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Sequential use of Midazolam and Dexmedetomidine for long term sedation may reduce weaning time in selected critically ill, mechanically ventilated patients: A randomized controlled study

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Background: Current sedatives have different side effects in long-term sedation. The sequential use of midazolam and dexmedetomidine for prolonged sedation may have distinct advantages. We aimed to evaluate the efficacy and safety of the sequential use of midazolam and either dexmedetomidine or propofol, and the use of midazolam alone in selected critically ill, mechanically ventilated patients.

Methods: This single center, randomized controlled study was conducted in medical and surgical ICUs in a tertiary, academic medical center. Patients enrolled in this study were critically ill, mechanically ventilated adult patients receiving midazolam, with anticipated mechanical ventilation for ≥ 72 hours. They passed the spontaneous breathing trial (SBT) safety screen, underwent a 30-min-SBT without indication for extubation and continued to require sedation. Patients were randomized into group M-D (midazolam was switched to dexmedetomidine), group M-P (midazolam was switched to propofol), and group M (sedation with midazolam alone), and sedatives were titrated to achieve the targeted sedation range (RASS -2 to 0).

Results: Total 252 patients were enrolled. Patients in group M-D had an earlier recovery, faster extubation, and more percentage of time at the target sedation level than those in group M-P and group M (all $P < 0.001$). They also experienced less weaning time (25.0 hours vs. 49.0 hours; HR 1.47, 95% CI 1.05 to 2.06; $P = 0.025$), and a lower incidence of delirium (19.5% vs. 43.8%, $P = 0.002$) than patients in group M. Recovery ($P < 0.001$), extubation ($P < 0.001$), and weaning time ($P = 0.048$) in group M-P were shorter than in group M, while the acquisition cost of sedative drug was more expensive than other groups (both $P < 0.001$). There was no significant difference in adverse events among these groups (all $P > 0.05$).

Conclusions: The sequential use of midazolam and dexmedetomidine was an effective and safe sedation strategy for long-term sedation and could provide clinically relevant benefits for selected critically ill, mechanically ventilated patients.

Trial Registration: clinicaltrials.gov, NCT02528513.

Recent Publications:

1. Zhang, Q., Xu, L., Zhang, Y. et al. A novel ViewRNA in situ hybridization method for the detection of the dynamic distribution of Classical Swine Fever Virus RNA in PK15 cells. *Virology* 14, 81 (2017). <https://doi.org/10.1186/s12985-017-0734-4>
2. Liu, H., Liu, J., Wang, S. et al. Enterolactone has stronger effects than enterodiol on ovarian cancer. *J Ovarian Res* 10, 49 (2017). <https://doi.org/10.1186/s13048-017-0346-z>
3. Ma, G., Jiang, A., Luo, Y. et al. Aquaporin 1 is located on the intestinal basolateral membrane in *Toxocara canis* and might play a role in drug uptake. *Parasites Vectors* 12, 243 (2019). <https://doi.org/10.1186/s13071-019-3500-1>

Biography

Zhou has her expertise in respiratory care and analgesia and sedation in critical care. After years of experiences in clinical practice, teaching, and research in West China Hospital of Sichuan University, as the principal research member, she developed a novel sedation strategy—the sequential use of midazolam and dexmedetomidine based on ventilator weaning process in selected critically ill, mechanically ventilated patients for improving outcomes. This approach was built based on the previous sequential use of midazolam and propofol. This sedation strategy was a safe and more effective sedation strategy and may provide clinical benefits for selected critically ill, mechanically ventilated patients.

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