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What's New in the Patient Safety World

March 2024

Gabapentinoids and COPD Exacerbation

Add another downside to the use of gabapentinoids. Rahman et al. (Rahman 2024) looked at patients with COPD in Quebec who were begun on gabapentinoids for indications of epilepsy, neuropathic pain, or other chronic pain. Compared to matched COPD patients not taking gabapentinoids, there was an increased risk for severe COPD exacerbation across the indications of epilepsy (HR 1.58), neuropathic pain (HR 1.35), and other chronic pain (HR 1.49) and overall (HR 1.39). The authors conclude that their results support recent warnings from Health Canada and the US FDA about breathing difficulties associated with gabapentinoids.

However, there has also been an interesting positive study regarding gabapentin. In general, gabapentinoids have not been very successful in reducing the need for opioids in patients undergoing surgery and have possibly increased the risk of postoperative respiratory depression in patients also receiving opioids (see, for example, our December 2023 What's New in the Patient Safety World column "Postop Gabapentin No Better Than Placebo"). But the new study from Sweden found that using gabapentin as part of a multimodal analgesia bundle did reduce the need for opioids in patients undergoing colorectal surgery (Gedda 2023).

A care bundle consisting of an individualized opioid regimen, regular gabapentinoids, and clonidine as a rescue analgesic was introduced gradually in 842 patients who underwent major colorectal surgery. Over the study period, median opioid usage decreased from 75 MME (morphine milligram equivalents) in 2016 to 22 MME in 2019 ($P < .001$), and the proportion of patients receiving 45 MME or less increased from 35% to 66% ($P < .001$). An individualized opioid strategy, the use of gabapentin, and increasing age were factors associated with less opioid consumption, while the use of clonidine was associated with more opioid intake. The authors concluded that regular gabapentin and an individualized opioid regimen were particularly strongly associated with this decrease and should be further evaluated as components of multimodal, opioid-free postoperative analgesia.

In the Gedda study, regular gabapentinoids were implemented as a standard order set of oral gabapentin 300 mg twice on the day of surgery followed by 300 mg 3 times daily

from day 1 until 7 to 10 days after surgery. A lower dose was used in patients aged 80 years or older and in patients with a reduced renal clearance (eGFR of less than 50). Those doses were chosen to minimize the risk of adverse events. Only 2% of study participants discontinued gabapentin due to a suspected adverse reaction. The adverse reactions were all mild and fully reversible.

The authors note that their results contradict findings in a meta-analysis on gabapentinoids in postoperative analgesia (Verret 2020), which concluded that gabapentinoids provide clinically irrelevant analgesia and are associated with too many serious adverse effects to be considered effective. Gedda et al. believe that dosing and the timing of the doses can be a part of an explanation, since the dose of gabapentin used was in the low dosage range. In addition, most participants in their study consumed no or small amounts of opioids, which may explain the absence of respiratory depression. Also, many previous studies began gabapentinoids pre-operatively, whereas in the Gedda study they were only used post-operatively. Note also that, in our December 2023 What's New in the Patient Safety World column "Postop Gabapentin No Better Than Placebo"), we noted that in the GAP trial opioid use did favor gabapentin for non-cardiac thoracic and abdominal procedures over the first few post-operative days, being roughly 30% lower at several time points. But it was felt that this was statistically significant but not clinically significant. Maybe not so insignificant, in view of the Gedda study!

Particularly in view of the negative effect of opioids on bowel function, it is desirable to find regimens that reduce the need for opioids in major colorectal surgery. Maybe it's too early to give up on gabapentinoids to reduce the need for post-op opioids, but we still need to keep in mind the many potential downsides they may have.

Some of our prior columns on safety issues with gabapentinoids:

- November 2017 "Bad Combination: Gabapentin and Opioids"
- March 2019 "Gabapentin and Pregabalin on the Radar Screen"
- January 2020 "FDA Warning on Gabapentinoids"
- February 25, 2020 "More on Perioperative Gabapentinoids"
- January 2021 "Gabapentinoids Again"
- June 2022 "Gabapentin and Overdoses"
- September 27, 2022 "More Bad News for Gabapentin"
- December 2023 "Postop Gabapentin No Better Than Placebo"

References:

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Gedda C, Nygren J, Garpenbeck A, et al. Multimodal Analgesia Bundle and Postoperative Opioid Use Among Patients Undergoing Colorectal Surgery. JAMA Netw Open 2023; 6(9): e2332408
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Verret M, Lauzier F, Zarychanski R, et al. Canadian Perioperative Anesthesia Clinical Trials (PACT) Group. Perioperative use of gabapentinoids for the management of postoperative acute pain: a systematic review and meta-analysis. Anesthesiology 2020; 133(2): 265-279
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Gabapentin in post-surgery pain (GAP trial)
https://www.isrctn.com/ISRCTN63614165

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