

**Hale ME, Dvergsten C, Gimbel J. Efficacy and Safety of Oxymorphone Extended Release in Chronic Low Back Pain: Results of a Randomized, Double-Blind, Placebo-and Active-Controlled Phase III Study. J Pain 2005;6(1):21-28.**

Design: Randomized clinical trial

Population/sample size/setting:

- 329 patients (174 men, 155 women, mean age 46) treated for chronic low back pain by a contract research organization in Virginia and Arizona
- Eligible patients were 18 to 75 years old, with moderate to severe low back pain present at least 15 days per month for several hours per day for at least 2 months, and were taking a stable dose of opioids for at least 3 days before screening
- Exclusion criteria were fibromyalgia, CRPS, acute spinal cord compression and other spinal surgical emergencies, diskitis, tumor, psychiatric illness, seizure disorders, drug/alcohol dependence, or opioid hypersensitivity; surgical procedures within 2 months, nerve blocks within 4 weeks, and active or pending litigation involving back pain were also exclusion criteria

Main outcome measures:

- 330 patients were randomized to oxycodone (n=164) or oxymorphone (n=166) in a 1:1 ratio for a double-blind titration phase lasting 14 days; the study drug was given at 8 AM and 8 PM
- Titration for oxymorphone was to a dose of 110 mg q 12 h, and for oxycodone was to a dose of 220 mg q 12 h (equivalent to 660 mg morphine per day)
- Attrition due to adverse effects or lack of efficacy during the dose titration phase was similar in the two groups; 53 oxymorphone patients and 42 oxycodone patients withdrew
- 235 patients who completed the titration phase then entered an 18 day double-blind trial phase
- The pain VAS at the end of the titration phase was taken as the baseline for the primary outcome analysis, which was the change from baseline between baseline and the study end point
- Patients entering the 18 day phase either continued with their current treatment at the fixed dose established during the titration phase, or were randomized to placebo; the randomization was to oxymorphone (n=80), placebo (n=75), or oxycodone (n=80)
- Rescue medication in the form of oral morphine was allowed on an unlimited basis for the first 4 days of the second phase of the study, but was limited to 30 mg/d thereafter
- Pain VAS was recorded daily for each of the 18 days of the double-blind trial phase; the VAS was recorded 4 hours after the AM dose of the study drug
- 213 of the 235 patients had at least one VAS pain intensity measurement and were available for intent-to-treat analysis, and 139 patients completed the study

- 22 oxymorphone patients and 21 oxycodone patients discontinued treatment during the 18 day trial; 16 oxymorphone and 13 oxycodone patients stopped treatment for lack of efficacy
- 53 placebo patients discontinued the study during the 18 day trial, 44 for lack of efficacy
- During the 18 day trial, pain VAS increased in the placebo group compared to both oxymorphone and oxycodone; for oxymorphone, the difference with placebo was 18.22 points and for oxycodone the difference was 18.55 points
- Moderate to complete pain relief was reported by 61% of oxymorphone and oxycodone groups, but by only 28% of placebo patients
- Use of rescue medication with oral morphine at the end of the study was similar in all three groups, and was less than 15 mg/d on average
- Most adverse effects of oxymorphone and oxycodone were mild to moderate in severity; constipation and sedation were the most common side effects

#### Authors' conclusions:

- Both oxymorphone and oxycodone are safe and effective treatment options for chronic low back pain; oxymorphone is equianalgesic with oxycodone at one half the milligram dose
- Because oxymorphone is not metabolized by the cytochrome P450 system, it may have fewer drug interactions than oxycodone
- High risk patients for drug abuse were excluded from this trial, and issues related to prolonged use are not addressed

#### Comments:

- The study design is a variant of the enriched enrollment design of other analgesics, in which randomization is done after patients are shown to tolerate and respond to the study drugs
- Presumably, the placebo group drew equally from the oxymorphone and oxycodone treatment groups at the time of randomization; the numbers from each are not reported in the flow diagram
- Pain VAS scores are reported graphically in Figure 3, but not in tabular form; from the graph, it appears that all three groups had at least some increase in pain during the 18 days of the trial (all changes are positive); the author has been e-mailed for clarification
- Presumably, monitoring for compliance with treatment is easier when controlled substances are studied, since accountability for their dispensing is strict; it is likely that the study drugs were taken as instructed
- From Table 1, it appears that at the end of the study, there was still considerable pain in all three treatment groups; for example, the two opioid groups had average "least pain" scores of about 4 on a scale from 0 to 10
- Because moderate to complete pain relief was reported by 61% of the opioid groups, the "least pain" scores of 4 and "pain right now" scores of about 6 are difficult to interpret

- Making this interpretation more difficult is the fact that baseline characteristics are not reported in tabular form; the baseline VAS pain scores and the VAS scores at the time of randomization are missing from the report
- The randomization appears to be adequate and complete blinding was unlikely, since the placebo group could be expected to recognize the change in drug efficacy fairly quickly; the risk of bias is low to moderate
- While many important data elements are absent, the available data are sufficient to show that the analgesic effects of oxymorphone and oxycodone are not likely to differ greatly

Assessment: Adequate for evidence that oxymorphone has analgesic effects similar to those of oxycodone