Treating Pain in Advanced CKD & Dialysis Patients
Clinical Algorithm & Preferred Medications

Coalition for Supportive Care of Kidney Patients
www.kidneysupportivecare.org

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Overview of Essentials of Pain Management

1. Assess pain intensity on a 0-10 scale in which 0 = no pain at all and 10 = the worst pain imaginable. Determine if the pain is mild (1-4), moderate (5-6), or severe (7-10).

2. Prescribe pain medications and dosages according to the World Health Organization 3-Step Analgesic Ladder adapted for patients with chronic kidney disease (see page 3).

3. Assess the character of the patient’s pain and determine whether it is nociceptive, neuropathic, or both. Patients may have more than one type of pain; each pain syndrome should be diagnosed and treated.

   Nociceptive pain involves intact pain receptors and is described by patients as aching, dull, throbbing, cramping, or pressure.

   Neuropathic pain involves injury to pain receptors and is described by patients as tingling, burning, stabbing, or numb (see page 6).

4. Assess pain regularly for site, relieving and aggravating factors, and temporal relationships, and assess treatment regularly for effect on functioning and quality of life.

ALWAYS...

- Ask your patients about their symptoms and pain. Believe the patient’s report of pain unless history of substance and/or drug misuse.
- Consider depression as a potential contributor.
- Recommend non-pharmacological interventions (e.g., heat, ice, TENS unit, etc.), as appropriate.
- Use adjuvant medications to reduce pain and side effects.
- Anticipate and treat constipation.
- Be alert for patients with opioid use disorder.

Chronic pain is common and can be severe in ESRD patients, greatly reducing quality of life.
**Pain Assessment**

**Instructions:** Please have your patient describe his/her level of pain by circling the appropriate number or the face that best describes the intensity of pain. Determine if the pain is nociceptive or neuropathic by the descriptors the patient uses to describe the pain (see algorithm below). Repeat the pain assessment on subsequent patient visits.

<table>
<thead>
<tr>
<th><strong>Recommended Practices</strong></th>
<th><strong>A</strong></th>
<th><strong>B</strong></th>
<th><strong>C</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Educate</strong> patient/caregivers on pain assessment and charting at home, goals of therapy, management plan, and potential complications.</td>
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<td><strong>Aim to achieve control at a level acceptable to the patient; it may not be necessary or possible to make the patient completely pain-free. Provide PRN doses for breakthrough pain.</strong></td>
<td><strong>Schedule doses over 24 hours on a regular basis for chronic pain. Provide PRN doses for breakthrough pain.</strong></td>
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1. **“Are you having any pain?”**
   
   ```
   Verbal: “How much pain are you having, from 0 (no pain) to 10 (worst pain imaginable)?”
   Written: “Circle the number that describes how much pain you are having.”
   ```

2. **“Where is the pain located?”**
   
   Record, screen, and address each site.

3. **“What is the character of the pain?”**
   
   **Nociceptive**—Patient descriptors: *aching, dull, throbbing, cramping, pressure*
   
   **Neuropathic**—Patient descriptors: *tingling, numbness, burning, stabbing, increased pain to light touch*
   
   Both Nociceptive and Neuropathic

4. **“What relieves the pain?” “What aggravates the pain?”**

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WHO 3-Step Analgesic Ladder (adapted for advanced CKD)

Freedom from Pain
Severe Pain (7-10)
Hydromorphone – start at 1 mg PO q 4-6hr + 1 mg PRN for breakthrough pain q 2hr
Please note: Hydromorphone is potentially unsafe if the patient stops dialysis OR is CKD stage 4 or 5. The kidney-excreted active metabolite, hydromorphone-3-glucuronide, builds up because it is not adequately cleared in worsening CKD.

Pain Persisting or Increasing
Moderate Pain (5-6)
Hydrocodone – start at 5 mg PO q 4hr PRN
Oxycodone – start at 5 mg PO q 4hr PRN
Tramadol – start at 25 mg PO q d
± Nonopioid analgesics ± Adjuvants

Pain Persisting or Increasing
Mild Pain (1-4)
Acetaminophen
Avoid NSAIDS
± Adjuvants

Titrate upwards, increasing the dose until either analgesia or intolerable side effects occur. For mild-moderate pain, increase dose by 25-50%; for severe pain, increase dose by 50-100%.

Adjuvants, include medications such as anticonvulsants for neuropathic pain. It may also refer to medications that are given to manage an adverse effect of an opioid, or to enhance analgesia, such as steroids for pain from bone metastases.

When using products that combine opioids with acetaminophen do not exceed 3.2g of acetaminophen per day to avoid hepatotoxicity.
# Pain Medications in CKD/ESRD

<table>
<thead>
<tr>
<th><strong>Recommended</strong></th>
<th><strong>Use with Caution</strong></th>
<th><strong>Do Not Use</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Tramadol</td>
<td>Morphine</td>
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<tr>
<td></td>
<td>Limit dose to 50 mg BID. Higher doses have been used but caution needs to be taken since pharmacokinetics are not well established.</td>
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<tr>
<td>Hydromorphone</td>
<td>Hydrocodone/Oxycodone</td>
<td>Codeine</td>
</tr>
<tr>
<td>Hydromorphone is potentially unsafe if the patient stops dialysis OR is CKD stage 4 or 5. The kidney-excreted active metabolite, hydromorphone-3-glucuronide, build ups because it is not adequately cleared in worsening CKD.</td>
<td>Insufficient pharmacokinetic evidence to establish safety in CKD, but literature reports use without major adverse effects.</td>
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<tr>
<td>Fentanyl</td>
<td>Desipramine/Nortriptyline</td>
<td>Meperidine</td>
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<td></td>
<td>Alternative to treat neuropathic pain, but more adverse effects than gabapentin and pregabalin.</td>
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</tr>
<tr>
<td>Methadone</td>
<td>Gabapentin</td>
<td>Propoxyphene</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Doses in ESRD up to 300mg/d are generally considered safe, but higher doses should be used with caution; note that gabapentin use for neuropathic pain is off-label but effectiveness has been documented.</td>
<td>Renally excreted metabolites accumulate in CKD causing neurotoxicity.</td>
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<tr>
<td>Pregabalin</td>
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<tr>
<td>Doses up to 100 mg/d are generally considered safe in ESRD.</td>
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Algorithm to Treat Severe Chronic Pain in Dialysis Patients

