FAST FACTS AND CONCEPTS #161
OPIOID USE IN RENAL FAILURE

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Background Chronic pain is common in chronic kidney disease impacting 50% of hemodialysis patients, 82% of whom experience moderate to severe pain. The absorption, metabolism, and renal clearance of opioids are complex in renal failure. However, with the appropriate selection and titration of opioids, patients with renal failure can achieve analgesia with minimal risk of adverse effects. This *Fast Fact* offers best practice suggestions for opioid use in the setting of renal failure.

Not Recommended for Use:

- **Meperidine** is not recommended in renal failure due to accumulation of normeperidine, which may cause seizures.
- **Codeine** has been reported to cause profound toxicity which can be delayed and may occur after trivial doses. We recommend that codeine be avoided in patients with a Glomerular Filtration Rate (GFR) <30 mL/min.
- **Dextropropoxyphene** is associated with central nervous system (CNS) and cardiac toxicity and is not recommended for use in patients with renal failure.
- **Morphine and hydromorphone** both have 3-glucuronide metabolites that accumulate in renal failure and may case neurotoxicity, so these should be utilized with caution for chronic use in renal insufficiency (GFR <30 mL/min) due to the rapid accumulation of these metabolites. If one must be used, hydromorphone may be preferable, although there is not clear consensus on this. For patients receiving hemodialysis, the metabolities associated with hydromorphone appear to be more effectively removed via dialysis. Therefore, with careful monitoring, low to moderate doses (oral morphine daily equivalent of <60 mg) may be used safely. Minimize the use of long-acting preparations of morphine if possible and monitor closely for toxicity (see *Fast Facts* #57, 58).

Use with Caution:

- **Oxycodone** is metabolized in the liver with 19% excreted unchanged in the urine. While oxycodone does have metabolites, they do not appear to be as associated with clinically-significant neurotoxicity. However, the parent compound does accumulate in renal failure, and there are reports of accumulation of oxycodone in patients with renal failure resulting in overdose. Adjustment of dose and/or frequency is recommended, along with careful monitoring, especially if scheduled.

Less Associated Risk in Renal Insufficiency:

- **Fentanyl** is considered relatively safe in renal failure as it has no active metabolites. However, very little pharmacokinetic data exist regarding fentanyl in end stage renal disease. While some studies have shown decreased clearance in renal failure, most studies do not show drug accumulation. Fentanyl is not dialyzable due to high protein binding and a high volume of distribution. Caution with dosage and close monitoring for sedation is still recommended.
- **Methadone** is considered relatively safe in renal failure. It has no active metabolites and limited plasma accumulation in renal failure due to enhanced elimination in the feces. However, precautions regarding the use of methadone exist (See *Fast Facts* # 75, 86). Methadone does not appear to be removed by dialysis.
- **Burpenorphine** is considered by many experts to be a good option in renal failure due to lack of active metabolites or accumulation of parent compound. However, there is less data on the safety and efficacy on buprenorphine in palliative or cancer pain than many other opoids. Also, the pharmacokinetics are different than many opioids (see *Fast Fact* #268), so caution is still advised.

Dosing Given the paucity of pharmacokinetic and pharmacodynamic data of opioids in renal failure, it is difficult to advocate for specific opioid dosing algorithms. Broadbent et al recommended decreasing the dose morphine, oxycodone, or hydromorphone by 25% if Cr Cl is 10-50ml/min and 50% if CrCl <10mL/min. Methadone and buprenorphine likely do not require dose adjustment in renal insufficiency.

Some experts suggest that clinicians focus on PRN opioid dosing that adequately relieves pain without unacceptable side effects (see *Fast Fact* #20) and use caution with scheduled dosing. While many opioids can be used when GFR is <50, they require closer monitoring and constant reassessment to ensure that accumulation of active metabolites does not result in toxicity or overdose. This should not preclude the effective use of opioids in these patients, however.

Multimodal Therapy: A multimodal approach to pain therapy is recommended if feasible for patients with renal impairment. While beyond the scope of this *Fast Fact*, other analgesic options including acetaminophen, nortriptyline, renally-dosed gabapentin or pregabalin, corticosteroids, tizanidine, interventional therapies, and physical therapy should be considered.

References:

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