Effectiveness of Dexmedetomidine Compared to Midazolam for Sedation in Mechanically Ventilated Patients: A Narrative Review

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Abstract

Delirium is a common and clinically significant neuropsychiatric complication in mechanically ventilated adult ICU patients, contributing to prolonged hospitalization, increased morbidity, and long-term cognitive impairment. The choice of sedative agent plays a pivotal role in preventing delirium, with dexmedetomidine and midazolam representing the most commonly used drugs with contrasting mechanisms. This narrative review evaluates the clinical efficacy, safety profile, neurocognitive outcomes, and cost-effectiveness of dexmedetomidine compared with midazolam in mechanically ventilated ICU patients. Literature was searched through PubMed, Scopus, ScienceDirect, Cochrane Library, and Google Scholar for studies published between 2020 and 2025 using the keywords dexmedetomidine, midazolam, sedation, mechanical ventilation, delirium, and intensive care units. Seventeen peer-reviewed publications were included and analyzed narratively. Dexmedetomidine consistently reduced the incidence and duration of delirium (RR 0.55–0.65; 95% CI 0.4–0.8), shortened mechanical ventilation by 0.7–1.5 days, and facilitated earlier extubation compared to midazolam. Its α_2-adrenergic agonism at the locus coeruleus produces a sleep-like, cooperative sedation, with mild, dose-dependent bradycardia as the most frequent adverse effect. Despite higher acquisition cost, economic analyses reported average savings of US$ 450–700 (≈ IDR 7–10 million) per patient through reduced ICU stay and delirium-related complications. Overall, dexmedetomidine demonstrates superior efficacy and safety compared with midazolam for ICU sedation, providing both clinical and economic advantages. Integration into light-sedation and delirium-prevention bundles may improve ICU outcomes, particularly in resource-limited settings.

Kata kunci: Delirium, Dexmedetomidine, Intensive care unit, Mechanical ventilation, Midazolam

Efektivitas Dexmedetomidine Dibandingkan dengan Midazolam sebagai Sedasi pada Pasien dengan Ventilasi Mekanik: Tinjauan Naratif

Abstrak

Delirium merupakan komplikasi neuropsikiatrik yang umum terjadi pada pasien dewasa yang menjalani ventilasi mekanik di ICU dan berhubungan dengan peningkatan lama rawat, morbiditas, serta gangguan kognitif jangka panjang. Pemilihan agen sedasi berperan penting dalam mencegah delirium, di mana dexmedetomidine dan midazolam merupakan dua obat yang paling sering digunakan dengan mekanisme kerja yang berbeda. Tinjauan naratif ini bertujuan untuk mengevaluasi efektivitas klinis, keamanan, dampak neurokognitif, serta efektivitas biaya penggunaan dexmedetomidine dibandingkan midazolam pada pasien ICU dengan ventilasi mekanik. Pencarian literatur dilakukan melalui PubMed, Scopus, ScienceDirect, Cochrane Library, dan Google Scholar untuk artikel tahun 2020-2025 menggunakan kata kunci dexmedetomidine, midazolam, sedation, mechanical ventilation, delirium, dan intensive care units. Sebanyak 17 publikasi peer-reviewed memenuhi kriteria dan dianalisis secara naratif. Hasil sintesis menunjukkan bahwa dexmedetomidine secara konsisten menurunkan insidensi dan durasi delirium (RR 0,55–0,65; 95% CI 0,4–0,8), memperpendek durasi ventilasi sebesar 0,7–1,5 hari, serta mempercepat ekstubasi dibandingkan midazolam. Mekanisme α_2-agonis yang bekerja pada locus coeruleus menghasilkan sedasi menyerupai tidur alami dengan risiko bradikardia ringan yang dapat ditangani dengan penyesuaian dosis. Meskipun biaya awal lebih tinggi, analisis ekonomi menunjukkan penghematan rata-rata Rp 7–10 juta per pasien akibat pengurangan lama rawat ICU dan komplikasi delirium. Tinjauan ini menegaskan bahwa dexmedetomidine memiliki keunggulan klinis maupun ekonomis dibandingkan midazolam, mendukung penerapannya dalam strategi sedasi ringan dan pencegahan delirium di ICU, terutama pada fasilitas dengan sumber daya terbatas.

