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COMPARATIVE EFFICACY OF DEXMEDETOMIDINE AND MIDAZOLAM IN ANESTHESIA-RELATED SEDATION FOR MECHANICALLY VENTILATED ICU PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Sedation is an essential aspect of mechanically ventilated patient management in the Intensive Care Unit (ICU). Selection of the sedative agent may have a major impact on the outcome of patients. This trial seeks to compare the safety and efficacy of dexmedetomidine and midazolam in anesthesia-related sedation in mechanically ventilated ICU patients.

Methods: A randomized controlled trial was carried out in Lady Reading Hospital, Peshawar, on 100 adult mechanically ventilated ICU patients. Participants were randomly allocated to be administered either dexmedetomidine or midazolam. The depth of sedation was measured by Richmond Agitation-Sedation Scale (RASS), and measures like time to extubation, mechanical ventilation duration, ICU stay, need for opioids, and delirium incidence were documented and analyzed.

Results: Dexmedetomidine-sedated patients had superior RASS control, had much reduced mechanical ventilation and ICU stays, and had fewer ICU-associated delirium events than midazolam-treated patients. The dexmedetomidine group also needed less opioid supplementation. Bradycardia was more prevalent in the dexmedetomidine group but was controllable with titration of doses.

Conclusion: Dexmedetomidine was found to be superior and safer than midazolam for sedation of mechanically ventilated ICU patients. Its application may improve recovery, decrease ICU burden, and enhance global patient outcomes, especially under resource-scarce conditions.

INTRODUCTION

Management of critically ill patients in the intensive care unit (ICU) frequently requires mechanical ventilation, a life-saving technology that is linked with significant physiological and psychological stress(Telias et al., 2022). Effective sedation is one of the cornerstones of the management of mechanically ventilated patients, being responsible for comfort, safety, synchrony with the ventilator, and the prevention of psychological trauma. Benzodiazepines like midazolam have been classically used for sedation in the intensive care unit because of their effective anxiolytic as well as hypnotic effects(Scholarworks & Lord, 2020). However, concerns regarding their adverse effects, including respiratory depression, prolonged sedation, delirium, and withdrawal phenomena, have prompted the exploration of alternative agents(Agar et al., 2022) Dexmedetomidine, a selective alpha-2 adrenergic receptor agonist, has gained attention as an innovative sedative drug, with possible advantages of sedation quality, arousability of the patient, and diminished delirium(Bosch et al., 2023).

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The best sedative agent for ICU patients would ideally offer effective anxiolysis and hypnosis, facilitate easy titration to desired levels of sedation, ensure rapid recovery, and have minimal respiratory and hemodynamic compromise(Boncyk et al., n.d.). In addition, it must have little drug accumulation in patients with hepatic or renal failure, which is frequently found in critically ill patients. Although midazolam meets a number of these qualifications, it has been linked with an increased rate of ICU delirium, mechanical ventilation, and extubation delay. These results have important implications regarding patient morbidity, ICU stay, and overall health costs(R. Nelson et al., 2022). Dexmedetomidine, cleared by the U.S. FDA for sedation in adult ICU patients for durations of up to 24 hours, induces sedation more similar to natural sleep and lacks a severe respiratory depressive effect. It provides the benefit of arousable sedation, with the ability to keep patients cooperative and communicative, which is valuable for neurological examinations and early mobilization procedures. In addition, dexmedetomidine has been demonstrated to provide opioid-sparing effects and may decrease the rate of opioid-related complications in ICU patients(Gambadoro et al., n.d.) Its sedative and analgesic effects with minimal respiratory function depression imply a therapeutic advantage over standard benzodiazepines in critical care sedation.

Several clinical trials have compared dexmedetomidine with midazolam in different clinical situations, but comparative efficacy and safety of the two in long-term sedation of ICU patients, especially mechanically ventilated ones, is an area of continued controversy(Wen et al., 2023). Various randomized controlled trials and meta-analyses have shown that dexmedetomidine decreases mechanical ventilation duration and delirium incidence, but some have questioned its hemodynamic safety profile in that it may cause bradycardia and hypotension. Such conflicting results highlight the need for well-powered, high-quality studies to clarify the clinical usefulness of dexmedetomidine over midazolam, particularly within real-world ICU environments where polypharmacy and comorbidities are the rule rather than the exception.

Sedation for anesthesia in ICU environments requires not just pharmacologic effectiveness but also consideration for all patient outcomes, such as ease of arousability, extubation time(*Improving Understanding of Anesthetic Considerations... - Google Scholar*, n.d.). ICU stay length, post-ICU cognitive function, and long-term psychological impact. SAS or RASS are routinely utilized to assess the depth of sedation, and the ideal sedative would sustain the intended RASS level with minimal fluctuations. Dexmedetomidine is in contrast to midazolam, facilitating a "cooperative sedation," where the patient is relaxed but easily arousable, possibly reducing delirium occurrence, patient interaction, and rehabilitation complication.

