

# PALLIATIVE CARE PHARMACY PHAST PHACT



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## Palliative Care Pharmacy Team:

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If you have a topic you  
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## TODAY'S TOPIC:

### Opioids in Renal Dysfunction: Should Hydromorphone Be Preferred? Week 4: Palliative Care's Viewpoint

#### **Background:**

The presence of renal dysfunction affects 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. Oncologists also appreciate the importance of this dilemma and published a systematic review in 2016.

#### **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:**

- [J Palliat Med. 2016;19\(11\):1179–1187.](#)  
Evidence for Neurotoxicity Due to Morphine or Hydromorphone Use in Renal Impairment: A Systematic Review.
  - Objective: To identify and assess the quality of evidence for neurotoxic effects in patients with renal impairment receiving morphine or hydromorphone.
  - Methods: Studies were included if they reported neurotoxic effects of either morphine or hydromorphone for chronic or malignant pain in patients with renal impairment. Review articles and case reports were excluded.

- **Results:** Six original articles, three prospective and three retrospective studies were identified and assessed. No relevant randomized clinical trials were identified.

**Morphine:**

- Of 109 cancer patients who received either oral or IV morphine, 26% (n = 28) developed myoclonus and 40% (n=43) had cognitive impairment
- Of 36 patients who received oral or subcutaneous morphine, increased SCr was associated with adverse effects, including increased delirium (p=0.031)
- 581 out of 1147 cancer patients received morphine, of which 11-15% had moderate/severe renal impairment. Patients with high serum M3G (inactive metabolite of morphine) were more likely to report severe cognitive dysfunction (OR: 1.63, 95% CI: 1.03–2.56; p = 0.04). However, cognitive dysfunction was not significantly associated with renal function

**Hydromorphone:**

- Of 55 palliative care patients switch to oral hydromorphone, there was no statistically significant difference between patients with and without renal impairment for drowsiness and/or hallucinations. 46/55 patients (83%) had switched from morphine.
  - Of 54 patients receiving hydromorphone continuous infusion, no neuroexcitatory effects were seen in patients in the lowest quartile of dose or duration. Increased agitation and cognitive dysfunction were associated with increased quartile of hydromorphone dose (agitation p < 0.0001; cognitive dysfunction p < 0.0001) and duration (agitation p < 0.0002; cognitive dysfunction <0.002).
  - Of 156 inpatient hospice patients on scheduled IV hydromorphone regimen 6.4% (n=10) developed neurotoxic symptoms. Mean hydromorphone dose of patients with neurotoxic symptoms (2.15 mg/h) was significantly higher than mean dose of patients without neurotoxic symptoms (0.88 mg/h).
- **Conclusions:** “Although morphine and hydromorphone use may be associated with neurotoxic effects in patients with renal impairment, current evidence consists of very low-quality studies with conflicting findings. Clinicians may consider using either morphine or hydromorphone in mild-to-moderate renal impairment, while closely monitoring for neurotoxic effects, particularly when used in high doses and for extended duration.”

### **So... What does this all mean Jenn Sami?**

- The palliative care providers also agree – this topic is not black and white. As you can see, they concluded you could consider morphine or hydromorphone in patients with mild-to-moderate renal impairment
- The true prevalence of opioid-related myoclonus remains unknown. In one review, the authors reported a prevalence of anywhere between 2.7% to 87%
- Per this study, hydromorphone does appear to be more tolerable in patients with renal impairment, but this is subjective. For

example, in patients who switched from their previous opioid therapy to hydromorphone, there was an improvement in side effects for >80% of patients

- As with our other clinician viewpoints, there is no significant association between renal function and metabolite accumulation. However, it does appear higher doses will put a patient at a higher risk of adverse drug reactions
- In this review, the authors found cognitive effects appeared on day 6 of therapy on average, so monitoring for these symptoms is important in the first week of therapy or when doses are increased
- Consider monitoring the patient more than their objective lab values

**CLINICAL PEARL:**

**The use of morphine and hydromorphone is controversial in patients with renal dysfunction.**