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FAST FACTS AND CONCEPTS #161

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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 reviews recommendations for opioid use in the setting of renal failure and in patients receiving chronic dialysis.

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** is not recommended for chronic use in renal insufficiency (GFR < 30 mL/min) due to the rapid accumulation of active, nondialyzable metabolites that are neurotoxic. If morphine must be used, avoid long-acting preparations 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. There are reports of accumulation of both the parent compound and metabolites in renal failure resulting in CNS toxicity and sedation.
- **Hydromorphone**, as the parent drug, does not substantially accumulate in hemodialysis patients. Conversely, an active metabolite, hydromorphone-3-glucuronide, quickly accumulates between dialysis treatments but appears to be effectively removed during hemodialysis. With careful monitoring, hydromorphone may be used safely in dialysis patients. However, it should be used with caution in patients with a GFR < 30mL/min who have yet to start dialysis or who have withdrawn from dialysis.

Safest 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.
- **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). It does not appear to be removed by dialysis.

Opioid Dosing Given the lack of pharmacokinetic and pharmacodynamic data of opioids in renal failure, it is difficult to advocate for specific analgesic treatment algorithms. However, the following guide has been proposed (Broadbent 2003) for the initial dosing of the safer opioids in renal failure.

- Creatinine Clearance > 50 mL/min: normal dosing.
- Creatinine Clearance of 10-50 mL/min: 75% of normal.
- Creatinine Clearance < 10 mL/min: 50% of normal.

The “normal opioid dose” for any given patient is the dose that adequately relieves pain without unacceptable adverse effects (see *Fast Fact #20*). While opioids can be used in renal insufficiency, they require closer monitoring and constant reassessment to ensure that accumulation of active metabolites does not result in toxicity. This should not preclude the effective use of opioids in these patients.

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Version History: This Fast Fact was originally edited by David E Weissman MD and published in August 2006. Current version re-copy-edited in April 2009.

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ACGME Competencies: Medical Knowledge, Patient Care

Keyword(s): Pain – Opioids

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