PAIN CONTROL FOR THE CKD PATIENT

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LEARNING OBJECTIVES

• Review the types of pain
• Review the common causes of pain in renal patients
• Pharmacy 101 – medications used in pain management and what is safest in renal population
• Understand the contraindications for use of some medications in the face of renal failure
WHAT IS PAIN?

“Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”

American Pain Society, 1992
TYPES OF PAIN

1. Acute Pain

- Usually self-limiting/short duration
- Warning of injury or disease
- Potential to be treated effectively
- If undertreated may go on to become chronic pain
2. Chronic Pain

- May persist for years
- Often inadequately controlled by medications or other pain management therapies.
- Often requires complex treatment strategies.

- Acute and Chronic Pain is often subcategorized into mechanism-based categories: *Neuropathic* and *Nociceptive*
- Neuropathic – associated with a nerve injury.
- Nociceptive – caused by or from responding to a painful stimulus.
- Nociceptors in skin, muscle and other body tissues carry pain signals to the CNS.
- Simplistic approach because multiple pathophysiologival mechanisms are probably involved.
- ? Neuropathic origin - response to opioid analgesics is less with neuropathic pain.
PREVALENCE IN RENAL PATIENTS

Literature suggests:

- 37-50% HD patients experience chronic pain
- 82% of these patients rate their pain as moderate to severe in intensity
- Pain is present in 42% of patients withdrawing from dialysis

MULTIFACTORIAL CAUSES

1. Co-morbidities
   - DM neuropathy
   - PVD with ischemic limbs
   - Musculoskeletal

2. ESRD
   - renal bone disease (calciphylaxis, renal osteodystrophy)
   - HD related (needle insertion, muscle cramps, headaches)
   - PD related (peritonitis, abdominal distension/back pain)
   - Primary kidney disease (PCKD)
   - Chronic infections related to central lines/AV fistulas

What are specific issues related to pain management in renal patients?
A typical renal patient has...

- Multiple co-morbidities
- Advanced age
- Altered pharmacokinetics and pharmacodynamics of medications
- Polypharmacy

Sensitivity to medications !!
BARRIERS TO ADEQUATE PAIN RELIEF

- Patients may under-report pain (assume pain is part of dialysis/disease) or may wait until pain becomes severe
- Pain is often multifactorial
- Lack of research in pain management in ESRD
- Lack of analgesic pharmacokinetic/pharmacodynamic data in ESRD
- Increased risk of adverse effects/toxicity due to advanced age, polypharmacy, co-morbidities

Davison, SN J Palliative Med 2007; 10: 1277-87
ANALGESIC USE IN ADVANCED RENAL DISEASE
NON-OPIOID ANALGESICS
1. Acetaminophen

- Recommended as the non-narcotic analgesic of choice in CKD patients. (The National Kidney Foundation)

- For mild to moderate nociceptive pain.

- Lack of GI toxicity and platelet dysfunction make it an attractive alternative to NSAIDs.
- Does not accumulate in ESRD – inactive metabolites renally excreted – removed by dialysis.

- 4g recommended as maximum daily dose by several references – Bennett's recommends 50% reduction when GFR < 30 mL/min

- Some references suggest extending dosing interval

- Chronic daily dosing → liver damage in some patients. Caution if history of EtOH
2. **NSAIDs (Selective /Non-selective)**

- **Mild to moderate pain, inflammation, bone pain and rheumatoid conditions**
- **Work by reducing production of PGs** that promote pain, inflammation and fever
- **PGs** also protect the lining of stomach and promote blood clotting by platelet activation

- **Enzymes** that produce PGs are called **cyclooxygenase** or **COX**
  - **Celecoxib**
  - **Ibuprofen, ASA, Naproxen**
- Both enzymes produce PGs that promote pain, inflammation and fever. Only COX-1 produces PGs that activate platelets and protect stomach