From a pharmacokinetic perspective, midazolam is metabolized in the liver by cytochrome P450 enzymes and has been noted to accumulate with extended infusion, especially in patients who have hepatic impairment(Fung et al., 2022). Conversely, dexmedetomidine has a more stable elimination half-life, but caution is indicated because of its potential cardiovascular side effects of hypotension and bradycardia, especially with loading doses or bolus titration.

In addition, sedation strategy is a crucial component of putting in place strategies like daily sedation interruption, spontaneous breathing trials, and early mobilization, all of which are critical components of contemporary ICU practice for limiting ventilator-associated complications. In this regard, dexmedetomidine's pharmacodynamic profile can facilitate more effective deployment of these strategies relative to midazolam, and it may result in better clinical outcomes and less ICU burden(Castillo et al., 2020).

The COVID-19 pandemic has again emphasized the importance of ideal sedation practice in the ICU, with most patients necessitating extended sedation and ventilation(Landoni et al., n.d.). Drug shortages, increased sedation demands, and shifting clinical guidelines have prompted clinicians to reassess sedative choices. Emerging evidence suggests that dexmedetomidine may also gain by decreasing prolonged ICU stays and avoiding ICU-delirium in COVID-19 and other critically ill patients, further validating its consideration in clinical trials.

This study will conduct a rigorous randomized controlled trial between the efficacy of dexmedetomidine and midazolam in sedating

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mechanically ventilated patients in the ICU under anaesthesia-related care(Zhao et al., 2023). The main outcome will be the sustenance of target sedation levels as measured by the Richmond Agitation-Sedation Scale (RASS), whereas secondary outcomes will be duration of mechanical ventilation, delirium incidence, hemodynamic stability, total dose of sedatives, opioid-sparing, time to extubation, and ICU stay.

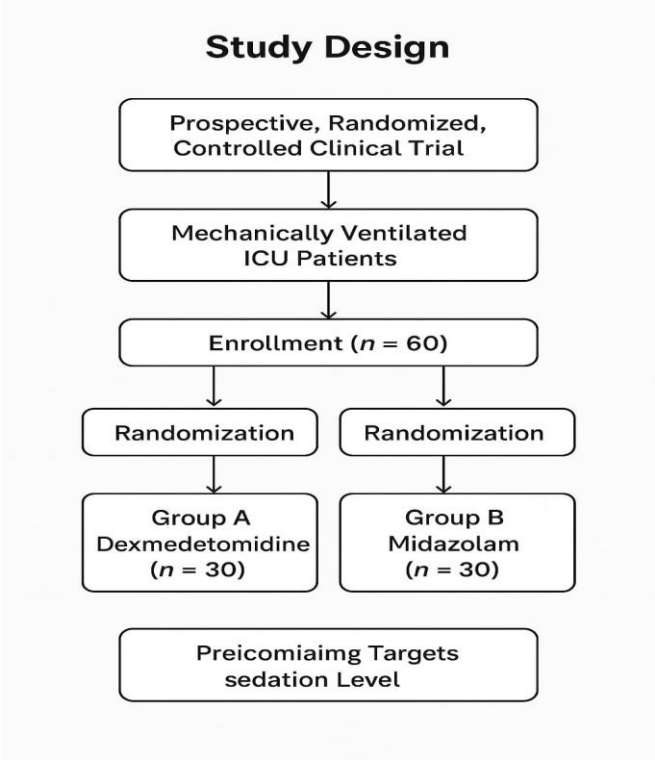
By comparing head-to-head the two commonly used agents, the study aims to influence clinical decision-making and support evidence-based ICU sedation practice guidelines. The results have important implications for anesthesiologists, intensivists, and critical care staff when choosing the most suitable sedation agent for patients receiving mechanical ventilation, thus optimizing patient outcomes and maximizing resource use in high-dependency environments.

In summary, comparative effectiveness of dexmedetomidine and midazolam for anesthesia-associated sedation in mechanically ventilated ICU patients is an important area of clinical research. Considering the magnitude of stakes involved in the care of ICU patients—both in relation to safety of the patient and costs of healthcare—it is crucial to determine the ideal sedative drug. This research aims to fill this important gap with a randomized controlled trial that will yield strong evidence of the clinical benefits and drawbacks of each agent, opening the door to improved and personalized sedation practices in the ICU.

