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Letter to the Editor

REVISITING A COMPARATIVE STUDY OF MELATONIN WITH PLACEBO IN ATTENUATION OF HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND INTUBATION

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Dear Editor,

An indolamine called melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone primarily synthesized and secreted by the pinecone-shaped gland of the cerebrum, named the conarium or epiphysis cerebri, from the amino acid tryptophan. Melatonin itself was first isolated in 1958 from the bovine pineal gland by Lerner et al., while the 17th-century philosopher René Descartes hypothesized the pineal gland of the brain (epiphysis cerebri) as the seat of the human soul—a structure paleontologists have described as an ancestral "third eye" (1–5). We do pen these lines concerning the article entitled *"A comparative study of melatonin with placebo in attenuation of hemodynamic responses to laryngoscopy and intubation,"* published in *Sanamed*, volume 19 (6). Jamwal et al. (6) reveal and address an important clinical issue—the attenuation of hemodynamic responses during laryngoscopy and endotracheal intubation—and explore the potential role of oral melatonin as premedication.The findings suggest that oral melatonin at doses of 3 mg and 6 mg effectively attenuate these pressor changes and also provides analgesic and anxiolytic effects, with the 6 mg dose showing greater effectiveness.These outcomes are valuable and align with other research indicating melatonin's potential benefits in the perioperative period. However, while the results are promising, we wish to highlight a significant methodological aspect mentioned by the authors themselves, which warrants careful consideration when interpreting the findings. The study design allocated patients to Melatonin 3 mg, Melatonin 6 mg, and Placebo groups at the discretion of the attending anesthesiologist, rather than through a formal randomization process. As the authors correctly point out, this lack of randomization might introduce selection bias due to subjective considerations during allocation. Although the demographic characteristics, ASA grade, and Mallampati grading were reported as comparable across the groups at baseline, the non-random allocation method means that other potentially confounding factors, not explicitly measured or reported, could have differed systematically between the groups, influencing the outcomes observed. Furthermore, the study population was limited to patients undergoing elective surgery for supratentorial tumors. While this provides a focused cohort, it also limits the generalizability of these findings to patients undergoing other types of surgery or those with different underlying pathological conditions or comorbidities beyond those listed as exclusion criteria.In addition, the authors acknowledge that the size and location of these specific tumors could potentially influence postoperative recovery characteristics. Moreover, they appropriately suggest that future studies should be conducted using randomized controlled trials with larger sample sizes and standardized methodologies to further assess melatonin's efficacy and establish dose-response relationships. We support this recommendation. As such, a robust randomized design is crucial to minimize bias and provide more definitive evidence regarding melatonin's role in attenuating hemodynamic responses and providing anxiolysis and analgesia in a broader surgical population. In essence, the study provides interesting preliminary evidence supporting the use of oral melatonin premedication. Nevertheless, the methodological limitation regarding the lack of randomization may be a critical factor when interpreting

these findings. To this end, we look forward to future research, ideally using randomized controlled trial designs, that will build upon these findings and provide more explicit guidance on the clinical application of melatonin in perioperative care. This issue merits further investigation. We thank Jamwal et al. (6) for their valuable study on melatonin.

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