- NSAIDS block COX enzymes & reduce PG production

- All NSAIDs must be used with caution in CKD (stage 3 or higher) due to inhibition of renal vasodilatory PGs $E_2$ and $I_2$ (**COX-II inhibition**) ➔ hypertension, ↑GFR and ↑K+

- Caution in heart failure
- Inhibition of COX-1 results in antiplatelet effects and GI toxicity → COXibs (celecoxib) may, to a lesser extent, reduce risk of GI bleeds or upset
- Best to avoid – if necessary, short-term use and low dose (Celecoxib 100-200 mg/day)
- Consider gastroprotection with a PPI

- Topical formulations (localized pain)
OPIOID ANALGESICS

- Management of moderate to severe pain

- PK are more complex in ESRD patients more likely to experience opioid toxicity

- PK and pharmacodynamics yet to be studied in ESRD appropriate dosing remains unknown ??

- Start at small doses and titrate up
EFFECT OF OPIOID METABOLITES

- Most, other than fentanyl and methadone, have active metabolites which may accumulate in CKD
<table>
<thead>
<tr>
<th>OPIOID</th>
<th>ACTIVE METABOLITE</th>
<th>EFFECT</th>
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<tbody>
<tr>
<td>Morphine</td>
<td>Morphine-3-glucuronide (55%)</td>
<td>Neuroexcitatory</td>
</tr>
<tr>
<td></td>
<td>Morphine-6-glucuronide (10%)</td>
<td>Analgesic</td>
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<tr>
<td>Hydromorphone</td>
<td>HM-3-glucuronide (37%)</td>
<td>Neuroexcitatory</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Normeperidine</td>
<td>Seizures</td>
</tr>
<tr>
<td>Codeine</td>
<td>Codeine-6-glucuronide 10% to morphine</td>
<td>As for morphine</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Noroxycodone Oxymorphone</td>
<td>Weak analgesic</td>
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</tbody>
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CONSIDERATIONS IN CKD

1. Meperidine – AVOID due to accumulation of active metabolite (renally cleared)

2. *Morphine – AVOID due to accumulation of active metabolites (renally cleared)
   - If must be used, avoid long-acting preps and monitor closely for toxicity
   - Profound analgesia, sedation and ventilatory depression reported in CKD patients
3. **Codeine/compounds – CAUTION –** decrease starting dose by 50%

4. **Oxycodone – CAUTION** - insufficient PK evidence to establish long-term safety in CKD.
   - Literature reports use without major adverse effects.
   - Less constipating than codeine and less hallucinations compared to morphine.
   - Compounds
5. *Hydromorphone – CAUTION*

- High narcotic potency (7\(x\) narcotic analgesic effect of morphine)
- Less active metabolites compared to morphine (less accumulation)
- Better tolerated - reduced incidence of hallucinations & delirium with long-term use in CKD patients
- Less sedation, n/v, pruritis (\(\downarrow\) histamine release)
EQUIVALENT DOSES – Hydromorphone / Morphine

- ISMP has received many incident reports related to hydromorphone
- Different dosing acute vs. chronic:

1. In **acute** situations, 10 mg morphine po = 1.3 mg hydromorphone po

2. Pts on **chronic** opioids, 10 mg morphine po = 2.5 mg hydromorphone po
6. **Fentanyl** – **RECOMMENDED**

- For chronic pain in CKD → no active metabolites and parent compound doesn’t accumulate
- Good choice for patients with stable level of pain
- Do not use in the opioid-naïve patient
- Onset of patch – approx. 12 hours
- 12 mcg patch = 30-60 mg morphine po
7. Methadone – RECOMMENDED

- For severe chronic pain → no active metabolites
- Option if pain refractory to usual opioids
- Long and variable half-life (~23 hrs) → 4-9 days to reach steady-state (slow upward adjustments necessary)
- Physician needs special privilege to prescribe it (paperwork)
- Multiple drug interactions
CONCLUSION

- Conflicting/lack of data makes dosing of opioids difficult in CKD
- A greater understanding of the PK and pharmacodynamics of opioids is necessary to develop effective clinical approaches to pain management in this population.