

Comparison of Drug Liking and Positive Subjective Effects of Oral Intact Extended-Release Oxymorphone and Controlled-Release Oxycodone

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Purpose

Opioids are effective analgesics, but the potential for abuse remains a concern for prescribers. Positive subjective effects and drug liking might contribute to potential for abuse. Individuals susceptible to drug abuse are more likely to report positive subjective effects (Franques. *Drug Alcohol Depend.* 2003;69:121-126; Zacny. *Pharmacol Biochem Behav.* 2010; 95:113-120). This exploratory, randomized, double-blind, placebo-controlled, 5-treatment, 10-sequence crossover study compared drug liking and positive subjective effects of single, equianalgesic, intact oral doses of oxymorphone extended release (ER; 15 and 30 mg) and oxycodone controlled release (CR; 30 and 60 mg) in healthy, nondependent, recreational opioid users.

Method

Subjects aged 18-55 years who demonstrated the ability to discriminate the positive subjective effects of hydromorphone 8 mg against placebo during a qualification phase entered the treatment phase and received single intact oral doses of oxymorphone, oxycodone, and placebo separated by a ≥ 7 -day washout. Subjective assessments included the Addiction Research Center Inventory (ARCI) Morphine Benzedrine Group (MBG) scale, Visual Analog Scales (0-100 mm; Drug Liking, Good Effects, Overall Drug Liking, Take Drug Again, Subjective Drug Value), and pupillometry, performed between 0.5 and 24 hours postdose. Maximum effect (E_{max}) was calculated, and analysis of covariance or analysis of variance was used to compare the least squares (LS) mean (SE) difference between equianalgesic dose groups (oxymorphone ER 15 mg vs oxycodone CR 30 mg; oxymorphone ER 30 mg vs oxycodone CR 60 mg; based on conversion table in oxymorphone ER label). Safety assessments included adverse events (AEs), vital signs, laboratory tests, and electrocardiogram.

Results

35 of 40 (87.5%) subjects completed the study; 5 subjects withdrew because of an intolerable AE (n=2), administrative reasons (n=2), or noncompliance (n=1). Oxymorphone ER showed a significantly lower E_{max} than respective equianalgesic doses of oxycodone CR for Drug Liking (LS mean [SE] difference -21.2 [3.2] for oxymorphone ER 15 mg vs oxycodone CR 30 mg, $P < 0.001$; -18.9 [3.1] for oxymorphone ER 30 mg vs oxycodone CR 60 mg, $P < 0.001$) and Overall Drug Liking scales (-21.3 [3.6], $P < 0.001$; -9.9 [3.6], $P = 0.01$). For Take Drug Again, the difference was only significant for oxymorphone ER 15 mg vs oxycodone CR 30 mg (-24.2 [4.8], $P < 0.001$). Oxymorphone ER also showed a significantly lower E_{max} than respective equianalgesic doses of oxycodone CR for the Subjective Drug Value (-16.0 [3.1], $P < 0.001$; -8.2 [3.1], $P = 0.01$) and Good Effects scales (-34.6 [6.1], $P < 0.001$; -23.7 [6.1], $P < 0.001$) and on the ARCI-MBG (-1.9 [0.7], $P = 0.01$; -2.4 [0.7], $P < 0.001$). At equianalgesic doses, pupil diameter was significantly larger with oxymorphone ER than oxycodone CR (LS mean [SE] difference in minimum pupil diameter 1.1 [0.2], $P < 0.001$; 0.9 [0.2], $P < 0.001$). At least 1 AE was reported by 59.5% (15 mg) and 73.7% (30 mg) of subjects with oxymorphone ER and 87.5% (30 mg) and 97.5% (60 mg) of subjects with oxycodone CR. With oxymorphone ER, fewer euphoria-related AEs were observed (15 mg, 24.3%; 30 mg, 52.6%) compared with oxycodone CR (30 mg, 67.5%; 60 mg, 92.5%).

Conclusions

In this exploratory study using equianalgesic oral intact doses, oxymorphone ER was associated with less drug liking and lower subjective effects than oxycodone CR. These results suggest that oxymorphone ER may have a lower abuse potential than oxycodone CR.

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