

## **Opioid antagonists in the treatment of opioid-induced constipation and pruritus.**

Okuyama T, Tanaka K, Akechi T, Kugaya A, Okamura H, Nishiwaki Y, et al. J Pain Symptom Manage 2000; 22(1):554-4.

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### **Abstract:**

**Objective:** To describe the role of opioid antagonists in the treatment of opioid-induced constipation and pruritus.

**Data Sources:** A MEDLINE search was performed (1966-February 2000) for narcotics and opioid antagonists. Results were limited to English-language and clinical trials. Background information was obtained from pharmacology and pharmacotherapy references and review articles. Hand searching of selected bibliographies yielded several references.

**Study Selection and Data Extraction:** Studies were reviewed that examined the use of naloxone, naltrexone, and methylnaltrexone for opioid-related constipation and pruritus. Selected citations included various clinical trials and case series.

**Data Synthesis:** Opioids are used for cancer and nonmalignant pain. Peripheral opioid receptor stimulation due to endogenous (ie. endorphins) or exogenous (ie. morphine) stimulants may result in negative adverse effects, including constipation and pruritus. Adjuvant agents, such as laxatives and antihistamines, are often used to treat these adverse effects, but are themselves associated with adverse effects and are sometimes ineffective. Opioid antagonists have demonstrated reversal of peripheral opioid receptor stimulation. Clinical trials show adequate maintenance of pain control, as well as decreases in opioid-induced constipation and pruritus.

**Conclusions:** Opioid antagonists offer a therapeutic alternative to conventional adjuvant agents, with the risk of loss of analgesia at higher doses. Methylnaltrexone offers the advantage of peripheral action only and thus not reversing analgesia. Results are promising; however, larger clinical trials are necessary before opioid antagonists become the standard of care for opioid-induced constipation and pruritus.

### **Comments:**

**Strengths/uniqueness:** This is an up-to-date review of the options available if considering opioid antagonist treatment of constipation and pruritus. The authors point to the need for larger clinical trials to determine efficacy, appropriate dosing and preservation of pain control.

**Weakness:** The two most promising agents reviewed are not commercially available. Methylnaltrexone is available as an injection for experimental use only. The primary author is in the employ of Novo Nordisk Pharmaceuticals.

**Relevance to Palliative Care:** Constipation is an ever-present challenge in palliative care. The issue of prescribing opioid antagonists for constipation does surface occasionally...but soon disappears as an

option when the consequences of analgesia reversal are considered.