



Question: A patient developed opioid induced pruritus after receiving morphine via a CSCI. Is there any evidence to support opioid rotation to relieve the opioid-induced pruritus?

Date: January 2012.

Summary

- Pruritus occurs in about 2-10% of patients treated systemically with opioids.
- The risk is markedly increased when opioids are given intraspinally.
- The prevalence of itching also rises with increasing dosage.
- Evidence to support opioid rotation to treat opioid-induced itch is limited to a very small number of case reports.

Background

The pathogenesis of opioid-induced pruritus (OIP) is still not fully known, but two different mechanisms have been proposed: peripheral and central.¹ The prevalence of pruritus depends on the opioid used and the method of administration. Pruritus occurs in about 2-10% of patients treated systemically with opioids.¹ OIP affects 10–50% of patients receiving intravenous opioids and 20–100% of those receiving epidural or intrathecal opioid therapy.² The highest prevalence (up to 100%) is associated with intrathecal morphine. The prevalence of itching also rises with increasing dosage.¹

Histamine is thought to be a key mediator of itching produced by orally administered opioids.¹ The neuraxial opioid-induced pruritus (i.e due to epidurally, intracisternally, intraspinally or intrathecally administered opioids) seems to have a different mechanism, that of a central process mediated via the μ -opioid receptors, and the medullary dorsal horn may be a critical site of action of opioids producing pruritus.¹ It has been shown that activation of the kappa (κ) and gamma (δ) opioid receptors does not cause pruritus.³ However, central dopamine receptors (D₂), serotonin 5-HT₃ receptors, prostaglandins and the antagonism of GABA and glycine receptors in the CNS may all contribute to opioid induced pruritus.³

Opioid-Induced Pruritus

Opioids are reported to cause histamine release from mast cells to varying degrees.⁴ A study by Hermens et al found that skin mast cells incubated with morphine released histamine but oxymorphone and fentanyl did not cause histamine release.⁵ However, fentanyl has been shown to produce itch.⁴ There is varying incidence of itch associated with different opioids. (See table 1)

Table 1: Incidence of itch associated with different opioids.

OPIOID	REPORTED INCIDENCE OF ITCH
Morphine	Oral = $\geq 1\%$ Oral ⁶ IV/SC = $\sim 80\%$ ⁷
Oxycodone	Controlled-release = 13%; ⁸ Immediate-release = 3% or greater. ⁸
Hydromorphone	Extended-release = 1% to 8% ⁹
Fentanyl	All routes = 3%-10% ¹⁰
Alfentanil	0.3% - 1% ¹¹
Methadone	Incidence is not outlined but pruritus is listed as an adverse effect. ^{12,13}

Evidence to support opioid rotation to treat opioid-induced itch.

Katcher et al describe a case of severe morphine-induced itch unrelieved by antihistamines, which responded to a change to hydromorphone.¹⁴ The patient was admitted to hospital, receiving oral morphine, with uncontrolled pain and an intolerable itch.¹⁴ He was subsequently switched to a continuous subcutaneous infusion (CSCI) of morphine that was titrated to control the pain, however, the itch remained unresolved.¹⁴ He was rotated to hydromorphone via a CSCI.¹⁴ The itch stopped within 24 hours of starting the hydromorphone.¹⁴ Prior to discharge he was switched to oral hydromorphone. The authors discussed that both morphine and hydromorphone are pure mu-agonist opioids, and a receptor-based explanation for the relief of the itch seems unlikely.¹⁴ Oxycodone or fentanyl could have been chosen instead as they cause less histamine release.¹⁴ The authors conclude that the observation that oral and intravenous hydromorphone provided satisfactory analgesia without troublesome morphine-related itch suggests that opioid rotation may be a useful strategy for patients with severe opioid-induced itch.¹⁴

Search Strategy

Pubmed, Embase, CINAHL, PsycINFO and Cochrane Library were searched using the search term 'opioid-induced pruritus'. (A combined searched of 'opioid-induced pruritus' with 'opioid rotation' did not retrieve any relevant results.) No date restrictions were imposed. The limits of 'English language' and 'Human Species' were imposed. Articles were selected based on the information available in the abstract. The reference lists of retrieved articles were checked for additional studies. Standard reference sources (The British National Formulary, Summaries of Product Characteristics, Martindale, the complete drug reference, American Hospital Formulary Services and Micromedex) were searched to determine the incidence of pruritus with each opioid.

References

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