



## ARTICLE OF THE MONTH

### Intraoperative Infusion of Dexmedetomidine for Prevention of Postoperative Delirium and Cognitive Dysfunction in Elderly Patients Undergoing Major Elective Non-cardiac Surgery: A Randomized Clinical Trial

Deiner S, Luo X, Lin HM, Sessler DI, Saager L, Sieber FE, Lee HB, Sano M; and the Delirium Writing Group, Jankowski C, Bergese SD, Candiotti K, Flaherty JH, Arora H, Shander A, Rock P. *JAMA Surg.* 2017 Aug 16;152(8):e171505. doi: 10.1001/jamasurg.2017.1505. Epub 2017 Aug 16.

Welcome to the November 2017 installment of the SNACC Article of the Month! The featured study by Deiner *et al* is looking at the intraoperative use of dexmedetomidine in an elderly population undergoing non-cardiac surgery and its effects on the incidence and severity of postoperative delirium and postoperative cognitive decline. Dr Wei Zhou, this month's expert commentator, is sharing his take on this article he kindly selected.

Dr. Zhou is an assistant professor of anesthesiology in the Department of Anesthesia and Perioperative Care at UCSF. His research interest is on the basic mechanisms underlying anesthetics. Currently, he is studying the orexinergic neurons in the lateral hypothalamus, which are involved in sleep-wake control and energy homeostasis. Narcolepsy, a chronic sleep disorder, is thought to be caused by the lack of orexin neuropeptides. Dr. Zhou is hoping to find a way to facilitate postoperative recovery and to decrease the incidence of delirium by utilizing the orexin system.

We encourage all of our readers to tell us what they think by joining us on [LinkedIn](#) feed, the [Twitter](#) feed or on [Facebook](#).

~ Oana Maties, MD, Adrian Pichurko, MD and Nina Schloemerkerper, MD

### Commentary

Wei Zhou, MD, PhD

Delirium, an acute deterioration of mental status, occurs in 15-53% of older patients postoperatively and is associated with a high one-year mortality rate (35-40%).<sup>1</sup> Its etiology is unclear, but it is likely due to multiple factors related to baseline cognitive function, underlying disease, surgery and anesthesia. In the recent issue of

*JAMA Surgery*, Deiner *et al* published the results from a multicenter randomized clinical trial and concluded that intraoperative dexmedetomidine does not prevent postoperative delirium.<sup>2</sup>

Dexmedetomidine, an  $\alpha_{2A}$ -adrenergic agonist, is widely used in ICU and has been shown to decrease the incidence of ICU related delirium.<sup>3</sup> Deiner *et al* designed their study to evaluate whether intraoperative infusion of dexmedetomidine reduces postoperative delirium. Sixty-eight-year-old and older patients, ASA I – III, undergoing major elective noncardiac surgery, were selected for the study. The treatment group received 0.5  $\mu\text{g}/\text{kg}/\text{h}$  dexmedetomidine intraoperatively (no loading dose) that continued for up to two hours in PACU. Delirium was assessed using the Confusion Assessment Method (CAM) daily up to five days. Further cognitive function tests were done at three and six months. A total of 404 patients were randomized, with 197 patients being allocated to the dexmedetomidine group and 207 to the saline group. Twenty-three patients in the dexmedetomidine group (12.2%) and 23 in the saline group (11.4%) developed delirium. There was no significant difference in severity (mild, moderate or severe) by treatment group or by difference in subtype.

The initial plan for the study was to enroll over 700 patients, but the study was terminated early due to futility based on an interim analysis of primary outcome (postoperative delirium) in 2014. Baseline and surgical factors statistically significantly associated with postoperative delirium include educational level, baseline mild cognitive impairment, surgical procedure (orthopedic, spine, thoracic, urologic), surgery time (>four hours), and presence of PACU delirium. The analysis of the secondary outcome (postoperative cognitive decline) did not show significant treatment effect from dexmedetomidine either.

The results of this study contrast with previous reports on the effects of dexmedetomidine on postoperative delirium and agitation. Previous studies on delirium in the ICU setting compared dexmedetomidine and propofol sedation in cardiac surgery patients and found a significant reduction in the incidence, duration and severity of delirium in the dexmedetomidine group.<sup>3</sup> Additionally, a recent study comparing intraoperative dexmedetomidine versus propofol for sedation in patients having orthopedic surgery with regional anesthesia suggested that dexmedetomidine has benefit in reducing postoperative agitation.<sup>5</sup> There are a number of reports on the prevention of emergence delirium by the use of dexmedetomidine in pediatric population.<sup>6,7</sup>

Another randomized control trial studying the prevention of postoperative delirium in elderly patients after non-cardiac surgery showed significant benefit of low dose (0.1  $\mu\text{g}/\text{kg}/\text{h}$ ) dexmedetomidine infusion administered from postoperative admission to ICU until 8:00 am on POD 1 in decreasing the occurrence of delirium in the first seven days after surgery.

Dexmedetomidine works on the arousal pathways in the brain and is known to reduce MAC of other general anesthetics such as sevoflurane.<sup>4</sup> One limitation of this study is that the authors did not take the MAC reducing effect into account which potentially led to the patients in the treatment group having deeper level of anesthesia than the patients in the control group.

The results of this study are probably not surprising. The timing and dosage are always two important factors to consider when determining the effectiveness of a drug. However, given the multifactorial etiology of postoperative delirium, its management likely involves multiple components. Further research in the pathogenesis of postoperative delirium is required in order to answer the complex question of its prevention and treatment.

## References:

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