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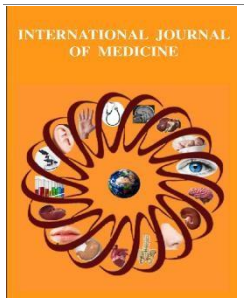

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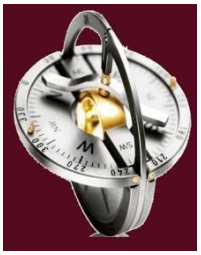

Research Article

Effectiveness of different sedation protocols in critically ill patients on mechanical ventilation

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Abstract

Background: Sedation is vital for comfort and safety in mechanically ventilated ICU patients, but excessive or inappropriate sedation can prolong ventilation and increase complications. Optimizing sedation protocols is essential to improve outcomes. ***Objective***: To compare the effectiveness and safety of three commonly used sedation agents, propofol, midazolam, and dexmedetomidine in critically i ll patients requiring mechanical ventilation. ***Methods***: This prospective, randomized comparative study was conducted at Gulbarga Institute of Medical Sciences, Kalaburagi India and included 105 ICU patients. Participants were randomly divided into three groups: propofol-based, midazolam-based, and dexmedetomidine-based sedation. ***Results***: Both dexmedetomidine and propofol were more effective than midazolam. The mean duration of ventilation was 4.2 ± 1.6 days with dexmedetomidine, 4.8 ± 1.9 days with propofol, and 6.3 ± 2.4 days with midazolam (p = 0.001). Delirium incidence was lowest with dexmedetomidine (8.6%), moderate with propof ol (14.3%), and highest with midazolam (28.6%). ICU stay was also shorter with dexmedetomidine (8.1 ± 2.4 days) compared to midazolam (10.4 ± 3.3 days) (p = 0.01). Dexmedetomidine caused mild, manageable bradycardia (17.1%), while propofol had the fastest onset (15.6 ± 3.8 minutes) and stable hemodynamics. ***Conclusion***: Both dexmedetomidine and propofol provide superior sedation quality and faster recovery compared to midazolam. Dexmedetomidine offers the added advantage of minimizing delirium and reducing ICU stay, making it the preferred agent for light, protocol-based sedation in mechanically ventilated patients.

Keywords: Sedation, dexmedetomidine, propofol, midazolam, mechanical ventilation, ICU outcomes, delirium, light sedation.

Introduction:

Sedation is a critical component of care for patients in the intensive care unit (ICU) who require mechanical ventilation. It serves multiple essential purposes, including alleviation of anxiety, reduction of pain and agitation, improvement of ventilator synchrony, and prevention of self-extubation or other harmful patient behaviors. However, while sedation improves comfort and safety, it is a double-edged sword, as both over-sedation and under-sedation can negatively affect outcomes [1]. Excessive sedation is linked to prolonged mechanical ventilation, delirium, hemodynamic instability, and increased mortality, whereas inadequate sedation can result in agitation, accidental extubation, and cardiopulmonary stress [2]. Thus, achieving the optimal depth of sedation through evidence-based and protocolized approaches has become a major focus of critical care medicine. Over the past two decades, sedation management has undergone a significant paradigm shift from deep, continuous sedation toward light or goal-directed sedation, guided by validated scoring systems such as the Richmond Agitation-Sedation Scale (RASS) and Sedation Agitation Scale (SAS) [3]. The Society of Critical Care Medicine (SCCM)guidelines now recommend maintaining patients in a state of light sedation, unless clinically contraindicated, to facilitate neurological assessments and promote early mobilization [4]. Furthermore, daily sedation interruption and protocolized sedation titration have emerged as strategies to prevent oversedation, reduce ICU stay, and improve survival outcomes [5]. Different pharmacologic agents are used for sedation in the ICU, each with unique mechanisms, benefits, and limitations. Benzodiazepines such as midazolam and lorazepam have long been the mainstay of ICU sedation due to their anxiolytic and amnestic effects. However, recent evidence associates benzodiazepine use with a higher incidence of ICU delirium, delayed awakening, and prolonged ventilation times [6]. Propofol, a short-acting hypnotic agent, offers rapid onset and easy titration, making it ideal for patients requiring frequent neurological evaluations or early extubation. Yet, it can cause hypotension, hypertriglyceridemia, and in rare cases, propofol infusion syndrome, limiting its use in hemodynamically unstable patients [7]. It also exhibits analgesic and sympatholytic properties and may reduce delirium incidence and duration of mechanical ventilation, as shown in multiple studies [8]. However, its use may be limited by bradycardia and hypotension, especially at higher doses or in patients with preexisting cardiovascular compromise [9]. Recent trends have emphasized sedation protocols tailored to the individual patient's needs and underlying conditions, often incorporating analgesia-first or analgesia-based sedation strategies to minimize sedative load. Protocolized approaches using agents such as propofol, midazolam, and dexmedetomidine have demonstrated better patient outcomes compared to non-protocolized sedation. Such strategies have been associated with shorter ventilation duration, reduced ICU stay, and lower incidence of delirium [10]. Despite international guidelines advocating protocolized, light sedation, significant variability in clinical practicepersists. Differences in patient populations, availability of drugs, ICU staffing ratios, and physician preferences contribute to inconsistent sedation management across centers. Additionally, studies comparing different sedation protocols are limited, particularly in low- and middle-income settings where resource constraints and drug availability influence protocol implementation [11].

