



ARTICLE OF THE MONTH

Perioperative Gabapentin Does Not Reduce Postoperative Delirium in Older Surgical Patients: A Randomized Clinical Trial

Leung JM, Sands LP, Chen N, Ames C, Berven S, Bozic K, Burch S, Chou D, Covinsky K, Deviren V, Kinjo S, Kramer JH, Ries M, Tay B, Vail T, Weinstein P, Chang S, Meckler G, Newman S, Tsai T, Voss V, Youngblom E; Perioperative Medicine Research Group. *Anesthesiology*. 2017 Jul 20 [Epub ahead of print]

This month's SNACC Article of the Month addresses the reduction of post-operative delirium, a common problem with potentially severe impact. Dr. Phillip Vlisides, this month's expert commentator, selected this article and provides insight into its significance.

Dr. Vlisides is an assistant professor of anesthesiology at the University of Michigan Medical School and serves as director of clinical neuroscience research in the Department of Anesthesiology. He completed an NIH-T32 fellowship in perioperative neuroscience research and served as University of Michigan site principal investigator for the PODCAST Trial, which examined the effect of ketamine on the prevention of postoperative delirium. He is currently leading a sub-study analysis of the PODCAST dataset to explore novel strategies for delirium risk reduction. Dr. Vlisides and his clinical research team also explore the impact of cerebrovascular disease on perioperative outcomes and advanced neuromonitoring techniques in the perioperative setting.

We welcome comments and discussion on this topic via SNACC's [LinkedIn](#) feed, the [Twitter](#) feed or on [Facebook](#).

~ Adrian Pichurko, MD; Oana Maties, MD; and Nina Schloemerkemper, MD

Commentary

Phillip E. Vlisides, MD

Delirium is a pressing public health concern, affecting up to 70% of adult surgical patients.¹ Furthermore, delirium is associated with increased mortality, persistent cognitive decline, prolonged hospital length of stay, and increased healthcare costs.²⁻⁴ In a large, single-center randomized controlled trial, Leung *et al.*⁵ assessed the effects of gabapentin on postoperative delirium, opioid use, and pain in older adults undergoing non-cardiac surgery. The trial was based on exciting pilot data that demonstrated reduced delirium and a trend towards decreased opioid use in surgical patients receiving gabapentin.⁶

Patients were randomized to placebo (N=347) or gabapentin (N=350), 900 mg, preoperatively and for the first three postoperative days. Delirium was the primary outcome, and incidence during the first three postoperative days did not significantly differ between the placebo (22.4%) and gabapentin (20.8%) groups ($P=0.30$). When

further stratifying by type of surgery or anesthesia, delirium incidence remained similar among subgroups. Gabapentin administration did reduce postoperative opioid administration (assessed by morphine equivalents), particularly during the first postoperative day (median 6.7 mg [IQR 1.3, 20.0] gabapentin group, 6.7 mg [2.7, 24.8] placebo group, $P=0.04$). Postoperative pain scores were not significantly different between groups, though patients experiencing high postoperative pain (visual analog scale 7-10) experienced higher rates of delirium (19.5%; 95% CI 14.9-24.1%) compared to those experiencing low pain scores (visual analog scale 1-3) (9.1%; 95% CI 6.3%-11.9%; $P=0.0001$).

In summary, preoperative gabapentin use did not reduce postoperative delirium incidence. Daily gabapentin administration did seem to confer a postoperative neurologic effect, as opioid administration was significantly reduced. Pain scores, however, remained the same for both groups across all three postoperative days. These findings suggest that pain itself may be a significant driver of postoperative delirium, as previously supported by the authors.⁷ Pain has been shown to interfere with cognitive flexibility in older adults,⁸ further supporting this notion. The authors also allude to the possibility that regional anesthetic techniques may have independently reduced opioid burden, and thus, mitigated delirium risk. Opioid use has indeed been associated with delirium,⁷ and pain and opioid administration may form a dynamic neural interplay that increases delirium risk, particularly given that opioids modulate cortical cholinergic transmission.⁹ Lastly, given the growing number of negative trials that explored various preventions for delirium, further investigation is needed to better understand the neurophysiologic substrates of delirium and related altered states of consciousness.

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