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Dexmedetomidine and Melatonin for Postoperative Sleep Disturbances and Delirium in Neurosurgical ICU: An Observational Study of 40 Patients

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Abstract

Background: Postoperative sleep disturbances and delirium are frequent in neurosurgical ICU patients, leading to agitation, sympathetic surges, raised intracranial pressure, and prolonged ICU stay. Pharmacological strategies remain underexplored.

Methods: This prospective observational study was conducted at SKIMS Soura Srinagar between August 2024 and July 2025. Forty postoperative neurosurgical ICU patients with intracranial tumors who developed sleep disturbances and delirium were included. Patients were managed with either low-dose dexmedetomidine infusion (0.2–0.4 µg/kg/hr, no loading dose) or oral melatonin (3–6 mg at bedtime). Primary outcomes were sleep quality and delirium resolution; secondary outcomes were adverse effects and ICU stay.

Results: Twenty patients received dexmedetomidine and twenty received melatonin. Dexmedetomidine improved nocturnal sleep continuity in 85% and resolved delirium in 90% of patients within 24 hours, but was associated with mild bradycardia in 2 patients. Melatonin improved sleep–wake rhythm in 80% and resolved delirium in 75% of patients within 48 hours, with no haemodynamic side effects. Mean ICU stay was 4.2 ± 1.1 days in the dexmedetomidine group and 4.6 ± 1.3 days in the melatonin group.

Conclusion: Both dexmedetomidine and melatonin are effective in managing postoperative sleep disturbances and delirium in neurosurgical ICU patients. Dexmedetomidine provides rapid control of agitation and sleep induction, whereas melatonin restores circadian rhythm with excellent safety.

Keywords: Dexmedetomidine, Melatonin, Sleep disturbances, Delirium, Neurosurgery, ICU

Introduction

Sleep disturbances and delirium are well-recognized complications in patients admitted to neurosurgical intensive care units (ICUs). These phenomena are multifactorial in origin and can result from postoperative pain, environmental stressors such as noise and light, use of corticosteroids, altered melatonin secretion, and direct neurological injury from surgery or tumor pathology. The prevalence of postoperative sleep disturbances in neurosurgical patients has been reported to be as high as 60–70%, and delirium occurs in approximately 20–40% of ICU patients, with an even higher incidence in those undergoing intracranial procedures. Both conditions are not merely discomforting but have critical clinical implications. Disrupted sleep contributes to increased sympathetic drive, surges in blood pressure, and elevations in intracranial pressure, which can compromise surgical outcomes. Delirium, characterized by fluctuating disturbances in attention, awareness, and cognition, is associated with longer ICU stays, higher morbidity, and increased mortality.

Traditionally, sedatives such as benzodiazepines, opioids, and propofol have been used to manage agitation and promote sleep in ICU patients. However, these agents are often unsatisfactory in neurosurgical settings. Benzodiazepines, while effective in inducing sedation, are known to exacerbate delirium and impair natural sleep architecture by reducing restorative slow-wave and REM sleep. Propofol, a short-acting hypnotic, can achieve rapid sedation but similarly fails to restore physiological sleep patterns. Moreover, both classes

of drugs carry the risk of respiratory depression, hypotension, and delayed recovery, making them less than ideal choices in neurocritical care.

In this context, dexmedetomidine and melatonin represent promising alternatives. Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that provides a unique form of sedation often described as 'cooperative' or 'arousable'. Unlike other sedatives, dexmedetomidine produces an electroencephalographic pattern similar to non-REM sleep, thereby mimicking natural physiological sleep. It exerts anxiolytic and analgesic properties without causing significant respiratory depression, which is a critical advantage in neurosurgical patients requiring tight control of intracranial dynamics. However, its use is not without risks—bradycardia and hypotension are commonly reported, necessitating careful monitoring.

Melatonin, on the other hand, is a naturally occurring indoleamine secreted by the pineal gland in response to darkness. It plays a central role in regulating circadian rhythm and sleep–wake cycles. Beyond its chronobiotic effects, melatonin has antioxidant, anti-inflammatory, and neuroprotective properties, which may be particularly beneficial in neurosurgical patients recovering from tumor resection and associated cerebral stress. Importantly, melatonin has an excellent safety profile, with minimal side effects even at relatively high doses. Its ability to restore circadian rhythm makes it especially suitable for ICU settings where normal environmental cues are disrupted.