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Objective

To compare the effectiveness and safety of three commonly used sedation agents, propofol, midazolam, and dexmedetomidine in critically ill patients requiring mechanical ventilation..

Materials and Methods

This was a prospective, randomized, comparative study conducted at Gulbarga institute of medical sciences from Jan 2025 to May 2025 . A total of 105 patients admitted to the intensive care unit (ICU) and requiring sedation for mechanical ventilation were enrolled.

Inclusion Criteria

- Adult patients aged 18 to 75 years.
- Patients admitted to the ICU requiring mechanical ventilation for more than 24 hours.
- Patients requiring continuous intravenous sedation as determined by the treating physician.
- Written informed consent obtained from the patient's legal representative.

Exclusion Criteria

- Known neurological disorders (e.g., coma, traumatic brain injury, stroke).
- Severe hepatic or renal impairment (Child-Pugh C, eGFR <30 mL/min).
- Pregnant or lactating women.
- Allergy or known hypersensitivity to propofol, midazolam, or dexmedetomidine.
- Patients with hemodynamic instability unresponsive to fluid resuscitation.
- Patients on neuromuscular blocking agents for prolonged paralysis.

Data Collection

Data were collected prospectively from all enrolled patients during their ICU stay. After randomization, patients were assigned to one of three groups based on the sedation protocol propofol-based, midazolam-based, or dexmedetomidine-based. Each patient received continuous intravenous sedation titrated to achieve a target Richmond Agitation-Sedation Scale (RASS) score between −2 (light sedation) and 0 (alert and calm). Baseline characteristics such as age, gender, body mass index (BMI), primary diagnosis, and APACHE II score were recorded upon ICU admission. Continuous monitoring of heart rate, mean arterial pressure (MAP), and oxygen saturation (SpO_2) was maintained throughout the sedation period. The primary outcomes included the duration of mechanical ventilation and ICU length of stay, while secondary outcomes were the incidence of delirium, hemodynamic instability, and ICU mortality. Delirium was assessed twice daily using the Confusion Assessment Method for the ICU (CAM-ICU), and hemodynamic instability was defined as a greater than 20% drop in MAP or heart rate requiring pharmacological intervention. Sedation depth and clinical response were evaluated hourly, and all adverse effects, such as hypotension, bradycardia, or propofol infusion syndrome, were documented. Data were collected at baseline, 24 hours, 48 hours, and at the time of extubation, and recorded in standardized data collection sheets by trained ICU nurses under the supervision of attending intensivists.

Statistical Analysis

All collected data were entered into SPSS version 25.0 (IBM Corp., Armonk, NY, USA) for statistical analysis. Quantitative variables, including age, duration of mechanical ventilation, and ICU stay, were presented as mean ± standard deviation (SD), while qualitative variables such as gender, delirium occurrence, and mortality were expressed as frequencies and percentages. A p-value < 0.05 was considered statistically significant

