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LETTER TO THE EDITOR

Reply to the letter by Shuyu Zhang

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To the Editor

We sincerely appreciate the thoughtful and constructive comments provided by Dr. Zhang on our recently published article "Comparison of reversal of rocuronium-induced neuromuscular blockade with sugammadex under remimazolam versus propofol anesthesia: a randomized clinical trial" [1].

One of the key issues raised is the influence of flumazenil. In our study, flumazenil was administered as needed by the attending anesthesiologist. Therefore, as Dr. Zhang correctly pointed out, the timing and use of flumazenil varied among patients. Specifically, among the 13 patients in the remimazolam group included in the analysis, flumazenil was used in 10, with three of them receiving it after extubation. However, we believe that this variation did not influence the primary outcome of our study, because remimazolam was discontinued once the train-of-four (TOF) ratio had recovered to > 90% of the baseline value, as described in the Methods section, and flumazenil was administered thereafter. The median time from the discontinuation of remimazolam to the administration of flumazenil was 10.5 min (range, 2–19 min).

In addition, TOF responses in our study were not assessed after the discontinuation of anesthetic drugs or the administration of flumazenil, as TOF stimulation can cause patient discomfort or pain. Further, although low-current stimulation causes less discomfort, it compromises monitoring accuracy [2]. In future, well-designed protocols are needed to clarify the time course of TOF responses after flumazenil administration.

Another key issue highlighted was the difference in recovery of TOF responses depending on the muscle group and monitoring modality. Although the potential limitation of using electromyography at the abductor digiti minimi muscle was acknowledged prior to the study, we conducted the study using this monitoring method due to its advantages (e.g., no need for normalization and immobilization) [3]. A recent clinical study also demonstrated that electromyographic neuromuscular monitoring is less variable than acceleromyography, and is comparable to mechanomyography [4], which is the "gold standard" for neuromuscular monitoring [5], supporting the appropriateness of our method. However, as Dr. Zhang pointed out, our findings should be interpreted with caution in clinical practice when using acceleromyography at the adductor pollicis muscle, since acceleromyographic TOF responses are generally reported to recover more rapidly than electromyographic TOF responses [6–8]. We fully agree that concurrent monitoring using both modalities enhances scientific rigor and clinical relevance.

We would like to once again express our sincere appreciation to Dr. Zhang for facilitating this valuable discussion and for providing us with the opportunity to address the concerns raised. We look forward to further contributing to research on the compatibility of remimazolam or flumazenil with sugammadex.

Declarations

Conflict of interest T. Kawasaki has no conflict of interest; M. Fujimoto has received speaker's fees from MSD Inc, Century Medical Inc, and Nihon Kohden Corporation. However, none of these entities provided financial support for his participation in this study; N. Hirata has received honoraria and speaker's fees from Mundipharma, Maruishi

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Pharmaceutical Corporation, and Nihon Kohden Corporation. However, none of these entities provided financial support for his participation in this study. He has also received speaker's fees from Asahi Kasei Corporation and Otsuka Pharmaceutical Factory.

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