PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #58
NEUROEXCITATORY EFFECTS OF OPIOIDS: TREATMENT

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Background *Fast Fact* #57 reviewed the pharmacology and patient assessment aspects of opioid induced neurotoxicity, notably myoclonus. This *Fast Fact* discusses treatment.

General Approach Decisions about the most appropriate treatment approach need to take into account features of the physical examination (the frequency and intensity of symptoms, hydration status, and estimated prognosis) and information from the medical record (temporal pattern of opioid use and dose escalation, other medications, the presence of electrolyte abnormalities and major organ dysfunction). Whenever medically appropriate, easily treatable causes or exacerbating factors should be corrected (e.g. correct hypomagnesemia).

Treatment Strategies The range of options for management of pain and direct opioid neurotoxic effects divides into strategies to treat the myoclonus and strategies to reduce the offending opioid.

1. **Observation.** Mild myoclonus may trouble family members more than the patient. If the patient is satisfied with current therapy, explaining the cause/progression of symptoms may be all that is necessary.
2. **Opioid dose reduction.** Seeing that some observational studies suggest that neuroexcitatory symptoms from opioid may not develop until a certain neuroexcitatory threshold of 3-glucoronide metabolites is surpassed, myoclonus may resolve over a few days with a decrease in opioid dose. However, make sure you are not reducing the opioid dose solely to control myoclonus at the expense of good pain control.
3. **Rotate to a dissimilar opioid.** Rotating to a lower dosage of a structurally dissimilar opioid will often reduce myoclonus and other neuroexcitatory effects within 24 hours, while achieving comparable pain control (*Fast Fact* #175 discusses opioid structural classes.) Rotation is especially important in patients with opioid-induced hyperalgesia. As a general rule, decrease the morphine equianalgesic dose by at least 50% when switching to a new medication (see *Fast Fact* # 36). For patients on very high doses, rotate to a new opioid at 20-25% of the morphine equianalgesic dose. Historically, methadone and fentanyl have been considered to be better opioids to rotate to as they have no active metabolites (which are implicated in the neuroexcitatory effects of other opioids). This observation is empiric, and has not been evaluated in clinical trials; clinicians should be cautious of using methadone without familiarity with its pharmacology (see *Fast Facts* #75, 86).
4. **Adjuvant and other analgesic therapy.** Adjuvant analgesics (e.g. anticonvulsants, antidepressants, corticosteroids) or non-drug therapies (e.g. acupuncture, TENS, heat, cold) may allow for opioid reduction, with preservation of analgesia.
5. **Benzodiazepines and other drugs to reduce myoclonus.** The addition of a benzodiazepine can reduce myoclonus without alteration of the opioid dose, although increasing sedation may be an unwanted side effect. Start with clonazepam 0.5-1 mg at night or 0.5 mg 2-3 times a day. Alternative agents include lorazepam orally or sublingually, starting at 1-2 mg q8 hours. A continuous infusion of midazolam is an expensive but effective option. Alternatives to benzodiazepines include baclofen, gabapentin, and nifedipine. Start baclofen at 5 mg 3 times a day and increase as needed/tolerated to 20 mg 3 times a day. Start gabapentin at 100 mg 3 times a day and increase as needed to 900-3600 mg total a day. Nifedipine (10 mg 3 times a day) can also be used.

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