

Subcutaneous Methylnaltrexone for Treatment of Opioid-Induced Constipation in Patients With Chronic, Nonmalignant Pain: A Randomized Controlled Study

Presented by, Amol Saincher PGY2

Reference: [J Pain](#). 2011 May;12(5):554-62. doi: 10.1016/j.jpain.2010.11.008. Epub 2011 Mar 22.

[Michna E](#), [Blonsky ER](#), [Schulman S](#), [Tzanis E](#), [Manley A](#), [Zhang H](#), [Iyer S](#), [Randazzo B](#).

Abstract: Methylnaltrexone is effective for opioid-induced constipation (OIC) in advanced illness patients. This 4-week, double-blind, randomized, placebo-controlled study investigated the effect of subcutaneous methylnaltrexone on OIC in patients receiving opioids for chronic, non-malignant pain. Patients (N = 460) received subcutaneous methylnaltrexone 12 mg once daily (QD) or every other day (alternating with placebo) compared with placebo. Assessments included bowel movement count, time of bowel movement, straining, sense of complete evacuation, Bristol Stool Form Scales, and quality of life. Within 4 hours of first dose, 34.2% of patients in both methylnaltrexone groups had rescue-free bowel movements (RFBMs) versus 9.9% on placebo (P < .001). The estimated number needed to treat was about 4. On average, 28.9% of methylnaltrexone QD and 30.2% of methylnaltrexone alternate-day dosing resulted in RFBMs within 4 hours versus 9.4% QD and 9.3% alternate-day placebo injections (both P < .001). Both methylnaltrexone groups had significantly shorter time to first RFBM (P < .001) and greater increase in number of weekly RFBMs (P < .05) versus placebo. Adverse events included abdominal pain, diarrhea, nausea, and hyperhidrosis. Bristol Stool Form Scale scores (P = .002) and sensation of complete evacuation (P < .04) were significantly superior with methylnaltrexone QD; both methylnaltrexone groups reported no or mild straining during RFBMs in the first 2 weeks (P < .02). At 4 weeks, a significantly greater improvement in patient-reported, constipation-specific quality of life was seen in the alternate-day dosing (P < .05) and QD (P < .001) groups.

Perspective: We present data demonstrating that subcutaneous methylnaltrexone 12 mg given once daily (QD) or every other day provides significant relief of OIC and was generally well tolerated in patients with chronic, non-malignant pain. These results expand on prior effectiveness observed for the treatment of OIC in advanced illness patients to a broader population.

Results: Described in above abstract. Results that were omitted above are the following. After 4 weeks, 58.7% of daily treatment group (NNT – 5), 45.3% of alternate days (NNT – 14) and 38.3% of placebo had greater than or equal to 3 BM/week. As well, 62% of placebo versus 39% of daily treatment group and 50% of the alternating treatment group used rescue laxatives. These numbers and the ones mentioned in the abstract were statistically significant.

Strengths: A well designed study since it was randomized, placebo-controlled, double blind with allocation concealment. It had a good sample size of 460.

Weaknesses: Weaknesses included limited trial duration of 4 weeks. There was no attempt to show whether this drug is superior or more effective than a typical bowel routine. There is uncertainty about whether titrating opioids reduces the effect of this drug. This was an industry sponsored study and the cost of medication was not discussed.

Relevance to Palliative Care: Palliative care frequently involves treatment of chronic pain with large doses of opioids. As a result, opioid-induced constipation is a common concern in the palliative setting. methylnaltrexone is administered subcutaneously which helps in patients unable to tolerate or who have failed enteral medications.