Results

The total study population comprised 105 critically ill patients equally divided into three groups–Propofol (n=35), Midazolam (n=35), and Dexmedetomidine (n=35). The overall mean age was 56.8 ± 13.2 years, with group means of 57.4 ± 12.6, 55.9 ± 13.8, and 57.1 ± 13.2 years respectively (p=0.82). Males were predominant, with a male-to-female ratio of 63:42 across all patients (Propofol 22:13, Midazolam 20:15, Dexmedetomidine 21:14; p=0.89). The mean BMI was similar across groups (26.3 ± 3.8 kg/m² overall; p=0.91). Sepsis was the pri mary diagnosis in 38.1% of patients, distributed as 37.1% in the Propofol group, 42.9% in Midazolam, and 34.3% in Dexmedetomidine (p=0.7 1). The mean APACHE II score was 22.6 ± 5.7, showing comparable severity between groups (p=0.78). Hypertension and diabetes were common comorbidities, reported in 45.7% and 37.1% of patients respectively, with no statistical difference among the three groups (p=0.89 and p=1.00).

Table 1: Baseline Demographic and Clinical Characteristics of Patients (n = 105)

Variable	Total (n=105)	Propofol Group (n=35)	Midazolam Group (n=35)	Dexmedetomidine Group (n=35)	p-value
Age (years), mean ± SD	56.8 ± 13.2	57.4 ± 12.6	55.9 ± 13.8	57.1 ± 13.2	0.82
Gender (Male/Female)	63 / 42	22 / 13	20 / 15	21 / 14	0.89
BMI (kg/m²), mean ± SD	26.3 ± 3.8	26.1 ± 3.7	26.5 ± 3.9	26.3 ± 3.8	0.91
Primary Diagnosis - Sepsis (%)	40 (38.1%)	13 (37.1%)	15 (42.9%)	12 (34.3%)	0.71
APACHE II Score, mean ± SD	22.6 ± 5.7	22.8 ± 5.9	23.1 ± 5.5	22.0 ± 5.6	0.78
Comorbidities - Hypertension (%)	48 (45.7%)	17 (48.6%)	16 (45.7%)	15 (42.9%)	0.89
Comorbidities – Diabetes Mellitus (%)	39 (37.1%)	13 (37.1%)	13 (37.1%)	13 (37.1%)	1.00

Target sedation levels (RASS goals) were achieved in 90.5% of all patients, with rates of 94.3% for Propofol, 85.7% for Midazolam, and 91.4% for Dexmedetomidine (p=0.37). The mean sedation onset time was significantly faster in the Propofol group at 15.6 ± 3.8 minut es compared to 20.8 ± 4.3 minutes in the Midazolam group and 18.1 ± 4.1 minutes in the Dexmedetomidine group (p=0.01). Mean sedation duration was 64.3 ± 20.2 hours overall (Propofol 61.7 ± 19.4, Midazolam 68.9 ± 22.1, Dexmedetomidine 62.4 ± 19.1; p=0.29). Sedation interr uption was performed in 78.1% of all cases (82.9% in Propofol, 68.6% in Midazolam, and 82.9% in Dexmedetomidine; p=0 .18).

Table 2: Sedation Depth and Maintenance Parameters

Variable	Total (n=105)	Propofol	Midazolam	Dexmedetomidine	p-value
Target RASS Achieved (%)	95 (90.5%)	33 (94.3%)	30 (85.7%)	32 (91.4%)	0.37
Mean Sedation Onset Time (min), mean ± SD	18.2 ± 4.6	15.6 ± 3.8	20.8 ± 4.3	18.1 ± 4.1	0.01*
Mean Sedation Duration (hours), mean ± SD	64.3 ± 20.2	61.7 ± 19.4	68.9 ± 22.1	62.4 ± 19.1	0.29
Sedation Interruption Performed (%)	82 (78.1%)	29 (82.9%)	24 (68.6%)	29 (82.9%)	0.18
Mean Daily Sedative Dose (mg/kg/h), mean ± SD	—	2.4 ± 0.7	0.05 ± 0.02	0.8 ± 0.3	—

Baseline mean arterial pressure (MAP) was consistent across all groups (Propofol 83.2 ± 10.6 mmHg, Midazolam 82.4 ± 11.2 mmHg, Dexmedetomidine 84.1 ± 10.8 mmHg; p=0.81). However, at 24 hours, Dexmedetomidine patients exhibited a lower MAP (74.2 ± 8.5 mmHg) compared to Propofol (77.9 ± 9.4 mmHg) and Midazolam (79.1 ± 9.9 mmHg), with statistical significance (p=0.04). The mean heart rate at 24 hours was notably lower with Dexmedetomidine (74.8 ± 10.4 bpm) than with Propofol (86.8 ± 12.5 bpm) and Midazolam (88 .2 ± 11.7 bpm), highly significant at p<0.001. Bradycardia occurred in 17.1% of Dexmedetomidine patients, versus 2.9% in Propofol and 0% in M idazolam (p=0.01).

