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RESPONSE TO LETTER

Preserving Airway Reflexes During Awake Intubation: A Cautionary Note on Deep Sedation Protocols [Response to Letter]

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Dear editor

We would like to sincerely thank Dr. Ahmet Yüksek and Dr. Mehmet Yılmaz for their valuable comments and constructive suggestions on our paper, Efficacy and Safety of Remimazolam versus Dexmedetomidine and Midazolam in Awake Endotracheal Intubation for Difficult Airway Patients: A Randomized Controlled Study.

We highly appreciate their attention to optimizing sedation strategies for awake tracheal intubation (ATI), a key clinical issue. We also thank them for recognizing the strengths of our study, including the challenges of conducting a prospective randomized controlled trial in patients with difficult airways, the rationale behind including 90 ATI patients, and the work done to clearly define the ideal characteristics of sedative drugs.

In response to their comments, we fully agree with the core issues raised. Current airway management guidelines emphasize the use of minimal to moderate sedation during ATI to maintain the patient's airway protective reflexes and spontaneous ventilation.[1] Based on the clinical characteristics of the patients in our study and the sedation protocol design, we set the ideal sedation depth at a MOAA/S score of 2–3, with the actual sedation target being MOAA/S = 2. This approach allowed us to achieve moderate sedation, improving intubation tolerance, while always prioritizing airway safety and ventilation function. To ensure patient safety, we have outlined specific preventive measures, including regular reassessment of the MOAA/S score. In cases of over-sedation (MOAA/S $\leq$ 1), sedation medication was immediately stopped, and flumazenil (0.2 mg intravenously) was administered. If the sedation depth did not improve after 1 minute, additional doses were administered to minimize the risk of respiratory depression and excessive sedation.

We also agree with the authors' suggestion that some ATI patients may not require sedation, and the emphasis should be on a personalized minimal sedation strategy. This suggestion is valuable for optimizing clinical ATI sedation practices. Furthermore, we have carefully reviewed the "Difficult Airway Society 2025 Guidelines for Management of Unanticipated Difficult Tracheal Intubation in Adults" provided by the authors, which offered important insights and will guide the further optimization of sedation strategies in future research, ensuring better alignment with clinical practice.[2]

The pharmacological properties of different sedative drugs vary significantly, and these differences determine their suitable administration methods.[3] In this study, we adopted different administration protocols for remimazolam, midazolam, and dexmedetomidine based on their pharmacological characteristics. Remimazolam and midazolam were administered via intravenous bolus injection, while dexmedetomidine was given via continuous intravenous infusion. This approach ensured that each drug could exert its full sedative effect, ensuring both the scientific validity of the study design and patient safety. We also acknowledge that titration to the preset sedation threshold after a fixed initial dose could introduce potential bias when comparing drugs with different pharmacokinetic characteristics and administration methods. Furthermore, the differences in

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administration methods may cause the time required to reach the desired sedation level to be influenced more by the drug administration strategy than by the drug's intrinsic pharmacological properties.

Regarding the choice of first-attempt intubation success rate as the primary outcome, we understand that this outcome is influenced by multiple factors, including the effects of the sedative drugs, the clinical experience of the operator, the patient's airway anatomical features, and the adequacy of local anesthesia. In our study, all intubations were performed by anesthesiologists with extensive clinical experience, which likely increased the success rate but may limit the external validity of our findings.

On the issue of blinding, this study employed a double-blind design, with independent drug administrators to minimize bias. However, due to the different administration methods (dexmedetomidine via intravenous infusion and remimazolam and midazolam via bolus injection), it was not possible to fully blind the anesthesiologists. We were able to maintain effective blinding between remimazolam and midazolam. We have taken extensive measures to reduce potential bias in the blinding process. We agree with the authors' perspective, and we will further refine the blinding design in future research to reduce the impact of the differences in administration methods, further enhancing the internal validity of the study.

Regarding the interpretation of sedation depth and patient comfort, the authors' point that "initial sedation levels may differ across groups" is of great value. While we made efforts to control for baseline characteristics to ensure comparability between groups, clinical studies inevitably involve individual differences, which may slightly affect the interpretation of the outcomes. Additionally, regarding the confounding factor of sulfentanyl use in all groups, we used sulfentanyl based on routine clinical practice to assist with sedation and alleviate pain during intubation.

We recognize that excluding patients with significant comorbidities may limit the generalizability of the study's conclusions. The exclusion of such patients in this study was primarily to ensure maximum patient safety during the study, based on our sedation scoring system, while also minimizing the interference of comorbidities on the study outcomes.

Once again, we sincerely thank Dr. Yüksek and Dr. Yılmaz for their valuable comments and the journal for providing us with the opportunity to respond. Their suggestions offer crucial guidance for our future research and will help refine sedation strategies for ATI. We will carefully consider these recommendations in future studies, continuing to optimize research design and protocols to provide more reliable and clinically relevant evidence for the management of difficult airways.

Disclosure

The authors declare no conflicts of interest regarding this communication.

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