UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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

TODAY'S TOPIC:

Gabapentin and Opioid Co-Administration

Background:

Gabapentinoids such as gabapentin and pregabalin were originally developed as antiseizure medications but are now used often for the treatment of neuropathic pain. They are currently FDA indicated for partial seizures and postherpetic neuropathy. However, over time gabapentinoid use has increased, potentially a result of the opioid epidemic and the push for non-opioid analgesia.

Recap from Previous Issues of *The Tablet* surrounding Gabapentinoids

Vol. 1, No. 9 - Pregabalin at oral doses of 300mg-600mg/day has proven to be beneficial for PHN and PDN; evidence for other types of neuropathic pain, like cancer-related cancer pain, is very limited.
Vol. 1, No.10 – Amitriptyline and gabapentinoids are effective in relieving neuropathic pain in patients with cancer, although pregabalin may reduce neuropathic pain more compared to other medications.
Vol. 1, No.11 - No significant association of respiratory depression with opioid coadministration in gabapentinoid group versus nongabapentinoid group. Gabapentinoids might have dose-related effects on respiratory depression. Odds of an opioid-related death was 49% higher among individuals recently exposed to gabapentin and opioids concomitantly compared to those exposed to just opioids.
Vol. 1, No. 19 - Possibility that dosing conversion is not linear between gabapentin and pregabalin. If using the 6:1 ratio of gabapentin to pregabalin dosing, this conversion may be too conservative whereas at other doses/situations it may be too aggressive.
Vol. 1, No. 27 - It is difficult to determine onset of analgesia versus peak analgesia of various neuropathic pain agents such as gabapentin, pregabalin, duloxetine, venlafaxine, etc. as onset of analgesia is not well-reported in available studies.

Importance:

Reports have found using gabapentinoids concomitantly with opioids increases the risk of opioid-related adverse events including respiratory depression and opioid-related deaths. Combined use is not recommended per the Beers Criteria due to increased risk of sedation, respiratory depression, and potential death. Palliative care clinicians should be aware of this warning, other data behind this warning, and its implications for clinical practice.

The Literature:

Am J Hosp Palliat Care. 2021 Aug 19;10499091211040231.

Gabapentinoid dosing and associated toxicities in patients w/wo concomitant opioids during hospitalization

Objective**:** To determine if there is a difference in administered dose of gabapentin, reported sedation, fall risk score, or CNS related adverse effects in hospitalized patients with or without concomitant opioid use
Methods: Retrospective, multi-centered, cross-sectional, descriptive study; n = 499, age18-85 years old, administered at least 1 dose of a gabapentinoid during a hospital admission between Jan 2018-Dec 2018
Outcomes**:**

- Primary Outcome: Difference in administered gabapentinoid total daily dose in patients with or without concomitant opioid use
- Secondary Outcome: Difference in sedation documentation, renal function, fall risk scores using the Hester Davis Fall Risk Scale, and central nervous system related side effects

Results**:**

- Average total daily dose of gabapentin was higher in patients taking opioids concomitantly with gabapentin than patients taking gabapentin monotherapy

Primary Outcome	**Opioid (n = 159)**	**Non-opioid (n = 340)**	**P-value**
Avg total daily dose	860mg (SD = 553 mg)	706mg (SD = 614 mg)	0.007

- Secondary Outcomes
  - Sedation documentation was missing more so in the non-opioid group than the opioid group ($p < 0.001$)
  - Fall risk score recorded via Hester Davis fall risk score was similar between both groups
  - Adverse effects such as ataxia, confusion, dizziness, and blurred vision were similar between both groups
  - Number of patients with total daily dosage above recommended maximum
    - Differences in doses based on renal function was not significant

Conclusions**:**

- Gabapentin average total daily dosage of hospitalized patients were higher in patients who also required opioids
- Sedation documentation is less frequent in patients on gabapentin monotherapy

Bottom Line (Evan's thoughts):

- Main reason for this comparison is that the dosing of gabapentin, in combination with opioids, is related to morbidity and mortality, however this study's main outcome was simply looking at total doses of gabapentin in both groups (with concomitant opioids and without)…
- The average dose of gabapentin in both groups is rather low… 860mg (with a large standard deviation +/- ~600mg) compared to our typical analgesic dose target of 1800mg/day… hard to say out this influenced adverse effects described in this article
- Is a difference of 154mg of total daily dose gabapentin clinically significant? Probably not…
- Of note, they found sedation documentation was missing more so in the gabapentin monotherapy group… should we try to increase our documentation of sedation for patients receiving gabapentin monotherapy? Seems appropriate to me… maybe we are missing sedation related to gabapentin alone…
- Gabapentinoid side effects such as sedation, ataxia, confusion, and dizziness are well recognized and included on the drug package inserts but are underreported in literature
- Demographics such as age & CHF were significantly different and were not controlled for- maybe this made a difference in dosing strategies or in secondary outcomes?
- Retrospective nature relied on EMR documentation… information that I would have liked to see was missing such as pain scores, indications, other meds, comorbidities, if patient was on newly prescribed gabapentin or was a continued home med etc.

CLINICAL PEARL: Monitor for potential side effects of gabapentin, including sedation, as these may be underreported/not documented well in clinical practice