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# GABAPENTIN FOR ACUTE POSTOPERATIVE PAIN

## *Evidence Based Medicine Guideline*

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Approved: 11/18/2022 Previous Revision dates: 09/28/2016

**SUMMARY**
Gabapentin (Neurontin™) has gained significant interest as part of a multi-modal pain management strategy for the control of acute pain. There has been considerable variation in both the dose and the regimen used in recent clinical trials. Most have relied on pre-operative dosing and have utilized a single dose of 300 to 1200 mg. Higher doses seem to show a decrease in postoperative pain, a reduction in narcotic requirement, and reduction in narcotic related adverse effects such as nausea, vomiting, and ileus, with a propensity for causing sedation and dizziness.

**RECOMMENDATIONS**

- **Level 1**
  - **None**
- **Level 2**
  - **Pre-operative gabapentin (600-1200 mg) reduces the amount of narcotics required in the post-anesthetic care unit (PACU).**
  - **Pre-operative gabapentin does not decrease long-term narcotic use and is associated with increased side effects of respiratory depression, sedation, and falls.**
  - **Post-operative gabapentin (600 mg) may be equally effective as a preoperative dose in decreasing PACU narcotic use.**
- **Level 3**
  - **Concomitant administration of gabapentin as part of a multi-modal pain management strategy including narcotics, non-steroidal anti-inflammatory drugs (NSAIDS), and muscle relaxants does not improve pain scores.**

## INTRODUCTION

Gabapentin and other anticonvulsant medications have been established as an effective treatment for chronic neuropathic pain and are commonly used for such conditions as herpetic neuralgia, diabetic neuropathy, and phantom limb pain following amputation. These medications act by reducing the activity of calcium channels in GABA-ergic neurons thereby activating the noradrenergic spinal pathway which in turn reduces the expression of the spinal cord excitatory amino acids glutamate and aspartate. Recently, there has been interest in gabapentin as an adjunct for the treatment of acute pain as part of a multi-modal pain management strategy.

## LITERATURE REVIEW

In 2004, Pandey et al. investigated the use of a single 300 mg dose of gabapentin preoperatively in patients undergoing single level lumbar discectomy (1). They found that patients receiving gabapentin preoperatively had a decrease in the requirement for post-operative fentanyl (234 ± 142 mcg vs. 360 ± 104 mcg). In a follow up study

**LEVEL OF RECOMMENDATION DEFINITIONS**

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

in 2005, they evaluated increasing gabapentin dosages to determine the optimal pre-operative dose (2). Patients were divided into 5 groups and received placebo, 300 mg, 600 mg, 900 mg, or 1200 mg. They found that pre-operative gabapentin decreased patient use of fentanyl at all dosages. There was no advantage found in raising the dose from 600 mg to 1200 mg. They concluded 600 mg was the optimal dose for pre-operative gabapentin administration.

In 2006, Ho et al. performed a review of 16 randomized controlled trials (RCTs) evaluating the use of preoperative gabapentin in controlling postoperative pain (3). This was a heterogeneous group that included orthopedic, gynecologic, urologic, breast, and head/neck surgery trials. They found that a single preoperative dose of 1200 mg effectively reduced postoperative pain and opioid use. Multiple doses of gabapentin preoperatively, and continued postoperatively, did not appear to reduce pain scores. Incidence of opioid adverse effects such as vomiting and pruritus were lower in the gabapentin group. Although not statistically significant, there was a trend toward a lower incidence of nausea, urinary retention, and constipation in the gabapentin group. The incidence of sedation was higher in the gabapentin group and there was a trend towards increased dizziness.

