



## ARTICLE OF THE MONTH

### Preoperative Gabapentin Administration Improves Acute Postoperative Analgesia in Patients Undergoing Craniotomy: A Randomized Controlled Trial

Zeng M, Dong J, Lin N, Zhang W, Zhang K, Peng K, Wang D, Zhao Y, Peng Y, Han R.  
*J Neurosurg Anesthesiol.* 2019 Oct;31(4):392-398. doi: 10.1097/ANA.0000000000000533. PMID: 30134301.

Welcome to another session of the Article of the Month, July 2021. This month we discuss a study looking at the effects of perioperative administration of gabapentin on acute postoperative analgesia for patients undergoing a craniotomy. Our expert commentators this month are Una Srejjic, MD and Matthew Pearn, MD, PhD from University of California San Diego.

As always, readers are welcome to join us for further discussion and feedback on the SNACC [Twitter](#) feed, or on [Facebook](#).

- Oana Maties, MD, Shilpa Rao, MD, Amie Hoefnagel, MD, and Nina Schloemerkerper, MD

#### **Una Srejjic, MD - Biographical Sketch**

Dr. Una Srejjic is a Clinical Professor of Anesthesiology and Program Director of the Neuro-Anesthesia Fellowship Training Program at the University of California, San Diego UCSD. She has been in practice for 22 years. She completed her anesthesiology training at Baylor College of Medicine in Houston, Texas where she subsequently practiced for 11 years (Baylor College of Medicine Ben Taub General Hospital for two years, Level 1 Trauma, and then MD Anderson Cancer Center in Houston, Texas as a member of the Neuroanesthesia team for nine years). She then moved West and has been in the University of California system since 2011.

She joined the Neuroanesthesia Faculty at University of California, San Francisco UCSF where she did clinical work and clinical research for eight years and has since relocated to University of California, San Diego where she has been practicing in the Neuroanesthesia Group for three years. Dr. Srejjic's research interests lie in regional anesthesia and pain management in neurosurgery and she has been active in this field at UCSF/UCSD. She has several peer reviewed publications in highly regarded journals including Anesthesia and Analgesia and The British Medical Journal BMJ.

#### **Matthew Pearn, MD, PhD - Biographical Sketch**

Dr. Matthew Pearn has been a Clinician Scientist for more than 15 years. He is currently an Associate Professor of Anesthesiology and Researcher at UCSD. A former UCSF Medical School graduate, he completed his anesthesiology residency at UCSD. Dr. Pearn has published and serves as a reviewer on several highly regarded medical journals including the British Journal of Anesthesia and Neuroscience amongst others. Dr. Pearn's Academic/Research Interests

focus on the Basic Science of Anesthetic Neurotoxicity, and more specifically: The role of caveolin-1 on anesthetic-mediated neurotoxicity for which he holds a large research grant.

## Commentary

**Una Srejjic, MD and Matthew Pearn, MD, PhD**  
*University of California, San Diego*

The authors Zeng et al. report results of a randomized placebo controlled double blinded trial:

Preoperative Gabapentin Administration Improves Acute Postoperative Analgesia in Patients Undergoing Craniotomy in the Journal of Neurosurgical Anesthesiology Oct. 2019. This was a single center study (Beijing Tiantan Hospital) from China that looked at introducing gabapentin to the peri-operative multi-modal analgesia regimen in posterior fossa craniotomy patients (sub-occipital and sub-temporal), known to have higher rates of post-operative pain as compared to other types of craniotomies. One hundred and twenty-two patients were randomized to either placebo (B vitamin) or gabapentin in a dose of 600 mg (night before surgery) and 600 mg once two hours before surgery for a total of 1200 mg preoperatively.

### Primary Outcome:

1. Postoperative score on head movement at 24 hours

### Secondary Outcomes:

1. Postoperative pain score at other time points
2. Nausea and vomiting
3. Sedation
4. Analgesic consumption

### Results:

1. Gabapentin reduced postoperative pain scores at and before 24 hours
2. Gabapentin did NOT decrease postoperative nausea
3. Gabapentin decreased postoperative vomiting and rescue antiemetic
4. Gabapentin increased postoperative sedation at 2 hours
5. Gabapentin did NOT decrease postoperative opioid consumption

Although gabapentin did not decrease opioid consumption, it decreased pain scores at 24 hours and it decreased post-operative vomiting, without decreasing post-operative nausea. Sedation was increased post-operatively at two hours.