Table 3: Hemodynamic Parameters and Stability During Sedation

Parameter	Propofol (n=35)	Midazolam (n=35)	Dexmedetomidine (n=35)	p-value
Baseline MAP (mmHg), mean ± SD	83.2 ± 10.6	82.4 ± 11.2	84.1 ± 10.8	0.81
MAP at 24 hours (mmHg), mean ± SD	77.9 ± 9.4	79.1 ± 9.9	74.2 ± 8.5	0.04*
Heart Rate at 24 hours (bpm), mean ± SD	86.8 ± 12.5	88.2 ± 11.7	74.8 ± 10.4	<0.001*
Incidence of Bradycardia (%)	1 (2.9%)	0 (0%)	6 (17.1%)	0.01*
Incidence of Hypotension (%)	4 (11.4%)	3 (8.6%)	5 (14.3%)	0.70
Vasopressor Use (%)	9 (25.7%)	8 (22.9%)	10 (28.6%)	0.86

Delirium incidence differed significantly between groups, with Midazolam showing the highest rate at 28.6%, compared to 14.3% for Propofol and 8.6% for Dexmedetomidine (p=0.04). The mean delirium duration was shortest in the Dexmedetomidine group (1.3 ± 0.5 days) and longest in the Midazolam group (3.1 ± 1.2 days), while Propofol averaged 1.8 ± 0.7 days (p=0.02). Patients in the Dexmedetomidine group also achieved earlier awakening (6.3 ± 2.8 hours) than those in the Midazolam group (8.1 ± 3.6 hours), while Propofol patients averaged 5.9 ± 2.4 hours (p=0.01). The mean RASS at extubation was –0.3 ± 0.4 for Propofol, –0.6 ± 0.5 for Midazolam, and –0.2 ± 0.3 for Dexmedetomidine, indicating a lighter sedation level with Dexmedetomidine (p=0.03).

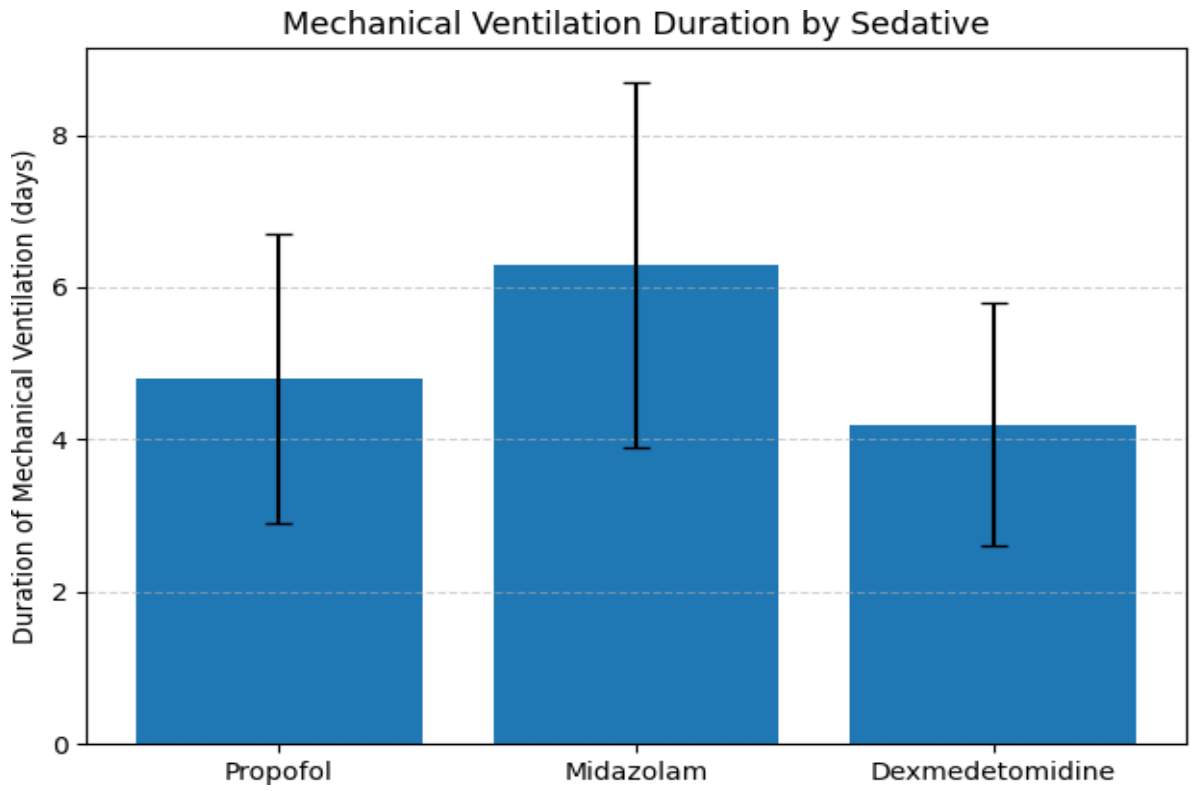
Table 4: Delirium and Neurological Outcomes