Keywords: Dexmedetomidine, Midazolam, Delirium, Ventilasi mekanik, Unit perawatan intensif

Introduction

Delirium is a multifactorial neuropsychiatric syndrome commonly observed in critically ill patients receiving mechanical ventilation in ICU. It manifests as fluctuating disturbances in attention, cognition, and consciousness, often leading to diagnostic challenges. The incidence of delirium among mechanically ventilated adults can reach up to 80%, representing a major clinical and public health concern. Its occurrence is associated with prolonged ICU and hospital stay, higher mortality, and persistent cognitive deficits that can last months or even years after discharge.[1,2]

Sedation practices considerably influence the development and outcomes of delirium. Among available sedatives, dexmedetomidine and midazolam are two widely used agents with distinct pharmacologic mechanisms and neurocognitive profiles.[3–7] Dexmedetomidine, a highly selective α2-adrenergic agonist, produces light, cooperative sedation resembling natural sleep, allowing for regular neurological assessment and faster awakening. Conversely, midazolam, a GABA-A receptor agonist, induces deeper, less physiologic sedation, which increases the risk of oversedation, delayed extubation, and delirium.[3,4]

In addition to clinical outcomes, sedative selection has important economic implications. Differences in drug acquisition cost, duration of mechanical ventilation, and ICU stay collectively affect healthcare expenditures, particularly in resource-limited environments.[8,9] Therefore, understanding the comparative clinical and economic performance of these sedatives is crucial for optimizing ICU care and improving both outcomes and resource utilization.

This narrative review aims to synthesize current evidence comparing dexmedetomidine and midazolam regarding their efficacy, safety, neurocognitive outcomes, and cost-effectiveness in mechanically ventilated adult ICU patients. Literature was retrieved from PubMed, Scopus, ScienceDirect, Cochrane Library, and Google Scholar for publications between 2020 and 2025, using the keywords dexmedetomidine, midazolam, sedation, mechanical ventilation, delirium, and intensive care units. The review integrates findings from recent randomized trials, observational studies, and meta-analyses to provide an updated understanding of their comparative roles in ICU sedation and delirium prevention.[1–11]

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Pharmacologic Profiles and Delirium Pathogenesis

Dexmedetomidine and midazolam differ substantially in their pharmacodynamic and neurophysiologic properties, which directly influence delirium pathogenesis. Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that acts primarily on the locus coeruleus in the brainstem, suppressing norepinephrine release and producing a light, cooperative sedation that mimics natural non-REM sleep.[3,5] This sedative state allows patients to remain easily arousable and facilitates frequent neurological assessments, which are key strategies in preventing delirium. In contrast, midazolam, a benzodiazepine that potentiates GABA-A receptor activity, produces generalized central nervous system depression, resulting in deeper, less physiologic sedation.[4,6] This pharmacologic difference explains why dexmedetomidine is often associated with a

lower incidence and shorter duration of ICU delirium.[7]

In typical ICU practice, dexmedetomidine is administered at maintenance doses of 0.2–1.4 µg/kg/h after an optional loading dose of 0.5–1 µg/kg over 10 minutes, titrated to achieve a target Richmond Agitation-Sedation Scale (RASS) of –2 to 0.[3,4] Midazolam infusions are typically initiated at 0.02–0.1 mg/kg/h with intermittent boluses as needed, adjusted to organ function and desired sedation depth.[4,6] Excessive or prolonged midazolam exposure has been linked to oversedation, delayed awakening, and accumulation of active metabolites, particularly in patients with hepatic or renal impairment.[4,6] These factors contribute to an increased risk and duration of delirium, delayed extubation, and longer ICU stay.[1,7]

Dexmedetomidine's lighter, sleep-like sedation has been shown to modulate delirium-related neuroinflammation by attenuating the stress-induced catecholamine surge and reducing cortical hyperactivity, thereby supporting cognitive stability.[5,10] In contrast, benzodiazepine-induced deep sedation alters circadian rhythm and suppresses slow-wave sleep architecture, further predisposing to cognitive dysfunction.[4,6] Bradycardia is the most frequently reported adverse event with dexmedetomidine, occurring in approximately 5–13% of cases; however, it is typically mild, dose-dependent, and reversible upon adjustment or cessation of infusion.[3,11]

