Oral methylnaltrexone does not negatively impact analgesia in patients with opioid-induced constipation and chronic noncancer pain

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Introduction

An oral formulation of methylnaltrexone has been developed and approved for treatment of opioid-induced constipation (OIC) in patients with chronic noncancer pain. Because methylnaltrexone is a peripherally acting mu-opioid receptor antagonist, an analysis was conducted to determine the potential impact of oral methylnaltrexone on opioid analgesia.

Materials and methods (NA for case report)

In a phase 3, randomized, double-blind, placebo-controlled trial, adults with chronic noncancer pain for ≥2 months who had been receiving a daily dose of ≥50 mg/d oral morphine equivalents (MEDs) for ≥14 days and had OIC (defined as <3 rescue-free bowel movements [RFBMs] per week associated with ≥1 of the following: ≥25% of RFBMs categorized as type 1 or type 2 on the Bristol Stool Form Sale; straining during ≥25% of RFBMs; or ≥25% of RFBMs with a sensation of incomplete evacuation) were randomized to receive oral methylnaltrexone (150 mg, 300 mg, or 450 mg) or placebo once daily (QD) for 4 weeks followed by 8 weeks of oral methylnaltrexone as needed. Double blinding was maintained throughout the study. The study design and assessments were approved by the appropriate institutional review board. Opioid use was recorded daily; changes in pain intensity scores (rated from 0 = “no pain” to 10 = “worst possible pain”) and opioid withdrawal (assessed using the objective opioid withdrawal scale [OOWS]) were evaluated on study days 1, 14, and 28 during the QD period and on days 42, 56, and 84 during the as-needed period.

Results/Case report

A total of 803 patients received >1 dose of study medication (oral methylnaltrexone 150 mg, n=201; 300 mg, n=201; 450 mg, n=200; placebo, n=201). At baseline, the primary pain condition requiring opioid use was back pain, which was reported by 66.9% of patients who received oral methylnaltrexone (all groups combined) and 72.1% of patients who received placebo. Baseline pain intensity scores were similar among treatment groups (mean range, 6.2–6.4) and remained stable throughout the 4-week double-blind (mean range, 6.1–6.5) and 8-week “as needed” (mean range, 6.3–6.5) periods. Baseline mean MEDs were comparable between oral methylnaltrexone 150 mg (200 mg/d) and oral methylnaltrexone 450 mg/d (218 mg/d) and placebo (210 mg/d), but were slightly higher in the oral methylnaltrexone 300 mg group (253 mg/d). Nonsignificant, minimal changes in mean MEDs were observed after 4 weeks of daily treatment (range, 214.5–235.6 mg/d) and at the end of the “as needed” phase (range, 202.4–234.9 mg/d). The percentage of patients who initiated new opioid medications was similar in the placebo (39.8%) and oral methylnaltrexone groups (150 mg, 44.8%; 300 mg, 43.3%; 450 mg, 35.0%). Mean changes from baseline in OOWS score were minimal in all groups (mean range, -0.16 to 0.06) and were comparable across groups, including when abdominal cramping (which may be a confounding factor because of its association with constipation and methylnaltrexone mechanism of action) was excluded from the analysis.

Discussion

Oral methylnaltrexone does not elicit opioid withdrawal or interfere with opioid analgesia.

References (Maximum 5)

N/A

Disclosures

I confirm that I am aware of conflicts of interest in my presentation.
Details:

Disclosures
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Joseph R. Harper is an employee of Salix Pharmaceuticals.
Robert J. Israel is an employee of Salix Pharmaceuticals or its affiliates.