



Will opioid rotation resolve an opioid induced itch?

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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 itch 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 Peripheral involves an allergic reaction related to cutaneous histamine release; it responds well to antihistamines and a switch of opioid. Central is less histamine-dependent, in palliative care it is rare; centrally acting opioid antagonists may provide relief but can also antagonise the analgesic effect.² 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.³ 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 (D_2), serotonin 5-HT₃ receptors, prostaglandins and the antagonism of GABA and glycine receptors in the CNS may all contribute to opioid induced pruritus.⁴

Opioid-Induced Pruritus

Opioids are reported to cause histamine release from mast cells to varying degrees.⁵ 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.⁶ However, fentanyl has been shown to produce itch.⁵ 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	Up to 80% ⁷
Oxycodone	Controlled-release = 13% ⁸ Immediate-release = 3% or greater ⁸
Hydromorphone	Extended-release = 1% to 8% ⁹
Fentanyl	Transdermal route = 3% to 10% ¹⁰ Sublingual route = 1% or greater 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 and Walsh 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

References

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