PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #20
OPIOID DOSE ESCALATION IN END-OF-LIFE CARE

David E Weissman MD, Andrew Kamell MD

Background A common question from trainees is "*How fast, and by how much, can opioids be safely dose escalated in terminally ill patients?"* Consider the analogy of furosemide (Lasix) when discussing this topic. An increase in Lasix from 10 mg to 11 mg is unheard of, yet that is precisely what often happens with opioids, especially parenteral infusions. For example, increasing a morphine infusion from 1 to 2 mg/hr is a 100% does increase; while going from 5 to 6 mg/hr is only a 20% increase. Yet, many orders are written, "increase drip by 1 mg/hr, titrate to comfort." Some hospitals and nursing units even have this as a standing order or nursing policy. Such titration orders are unlikely to lead to be effective.

Key clinical considerations for appropriate opioid escalation:

1. *Is an opioid dose escalation appropriate?* To answer that question, clinicians need to consider:
   - **a.** Is the patient tolerating opioids well with little adverse effects?
   - **b.** Is the pain or dyspnea expected to continue at a similar or progressive pattern (particularly relevant for scheduled medications or infusions) or might it be temporary?
   - **c.** Is the source of discomfort opioid responsive?
   - **d.** Is there evidence of hyperalgesia or neurotoxicity from opioids? See *Fast Facts* #57,58, and 142.
   - **e.** Is the pain related to a chronic, non-malignant source in which the patient has an extended prognosis? If so, then aggressive opioid titrations may not be the best long-term solution.

2. *How quickly can one increase the dose?* The recommended frequency of dose escalation depends on the half-life of the opioid.
   - *As-needed* short-acting single-agent hydrophilic opioids (e.g. morphine, oxycodone, hydromorphone) can be titrated up even after 1-2 doses if they are minimally effective and no drowsiness. If such agents are written as *scheduled* medications, then they will approach a steady state after about 3 doses and so can be safely titrated up.
   - Morphine or hydromorphone infusions can typically be titrated after about 4 half-lives, so 12-18 hours is generally safe.
   - Sustained-release oral morphine or oxycodone can be escalated every 24 - 48 hours.
   - Titration of lipophilic medications such as methadone, levorphanol, buprenorphine, or transdermal fentanyl should only occur every 7 days, although when patients are nearing death and goals of care are comfort in focus, more rapid escalation can be done with close monitoring and education (see *Fast Fact* # 75 about methadone and *Fast Fact* #103 about transdermal fentanyl).

3. *How much do I increase the dose of the opioid?* While there is a paucity of clinical data available to guide clinical decision-making, generally, dying patients are unlikely to notice a change in analgesia when dose increases are less than 25% above baseline. Below are two common analgesic approaches for patients nearing the end of life with comfort care goals. For the elderly or those with renal or liver disease, a more cautious dose-escalation schema may be necessary (see *Fast Facts* 161, 260, 307, and 357):
   - For ongoing *mild to moderate* pain, increase by 25-50%, *irrespective of starting dose*. For ongoing *moderate to severe* pain, increase by 50-100%, *irrespective of starting dose.*
   - An alternative approach is to order an equivalent amount of scheduled oral opioid (or an opioid infusion) that is approximately equivalent to the total opioid used (PRN + scheduled) over a 24-hour period. Then, order an adequate PRN dose as well. A reasonable among of opioid for a PRN dose is about 10-15% of the total daily opioid dose. For oral opioids, that dose should be provided every 2 hours as needed; for parenteral, every 1-hour PRN would be reasonable. For a PCA with a basal rate, consider providing the hourly rate as a prn bolus dose and order it to be available every 15 minutes as needed. For example, Mr. H received SR Morphine 30 mg po BID and requires 6 doses of IR morphine 7.5 mg every 24 hours. Total 24-hour dose = (30 mg x 2)

plus (7.5 mg x 6) = 60 +45 = 105 mg/day. The provider adjusts the SR morphine to 45 mg po BID and the PRN dose to 10 mg po q2hr PRN (just over 10% of the total daily scheduled dose).

- Do not escalate long-acting opioids or opioid infusions more than 100% at any time, irrespective of how many bolus/breakthrough doses have been used.
- These guidelines assume the patient is tolerating the opioid well (with no or minimal sedation). Clinicians will need to be more cautious and should consider expert help for patients with ongoing uncontrolled pain despite sedation from opioids or another cause.

See related *Fast Facts*: #18 Oral opioid dosing intervals**;** # 51 Opioid combination products**;** # 70 PRN range orders**;** # 74 Good and Bad analgesic orders**;** # 215 Opioid poorly-responsive cancer pain

References:

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3. Handbook of Cancer Pain Management. 5th Edition. Wisconsin Cancer Pain Initiative; 1996.
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Version History: This *Fast Fact* was originally edited by David E Weissman MD. 2nd Edition published July 2005; 3rd Edition May 2015 after a revision in December 2012 to add clarifying language about opioid escalation in sedated patients; transbuccal fentanyl language added. Updated again in August 2020 by Andrew Kamell MD.