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FAST FACTS AND CONCEPTS #142

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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-glucuronide).
- Central sensitization as a result of opioid-related activation of N-methyl-D-aspartate (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 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.

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