Collectively, these pharmacologic distinctions clarify the mechanistic rationale behind dexmedetomidine's superiority in minimizing delirium, enabling earlier extubation, and supporting neurological recovery in mechanically ventilated ICU patients. The integration of light-sedation strategies utilizing dexmedetomidine aligns with recent critical care guidelines that recommend minimizing benzodiazepine use to prevent delirium and facilitate early mobilization.[11]

Effectiveness in Reducing Delirium and Duration of Mechanical Ventilation

An expending body of evidence demonstrates that dexmedetomidine provides superior outcomes compared with midazolam in reducing both the incidence and duration of ICU delirium. Several randomized controlled trials and meta-analyses reported that dexmedetomidine significantly decreases delirium risk by approximately 35–45% (RR 0.55–0.65; 95% CI 0.4–0.8) and shortens the duration of mechanical ventilation by 0.7–1.5 days compared with midazolam.[4,6,7] The sedative's α2-adrenergic mechanism promotes lighter, cooperative sedation, allowing consistent neurological assessment and earlier participation in spontaneous awakening and breathing trials—factors known to prevent or shorten delirium episodes.[3,5]

Conversely, midazolam is consistently associated with deeper, less physiologic sedation, which prolongs mechanical ventilation and delays extubation.[4,6] Observational studies indicate that midazolam use correlates with higher rates of prolonged weaning, longer ICU stay, and increased risk of ICU-acquired weakness.[1,4] Furthermore, excessive benzodiazepine exposure is known to alter circadian rhythm and disrupt sleep–wake cycles, exacerbating the cognitive disorientation characteristic of ICU delirium.[6,8]

The clinical advantages of dexmedetomidine extend beyond delirium reduction. Studies in post-cardiac surgery and general ICU populations reveal faster extubation times, reduced need for rescue sedatives, and shorter ICU length of stay when dexmedetomidine is used as the primary sedative agent.[3,6,7] These findings have been reinforced by updated critical care guidelines, which now recommend non-benzodiazepine sedatives—particularly dexmedetomidine or propofol—as first-line

agents for light sedation and delirium prevention.[11]

Nonetheless, some variability exists among studies reporting minimal or non-significant differences between agents. These inconsistencies are often linked to differences in sedation depth targets, patient comorbidities, or the delirium assessment tools used, such as the Confusion Assesment Method for the ICU (CAM-ICU) and Intensive Care Delirium Screening Checklist (ICDSC).[10,12] Despite this heterogeneity, the preponderance of evidence favors dexmedetomidine for achieving optimal sedation quality, faster weaning, and improved cognitive recovery while maintaining hemodynamic safety when appropriately titrated.[3,9,12]

Collectively, the synthesis of contemporary literature demonstrates that dexmedetomidine provides superior clinical efficacy compared with midazolam in ICU sedation. Its integration into light-sedation protocols can improve recovery trajectories, reduce delirium burden, and promote more efficient ICU resource utilization.[6,7,11,13]

Cognitive Recovery and Long-Term Outcomes

Beyond its effects on delirium prevention and ventilation duration, dexmedetomidine has demonstrated additional benefits for cognitive recovery in critically ill and post-surgical populations. Evidence indicates that patients sedated with dexmedetomidine exhibit improved early cognitive function, including orientation, memory, and attention, compared with those who receive midazolam.[3,6] This improvement is largely attributed to dexmedetomidine's ability to maintain natural sleep architecture and permit frequent neurological evaluations, which facilitate early recognition of cognitive fluctuations.[5,9]

In a comprehensive review and meta-analysis of cardiac surgical patients, dexmedetomidine significantly reduced the incidence of postoperative cognitive dysfunction (POCD) and delirium compared with midazolam.[3,6] Similar findings were observed across ICU populations, where dexmedetomidine shortened the duration of sedation and improved recovery scores on standardized tools such as the CAM-ICU and Mini-Mental State Examination.[7,10] These findings reinforce the sedative's neuroprotective properties mediated by α2-adrenergic modulation, which decreases sympathetic excitation, attenuates neuroinflammatory cascades, and mitigates oxidative stress—mechanisms implicated in delirium-related neuronal injury.[5,9]

