

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 3: Oncology'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:

- [Support Care Cancer. 2017;25\(2\):661-675.](#)
The Use of Opioids in Cancer Patients With Renal Impairment-A Systematic Review
 - o **Methods:** Eligible studies met the following criteria: patients with cancer pain taking an opioid (defined as per the WHO ladder); >18 years; renal impairment (serum creatinine > normal range (study dependent), creatinine clearance (CrCl) or glomerular filtration rate (GFR) measurements <90 ml/min, or as per the study definition); clinical outcome related to renal impairment.
 - o **Results:** Eighteen studies (n = 2422) were eligible but heterogeneity meant meta-analysis was not possible. Morphine was examined in eight studies (n = 1418), oxycodone in two studies

(n = 325), and fentanyl, alfentanil or sufentanil were discussed in six studies in total (n = 442). No recommendations could be formulated on the preferred opioid in patients with renal impairment.

- Below are 8 of the 18 morphine studies to help illustrate the discrepancies:

Study:	Result:
Somogyi et al, 1993	No relationship observed between creatinine clearance and clearance of morphine, M3G, or M6G.
Klepstad et al, 2003	No relationship between serum morphine, M3G, or M6G concentration and opioid-induced side effects including nausea, constipation, sedation, and impaired cognition
Riley et al, 2006	Mild-moderate elevation in serum creatinine was not found to be a significant predictor of morphine intolerance
Kurita et al, 2015	Patients with higher serum morphine concentrations were more likely to experience severe constipation (p<0.001) and patients with higher M3G concentrations were more likely to have severe cognitive dysfunction (p<0.05)

- Two palliative care pertinent studies are the following:
 - [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 lack of consensus within the existing literature on the relationship between morphine, creatinine levels and morphine-related side effects. Based on the current evidence, morphine should be used with caution; however, more evidence is needed. Fentanyl, alfentanil and sufentanil are recommended in patients with renal impairment based on pharmacokinetics and clinical experience. However, the present systematic review found very little clinical evidence for this. Overall, the quality of the existing evidence on opioid treatment in cancer patients with renal impairment is low. There remains a need for high-quality clinical studies examining opioids in patients with renal impairment.”

So... What does this all mean Jenn Amy?

- The oncologists have come right out and disclosed that there is a lack of consensus within the existing literature on the relationship between morphine, creatinine levels and morphine-related side effects
 - Ever wonder where that CrCl <30mL/min came from? While it appears to be a reasonable threshold – it is not evidence based
- They also did not conclude that morphine had worse outcomes compared to fentanyl or oxycodone
- So, it is reasonable to consider the use of morphine in patients with renal impairment? Maybe – it is probably more important to monitor for adverse effects than make changes based on lab numbers

CLINICAL PEARL:

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