Outcome	Propofol	Midazolam	Dexmedetomidine	p-value
Incidence of Delirium (%)	5 (14.3%)	10 (28.6%)	3 (8.6%)	0.04*
Delirium Duration (days), mean ± SD	1.8 ± 0.7	3.1 ± 1.2	1.3 ± 0.5	0.02*
Time to First Awakening (hours), mean ± SD	5.9 ± 2.4	8.1 ± 3.6	6.3 ± 2.8	0.01*
RASS at Extubation, mean ± SD	–0.3 ± 0.4	–0.6 ± 0.5	–0.2 ± 0.3	0.03*

Patients sedated with Dexmedetomidine required significantly shorter mechanical ventilation duration (4.2 ± 1.6 days) compared to Midazolam (6.3 ± 2.4 days) and Propofol (4.8 ± 1.9 days) with p=0.001. ICU stay followed a similar pattern, with Dexmedetomidine patients staying for an average of 8.1 ± 2.4 days, shorter than Midazolam's 10.4 ± 3.3 days and Propofol's 8.9 ± 2.7 days (p=0.01). Unplanned extubation occurred in 5.7% of Propofol, 8.6% of Midazolam, and 2.9% of Dexmedetomidine patients (p=0.59).

Table 5: Ventilation and ICU Outcome Parameters

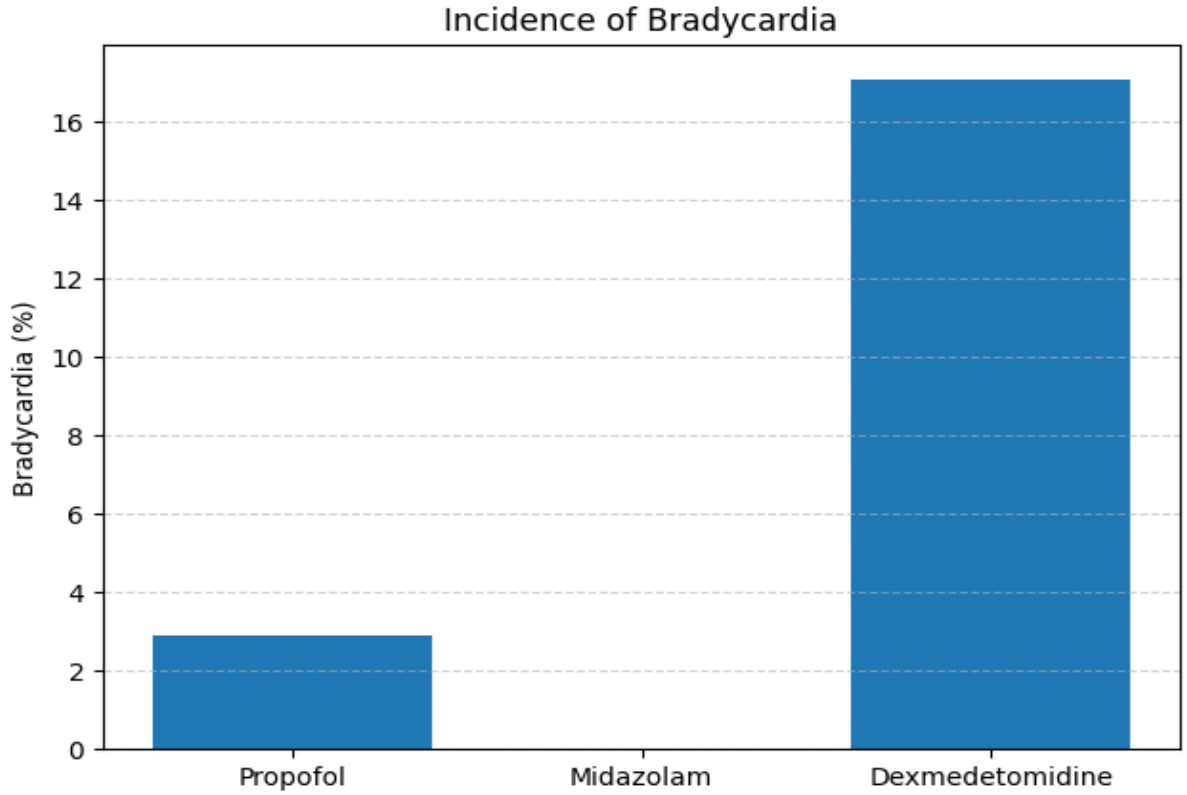
Variable	Propofol	Midazolam	Dexmedetomidine	p-value
Duration of Mechanical Ventilation (days), mean ± SD	4.8 ± 1.9	6.3 ± 2.4	4.2 ± 1.6	0.001*
ICU Length of Stay (days), mean ± SD	8.9 ± 2.7	10.4 ± 3.3	8.1 ± 2.4	0.01*
Unplanned Extubation (%)	2 (5.7%)	3 (8.6%)	1 (2.9%)	0.59
Reintubation within 48 hours (%)	1 (2.9%)	3 (8.6%)	1 (2.9%)	0.41



