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. 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. 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. OIP affects 10–50% of patients receiving intravenous opioids and 20–100% of those receiving epidural or intrathecal opioid therapy. The highest prevalence (up to 100%) is associated with intrathecal morphine. The prevalence of itching also rises with increasing dosage. Histamine is thought to be a key mediator of itching produced by orally administered opioids. 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. It has been shown that activation of the kappa (κ) and gamma (δ) opioid receptors does not cause pruritus. 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.

**Opioid-Induced Pruritus**

Opioids are reported to cause histamine release from mast cells to varying degrees. 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. However, fentanyl has been shown to produce itch. There is varying incidence of itch associated with different opioids (see table 1).

**Table 1: Incidence of itch associated with different opioids**

<table>
<thead>
<tr>
<th>OPIOID</th>
<th>REPORTED INCIDENCE OF ITCH</th>
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<tbody>
<tr>
<td>Morphine</td>
<td>Up to 80%</td>
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<tr>
<td>Oxycodone</td>
<td>Controlled-release = 13%</td>
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<tr>
<td></td>
<td>Immediate-release = 3% or greater</td>
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<tr>
<td>Hydromorphone</td>
<td>Extended-release = 1% to 8%</td>
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<tr>
<td>Fentanyl</td>
<td>Transdermal route = 3% to 10%</td>
</tr>
<tr>
<td></td>
<td>Sublingual route = 1% or greater</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>0.3% - 1%</td>
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<tr>
<td>Methadone</td>
<td>Incidence is not outlined but pruritus is listed as an adverse effect</td>
</tr>
</tbody>
</table>

**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. The patient was admitted to hospital, receiving oral morphine, with uncontrolled pain and an intolerable itch. He was subsequently switched to a continuous subcutaneous infusion (CSCI) of morphine that was titrated to control the pain, however, the itch remained unresolved. He was rotated to hydromorphone via a CSCI. The itch stopped within 24 hours of starting the hydromorphone. 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. Oxycodone or fentanyl could have been chosen instead as they cause less histamine release. 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.

References