

Author Response: Continuous Infusion of Propofol or Dexmedetomidine should not be the First Choice to Prevent Postoperative Delirium in Patients after Hip Fracture

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Keywords: Critically ill patients, Dexmedetomidine, Geriatric population, Hip fracture surgery, Postoperative delirium, Propofol.
Indian Journal of Critical Care Medicine (2025); 10.5005/jp-journals-10071-24869

Dear Editor,

We sincerely appreciate the thoughtful comments and insights provided by Finsterer and Marques.¹ In response to our article, "A comparison of efficacy between low-dose dexmedetomidine and propofol for prophylaxis of postoperative delirium in elderly patients undergoing hip fracture surgery: A randomized controlled trial".²

Thank you for highlighting the importance of monitoring for delirium immediately after anesthesia. To clarify that, as outlined in our methods, we excluded participants with a Richmond Agitation-Sedation Scale (RASS) of -2 or lower before starting sedation in the intensive care unit (ICU) (Supplementary data 1). Additionally, as shown in Table 2 of our manuscript, no cases of delirium were reported at the starting point (0-hour), which reinforces the robustness of our inclusion criteria and baseline assessments.

We agree that propofol-related infusion syndrome (PRIS) is a serious complication associated with propofol infusion. However, PRIS is extremely rare to occur with low-dose propofol infusions, such as those used in our study. Specifically, we used propofol infusion dose 0.5–1.75 mg/kg/hr from 8 p.m. to 6 a.m. (10 hours). Propofol-related infusion syndrome is most commonly observed in patients receiving continuous propofol infusions at doses exceeding 4 mg/kg/hr for more than 48 hours. This threshold is significantly higher and longer than the dosing regimen applied in our study, reducing the likelihood of PRIS development. These findings are consistent with existing clinical evidence, which supports the safety of lower-dose, short-duration propofol infusions.^{3–5}

While some animal studies have shown that propofol can induce post-traumatic stress disorder (PTSD) in mice, some studies have indeed suggested that propofol may have a protective effect against PTSD.⁶ In human patients, the risk of PTSD from propofol use is not well-established, and the potential effects are not a primary concern in clinical practice. Propofol is widely used in low doses for sedation, especially in the operating room and ICU, without significant evidence of inducing PTSD. Moreover, agitated critically ill patients who can recall delusional memories are at risk of developing PTSD. Optimizing sedation may help reduce this risk.

Several studies have shown that the use of midazolam, a benzodiazepine, in ICU settings increases the incidence of delirium. The clinical practice guidelines for the prevention of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU (PADIS guidelines) also recommend avoiding the use of benzodiazepines when possible.⁷ These guidelines emphasize the importance of minimizing the risk of delirium in critically ill

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How to cite this article: Ekkapat G, Chokengarmwong N. Author Response: Continuous Infusion of Propofol or Dexmedetomidine should not be the First Choice to Prevent Postoperative Delirium in Patients after Hip Fracture. *Indian J Crit Care Med* 2025;29(1):88–89.

Source of support: Nil

Conflict of interest: None

patients, as benzodiazepines like midazolam can impair cognitive function and contribute to agitation, leading to higher delirium rates. Alternatives such as dexmedetomidine and propofol are increasingly preferred, as they offer sedative effects with a lower risk of delirium and cognitive impairment.

In conclusion, preventing delirium is a multifaceted process that requires a comprehensive, multidisciplinary approach. No single intervention can effectively prevent delirium in all patients. Rather, a combination of strategies, such as optimizing sedation practices, minimizing the use of benzodiazepines, and incorporating non-pharmacological interventions like early mobilization and cognitive stimulation, has been shown to reduce delirium incidence. The selection of sedative agents should be tailored to the individual patient's needs and the specific clinical context. Ultimately, effective delirium management hinges on continuous assessment, individualized care, and collaboration across healthcare teams to ensure the best outcomes for patients.

We sincerely thank you once again for your valuable input and engaging with our work. We hope this response provides clarity regarding our study findings and limitations.

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