

Journal Watch
**METHYLNALTREXONE FOR REVERSAL OF CONSTIPATION DUE TO CHRONIC
METHADONE USE**

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ABSTRACT

Context: Constipation is the most common chronic adverse effect of opioid pain medications in patients who require long-term opioid administration, such as patients with advanced cancer, but conventional measures for ameliorating constipation often are insufficient.

Objective: To evaluate the efficacy of methylnaltrexone, the first peripheral opioid receptor antagonist, in treating chronic methadone-induced constipation.

Design: Double-blind, randomized, placebo-controlled trial conducted between May 1997 and December 1998.

Setting: Clinical research center of a university hospital.

Participants: Twenty-two subjects (9 men and 13 women; mean [SD] age, 43.2 [5.5] years) enrolled in a methadone maintenance program and having methadone-induced constipation.

Main Outcome Measures: Laxation response, oral-cecal transit time, and central opioid withdrawal symptoms were compared between the 2 groups.

Results: The 11 subjects in the placebo group showed no laxation response, and all 11 subjects in the intervention group had laxation response after intravenous methylnaltrexone administration ($P < .001$). The oral-cecal transit times at baseline for subjects in the methylnaltrexone and placebo groups averaged 132.3 and 126.8 minutes, respectively. The average (SD) change in the methylnaltrexone-treated group was -77.7 (37.2) minutes, significantly greater than the average change in the placebo group (-1.4[12.0] minutes; $P < .001$). No opioid withdrawal was observed in any subject, and no significant adverse effects were reported by the subjects during the study.

Conclusions: Our data demonstrate that intravenous methylnaltrexone can induce laxation and reverse slowing of oral cecal-transit time in subjects taking high opioid dosages. Low-dosage methylnaltrexone may have clinical utility in managing opioid-induced constipation.

COMMENTS:

Strengths: Double blind, randomized, placebo controlled trial. Good outcome measures, informed written consent obtained, included inclusion and exclusion criteria, funded by Institutional America Cancer Society Grant.

Weakness: Sample size was small, safety profile of the study drug cannot be

determined. No indication as to why the sample population was enrolled on a methadone maintenance program, patients with other co-morbidities were excluded(not a true representative of our patient population)

Relevance to Palliative Care: Most of the patients with advanced cancer get treated with opioids and many suffer from constipation. Opioid-related constipation is not only a frequent but also a distressing symptom and difficult to treat. The data from this study suggest that cancer patients receiving long term opioid treatment also may benefit from Methylnaltrexone in managing opioid induced constipation, thus improving the quality of life for these patients. However, there is a need for larger clinical trials to determine the safety profile of this drug in larger populations, especially those with terminal illnesses and additional co-morbidities.