

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

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Dear editor

We read with great interest the randomized controlled trial by Tang et al entitled “Efficacy and Safety of Remimazolam versus Dexmedetomidine and Midazolam in Awake Endotracheal Intubation for Difficult Airway Patients”.¹ This study addresses a clinically important and evolving topic, about optimization of sedation strategies for awake tracheal intubation (ATI). The comparison of remimazolam (an agent not yet extensively studied in this context) with commonly used sedatives such as dexmedetomidine and midazolam represents a valuable and timely contribution to the literature.

The authors should be commended for several strengths. First, conducting a prospective randomized study in a difficult airway population is inherently challenging, and the inclusion of 90 patients undergoing ATI is noteworthy.^{2,3} Second, the manuscript clearly outlines the desirable characteristics of an ideal sedative agent in this setting with rapid onset, maintenance of spontaneous ventilation, hemodynamic stability, and rapid recovery. Which provides a solid conceptual framework.

Nevertheless, we would like to raise several points for consideration that may help contextualize the findings and guide future research.

A central concern relates to the sedation strategy employed. The study targeted a MOAA/S score ≤ 2 , which corresponds to deep sedation. However, current airway management principles emphasize minimal to moderate sedation during ATI in order to preserve airway reflexes and spontaneous ventilation.⁴ In fact, the authors themselves define the ideal sedation depth as MOAA/S 2–3, yet the protocol required progression to deeper levels, even including disappearance of the corneal reflex. This approach may not reflect routine clinical practice and could introduce safety concerns, particularly in a population already at risk of difficult ventilation. Moreover, some patients undergoing ATI may not require sedation at all, highlighting the importance of individualized, minimal sedation strategies.

Related to this, the use of fixed initial doses followed by titration until a deep sedation threshold is reached may introduce bias when comparing agents with inherently different pharmacokinetics and administration routes. In the present study, midazolam and remimazolam were administered as boluses, whereas dexmedetomidine was given as an infusion. Comparing the time required to reach a predefined sedation level under these conditions may therefore be influenced more by the administration strategy than by intrinsic drug properties. Indeed, small modifications in dosing (eg., a lower midazolam dose) could plausibly alter the observed differences, raising questions about the robustness and reproducibility of the findings.

The choice of primary outcome as first-attempt intubation success rate also deserves further reflection. While clinically meaningful, this outcome is multifactorial and depends not only on sedation but also on operator experience, airway anatomy, and adequacy of topical anesthesia. In this study, all intubations were performed by a highly experienced anesthesiologist, which likely contributed to the very high success rates, particularly in the remimazolam group. This

may limit the external validity of the results and reduce the ability of the study to detect differences attributable solely to the sedative agents.

The blinding methodology, although carefully described, may also be difficult to maintain in practice. The use of different administration techniques (bolus versus infusion) and the need for ongoing sedation assessment in the same clinical environment may have allowed unintentional unblinding. Additionally, there appears to be an inconsistency, as the study is described as double-blind in the methods, while the limitations section acknowledges the absence of blinding. Clarification of this point would strengthen confidence in the internal validity of the study.

Another important consideration is the interpretation of sedation depth and comfort outcomes. The reported MOAA/S values suggest that patients in different groups may not have started from comparable sedation levels, which could influence both comfort scores and time to intubation readiness. For example, deeper initial sedation in some groups may facilitate intubation but at the cost of safety, while lighter sedation may prolong preparation time. This raises the possibility that the groups were not evaluated under equivalent clinical conditions.

The use of concomitant sufentanil in all groups, although reflective of clinical practice, introduces an additional confounding factor. Without detailed reporting of opioid effects or standardized titration, it becomes difficult to isolate the independent contribution of each sedative agent to respiratory and hemodynamic outcomes. Similarly, the assessment of adverse events and patient comfort relies on relatively simple and non-validated scales, limiting the granularity of these findings.

We also note that the study population excludes patients with significant comorbidities, who often represent a substantial proportion of individuals with difficult airways in real-world settings. This may limit the generalizability of the safety conclusions, particularly given that respiratory depression was observed in the remimazolam group, albeit in a small number of patients.

Finally, while the authors highlight the pharmacokinetic advantages of remimazolam, the discussion occasionally juxtaposes criticisms of midazolam with statements emphasizing pharmacological similarities between the two agents. A more consistent interpretation of these properties would further strengthen the manuscript.

In conclusion, this study provides valuable preliminary evidence supporting the potential role of remimazolam in ATI and contributes meaningfully to an area of ongoing clinical interest. At the same time, the findings should be interpreted in light of the methodological considerations outlined above, particularly regarding sedation strategy, outcome selection, and comparability between groups. We believe that future studies incorporating guideline-consistent sedation targets, standardized administration protocols, and broader patient populations will help to further clarify the optimal role of remimazolam in difficult airway management.

We congratulate the authors for their important work and believe that their study will stimulate further research in this field.

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