UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

PALLIATIVE CARE PHARMACY PHAST PHACT

February 13th, 2020 Vol. 6, No. 6

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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

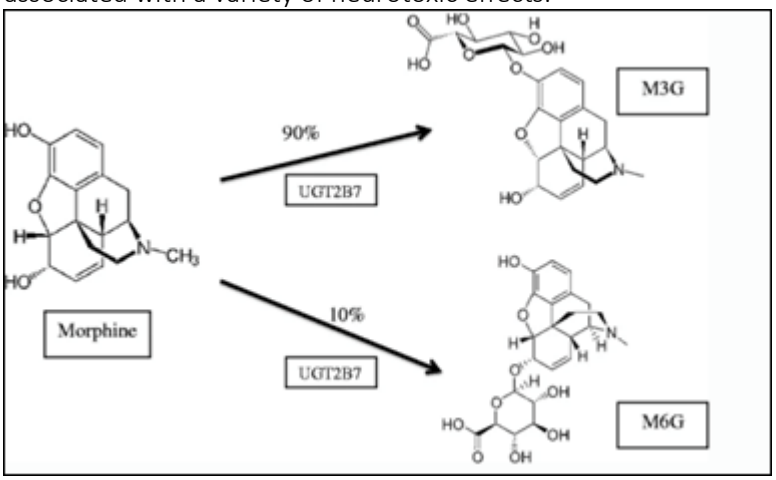
TODAY'S TOPIC:

Opioids in Renal Dysfunction: Should Hydromorphone Be Preferred?

Week 1: Overview

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 (GFR) however opioids are weak organic bases. Changes in the urine pH can alter tubular handling and therefore can alter this relationship. For example: morphine is often cautioned in patients with renal dysfunction due to the potential risk of active metabolite accumulation. In the liver morphine is metabolized to morphine-3-glucuronide (M3G) and M6G. M6G is analgesic, but has also been associated with a variety of neurotoxic effects.



However, hydromorphone shares a similar pathway.

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 Literature:

- J Pain Symptom Manage. 2004;28(5):497–504.
  Opioids in Renal Failure and Dialysis Patients
  - Review article
  - Morphine: "M6G achieves high serum levels in patients with reduced renal function, and although it crosses the blood–brain barrier slowly, once in the CNS its effects can be prolonged. There may be two forms of M6G—one that is extended and hydrophilic, and the second, occurring in water-poor tissue, that is folded and more lipophilic. For this reason, after discontinuing morphine or dialyzing to remove the M6G, theCNSeffectsmaypersistforsometimeastheM6Gslowly re-equilibrates across the blood-brain barrier back into the systemic circulation."
    - Do not use in renal failure, due to the difficulty of managing the complicated adverse effects of the metabolites. Both the parent compound and the metabolites can be removed by dialysis"
  - Hydromorphone: "Hydromorphone is metabolized in the liver to hydromorphone-3-glucuronide (36.8%), dihydromorphine (0.1%) and dihydroisomorphine (1.0%), as well as small amounts of hydromor-phone-3-sulfate, norhydromorphone, and nor-dihydroisomorphone. All metabolites are excreted renally, along with a small amount of free hydromorphone. Although further metabolism of the dihydro- forms to hydromorphone-6-glucuronide has been suggested"
    - Use carefully. Although the 3-glucuronide metabolite is neuro-excitatory and can accumulate in renal failure, hydromorphone has been used in renal failure patients with no adverse effects. Hydromorphone has been used without adverse effects in dialysis patients. The parent drug is partly removed by dialysis, but there are no data concerning dialysis of the metabolites, and metabolite accumulation is a risk."

So… What does this all mean Jenn?

- Did you notice that hydromorphone has a similar metabolism pathway to morphine? And some believe they both carry a similar risk of neurotoxicity. Notice they also carry the same recommendation per this article by Dean?
- Did you ever wonder where that CrCl 30 mL/min threshold came from?
- Over the next few weeks, we will present what data exists regarding this topic. It may surprise you…

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