

Oral naloxone reverses opioid-associated constipation.

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Abstract:

Opioid-related constipation is one of the most frequent side effects of chronic pain treatment. Enteral administration of naloxone blocks opioid action at the intestinal receptor level but has low systemic bioavailability due to marked hepatic first-pass metabolism. The aim of this study was to examine the effects of oral naloxone on opioid-associated constipation in an intraindividually controlled manner. Twenty-two chronic pain patients with oral opioid treatment and constipation were enrolled in this study. Constipation was defined as lack of laxation and/or necessity of laxative therapy in at least 3 out of 6 days. Laxation and laxative use were monitored for the first 6 days without intervention ('control period'). Then oral naloxone was started and titrated individually between 3x3 to 3x12 mg/day depending on laxation and withdrawal symptoms. After the 4-day titration period, patients were observed for a further 6 days ('naloxone period'). The Wilcoxon signed rank test was used to compare number of days with laxation and laxative therapy in the two study periods. Of the 22 patients studied, five patients did not reach the 'naloxone period' due to death, operation, systemic opioid withdrawal symptoms, or therapy-resistant vomiting. In the 6 day 'naloxone' compared to the 'control period', the mean number of days with laxation increased from 2.1 to 3.5 ($P<0.01$) and the number of days with laxative decreased from 6 to 3.8 ($P<0.01$). The mean naloxone dose in the 'naloxone period' was 17.5 mg/day. The mean pain intensity did not differ between these two periods. Moderate side effects of short duration were observed in four patients following naloxone single dose administrations between 6 and 20 mg resulting in yawning, sweating, and shivering. Most of the patients reported mild or moderate abdominal propulsions and/or abdominal cramps shortly after naloxone administration. All side effects terminated after 0.5-6h. This controlled study demonstrates that orally administered naloxone improves symptoms of opioid associated constipation and reduces laxative use. To prevent systemic withdrawal signs, therapy should be started with low doses and patients carefully monitored during titration

Comments:

Strengths/uniqueness: This study is the first to assess the use of oral naloxone for the treatment of opioid-induced constipation. Patients were used as their own controls in the study, in contrast to previous studies of naloxone which were not controlled. This study clearly defined inclusion criteria and outcome measures. The titration of naloxone allowed for inter-individual differences.

Weaknesses: There were signs of systemic withdrawal of opioids during the naloxone-period. The study period of 6 days is perhaps too short to fully assess laxative needs. Diet and laxative therapy before the start of the study were not standardized. There is the possibility of a placebo effect.

Relevance to Palliative Care: Opioid-associated constipation is a pervasive problem for the palliative population and more effective treatment options would be very useful. This article does not inspire full confidence that patients will not experience withdrawal with loss of pain control when using naloxone.