PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #440
OPIOID ROTATION: CONSIDERATIONS, CONTROVERSY, & CLINICAL PRACTICE
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Background Opioid rotation is the clinical practice of replacing one opioid medication with another in an attempt to improve analgesia and/or reduce side effects (1,2). In multiple studies, opioid rotation has generally been shown to be helpful: 50-90% of patients have improved pain relief or reduced toxicity after rotation (2). This *Fast Fact* covers the indications for opioid rotation and some of the abiding clinical challenges with this common practice.

When to rotate opioids The decision to pursue opioid rotation is most often individualized and requires shared decision making between the patient and the clinician. The two most common reasons for opioid rotation are the development of intolerable adverse effects or uncontrolled pain despite escalating opioid doses (2-7). Intolerable side effects include common opioid toxicities (sedation, nausea), as well as opioid-induced hyperalgesia in which patients' pain thresholds are lowered due to opioid use, leading to poor pain control (2, 7-9) (see *Fast Fact* #142). The threshold to decide a patient has uncontrolled pain despite escalating opioid doses is a complex, individualized assessment, but a common scenario would be when one has escalated a patient's dose by over 100% without seeing much improvement in analgesia (14). Additional reasons for rotation are drug costs, formulary issues, need to change administration route (e.g., IV to oral), patient behavioral concerns (using an opioid unsafely), or renal or liver failure (7, 10-13) (see *Fast Facts #161, 260)*.

Opioids are not perfectly interchangeable All opioid medications act on opioid receptors, but individual patients can experience a wide range of effects – analgesic or otherwise - to different opioids (2-5,7,8,10-14). Opioid metabolism and action are affected by individualized differences including age, genetic polymorphisms in opioid receptors and metabolic enzymes, and organ function (2, 7,8,13,14). Importantly, individual opioid medications each have unique affinities for the different opioid receptors (13,15). In addition to the well-known mu-opioid receptor, kappa- and delta-opioid receptors also exist throughout various areas of the central nervous system and are involved in pain perception (13). Moreover, some opioid medications possess unique activities outside of their effects on opioid receptors. Tramadol, for example, possesses monoamine reuptake activity (13,15) while methadone is a known NMDA antagonist (2,13,15). All these variables help to explain the differences in effects between opioid medications at presumed equianalgesic doses.

There is more to opioid rotation than math

- When rotating to a new opioid, clinicians must consider the "relative potency" between opioids, also known as *equianalgesia* (10). This information can be found in published equianalgesic tables (10). Some experts argue that currently available opioid equianalgesic tables are outdated, based on limited data, and difficult to apply broadly given the varying degrees of response to opioids between individuals (10,11). Given this, for safety reasons experts have long recommend initiating the new opioid at a dose that is 25-50% lower than the 'expected equivalent' dose of the previous opioid based on the equianalgesic table (11-13). Indeed, patients often achieve good pain outcomes when switching to a different opioid at this 'lower-than-equianalgesic' dose (13).
- "Doing the math" however is typically the easiest part of the opioid rotation decision making. Patient characteristics are equally important, especially in shifting a clinician to be more or less conservative with the new opioid dose. For example, older age; kidney or liver insufficiency; baseline sedation or delirium; recent ineffective rapid opioid escalation; and the main reason for opioid rotation being side effects or the need for a change of administration route (not intractable pain) are all reasons to be more conservative (e.g., be more likely to dose-reduce by ~50%). Conversely, clinicians can typically be more liberal with the new opioid starting dose if a patient is being rotated in the context of severe, intractable pain, who is at steady state with their baseline opioids, who is in a closely monitored environment like a hospital, and who is not experiencing sedation or cognitive impairment at baseline.
- Use shared decision-making to come to an agreement about the rotation. Some patients are fearful of changing medications. Use empathetic, positive language to propose a change. For example: "I am

worried the meds I have you on just aren't working well. You are still in a lot of pain. I think I can help you feel better if we switch your current opioid pain medicine to a different one."

- **Importantly, methadone, buprenorphine, and fentanyl are complicated to switch to/from (among other issues, these opioids have less well-defined equianaglesic ratios) and transitioning patients to/from these meds should warrant expert consultation**. Expert input should also be sought when considering an opioid rotation at very high doses (e.g., baseline morphine equivalent daily dose over 100 mg). Expert consultation could include a pain or palliative care pharmacist or medical clinician. See *Fast Facts* #2, 36, 75, #86 and #358.

Conclusion Although many questions remain, most experts argue that opioid rotation is a worthwhile practice when patients have uncontrolled pain or toxic effects from increasing doses of an opioid medication (2,3,5,7,8,10-12). When used, opioid rotation must include a thorough and careful assessment of the unique patient factors which could affect their response to new opioid (2,7,8,11-14).

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