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LETTER TO THE EDITOR

Exploration of the safety and efficacy of flumazenil

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To the Editor,

Remimazolam has been available for general anesthesia in Japan since 2020, and the number of studies on this novel anesthetic has been increasing in recent years. It is an ultra-short-acting benzodiazepine and its properties, such as its ability to be antagonized by flumazenil [1] and its relatively low hemodynamic effects [2], have attracted significant clinical attention. The use of remimazolam has also been expanded to pediatric patients [3]. However, several studies have reported the risk of residual sedation after antagonizing remimazolam with flumazenil and have recommended caution from pharmacokinetic and pharmacodynamic perspectives [4, 5]. We are in full agreement with the recommendation that automatic/casual or routine-like use of remimazolam based on flumazenil administration should be avoided.

At the same time, we are concerned that this recommendation will be taken as instruction, to be strictly followed. Clinicians should not hastily conclude that the use of remimazolam-flumazenil combination should be avoided, but rather explore how it can be used more effectively. What should be avoided is using its antagonists without sufficient care. This novel anesthetic technique should not be hastily restricted as it has significant clinical potential when used with proper management. Remimazolam has unique benefits that are not provided by other anesthetics, including those mentioned above, and proper combined use of remimazolam with flumazenil allows for precise control of emergence from anesthesia.

In conclusion, we believe that the safe and effective use of flumazenil in remimazolam anesthesia should be explored, not restricted. To this end, we are currently conducting research focusing on the potential of remimazolam in areas such as deep extubation in general anesthesia [6], and as a part of this research, a randomized controlled trial named "rapid sequence awakeness method", that is, remimazolam-assisted deep extubation with flumazenil in pediatric anesthesia is ongoing (clinical trial registry: jRCTs021240059).

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Declarations

Conflict of interest The authors declare that they have no competing interests.

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References

1. Sneyd JR. A new pharmacological approach for tracheal intubation? Br J Anaesth. 2024;133:16–8.
2. Luo Z, Cao H, Luo L, Chen L, Feng D, Huang G. Comparison of remimazolam tosilate and propofol during induction and maintenance of general anesthesia in patients undergoing laparoscopic

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cholecystectomy: a prospective, single center, randomized controlled trial. BMC Anesthesiol. 2024;24:226.
3. Tobias JD. Clinical experience with remimazolam in pediatric anesthesiology: An educational focused review. Paediatr Anaesth. 2024;34:1095–106.
4. Obara S. Simulation of residual sedation effect of remimazolam: pharmacokinetic-pharmacodynamic simulation can be an additional standard anesthesia monitoring method. J Anesth. 2022;36:167–70.
5. Obara S, Kamata K, Nakao M, Yamaguchi S, Kiyama S. Recommendation for the practice of total intravenous anesthesia. J Anesth. 2024;38:736–46.
6. Araki H, Inoue S. Switching to remimazolam followed by flumazenil may be a promising combination for deep extubation. JA Clin Rep. 2023;9:52.