

## Patient Safety Tip of the Week

February 25, 2020

### More on Perioperative Gabapentinoids

Gabapentinoids have increasingly been used as an adjunct for analgesia in a variety of surgical procedures. They have been promoted as part of multimodal analgesia regimens intended to reduce the use of opioids. In our February 11, 2020 Patient Safety Tip of the Week [“ERAS Rocks!”](#) we noted that many ERAS (Enhanced Recovery After Surgery) protocols use them but we inserted our own warning about their use. Over the past 3 years we have done several columns on patient safety issues related to gabapentinoids (see list below).

In fact, a recent systematic review and meta-analysis on perioperative use of gabapentinoids ([Verret 2019](#)) found no clinically significant analgesic effect for the perioperative use of gabapentinoids, with low level of evidence, and an increased risk of adverse events with moderate level of evidence. The authors concluded that their results do not support the use of gabapentinoids for the management postoperative acute pain in adult patients.

Duke University researchers have also taken a look at the impact of gabapentinoids used in the perioperative period. Ohnuma et al. ([Ohnuma 2019](#)) analyzed data from a large administrative claims database, including 862,524 patients from 592 hospitals, who underwent elective primary THA or TKA between 2009 and 2014. They looked at the following drugs, alone or in combination, on the day of surgery for patients undergoing TKA or THA: acetaminophen, nonsteroidal anti-inflammatory drugs (NSAID's), gabapentinoids (gabapentin or pregabalin), or none of the three drugs.

Compared to none of the three drugs as the reference category, exposure to gabapentinoids was associated with increased odds of naloxone use after surgery (OR 2.11), noninvasive ventilation (OR, 1.45), invasive mechanical ventilation (OR 1.25), and ICU admission (OR 1.28). A similar increase was seen in analgesic combinations including gabapentinoids. The group receiving NSAID's plus acetaminophen showed the most protective associations with naloxone use after surgery (OR 0.59), invasive mechanical ventilation (OR, 0.72), and ICU admission (OR 0.69), and was associated with the lowest opioid consumption on the day before discharge.

The authors conclude that preoperative gabapentinoids were associated with significant increased risk of postoperative opioid-related respiratory depression. It also failed to find benefits for gabapentinoids in terms of postoperative opioid consumption and LOS. They recommend reconsideration of routine use of preoperative gabapentinoids in the adult TKA and THA population.

The researchers also looked at 108,616 patients who underwent elective colorectal surgery across the 605 hospitals, 2% of whom received gabapentinoids on the day of surgery ([Yan 2019](#)). They found that use of gabapentinoids was associated with higher odds of noninvasive ventilation (OR 1.39) and receipt of naloxone after surgery (OR 1.70). There was no difference in invasive mechanical ventilation, opioid consumption, or LOS. They cite other small studies showing increased risk of postoperative respiratory depression and naloxone use in patients receiving gabapentinoids, which may be explained by an interaction between gabapentinoids and opioids.

Our January 2020 What's New in the Patient Safety World column "[FDA Warning on Gabapentinoids](#)" summarized some of our previous concerns about gabapentinoids and discussed a new warning on gabapentinoids from the FDA ([FDA 2019](#)). The FDA warns that "serious breathing difficulties may occur in patients using gabapentin (Neurontin, Gralise, Horizant) or pregabalin (Lyrica, Lyrica CR) who have respiratory risk factors. These include the use of opioid pain medicines and other drugs that depress the central nervous system, and conditions such as chronic obstructive pulmonary disease (COPD) that reduce lung function. The elderly are also at higher risk."

The FDA notes that gabapentinoids are often being combined with CNS depressants (including opioids, anti-anxiety medicines, antidepressants, and antihistamines), which increases the risk of respiratory depression. It acknowledges that there is less evidence supporting the risk of serious breathing difficulties in healthy individuals taking gabapentinoids alone.

The FDA decision was based upon both reports it received and studies in the medical literature. Of fatal cases involving gabapentinoids reported to the FDA, all had at least one additional risk factor.

Keep in mind that the above data are not from randomized controlled trials (the FDA did review two RCT's in healthy people), It's doubtful that RCT's will be conducted on the use of gabapentinoids in this setting. But, in the absence of hard evidence for their efficacy in analgesia for perioperative pain, it's probably wise to exclude them from your protocols.

Gabapentinoids have been very valuable in the management of chronic neuropathic pain. But it appears they add little or no benefit to management of perioperative pain and they add additional risks.

## 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”](#)

## References:

Verret M, Lauzier F, Zarychanski R, et al. Perioperative Use of Gabapentinoids for the Management of Postoperative Acute Pain: A Systematic Review and Meta-analysis. 2019 annual meeting of the American Society of Anesthesiologists (ASA; abstract A2096). <http://www.asaabstracts.com/strands/asaabstracts/abstract.htm?year=2019&index=18&abnum=1927>

Ohnuma T, Raghunathan K, Ellis A, et al. Abstract S-344 Effects of Acetaminophen, NSAID's, Gabapentinoids and Their Combinations on the Day of Surgery in Total Hip and Knee Arthroplasties. Anesthesia & Analgesia 2019; 128(5): 741 <https://iars.app.box.com/v/AM19AbstractSupplement>

Yan R, Ohnuma T, Krishnamoorthy V, et al. Abstract S-353 Gabapentinoids on the Day of Colorectal Surgery Are Associated with Adverse Postoperative Respiratory Outcomes. Anesthesia & Analgesia 2019; 128(5): 760 <https://iars.app.box.com/v/AM19AbstractSupplement>

FDA (US Food and Drug Administration). FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR) When used with CNS depressants or in patients with lung problems. FDA 2019; 12-19-2019 <https://www.fda.gov/media/133681/download>

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