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LETTER TO THE EDITOR

Reply to Kawasaki et al. randomized clinical trial

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To the Editor:

We read with interest the recent article by Kawasaki et al., which compared the efficacy of sugammadex in reversing rocuronium-induced neuromuscular blockade (NMB) under remimazolam versus propofol anesthesia [1]. The authors should be commended for conducting a well-designed, prospective randomized trial addressing an emerging clinical question, especially as remimazolam gains wider anesthetic use due to its favorable pharmacokinetic profile. This study offers valuable insight into the compatibility and safety of remimazolam with neuromuscular blockade reversal using sugammadex.

We especially appreciate the authors' methodological clarity in the anesthesia protocol, neuromuscular monitoring, and timing of sugammadex administration. The findings support that remimazolam does not significantly delay NMB reversal compared with propofol, a conclusion that is reassuring for clinicians exploring remimazolam as an alternative to intravenous agents with longer half-lives. However, we respectfully suggest that several elements of the study would benefit from further clarification or contextualization to enhance scientific rigor and clinical relevance.

First, we found the reporting of the primary outcome definition recovery of train-of-four (TOF) ratio $\geq 90\%$ to be appropriate and consistent with current guidelines [2]. However, there is ambiguity around the influence of flumazenil, which was administered at the discretion of the attending anesthesiologist in the remimazolam group. In addition, the timing and use of flumazenil warrant closer examination. It remains unclear how the administration was standardized across patients, specifically regarding timing in relation to discontinuation of remimazolam and the onset of emergence. The proportion of patients who received flumazenil and the potential impact on recovery parameters were not reported. Given that flumazenil is a benzodiazepine antagonist, variability in its timing and administration may confound the assessment of remimazolam's recovery profile and the time to achieve TOF ratio of 1.0. It would be valuable to clarify whether all patients received flumazenil, and at what interval relative to drug discontinuation and TOF assessment. Future studies might benefit from explicitly defining and controlling this variable.

Although the authors mention that electromyography was used to monitor the abductor digiti minimi muscle, it is worth noting that previous studies have shown significant differences in TOF count and recovery times depending on the muscle group and monitoring modality [2–4]. The clinical interpretations for TOF should be made cautiously by the readers and to further support reproducibility. For example, acceleromyography of the adductor pollicis tends to yield earlier recovery signals than electromyography of the abductor digiti minimi muscle. Without concurrent monitoring or discussion of these differences, the clinical interpretation of TOF values and comparability with prior studies may be limited. Readers should interpret these values with caution.

In conclusion, this study represents an important step in evaluating remimazolam's compatibility with sugammadex, and the findings are reassuring for anesthesiologists navigating new pharmacologic combinations. With minor clarifications and expanded discussion on real-world application, this work could serve as a foundation for future multi-center trials evaluating efficacy and safety in broader surgical populations.

Sincerely,
Shuyu Zhang.

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References

1. Kawasaki T, Fujimoto M, Hirata N. Comparison of reversal of rocuronium-induced neuromuscular blockade with sugammadex under remimazolam versus propofol anesthesia: a randomized clinical trial. J Anesth [Internet]. 2025. https://doi.org/10.1007/s00540-025-03517-7.
2. Blobner M, Hunter JM, Meistelman C, Hoeft A, Hollmann MW, Kirmeier E, Lewald H, Ulm K. Use of a train-of-four ratio of 0.95 versus 0.9 for tracheal extubation: an exploratory analysis of POPULAR data. Br J Anaesth. 2020;124(1):63–72.
3. Sessler CN. Train-of-four to monitor neuromuscular blockade? Chest. 2004;126(4):1018–22.
4. Lagneau F, Benayoun L, Plaud B, Bonnet F, Favier J, Marty J. The interpretation of train-of-four monitoring in intensive care: what about the muscle site and the current intensity? Intensive Care Med. 2001;27(6):1058–63.