PALLIATIVE CARE NETWORK OF WISCONSIN

**FAST FACTS AND CONCEPTS #142**
**OPIOID-INDUCED HYPERALGESIA**

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**Background** Opioid-induced hyperalgesia is a clinical phenomenon, characterized by increasing in pain in patients who are receiving increasing doses of opioids. This *Fast Fact* reviews the clinical findings and treatment options. See also *Fast Fact* #215 on opioid poorly-responsive pain.

**Clinical features of opioid hyperalgesia:**

- *History*
  - Increasing sensitivity to pain stimuli (hyperalgesia).
  - Worsening pain despite increasing doses of opioids.
  - Pain that becomes more diffuse, extending beyond the distribution of pre-existing pain.
  - Can occur at any dose of opioid, but more commonly with high parenteral doses of morphine or hydromorphone and/or in the setting of renal failure.
- *Physical Examination*
  - Pain elicited from ordinarily non-painful stimuli, such as stroking skin with cotton (*allodynia)*
  - Presence of other opioid hyperexcitability effects: myoclonus, delirium or seizures (see *Fast Facts* #57,58).

**Proposed mechanisms:**

- Toxic effect of opioid metabolites (e.g. morphine-3-glucuronide or hydromorphone-3-glucronide).
- Central sensitization as a result of opioid-related activation of N-methyl-D-asparate (NMDA) receptors in the central nervous system.
- Increase in spinal dynorphin activity.
- Enhanced descending facilitation from the rostral ventromedial medulla.
- Activation of intracellular protein kinase C.

**Therapies:**

- Reduce or discontinue the current opioid.
- Change opioid to one with less risk of neurotoxic effects: fentanyl or methadone (see *Fast Fact* #75).
- Add an infusion of a non-opioid NMDA receptor antagonist such as ketamine (see *Fast Fact* #132).
- Add a non-opioid adjuvant such as gabapentin, baclofen, acetaminophen or an NSAID.
- Initiate epidural, intrathecal, regional or local anesthesia and taper/discontinue systemic opioids.
- Increase hydration if clinically appropriate.

**Conclusion** Opioids can lead to a paradoxical increase in pain. Opioid-induced hyperalgesia should be considered in any patient with increasing pain that is not responding to increasing opioids. Referral to pain/palliative care professionals is appropriate to help develop a management strategy.

**References**

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