PAIN MANAGEMENT AND ESRD

Onaona Gurney

PGY-4
WHY DOES IT MATTER?

- High incidence of ESRD
- We deal with post-operative pain daily
- Serious complications can ensue
HOW ARE ESRD PATIENTS DIFFERENT?

- Multiple co-morbid conditions
- Chronic Pain
- Impaired clearance of medications
- Reduced hepatic breakdown\(^1\) of medications
KIDNEY: Reduced Clearance (CL) ↓
  ↓ GFR
  ↓ Tubular Secretion

Accumulation of Uremic Toxins: ↑ IS, CMPF, PTH

Chronic Inflammation: ↑ Cytokines

KIDNEY: Reduced Clearance (CL) ↓
  ↓ GFR
  ↓ Tubular Secretion

Accumulation of Uremic Toxins: ↑ IS, CMPF, PTH
WHAT’S THE RISK?

- Drug accumulation leading to adverse events
- Delayed response to pain medication
- Inadequate pain control
COMMON DRUGS USED

- Non-opioids
- Morphine
- Hydromorphone
- Oxycodone
- Codeine
- Fentanyl
- Tramadol
KIDDING....... 

Just some relevant take home points
NON-OPIOID ANALGESICS

- Acetaminophen
  - Analgesic of choice in elderly & kidney disease
  - Standing order
  - Not necessary to adjust for GFR

- NSAIDs
  - Decrease opioid use by 30-50%²
  - Short term use
MORPHINE

- Metabolized by liver into M3G, normorphine, & M6G
- M6G accumulates in renal failure
- M6G crosses BBB
- Increasing dose reduction with worsening renal function
HYDROMORPHONE

- More potent than morphine
- Morphine analogue
- Shorter duration of action
OXYCODONE

- Metabolized by the liver to noroxycodone & oxymorphine
- Reduced clearance in renal failure, prolonged half life
- Use cautiously & start with reduced dose
CODEINE

- Metabolized by the liver to variety of active metabolites (including M6G, C6G, morphine)

- Prolongation of half life in HD patients

- Metabolites accumulate in renal failure

- USE WITH CAUTION
FENTANYL

- Metabolized by liver to inactive, nontoxic metabolites
- Potent and short acting
- No significant accumulation in CKD
TRAMADOL

- Metabolized by the liver to 1 active metabolite
- Centrally acting, opioid agonist & MAOI
- Increased half-life elimination
<table>
<thead>
<tr>
<th>IN CKD</th>
<th>Opioid</th>
<th>Comments</th>
<th>Dialyzability</th>
<th>Dose adjustment based on eGFR (mg/mL)</th>
<th>Recommendation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morphine</td>
<td>Metabolites accumulate in renal failure, CNS and Respiratory depression, 20–25% of patients may tolerate well</td>
<td>Yes, but M6G slowly re-equilibrates across the blood brain barrier, delaying the response to hemodialysis; Very small amount removed by CVVH or CVVHD</td>
<td>75–100% 2.5–5 mg q6h</td>
<td>50–75% 2.5–5 mg q6-8h</td>
</tr>
<tr>
<td></td>
<td>Hydromorphone</td>
<td>Metabolite H3G accumulates in renal failure, has no analgesic activity but possibly neuro-excitatory</td>
<td>Yes</td>
<td>1.3 mg q6h</td>
<td>75% Start with 0.5 mg q6-8h</td>
</tr>
<tr>
<td></td>
<td>Fentanyl</td>
<td>Inactive metabolite, highly protein bound, large volume of distribution (Vd), CNS and Respiratory depression reported with infusion and Transdermal patch</td>
<td>No</td>
<td>25–100 mcg q4-6h SC</td>
<td>100% 75% 50% q12h</td>
</tr>
<tr>
<td></td>
<td>Tramadol</td>
<td>20% protein bound</td>
<td>Slowly removed, 50% clearance by HD</td>
<td>50–100 mg q6h</td>
<td>100% 50% 50% q12h</td>
</tr>
<tr>
<td></td>
<td>Oxycodone</td>
<td>50% protein bound</td>
<td>To some extent</td>
<td>5–10 mg q6h</td>
<td>100% 50% 25–50% q8h</td>
</tr>
<tr>
<td></td>
<td>Buprenorphine</td>
<td>Partial opioid agonist, ceiling analgesic effect, 96% protein bound</td>
<td>unlikely</td>
<td>0.3 mg IM/IV 8–16 mg S/L</td>
<td>Reduce dose and increase interval Reduce dose and increase interval</td>
</tr>
<tr>
<td>IN CKD</td>
<td>Opioid</td>
<td>Comments</td>
<td>Dialyzability</td>
<td>Dose adjustment based on eGFR</td>
<td>Recommendation(s)</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------</td>
<td>-----------------------------------------------</td>
<td>---------------</td>
<td>-------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>NOT RECOMMENDED</td>
<td>Codeine</td>
<td>Both codeine and its metabolites accumulate in renal failure</td>
<td>Dialyzerable</td>
<td></td>
<td>100% q6h 75% q8h 50% q12h Not recommended in dialysis patients</td>
</tr>
</tbody>
</table>
## SUMMARY

<table>
<thead>
<tr>
<th>Pain intensity</th>
<th>WHO analgesic step</th>
<th>Agent(s) of choice</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild pain</strong></td>
<td>Non-opioid ± Adjuvant</td>
<td>Acetaminophen 500 mg q6h (by the clock) and 325 mg every 6–8h as required</td>
<td>Not to exceed total dose of 3 g in 24-hours; If unable to take orally, then consider suppository NSAIDs/Cox-2 inhibitors are not recommended, but may consider, for short-term ONLY, under close observation</td>
</tr>
<tr>
<td><strong>Score 1–3</strong></td>
<td>Moderate pain</td>
<td>Non-opioid ± Adjuvant ± Weak opioid</td>
<td>Maximum dose 200 mg in stage 4 CKD and 100 mg in stage 5 CKD, dose after dialysis</td>
</tr>
<tr>
<td><strong>Score 4–6</strong></td>
<td>Non-opioid ± Adjuvant ± Strong opioid</td>
<td>± Hydromorphone 1.3 mg every 8h or Oxycodone 2.5 mg every 8–12h or Fentanyl 25–50 mcg SQ every 4–6h or Buprenorphine 0.3 mg every 6h IM/IV 8–16 mg sublingual daily Transdermal Patch – 5 mcg/hr–20 mcg/hr or Morphine 1.25–2.5 mg every 8–12h (for short-term use)</td>
<td>Use laxatives to avoid constipation, when using opioids Do not write standing (or long-term) orders for opioids Reassess the need and dose of opioids every 24–48 hours Monitoring for CNS and respiratory effects is required for protracted periods Fentanyl and methadone are highly protein bound and not dialyzable Avoid fentanyl transdermal patch in opioid-naïve patients</td>
</tr>
</tbody>
</table>
REFERENCES