Bradycardia was notably more frequent in the Dexmedetomidine group (17.1%) than in Propofol (2.9%) and Midazolam (0%), showing statistical significance (p=0.01). Hypotension occurred in 11.4%, 8.6%, and 14.3% of Propofol, Midazolam, and Dexmedetomidine groups respectively (p=0.70). No cases of Propofol infusion syndrome were observed. Post-sedation withdrawal or agitation was highest in the Midazolam group (20%), followed by Propofol (8.6%) and Dexmedetomidine (5.7%) (p=0.10).

Table 6: Adverse Effects and Clinical Outcomes

Adverse Event	Propofol (n=35)	Midazolam (n=35)	Dexmedetomidine (n=35)	p-value
Bradycardia (%)	1 (2.9%)	0 (0%)	6 (17.1%)	0.01*
Hypotension (%)	4 (11.4%)	3 (8.6%)	5 (14.3%)	0.70
Propofol Infusion Syndrome (%)	0 (0%)	—	—	—
Withdrawal/Agitation After Stop (%)	3 (8.6%)	7 (20%)	2 (5.7%)	0.10
ICU Mortality (%)	5 (14.3%)	7 (20%)	4 (11.4%)	0.61



Discussion

This study compared the effectiveness and safety of three sedation protocols propofol, midazolam, and dexmedetomidine in critically ill patients undergoing mechanical ventilation. The analysis of 105 patients revealed significant differences among these agents in terms of sedation quality, hemodynamic stability, duration of ventilation, delirium incidence, and ICU stay. Overall, dexmedetomidine and propofol were more effective and clinically advantageous than midazolam, with dexmedetomidine showing particular superiority in maintaining light, arousable sedation, minimizing delirium, and reducing ICU stay duration. All three agents achieved adequate sedation, as reflected by the target RASS scores achieved in over 90% of patients, though their pharmacodynamic profiles influenced onset and control. Propofol provided the fastest sedation onset (15.6 ± 3.8 minutes), consistent with its known rapid onset and short half-life. In contrast, midazolam took longer (20.8 ± 4.3 minutes) due to its slower redistribution and longer elimination half-life, leading to prolonged sedative effects and delayed awakening. Dexmedetomidine provided a comparable onset (18.1 ± 4.1 minutes) while maintaining a lighter and more stable sedation level. These findings mirror previous research, which demonstrated that propofol enables quicker sedation titration, while dexmedetomidine offers more stable and easily reversible sedation compared to benzodiazepine-based regimens [12]. Hemodynamic monitoring revealed that dexmedetomidine induced a greater decrease in heart rate (74.8 ± 10.4 bpm) and MAP (74.2 ± 8.5 mmHg) compared with propofol and midazolam, with a bradycardia incidence of 17.1%. Despite these effects, hemodynamic compromise remained clinically manageable and did not require sedation discontinuation in most cases. These findings align with previous research, which reported dexmedetomidine-associated bradycardia and hypotension due to its α2-adrenergic agonism causing reduced sympathetic tone [13]. In contrast, propofol demonstrated moderate hypotensive effects related to vasodilation, while midazolam maintained relative cardiovascular stability but contributed to delayed recovery and oversedation. Collectively, this suggests that dexmedetomidine is hemodynamically safe in most patients but should be used cautiously in those with preexisting bradyarrhythmias or low baseline MAP. The incidence of delirium differed significantly among the groups, being lowest with dexmedetomidine (8.6%), intermediate with propofol (14.3%), and highest with midazolam (28.6%). The duration of delirium was also shorter in dexmedetomidine-treated patients (1.3 ± 0.5 days) compared to midazolam (3.1 ± 1.2 days). This reflects the unique sedative profile of dexmedetomidine, which provides an