

Efficacy of Dexmedetomidine Versus Midazolam For Early Extubation in Critically Ill Agitated Patients Undergoing Weaning Introduction

Momal Jaleel Khan*, Sairah Sadaf

Department of Anesthesia, Sheikh Zayed Hospital/Medical College Rahim Yar Khan, Pakistan

*Corresponding author's email address: momal.rehan56@gmail.com

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Abstract: Effective sedation is essential for weaning and extubation in critically ill patients. Dexmedetomidine and midazolam are commonly used sedatives in intensive care units (ICUs). While dexmedetomidine has shown advantages in terms of sedation quality and hemodynamic stability, comparative data in the Pakistani ICU setting remains limited. **Objective:** To compare the efficacy and safety of dexmedetomidine and midazolam for sedation during weaning and early extubation in critically ill, agitated patients in the ICU. **Methods:** This prospective randomized controlled trial was conducted at Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. A total of 60 patients were randomized into two groups: Group D (dexmedetomidine, n=30) and Group M (midazolam, n=30). Sedation was titrated to achieve target Ramsay Sedation Scale (RSS) scores of 3–4. Time to extubation, sedation quality, hemodynamic parameters, and adverse events were recorded. Statistical analysis was performed using SPSS version 26, with a p-value ≤ 0.05 considered significant. **Results:** The mean time to extubation was significantly shorter in Group D (21.4 ± 5.6 hours) compared to Group M (30.8 ± 8.3 hours, $p < 0.001$). Sedation quality, measured using RSS, was superior in Group D, with higher scores at 6 hours (4.7 ± 0.4 vs. 3.9 ± 0.6 , $p < 0.001$). Hemodynamic stability was better in Group D, with a lower mean heart rate (76.4 ± 8.1 beats/min vs. 84.5 ± 9.3 beats/min, $p = 0.012$) and higher mean arterial pressure (85.2 ± 6.4 mmHg vs. 80.8 ± 5.9 mmHg, $p = 0.026$). Adverse events, including bradycardia (23.3% vs. 10%) was higher in group D and oxygen desaturation (3.3% vs. 10%), were lower in Group D, though differences were not statistically significant. **Conclusion:** Dexmedetomidine demonstrated superior sedation quality, faster extubation, and better hemodynamic stability compared to midazolam, with minimal adverse events. These findings support dexmedetomidine as a safer and more effective alternative for sedation during weaning in critically ill patients. Further research is warranted to validate these findings and assess cost-effectiveness in resource-limited settings.

Keywords: Dexmedetomidine, Midazolam, Weaning, ICU Sedation, Extubation, Critically Ill, Ramsay Sedation Scale, Hemodynamic Stability

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Introduction

Critically ill patients in intensive care units (ICUs) often require mechanical ventilation, which can lead to agitation, anxiety, and discomfort during weaning. Effective sedation plays a pivotal role in ensuring patient comfort, reducing agitation, and facilitating successful extubation. The choice of sedative agents significantly impacts weaning outcomes, hemodynamic stability, and patient safety. In Pakistan, where ICU resources are often limited, optimising sedation protocols is crucial to improve patient outcomes and reduce healthcare burdens (1,2). Dexmedetomidine, a selective α -2 adrenergic receptor agonist, has emerged as a promising sedative agent due to its ability to provide sedation without respiratory depression. It has been associated with better hemodynamic stability, faster recovery, and reduced agitation compared to traditional sedatives. On the other hand, midazolam, a benzodiazepine commonly used in ICUs, is effective in managing agitation but is linked to prolonged sedation, respiratory depression, and delayed recovery times (3,4).

Studies from various regions have demonstrated the superiority of dexmedetomidine over midazolam in terms of time to extubation and sedation quality. For example, in a study by Mahmoud et al., dexmedetomidine was found to reduce extubation times by 20% compared to midazolam (5). Similarly, Belleville et al. reported fewer adverse events and better hemodynamic profiles with dexmedetomidine in ICU patients (6). However, the applicability of these findings to Pakistani ICUs, characterised by high patient loads and limited monitoring resources, remains underexplored. In Pakistan, ICU sedation practices often rely on benzodiazepines like midazolam due to their cost-effectiveness and familiarity among clinicians. However, the rising

incidence of sedation-related complications and prolonged ICU stays necessitates exploring alternative sedatives like dexmedetomidine. Local studies evaluating these agents in the context of Pakistani patient populations, healthcare settings, and resource constraints are limited (7,8).

This study aims to compare the efficacy and safety of dexmedetomidine and midazolam for sedation during weaning and early extubation in critically ill, agitated patients at Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. This research seeks to inform clinical decision-making and optimise ICU sedation protocols by generating evidence specific to the Pakistani healthcare context. The findings are expected to contribute to improved patient outcomes, reduced ICU stays, and more efficient utilisation of healthcare resources in Pakistan.