In 2007, Peng et al. published a meta-analysis of RCTs in the management of acute postoperative pain using gabapentin (4). This analysis of 1181 patients including open gynecologic procedures, orthopedic procedures of the spine and lower extremity, breast surgery, procedures of the head and neck, open nephrectomy, and laparoscopic cholecystectomy. The majority of studies used doses of 600 mg to 1200 mg preoperatively in addition to continued administration in the postoperative period. A study of laparoscopic cholecystectomy included in the analysis used a dose of 300 mg. They found that gabapentin resulted in a 35% reduction in total analgesic consumption in the first 24 hours following surgery. Gabapentin also resulted in 27% to 39% reduction in visual analog scale (VAS) pain scores in the first 24 hours postoperatively. Gabapentin use reduced opioid-related nausea, vomiting, and pruritus although there was an increase in dizziness and sedation. They did note that there was significant heterogeneity in the magnitude of the benefit from adding gabapentin. Subgroup analysis based on surgical procedure, gabapentin dosing, or study quality could not explain the heterogeneity observed.

In 2007, Solak et al. evaluated gabapentin in patients with chronic post-thoracotomy pain (5). This study compared increasing gabapentin dosages with naproxen. The gabapentin was increased in a stepwise fashion during the period of treatment until all patients were on 2400 mg daily by the end of the study period. Patients in the naproxen group received 1000 mg daily in divided doses. At the conclusion of the 60-day trial, patients in the gabapentin group showed improved VAS pain scores and improved Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scores compared to patients in the naproxen group.

In 2006, Sihoe et al. evaluated gabapentin in the treatment of chronic pain after chest surgery (6). Twelve patients were chest trauma victims, 22 were status post video assisted thoracoscopic surgery (VATS), 8 had undergone open thoracotomies, and 3 had median sternotomies. Patients were started on a dose of gabapentin 300 mg daily and titrated up to a total dose of 900 mg daily for uncontrolled symptoms. At the conclusion of the study, 73% of patients reported a reduction in their pain score, and 42% reported a reduction of 50% or more.

In 2010, the Cochrane Library published a review of four RCTs evaluating single-dose gabapentin in doses from 250 to 500 mg in treating acute pain (7). Three of these studies used a third molar dental extraction model, and one involved major orthopedic surgery. All patients were given gabapentin in combination with opioids or NSAIDs. This review found that there was a significant decrease in narcotic requirement and less need for rescue medication in the gabapentin group. They noted the number needed to treat (NNT) for a 50% pain reduction was 11. They noted that this dose of gabapentin was inferior to other analgesics such as ibuprofen 400 mg, naproxen 50 mg, or acetaminophen 1000 mg. The authors of this review questioned whether a dose response could be demonstrated and whether the combination of gabapentin with other analgesics provided better pain relief than either alone.

Gabapentin has also been evaluated as part of a multi-modal pain management regimen. In 2013, Paul et al. included gabapentin in a regimen including morphine, ketorolac, and acetaminophen (8). They used a dose of 600 mg orally preoperatively followed by 200 mg every 8 hours during the postoperative period. They assessed morphine requirements and VAS pain scores both at rest and during movement over the first 72 hours following surgery. They found that the addition of gabapentin did not result in a significant decrease in morphine requirement, nor did it affect the VAS pain score. Gabapentin as part of a multi-modal pain regimen was also evaluated by Monks et al. in women receiving cesarean delivery. In this study, gabapentin was added to a regimen which included spinal anesthesia as well as postoperative narcotics (9). Patients received a dose of 600 mg orally preoperatively and 200 mg every 8 hours in the postoperative period. They found a statistically significant, but

small decrease of 7 mg of morphine consumption in the gabapentin group, but an increase in sedation. There was also a statistically significant, but small decrease in the VAS pain score. There were no statistically significant differences at 48 hours. The authors concluded that gabapentin is of questionable benefit when given as part of a multi-modal pain regimen after cesarean delivery.

In 2016, Mayo Clinic published a retrospective review looking at associations between preoperative variables and respiratory depression in PACU (10). They found an increased likelihood of respiratory depression with associated OR of 1.26 [1.02-1.58, P=0.04] following laparoscopic surgery in patients who had received gabapentin as part of their pain control regimen.