arousable, non-deliriogenic sedation that mimics natural sleep architecture. Previous research similarly reported that dexmedetomidine reduces the incidence and duration of ICU delirium, facilitating improved cognitive recovery and earlier communication between patients and healthcare providers. Furthermore, propofol also exhibited a favorable neurological profile, with a faster awakening time (5.9 ± 2.4 hours) than midazolam (8.1 ± 3.6 hours), aligning with previous research that linked propofol-based sedation to earlier extubation and reduced delirium rates [14]. A major outcome of this study was the significant reduction in ventilation duration and ICU length of stay in the dexmedetomidine and propofol groups. The mean duration of mechanical ventilation was 4.2 ± 1.6 days with dexmedetomidine and 4.8 ± 1.9 days with propofol, compared to 6.3 ± 2.4 days for midazolam ($p = 0.001$). Similarly, ICU stay was shorter with dexmedetomidine (8.1 ± 2.4 days) than with midazolam (10.4 ± 3.3 days) ($p = 0.01$). These differences can be attributed to faster awakening, better ventilator synchrony, and reduced delirium observed with dexmedetomidine and propofol. Previous research supports these findings, demonstrating that both propofol- and dexmedetomidine-based sedation protocols lead to earlier extubation, shorter ICU stays, and lower hospital costscompared with benzodiazepine-based regimens [15]. Although all sedative agents were generally well tolerated, dexmedetomidine was associated with more bradycardia (17.1%) but fewer episodes of agitation and withdrawal compared to midazolam. Propofol showed mild hypotension (11.4%) without major complications such as propofol infusion syndrome, while midazolam demonstrated the highest frequency of agitation upon discontinuation (20%) and ICU mortality (20%), though not statistically significant. These findings parallel previous research, which documented hemodynamic suppression with dexmedetomidine, vasodilatory hypotension with propofol, and rebound agitation or withdrawal associated with benzodiazepine discontinuation [16]. Importantly, the overall mortality was lowest in the dexmedetomidine group (11.4%), suggesting potential long-term benefits of lighter and more physiological sedation. This study had several limitations. The sample size (n = 105) was moderate, and the study was conducted at a single center, potentially limiting generalizability. Moreover, long-term neurocognitive outcomes and post-discharge recovery parameters were not evaluated. Hemodynamic variations were closely monitored, but biochemical markers of stress response were not assessed. Future multicenter studies with larger sample sizes and extended follow-up periodsare needed to validate these findings and explore the impact of sedation choice on long-term functional recovery and ICU survivorship.

Conclusion

It is concluded that both dexmedetomidine and propofol are more effective and safer than midazolam for sedation in mechanically ventilated ICU patients. Dexmedetomidine provided the best overall outcomes, with a shorter ventilation duration (4.2 ± 1.6 days), reduced ICU stay (8.1 ± 2.4 days), and lower delirium incidence (8.6%), while propofol offered the fastest onset (15.6 ± 3.8 minutes) and easier titration. In contrast, midazolam was linked to prolonged sedation and higher delirium rates. Although dexmedetomidine caused mild bradycardia, it was well tolerated. Therefore, protocol-based light sedation using dexmedetomidine or propofol should be preferred over benzodiazepines to achieve faster recovery, earlier weaning, and improved ICU outcomes.

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