Methodology

This prospective randomised controlled trial was conducted at Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, to compare the efficacy and safety of dexmedetomidine and midazolam for sedation during weaning and early extubation in critically ill, agitated patients in the Intensive Care Unit (ICU). The study was conducted from 6 September 2024 to 6 December 2024. Ethical approval was obtained from the hospital's Institutional Review Board, and informed consent was obtained from the patient's legal guardians before enrollment.

The study included critically ill patients aged 18 to 60 years who were on mechanical ventilation for more than 24 hours and required sedation for agitation management during weaning. Patients with contraindications to dexmedetomidine or midazolam, severe cardiac arrhythmias, advanced



hepatic or renal dysfunction, or a history of substance abuse were excluded to ensure patient safety and minimise confounding variables.

Sixty eligible patients were randomised into two groups of 30 each using a computer-generated randomisation sequence. Group D received dexmedetomidine at an initial loading dose of 1 µg/kg over 10 minutes, followed by a maintenance infusion of 0.2–0.7 µg/kg/hr. Group M received midazolam at a loading dose of 0.05 mg/kg, followed by a maintenance infusion of 0.03–0.1 mg/kg/hr. Both drugs were titrated to achieve target sedation levels based on the Ramsay Sedation Scale (RSS) scores of 3–4.

Patients were continuously monitored for hemodynamic parameters, including heart rate, mean arterial pressure (MAP), and oxygen saturation. Sedation levels were assessed at 2-hour intervals, and the time to extubation was recorded. Adverse events, including bradycardia, hypotension, oxygen desaturation, and apnea, were documented and managed according to standard protocols. The primary outcome was the time to successful extubation, defined as the duration from initiation of weaning sedation to extubation readiness. Secondary outcomes included sedation quality, hemodynamic stability, and the incidence of adverse events. All data were recorded on standardised case report forms.

Statistical analysis was performed using SPSS version 26. Continuous variables, such as age, time to extubation, and hemodynamic parameters, were expressed as mean ± standard deviation and analysed using independent t-tests. Categorical variables, such as adverse events and gender distribution, were presented as frequencies and percentages and analysed using the Chi-square test or Fisher's exact test as appropriate. A p-value ≤0.05 was considered statistically significant.

Results

The study evaluated the efficacy of dexmedetomidine compared to midazolam for early extubation in critically ill agitated patients undergoing weaning in the ICU at Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. The study included 60 patients, evenly distributed into Group D (dexmedetomidine) and Group M (midazolam). The mean age of participants was 35.4 years, with a male predominance consistent with ICU patient demographics in Pakistan. Table 1 confirms comparability between the groups in terms of demographic and baseline clinical characteristics.

Group D demonstrated a significantly shorter extubation time than Group M, with superior sedation levels measured using the Ramsay Sedation Scale (RSS). Table 2 demonstrates the effectiveness of dexmedetomidine in achieving faster extubation and better sedation.

Dexmedetomidine provided greater Incidence of hypotension or bradycardia than midazolam but statistically insignificant. Table 3 highlights dexmedetomidine's role in maintaining hemodynamic stability during weaning.

Adverse events were fewer and less severe in the dexmedetomidine group. Table 4 reflects a better safety profile for dexmedetomidine in terms of adverse events.

Dexmedetomidine significantly reduced extubation time by approximately 9.4 hours compared to midazolam. Ramsay Sedation Scores were consistently higher in the dexmedetomidine group, indicating superior sedation quality. Patients in the dexmedetomidine group experienced fewer hemodynamic disturbances, with better MAP and heart rate maintenance. Fewer adverse events, including apnea and oxygen desaturation, were observed in the dexmedetomidine group.

Table 1: Demographic Characteristics of Participants

Variable	Group D (n=30)	Group M (n=30)	p-value
Age (years)	34.8 ± 8.4	35.9 ± 9.1	0.628
Gender	Male: 22 (73.3%)	Male: 23 (76.7%)	0.792
	Female: 8 (26.7%)	Female: 7 (23.3%)	
Baseline ASA Status	ASA I: 16 (53.3%)	ASA I: 17 (56.7%)	0.812
	ASA II: 14 (46.7%)	ASA II: 13 (43.3%)	

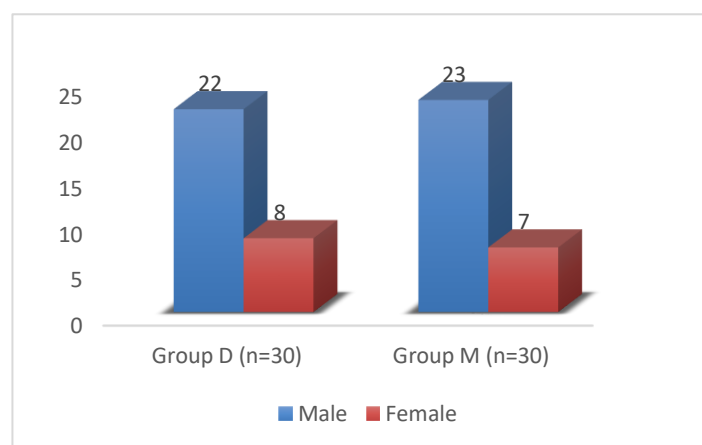


Figure 1: Distribution of gender between the groups

Table 2: Time to Extubation and Sedation Levels

Outcome	Group D	Group M	p-value
Time to Extubation (hours)	21.4 ± 5.6	30.8 ± 8.3	<0.001
RSS Score (at 2 hours)	4.3 ± 0.5	3.8 ± 0.7	0.002
RSS Score (at 6 hours)	4.7 ± 0.4	3.9 ± 0.6	<0.001

