# LETTER TO THE EDITOR

# Author Response

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**Keyword:** Cognitive dysfunction, Delirium, Melatonin, Post-cardiac surgery. *Indian Journal of Critical Care Medicine* (2024): 10.5005/jp-journals-10071-24619

#### Dear Editor,

Drs Suresh and Magoon have raised really pertinent points in their discussion of the index meta-analysis.<sup>1,2</sup> As rightly pointed out by them, assessment of preoperative cognitive function can control for a major potential covariate in the causation of postoperative delirium.<sup>3</sup> However, as they demonstrate with an informative table, trials actually measuring and reporting it are very few. Further, in the two trials objectively screening preoperative cognition, patients with observed deficits were excluded. Poor preoperative cognitive reserve is an important risk factor for postoperative delirium.<sup>4</sup> Exclusion of this high-risk cohort leaves aside the patients with the highest possible benefit from pharmacological prevention of postoperative delirium. Hence, it is our opinion that objective documentation of preoperative cognitive reserve is important, but the exclusion of patients with preoperative cognitive deficits runs the risk of overestimating the treatment effect of the intervention pragmatically. Moreover, the current paucity of trials assessing cognition makes evidence synthesis including only trials with preoperative cognitive assessment unfeasible.

Secondly, on-pump and off-pump surgeries constitute two distinct pathophysiology of cerebral insult.<sup>5</sup> Thus, they should be dealt with separately, and such a subgroup analysis was planned. However, as demonstrated in the table, studies reporting the primary outcome exclusively in the off-pump subgroup were very less, precluding a sufficiently powered analysis.

We welcome the points raised by Drs Suresh and Magoon, as they further expose the paucity of quality evidence about pharmacological neuroprotection in the perioperative milieu of cardiac surgeries, as well as the lack of standardized and clinically relevant interventions, outcomes, and management. This underlines the need for more high-quality trials using standardized interventions and outcomes in high-risk cohorts as recommended in our index study.

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How to cite this article: Niyogi SG, Naskar C, Singh A, Kumar B, Grover S. Author Response. Indian J Crit Care Med 2024;28(2):188. Source of support: Nil

Conflict of interest: None

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