

Journal Watch

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Title: Chamberlain BH, Cross K, Winston JL, Thomas J, Wang W, Su C, Israel RJ. Methylnaltrexone treatment of opioid-induced constipation in patients with advanced illness. *J Pain Symptom Manage* doi:10.1016/j.jpainsymman.2009.02.234.

Abstract: Methylnaltrexone, a peripherally acting mu-opioid receptor antagonist with restricted ability to cross the blood-brain barrier, reverses opioid-induced constipation (OIC) without affecting analgesia. A double-blind study in patients with advanced illness and OIC demonstrated that methylnaltrexone significantly induced laxation within 4 hours after the first dose compared with placebo. In this study, patients with advanced illness and OIC on stable doses of opioids and laxatives were randomized to methylnaltrexone 0.15 mg/kg (n=62) or placebo (n=71) subcutaneously every other day for 2 weeks. Laxation was assessed daily. Constipation distress, bowel status change, pain, laxative use, and opioid withdrawal symptoms were assessed weekly using standardized scales. Additional analyses to further characterize response to methylnaltrexone revealed that among patients with a bowel movement within 4 hours following the first dose, the median time to response was 0.5 hours for methylnaltrexone. Response rates among methylnaltrexone-treated patients who had responded to all previous doses were 57%-100% for doses two to seven. Among methylnaltrexone-treated patients who did not respond to the first or to the first two consecutive doses, 35% and 26% responded to the second and third dose, respectively. Higher percentages of patients and clinicians rated bowel status as improved in the methylnaltrexone than the placebo group. Fewer methylnaltrexone than placebo patients reported use of common laxative types, particularly enemas, during the study. Subcutaneous methylnaltrexone promptly and predictably induced laxation, improved constipation distress, and was associated with less laxative use in patients with advanced illness and OIC.

Strengths/uniqueness: The original trial appeared to be appropriately designed, executed, analyzed and reported.

Weaknesses: Given that the analyses presented are post-hoc in nature, the findings should be considered as exploratory rather than definitive.

Relevance to Palliative Care: One useful piece of information from this secondary analysis is that if laxation had not occurred after the first three doses of methylnaltrexone, then the likelihood of laxation after the fourth dose was less than 10 percent. In such situations, reasons for constipation other than opioids should be considered.