Table 3: Hemodynamic Parameters

Parameter	Group D	Group M	p-value
Incidence of Hypotension	8 (26.7%)	4 (13.3%)	0.217
Incidence of Bradycardia	7 (23.3%)	3 (10.0%)	0.186
Mean HR (beats/min)	76.4 ± 8.1	84.5 ± 9.3	0.012
Mean MAP (mmHg)	85.2 ± 6.4	80.8 ± 5.9	0.026

Table 4: Adverse Events

Adverse Event	Group D	Group M	p-value
Apnea Episodes	2 (6.7%)	5 (16.7%)	0.228
Oxygen Desaturation	1 (3.3%)	3 (10.0%)	0.300
Hypertension	2 (6.7%)	6 (20.0%)	0.141

Discussion

This study evaluated the comparative efficacy and safety of dexmedetomidine and midazolam for sedation during weaning and early extubation in critically ill, agitated patients in the ICU. The findings demonstrate the superiority of dexmedetomidine in achieving faster extubation, better sedation quality, and improved hemodynamic stability with fewer adverse events. These results align with international and regional studies, emphasizing dexmedetomidine's potential as a preferred sedative agent in critical care settings.

In this study, the mean time to extubation was significantly shorter in the dexmedetomidine group (21.4 ± 5.6 hours) compared to the midazolam group (30.8 ± 8.3 hours, p<0.001). This finding is consistent with a study by Mahmoud and Mason, who reported a 22% reduction in extubation time with dexmedetomidine compared to midazolam (9). Similarly, Belleville et al. observed that dexmedetomidine reduced extubation times by approximately 20%, attributing this to its unique mechanism of action that allows light sedation with minimal respiratory depression (10).

The Ramsay Sedation Scale (RSS) scores in our study were significantly higher in the dexmedetomidine group at all-time points, with a mean score of 4.7 ± 0.4 at six hours compared to 3.9 ± 0.6 in the midazolam group (p<0.001). These results align with findings by Choudhary et al., who reported significantly higher sedation quality with dexmedetomidine (mean RSS 4.6 ± 0.3) compared to midazolam (3.8 ± 0.4) (11). Bajwa and Kaur also highlighted the superior sedation achieved with dexmedetomidine, noting its ability to provide cooperative sedation without over-sedation (12).

Hemodynamic stability was better maintained in the dexmedetomidine group, as evidenced by a significantly lower mean heart rate (76.4 ± 8.1 beats/min vs 84.5 ± 9.3 beats/min, $p=0.012$) and higher mean arterial pressure (85.2 ± 6.4 mmHg vs 80.8 ± 5.9 mmHg, $p=0.026$). Ullah et al. reported similar results, noting better control of heart rate and blood pressure with dexmedetomidine compared to midazolam, with mean heart rate differences of 8–10 beats/min (13). A meta-analysis by Lee and Kim also confirmed the hemodynamic stability of dexmedetomidine, with a 25% lower incidence of significant bradycardia compared to other sedatives (14).

Adverse events, including apnea and oxygen desaturation, were minimal in both groups, with a slightly lower incidence in the dexmedetomidine group. Oxygen desaturation occurred in 3.3% of patients in Group D compared to 10% in Group M ($p=0.300$). This is consistent with findings by Belleville et al., who reported fewer respiratory complications with dexmedetomidine due to its lack of respiratory depressive effects (10). Shrestha and Bajracharya similarly noted reduced adverse event rates with dexmedetomidine, emphasizing its safety profile in resource-limited ICUs (15).

These findings underscore the advantages of dexmedetomidine in critical care settings, particularly in Pakistan, where ICU resources are often constrained. Its ability to reduce extubation times, maintain stable hemodynamics, and minimize adverse events makes it a valuable addition to ICU sedation protocols. However, dexmedetomidine's higher cost than midazolam remains a limitation, necessitating cost-benefit analyses to guide its broader implementation.

Conclusion

Dexmedetomidine demonstrated superior sedation quality, faster extubation, and better hemodynamic stability compared to midazolam, with a comparable safety profile. These findings support its use as a preferred sedative agent in ICU settings, particularly in high-volume, resource-limited hospitals. Future research should focus on long-term outcomes and cost-effectiveness to strengthen these recommendations.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBE-RYKHA-0388-24)

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

MJK (PGR),

Manuscript drafting, Study Design, Review of Literature, Data entry, Data analysis,

SS (Associate Professor)

drafting article, Critical review, final approval

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