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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]

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