In 2020, the Canadian Perioperative Anesthesia Clinical Trials Group performed a meta-analysis of randomized controlled trials to determine the efficacy and risks of perioperative use of gabapentanoids including gabapentin and pregabalin (11). They included 281 trials resulting in a pooled group of 24,683 participants. They converted pain scaling to a 100-point scale with a reduction in pain of 10 considered to be clinically significant. At the 6 hour, 12 hour, 24 hour, 48 hour, and 72 hour time points, there was a pain reduction on the 100-point scale of less than 10 for each time point suggesting a minimal improvement in pain reduction. There was no significant difference in postoperative chronic pain in the gabapentinoid groups. There was a reduction in required opioid requirement in the 72 hours after surgery. There was a moderate increased risk of ataxia, falls, and visual disturbance in the gabapentinoid group as well as a low increased risk of delirium, respiratory depression, and dizziness. With minimal reduction in pain and an increased risk of adverse events, they concluded that gabapentanoids should be used cautiously in the perioperative period.

In 2021, Young et al. studied gabapentanoids and prolonged opioid use in patients over 65 years old (12). This was a retrospective cohort study of nearly 14,000 patients of which 21% were given preoperative gabapentanoids. They did not demonstrate a statistically significant difference in pain control among patients that received pre-operative gabapentinoids and those who did not nor a reduced risk of prolonged outpatient opioid use.

**REFERENCES**


1. Pandey CK, Sahay S, Gupta D, Ambesh SP, Singh RB, Raza M, Singh U, Singh PK; Preemptive gabapentin decreases postoperative pain after lumbar discoidectomy; *Can J Anesth* 2004; 51(10): 986-989.
2. Pandey CK, Navkar DV, Giri PJ, Raza M, Behari S, Singh RB, Singh U, Singh PK. Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar discectomy: a randomized, double blind, placebo-controlled study; *J Neurosurg Anesthes* 2005; 17(2): 65-68.
3. Kok-Yuen Ho, Tong J Gan, Ashraf S. Habib; Gabapentin and postoperative pain – a systematic review of randomized controlled trials; *Pain* 2006, 126: 91-101.
4. Peng PWH, Wijeysundera DN, Li CCF. Use of gabapentin for perioperative pain control – A meta-analysis; *Pain Research and Management* 2007; 12(2): 85-92.
5. Solak O, Metin M, Esme H, Solak O, Yaman M, Pekcolaklar A, Gurses A, Kavuncu V. Effectiveness of gabapentin in the treatment of chronic post-thoracotomy pain; *Eur J Cardiothoracic Surg* 2007; 32: 9-12.
6. Sihoe AD, Lee TW, Wan IY, Thung KH, Yim AP; The use of gabapentin for post-operative and post-traumatic pain in thoracic surgery patients; *Eur J Cardiothoracic Surg* 2006; 29(5): 795-799.
7. Straube S, Derry S, Moore RA, Wiffen PJ, McQuay HJ; Single oral gabapentin for established acute postoperative pain in adults; *Cochrane Database of Systematic Reviews* 2010; 12(5).
8. Paul JE, Nantha-Aree M, Buckley N, Cheng J, Thabane L, Tidy A, DeBeer J, Winemaker M, Wismer D, Punthake D, Avram V; Gabapentin does not improve multimodal analgesia outcomes for total knee arthroplasty: a randomized controlled trial; *Can J Anesth* 2013; 60:423-431.
9. Monks DT, Hoppe DW, Downey K, Shah V, Bernstein P, Carvalho JCA; A perioperative dose of gabapentin does not produce a clinically meaningful improvement is analgesia after cesarean delivery; Anesthesiology 2015; 123(2): 320-326.
10. Cavalcante AN, Sprung J, Schroeder DR, Weingarten TN. Multimodal analgesic therapy with gabapentin and its association with postoperative respiratory depression. *Anesth Analg*. 2017; 125(1):141-146.
11. 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. *Anesthesiology* 2020; 133(2):265-279.
12. Young JC, Dasgupta N, Chidgey BA, et al. Day-of-surgery gabapentinoids and prolonged opioid use: A retrospective cohort study of medicare patients using electronic health records. *Anesth Analg*. 2021; 133(5):1119-1128.