized, placebo-controlled study of oxcarbazepine in painful diabetic neuropathy. Acta Neurol Scand 2006; 144: 177-180.

Design: Randomized clinical trial

Population/sample size/setting:

- 141 diabetic patients (78 men, 63 women, mean age 61) treated for neuropathic pain at 22 centers in the USA, Germany, and the UK
- Eligible patients had type 1 or 2 diabetes, at least 6 months but less than 5 years of neuropathic pain, stable HbA1c <11% at baseline, a pain rating of at least 50 on a 100 point VAS scale on the first screening visit, and an average VAS of 40 or more during 4 of the last 7 days prior to randomization
- Exclusion was done if the patient had previous or current treatment with oxcarbazepine, amputations other than toes, renal insufficiency, serum sodium levels under 135, chronic infectious disease

Main outcome measures:

- Randomized to placebo (n=70) or to oxcarbazepine (n=71)
- The study period consisted of a 2 week pre-randomization screening phase, followed by a 16 week double blind treatment phase: 4 weeks for dose titration and a 12 week maintenance phase of the study drug
- Starting dose of oxcarbazepine was 300 mg/d and titrated to a maximum of 1200 mg (600 mg bid)
- Acetaminophen was authorized for breakthrough pain; no other analgesics were permitted
- Primary efficacy measure was average VAS in the final week of treatment compared to baseline
- Secondary measures were global assessment of therapeutic effect (GATE) on a 7 point scale (-3 is very much improved and +3 is very much worse); time to onset of pain relief (20 point decrease from baseline VAS sustained for 2 consecutive days); sleep and SF-36 quality of life scales were also secondary outcome measures
- Of 71 oxcarbazepine patients, 42 completed the trial and 29 withdrew (18 of these for adverse events)
- Of 70 placebo patients, 53 completed the trial and 17 withdrew (4 of these for adverse effects)
- Mean oxcarbazepine dose during maintenance phase was 1091 mg/d
- Reduction in VAS scores did not differ between oxcarbazepine group (27.9%) and placebo group (31.1%)
- Secondary measures also did not differ between groups
- Most common adverse effects were headache, dizziness, and nausea; most of these occurred during the titration phase
- One patient in the oxcarbazepine group became hyponatremic (sodium was 122 mmol/L); the sodium normalized after discontinuing the drug

Authors conclusions:

- No significant differences were observed between oxcarbazepine and placebo for the primary or secondary outcomes
- A large placebo effect was observed, and this, together with premature discontinuation from the study, may contribute to the lack of an observed drug treatment effect

Comments:

- Although the percentage reductions in VAS appear to be approximately equal, the standard deviations are not given for any of the study variables; this precludes a power calculation for the study data and conclusions, and precludes the possibility of combining the results of this study with the results of similarly designed clinical trials
- The dose escalation from the starting dose to the final dose of 1200 mg took place over a 4 week period; it appears that the escalation schedule was the same for all participants
- If the dose titration needs to be tailored to the individual patient, a uniform dose escalation may not accurately represent the side effect profile that could be seen in clinical practice
- Details of randomization and blinding are lacking, but in a study which does not show group treatment differences, this is not likely to be a source of bias

Assessment: Inadequate (lack of sufficient information on the variability of the treatment response)