

Fixed-ratio combination oxycodone/naloxone compared with oxycodone alone for the relief of opioid-induced constipation in moderate-to-severe noncancer pain.

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Abstract

OBJECTIVE:

Opioid therapy is frequently associated with treatment-limiting constipation. Naloxone is an opioid antagonist with low oral systemic bioavailability. This Phase III clinical trial assessed the safety and efficacy of an oral fixed-ratio combination of oxycodone prolonged-release (PR) and naloxone PR compared with oxycodone PR in relieving opioid-induced constipation.

STUDY DESIGN:

This double-blind, multicenter trial was conducted in specialist and primary care centers in four European countries in an out-patients setting. The study included 322 adult patients with moderate-to-severe, noncancer pain requiring opioid therapy in a range of ≥ 20 mg/day and ≤ 50 mg/day oxycodone. Following a run-in phase patients were randomized to receive oxycodone PR/naloxone PR or oxycodone PR for 12 weeks. The primary outcome was improvement in constipation as measured using the Bowel Function Index (BFI). Secondary/exploratory assessments focused on pain intensity and additional bowel parameters.

TRIAL REGISTRATION:

[NCT00412152](#).

RESULTS:

A significant improvement in BFI scores occurred with oxycodone PR/naloxone PR compared with oxycodone PR after 4 weeks of double-blind treatment (-26.9 vs. -9.4, respectively; $p < 0.0001$), observed after only 1 week of treatment and continued until study end. A significant increase in the number of complete spontaneous bowel movements and decrease in laxative use were also reported. This improvement in bowel function was achieved without compromising the analgesic efficacy of the oxycodone component; pain intensity remained constant throughout the study. The incidence of adverse events was comparable in both groups and consistent with those expected of opioid analgesics. As the study was limited to a dose range of up to 50 mg oxycodone equivalent per day, further research on higher doses would be recommended.

CONCLUSION:

The fixed-ratio combination of oxycodone PR/naloxone PR is superior to oxycodone PR alone, offering patients effective analgesia while significantly improving opioid-induced constipation.

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