UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

PALLIATIVE CARE PHARMACY PHAST PHACT

March 26th, 2020 **Vol. 6, No. 12**

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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:

Breathing Problems with Gabapentin and Pregabalin

Background:

In December 2019, the FDA announced a formal safety concern warning of serious breathing problems with gabapentin and pregabalin for patients with respiratory risk factors. The risk factors includes opioids and other CNS depressants, older age, and respiratory conditions such as COPD. This risk appears to be less in patients taking gabapentinoids alone. Recently the FDA has seen an increase in gabapentionoid use, as well as misuse and abuse.

Importance:

Gabapentin and pregabalin are important neuropathic agents for palliative care providers. Patients with serious illness often suffer from neuropathic pain. These agents have traditionally been seen as more "benign" compared to other medication classes, therefore it is important to update this viewpoint as data is presented.

The Literature:

- FDA Adverse Event Reporting System (FAERS) Database:
  - The FDA reviewed several sources of data, including cases reports submitted to the FDA or published literature
  - Among 49 case reports submitted to FDA over the 5-year period from 2012 to 2017, 12 people died from respiratory depression with gabapentinoids, all of whom had at least one risk factor (of course this data is limited)
  - The FDA also reviewed the results of two randomized, double-blind, placebo-controlled clinical trials in healthy people, three observational studies, and several studies in animals

- Animal studies have showed pregabalin alone and pregabalin plus opioids can depress respiratory function
- One trial showed that using pregabalin alone and using it with an opioid pain reliever can depress breathing function
- The other trial showed gabapentin alone increased pauses in breathing during sleep
- Three observational studies at one academic medical center showed a relationship between gabapentinoids given before surgery and respiratory depression occurring after different kinds of surgeries

So… What does this all mean Jenn?

- For me this is not unexpected considering previous studies. You may remember several PCP Phast Phacts in 2018 were focused on this topic
- The important point is that the risk appears to be less in patients taking gabapentionoids alone - therefore they must be some synergy between gabapentinoids and other CNS depressant meds or respiratory conditions
- The real take home message is to start gabapentin and pregabalin at the lowest dose possible, and to have a lower threshold to taper off these agents if they are not found valuable
  - Literature suggests a target dose of 1,800mg/day of gabapentin. The literature is less clear on a target dose of pregabalin but it may be close to 300mg/day. An adequate duration of these medications is approximately 4 weeks
- Too add, remember gabapentin and pregabalin need to be adjusted for renal insufficiency. This is important as oversedation can occur if these meds are not adjusted

CLINICAL PEARL:
Palliative care providers should start gabapentin and pregabalin at the lowest dose possible and monitor patients for symptoms of respiratory depression when coprescribed other CNS depressants, or carry other risk factors.