### Background

Prior to this publication, gabapentin had only been studied in craniotomy pain in two other studies. Misra et al.<sup>1</sup> found that pre-operative gabapentin 600 mg did not reduce pain scores or opioid consumption at 24 hours. Ture et al.<sup>2</sup> showed that 1200 mg/day of gabapentin for seven days decreased total morphine consumption and lowered pain scores. Other studies have shown that up to 80 % of patients experience moderate to severe pain up to 48 hours post craniotomy and are often under-treated.<sup>3</sup>

Previously published studies involving large numbers of patients concluded the following about the use of gabapentin in the peri-operative period:

- (1) Gabapentin is known to be opioid sparing.<sup>4</sup>
- (2) Although post-operative opioid use was reduced, peri-operative administration of gabapentin did not result in a reduction of postoperative delirium or hospital length of stay.<sup>5</sup>
- (3) Incidence of over sedation was not different between the placebo and gabapentin treated groups (preoperatively and post-operative days 1-3, 300 mg TID).<sup>5</sup>
- (4) Some individuals are sensitive to the sedating effects of Gabapentin.<sup>6</sup>
- (5) In a 2019 Cochrane Review, gabapentin and pregabalin showed low grade evidence of decreased pain at 12, 24, and 48 hours postoperatively.<sup>7</sup>

There is a paucity of studies investigating the question of perioperative gabapentin use in patients undergoing craniotomy. While there are many issues with the design, including the choice of placebo, the choice of anesthetic regimen, the dose

of gabapentin and the details of chronic pain history of the patients included, this study could serve as a solid pilot study for future investigations. That gabapentin appears to decrease a patient's perception of pain within the first 24 hours postop is promising. However, the data isn't strong enough at this point to alter how a provider treats post neurosurgical pain. Gabapentin administered peri-operatively appears to pose little side effects, so incorporating it into practice seems to have little downside. It would have been useful if the authors described whether the increased sedation at two hours post-operatively was clinically significant or changed the postoperative management in any way. Early sedation that hinders a good neurological exam and cognitive assessment post-extubation may mask important surgical complications: hemorrhage, cranial nerve dysfunction, seizure, and status epilepticus.

1. Misra et al., The Effect of Gabapentin Premedication on Postoperative Nausea, Vomiting, and Pain in Patients on Preoperative Dexamethasone Undergoing Craniotomy for Intracranial Tumors, *J Neurosurgical Anesthesiol*, 2013;25:386-391
2. Ture et al. The Analgesic Effect of Gabapentin as a Prophylactic Anticonvulsant Drug on Postcraniotomy Pain: a Prospective Randomized Trial, *Anesth Analg*. 2009;109:1625-1631.
3. Mordhorst et al. Prospective Assessment of Postoperative Pain After Craniotomy. *J Neurosurg Anesthesiol*. 2010; 22:202-206
4. Hurley, Cohen, Williams et al., The Analgesic Effects of Peri-Operative Gabapentin on Post-operative Pain: A Meta-Analysis, *Reg Anesth Pain Med*. May-June 2006;31(3): 237-47
5. J M Leung, Chen, Ames et al., Peri-Operative Gabapentin Does Not Reduce Post-Op Delirium in Older Surgical Patients: A Randomized Clinical Trial, *Anesthesiology* 2017 Oct; 127(4): 633-644. (UCSF RCT 750 patients randomized.)
6. Fleet, Dixon, Kuwornu et al. Gabapentin dose and the 30-day risk of altered mental status in older adults: A Retrospective population-based study. (2018) PLoS ONE 13(3). <https://doi.org/10.1371/journal.pone.0193134>
7. Galvin, Levy, Day and Gilron, Pharmacological Interventions for the Prevention of Acute Postoperative Pain in adults following Brain Surgery. DOI: 10.1002/14651858.CD011931.pub2