**Hydromorphone:**
- Start at 0.5mg PO q 2 hours PRN pain. Titrate dosage every 2–3 days.
- If pain is not controlled, is continuous, and 24-hour dose exceeds 12 mg, substitute transdermal fentanyl 25 mcg/hr for regular dose of hydromorphone.
- If further “as needed” hydromorphone exceeds 12 mg/24 hours, increase dose of fentanyl patch by further 25 mcg. Titrate upwards in similar manner if pain is not controlled.

**Fentanyl Transdermal Patches:**
- Useful for patients with chronic, stable pain. Start after immediate-release opioid dose is established. Analgesia may not be obtained for 12-24 hours, so continue previous PRN analgesics for 12 hours to ensure a smooth transition.
- Initial dose for opioid-naïve patients is 12 mcg/hr (increase dose every 3–6 days as needed for pain). Useful choice if dialysis non-adherence or stopping dialysis are concerns.
- Fentanyl patches above 12 mcg/hr should not be used in opioid-naïve patients due to risk of respiratory depression.
- Since fentanyl patches are long acting, breakthrough pain medications should also be prescribed.

**CAUTION:** Toxic metabolite, H3G, can potentially accumulate if dialysis is stopped OR if patient is CKD stage 4 or 5.

**Methadone:**
- Only recommended to be used by knowledgeable physicians in consultation with a Pain Management specialist.
- Use if unable to control pain with fentanyl or hydromorphone (opioid-allergy, adverse effects, or refractory pain).
- Obtain baseline QTc (methadone may prolong QT interval) and repeat EKG if daily dose > 100 mg. 
  QTc < 500 ms considered safe.
- Beware of multiple drug interactions and adjust dose.
Treatment Based on Pain Type

Nociceptive Pain Treatment

- Confirm patient is able to swallow oral medications.
- Establish a pain control regimen utilizing short acting opioids and monitor for opioid toxicity and adverse effects.
- A rescue dose equivalent to 10% of the 24-hour dose of opioid should be available to be taken every 1-2 hours PRN for breakthrough pain. Remember to recalculate the rescue dose when increasing the base dose (long-acting dose).
- Long-acting opioids should be started after the needed dosage to control pain is established with short-acting opioids.
- If the patient is experiencing pain when he/she takes the long-acting opioid, he/she should take a rescue dose at the same time and not expect the long-acting opioid to relieve the breakthrough pain.

NOTE: Monitor for opioid toxicity (sedation, hallucinations, myoclonus, and/or asterixis) and opioid adverse effects (constipation, nausea, and vomiting).

Neuropathic Pain Treatment

Gabapentin:

- Start 100 mg PO qhs and increase weekly by 100 mg per night to a maximum of 300 mg qhs. Occasionally doses up to 600 mg a day can be safely used.
- If ineffective at maximum tolerated dose, discontinue and start pregabalin.

Pregabalin:

- 25 mg qhs and increase every few days to 100 mg a day.
- If pain control is inadequate at target dose for 2 to 4 weeks, or intolerable adverse effects, discontinue and start desipramine.

Desipramine:

- 10 mg PO qhs. Titrate to adequate pain control or maximum dose of 150 mg qhs.
- If pain control still remains inadequate, institute WHO 3-Step Analgesic Ladder (see page 3).
Management of Opioid Adverse Effects

Acute:

**Excessive sedation, compromised respiration with low O2 saturation**

- Dilute 0.4 mg of naloxone in 10 ml NS and administer 1 ml IV q 1-2 minutes until patient arouses.
- Continue to monitor for return of sedation or slowed respirations.

*Half-life of naloxone is shorter than half-life of opioids.*

Chronic:

**Nausea and/or vomiting**

- Prochlorperazine 2.5 to 10 mg PO, SC or PR QID PRN.
- Haloperidol 0.5 to 1 mg PO, SL, SC, IV BID-TID PRN (haloperidol solution is flavorless).
- Metoclopramide 5 to 10 mg PO, SC, IV QID PRN.
- Dimenhydrinate may be used 25 to 50 mg PO, SC, IV but is less effective, except if secondary to motion/dizziness. It also reduces opioid-induced pruritus.
- Ondansetron 4-8 mg PO or IV q8h PRN.
- Medications can be used alone or in combination.
- Consider mechanism for nausea in choosing agent.

**Constipation**

- Start stimulant laxative (e.g. senna, bisacodyl) at same time as opioids as preventative therapy.
- Lactulose 15-30 ml or polyethylene glycol 17g PO daily to BID is more effective for opioid-induced constipation, but patients may prefer medication in pill form.

**Cognitive impairment**

- Try decreasing the opioid dose to determine if function improves. If it does, consider using a lower dose or a different pain medication.