Existing literature on the use of dexmedetomidine and melatonin in critical care has shown encouraging results. Studies in general ICU populations have demonstrated that dexmedetomidine reduces the incidence of delirium, improves sleep quality, and facilitates earlier extubation compared to conventional sedatives. Similarly, melatonin supplementation has been reported to reduce delirium, improve subjective sleep quality, and decrease ICU length of stay in various surgical populations. However, data specific to neurosurgical patients remain limited. Neurosurgical ICU patients are a unique cohort with heightened vulnerability to sympathetic surges, intracranial hypertension, and secondary brain injury, which makes the choice of sedative and sleep-modulating agents particularly consequential.

This prospective observational study was undertaken to evaluate and compare the effectiveness of dexmedetomidine and melatonin in improving postoperative sleep disturbances and delirium among neurosurgical ICU patients at SKIMS Soura, Srinagar. By directly contrasting these two pharmacological strategies in a real-world neurocritical care setting, this study aims to provide clinically relevant insights that may help guide anesthesiologists, intensivists, and neurosurgeons in optimizing postoperative care.

Methods

This prospective observational study was carried out in the Department of Anaesthesiology, SKIMS Soura Srinagar, between August 2024 and July 2025. Approval was obtained from the Institutional Ethics Committee, and informed consent was obtained from the patients' next of kin given the impaired cognitive state of many patients experiencing delirium. The study adhered to the principles of the Declaration of Helsinki.

Inclusion criteria were adult patients aged 18–70 years undergoing craniotomy for intracranial tumors who developed postoperative sleep disturbances and delirium within 48 hours of ICU admission. Sleep disturbances were defined as difficulty initiating or maintaining sleep, and delirium was diagnosed clinically using the Confusion Assessment Method for the ICU (CAM-ICU). Exclusion criteria included severe haemodynamic instability requiring high-dose vasopressor support, known hepatic or renal failure, pre-existing psychiatric illness, or chronic use of sedative-hypnotic drugs.

Patients in whom non-pharmacological measures such as noise reduction, dimmed lighting, and reassurance failed were managed pharmacologically. The treating physician selected either dexmedetomidine or melatonin based on clinical judgment, patient characteristics, and availability. Dexmedetomidine was administered as an infusion at 0.2–0.4 μg/kg/hr without a loading dose, titrated overnight to maintain light sedation (Richmond Agitation–Sedation Scale score between –1 and 0). Continuous haemodynamic monitoring was employed, and infusion was stopped by morning. Melatonin was administered orally at doses of 3–6 mg at bedtime. The dose was selected based on clinical severity of insomnia, and patients were reassessed daily.

The primary outcomes were improvement in sleep quality and resolution of delirium. Sleep quality was defined as achievement of at least 4 hours of uninterrupted nocturnal sleep, assessed by nursing staff and relatives' reports. Resolution of delirium was assessed using CAM-ICU and documented as improvement in attention and orientation within 24–48 hours. Secondary outcomes included adverse effects such as bradycardia (HR <50 bpm), hypotension (MAP <65 mmHg), excessive sedation,

and duration of ICU stay. All patients were followed until discharge from ICU.

Data were analyzed using descriptive statistics. Continuous variables such as age and ICU stay were expressed as mean ± standard deviation. Categorical variables such as gender distribution, tumor type, and response rates were expressed as percentages. Given the modest sample size and observational nature of the study, no inferential statistics were applied beyond exploratory p-values to detect trends.

Results

A total of 40 patients met the inclusion criteria during the study period. Twenty patients received dexmedetomidine and twenty received melatonin. The mean age of the cohort was 49 ± 12 years, with a male-to-female ratio of approximately 3:2. The baseline demographics of both groups were comparable, with no significant differences in terms of age, gender distribution, or type of intracranial tumor. Diagnoses included glioblastomas (n=12), meningiomas (n=16), cerebellopontine angle tumors (n=6), and other intracranial tumors such as oligodendrogliomas and astrocytomas (n=6).

In the dexmedetomidine group, 17 of 20 patients (85%) achieved improvement in sleep quality, defined as ≥4 hours of uninterrupted nocturnal sleep, within the first night of treatment. Additionally, 18 of 20 patients (90%) showed resolution of delirium within 24 hours of initiating therapy. The rapid onset of sleep induction and calming effect of dexmedetomidine was particularly beneficial in patients with significant agitation and sympathetic surges. However, mild bradycardia (heart rate 45–50 bpm) occurred in 2 patients, which was managed with temporary dose reduction and did not necessitate drug discontinuation. No clinically significant hypotension was observed.