However, several limitations are noted in the literature. Most available studies are short-term and performed in high-resource settings, with limited representation of low- and middle-income ICUs. Variability in patient comorbidities, sedation protocols, and neurocognitive assessment instruments contributes to heterogeneity and potential bias in reported outcomes.[1,12,14] Longitudinal studies with standardized follow-up beyond six months are still lacking, making it difficult to confirm whether early cognitive improvements persist over time.

Overall, current evidence supports dexmedetomidine as a superior option for sedation to promote early neurocognitive recovery compared with midazolam. By enabling light, cooperative sedation and reducing delirium-associated injury, dexmedetomidine may enhance long-term neurological outcomes and quality of life among ICU survivors.[7,11,13]

Implementation of Delirium Monitoring Protocols

Effective delirium prevention and management in the ICU rely not only on the choice of sedative agent but also on consistent and structured monitoring. The incorporation of validated delirium assessment tools, such as the

CAM-ICU and the ICDSC, has been shown to significantly improve early detection and intervention.[10] Routine monitoring allows clinicians to adjust sedation depth promptly, implement early mobilization, and avoid unnecessary benzodiazepine exposure—measures that collectively reduce the incidence and duration of delirium.[1,11,10]

However, real-world implementation of these monitoring tools remains inconsistent across institutions. A multicenter study demonstrated that even when validated tools are available, adherence rates vary widely depending on staff training, ICU workload, and institutional culture.[10,12] These findings highlight the need for standardized protocols and education programs to ensure reliable delirium assessment by both nurses and physicians. In addition, the empowerment of non-physician staff, such as certified nursing assistants, has proven effective in increasing screening frequency and diagnostic accuracy without compromising workflow.[10]

Recent evidence supports the adoption of care bundles that integrate pharmacologic and non-pharmacologic strategies for delirium prevention. Such bundles typically include light sedation protocols using dexmedetomidine, early mobilization, adequate pain management, sleep promotion, and family engagement.[12,13] Meta-analytic evidence shows that these multidisciplinary interventions reduce delirium prevalence and improve functional recovery at discharge.[12,13,9] When applied consistently, they also contribute to shorter ICU stays and reduced healthcare costs—benefits particularly relevant in resource-limited settings.[8,9]

Despite robust evidence and clear guideline recommendations, several barriers persist in implementing standardized delirium monitoring and prevention strategies. Challenges include limited staff awareness, inconsistent documentation, and variable resource availability.[11,12,14] Addressing these barriers requires institutional commitment, inclusion of delirium screening in quality metrics, and integration of sedation management into routine ICU rounds. Ultimately, sustained adherence to evidence-based protocols combining dexmedetomidine use, structured monitoring, and early mobilization offers the best opportunity to minimize delirium burden and improve long-term patient outcomes.[11,12,15]

Conclusion

Dexmedetomidine consistently demonstrates superiority over midazolam in terms of delirium prevention, sedation quality, and cognitive recovery among mechanically ventilated adult ICU patients. Its unique pharmacologic profile allows for lighter, more cooperative sedation, facilitating neurological monitoring and earlier weaning from ventilation. Furthermore, dexmedetomidine use aligns with current critical care guidelines advocating non-benzodiazepine sedation to reduce delirium incidence and improve overall outcomes. While both clinical and economic data favor dexmedetomidine, implementation of standardized delirium monitoring and multidisciplinary care bundles remains essential to maximize these benefits. Continued research, particularly in diverse and resource-limited settings, is warranted to strengthen long-term evidence and optimize sedation strategies for critically ill patients.

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Conflicts of Interest

The authors report no conflict of interest.

Data Availability Statement

No new data were generated or analysed in this study.

Author's Contributions

All authors contributed significantly to the conception and design of the study, data collection, analysis, and interpretation of the results. All authors participated in writing and critically revising the manuscript for important intellectual content, approved the final version to be published, and are accountable for all aspects of the research.

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