UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

PALLIATIVE CARE PHARMACY PHAST PHACT

February 20th, 2020 **Vol. 6, No. 7**

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: pruskowskija@upmc.edu

TODAY'S TOPIC:

Opioids in Renal Dysfunction: Should Hydromorphone Be Preferred?
Week 2: Nephrology's Viewpoint

Background:

The presence of renal dysfunction affects of the pharmacokinetics of many drugs; especially opioids. The rate of elimination is in theory proportional to a patient's glomerular filtration rate (eGFR) however opioids are weak organic bases. Changes in the urine pH can alter tubular handling and therefore can alter this relationship. Nephrologist recognize the importance of this relationship and have published a 2017 systematic review explaining their viewpoint.

Importance:

Since approximately 20% of cancer patients have a CrCl <60 mL/min, it is important for palliative care providers to understand how renal dysfunction may impact the pharmacotherapy selection of opioids.

The Article:

- Pain Med. 2017 Aug 1;18(8):1416-1449.
  Opioid Use in Chronic Pain Patients with Chronic Kidney Disease: A Systematic Review.
  - Objective: To investigate the prevalence of chronic pain and opioid management among patients with chronic kidney disease (CKD)
  - Methods: A systematic search included citations from 1960 to May 2015 that highlighted the prevalence of pain; type, dose, and reason for opioid use; effectiveness of pain control and associated adverse effects of opioids in patients with an eGFR <60 mL/min/1.73 m^2
    - In this review, participants were adult (>18 years) patients with chronic pain (> 90 days) in all stages of CKD
  - Results: 12 observational studies from different countries were analyzed. There was variation between the studies in

what opioids were used, how effective the different opioids were, what dose and the duration of use. Two studies are of importance to palliative care providers:

- Lee et al: greater than 80% of palliative patients with renal impairment that experienced side effects of confusion, hallucinations, drowsiness, nausea and vomiting were improved when switching from morphine to hydromorphone; showing that a switch in opioids can reduce adverse effects
- Paramanandam et al: an increase in cognitive impairment and agitation was observed when the dose or duration of hydromorphone was increased in palliative patients with GFR <60 mL/min
  - This was significant in a duration of continuous infusion for ≥3 days and ≥2 mg/hour
  - No neuroexcitatory symptoms were reported when the duration was <2 days and dose was <0.5 mg/hour, suggesting this is the neuroexcitatory threshold
  - 14% prevalence of cognitive dysfunction when dose exceeded 3 mg/hour vs. 4% when dose was ≤3 mg/hour

- Conclusion: "There is fair evidence for the high prevalence of chronic pain among patients with CKD, as well as fair evidence for the inadequate use of opioid therapy for the treatment of CKD patients with chronic pain"

So… What does this all mean ~~Jenn~~ Kelly?

- The nephrologist view is not crystal clear. The objective of the above systematic review was to investigate the prevalence of pain in CKD patients
- Remember this review included patients with all stages of CKD, but provided special verbiage to adverse effects in patients with an eGFR <60 mL/min/1.73 m^2
- According to this study, there isn't a preferred opioid for patients with eGFR <60 60 mL/min/1.73 m^2, however according to the authors hydromorphone, transdermal fentanyl, methadone, and transdermal buprenorphine are considered "safer" and used more frequently because their metabolites are inactive and have less of a risk of side effects since active metabolites are not accumulating
- To add, the authors do not explicitly state how to monitor these patients. They hint that patients should probably be monitored frequently especially within 1-4 weeks of starting the opioid or after dose escalation(s). You should monitor for adverse effects such as impaired cognition, agitation, tremor, hypotension, and constipation
  - If an adverse effect arises, then the authors infer you should stop or decrease the opioid
- So, is hydromorphone preferred? Probably according to nephrologists

CLINICAL PEARL:
The use of morphine and hydromorphone is controversial in patients with renal dysfunction.