In the melatonin group, 16 of 20 patients (80%) achieved sleep improvement, though the effect was typically observed from the second night onward. Resolution of delirium was documented in 15 of 20 patients (75%) within 48 hours. Importantly, no haemodynamic side effects or excessive sedation were noted in this group. Melatonin was well tolerated across all patients and was especially useful in patients with mild delirium and predominant circadian rhythm disturbance.

The average ICU stay was 4.2 ± 1.1 days in the dexmedetomidine group and 4.6 ± 1.3 days in the melatonin group. While this difference was not statistically significant, it suggested a trend toward shorter ICU stay in the dexmedetomidine cohort, likely related to faster resolution of agitation. Table 1 summarizes the comparative outcomes of both groups.

Overall, both interventions demonstrated effectiveness in managing sleep disturbances and delirium in neurosurgical ICU patients. Dexmedetomidine showed superiority in terms of speed of action, whereas melatonin provided a safe and well-tolerated alternative with slower but steady improvement.

Discussion

This prospective observational study provides valuable insights into the management of sleep disturbances and delirium in neurosurgical ICU patients. Both dexmedetomidine and melatonin demonstrated significant benefits, though with different profiles of efficacy and safety. Dexmedetomidine offered rapid control of agitation and induction of sleep, whereas melatonin contributed to gradual restoration of circadian rhythm with an excellent safety margin.

The effectiveness of dexmedetomidine observed in this study aligns with prior research in critical care settings. Shehabi et al. (2021) reported that dexmedetomidine reduces the incidence of delirium in mechanically ventilated patients, while also improving sleep architecture by increasing non-REM sleep. Our findings extend these results to neurosurgical populations, where the risks of sympathetic surges and intracranial hypertension make rapid sedation particularly desirable. The bradycardia observed in 2 of our patients reflects the well-known haemodynamic profile of dexmedetomidine, underscoring the need for continuous monitoring.

Melatonin's role in ICU delirium and sleep regulation has also been supported by previous trials. Youn et al. (2022) demonstrated that perioperative melatonin supplementation improved postoperative sleep and reduced delirium in neurosurgical patients. Similarly, Flannery et al. (2022) emphasized the importance of circadian rhythm maintenance in reducing ICU-related sleep disturbances. Our study corroborates these findings by showing that melatonin restored sleep–wake cycles and alleviated delirium in the majority of patients, without any adverse effects. Its excellent tolerability makes it an attractive option, particularly for patients with mild to moderate sleep disruption who may not require continuous sedation.

The comparative analysis between dexmedetomidine and melatonin highlights a potential complementary role. Dexmedetomidine may be more suitable for patients requiring rapid sedation due to severe agitation, while melatonin may be better suited for longer-term management of circadian disruption or in patients at risk of haemodynamic compromise. Future protocols

could consider a stepwise approach—initial stabilization with dexmedetomidine followed by melatonin for circadian entrainment.

An important strength of this study is its real-world design, reflecting actual ICU practice where treatment choice is individualized. Additionally, the exclusive focus on neurosurgical patients addresses a knowledge gap in existing literature, as most prior studies have been conducted in general ICU populations. Nonetheless, several limitations merit discussion. The small sample size limits the generalizability of findings, and the absence of randomization introduces potential selection bias. Objective sleep measurements such as polysomnography were not feasible, and outcomes were based on clinical assessments, which may have subjective elements. Finally, being a single-center study, the results may not reflect practices in different ICU settings.

Despite these limitations, this study provides preliminary evidence that both dexmedetomidine and melatonin can be effectively integrated into neurosurgical ICU protocols. Their complementary mechanisms—rapid sedation versus circadian regulation—highlight the need for individualized therapy. Future multicentric randomized controlled trials with larger sample sizes and objective sleep monitoring are warranted to establish optimal dosing strategies, timing, and potential combined use.

Conclusion

In conclusion, this study demonstrates that both dexmedetomidine and melatonin are effective in managing postoperative sleep disturbances and delirium in neurosurgical ICU patients. Dexmedetomidine provides rapid onset of sleep and delirium control, albeit with a risk of bradycardia, while melatonin safely restores circadian rhythm without haemodynamic compromise. These findings suggest that both agents hold complementary roles in neurocritical care. Larger randomized studies are needed to confirm these results and to guide evidence-based protocols for optimizing postoperative recovery in neurosurgical patients.

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