Methodology

Study Design

This research was a prospective, randomized, controlled clinical trial aimed at evaluating the efficacy and safety of dexmedetomidine versus midazolam for sedation in mechanically ventilated patients receiving care in the intensive care unit (ICU)(Zhou et al., 2020). The study was undertaken for six months at the ICU of Lady Reading Hospital, Peshawar, which is one of the biggest tertiary care hospitals of Khyber Pakhtunkhwa, Pakistan. The purpose of the study was to assess the efficacy of every drug in sustaining target sedation and enhancing clinical outcomes among mechanically ventilated patients under anesthesia-related treatment(Cui et al., n.d.).



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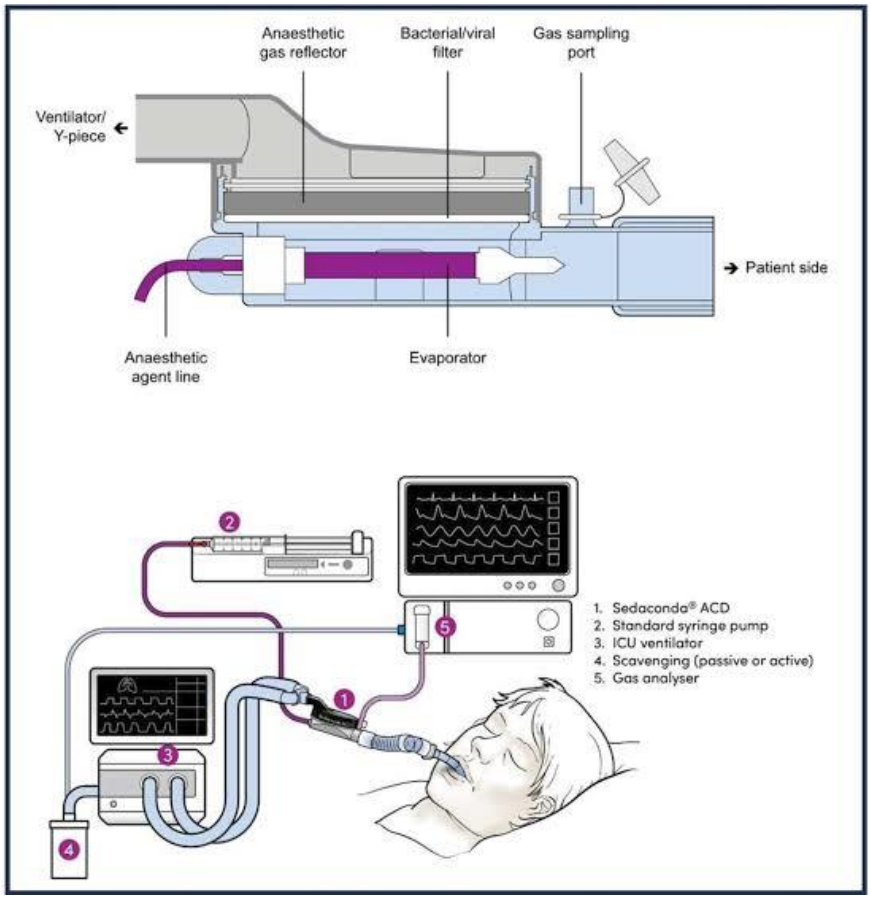
Ethical Considerations

Ethical permission for the study was received from the Institutional Review Board (IRB) of Lady Reading Hospital, Peshawar, before the start of the trial. The ethical principles set forth in the Declaration of Helsinki were adhered to strictly, and every attempt was made to preserve the dignity, rights, and welfare of the patients involved(Buruk et al., 2023). Because the patients were critically ill, sedated, and thus unable to give informed consent themselves, written informed consent was signed on their behalf by their legally authorized representatives or next of kin. Confidentiality and anonymity of all participants were ensured during the study.

Study Population

The study population included adult patients admitted to the ICU for over 24 hours of mechanical ventilation. The inclusion criteria were adult patients aged 18 to 65 years and hemodynamically stable with MAP equal to or greater than 65 mmHg and needed continuous sedation for mechanical ventilation(Carayannopoulos et al., n.d.). The desired sedation was a Richmond Agitation-Sedation Scale (RASS) of -2 to -3. Patients were recruited irrespective of the reason for ICU admission, from post-op care and trauma to sepsis and respiratory failure.



Patients were excluded from the study if they had a known allergy or contraindication to dexmedetomidine or midazolam, or if they had severe hepatic or renal impairment(Mohamed et al., n.d.). Those with existing neurological or psychiatric conditions, hemodynamic instability necessitating high doses of vasopressors, or a history of alcohol or substance abuse were excluded, too. Pregnant or breastfeeding women were also not included because of the risk to the fetus or newborn.

Sample size and randomization

60 patients were recruited for the study and randomly allocated to one of two groups by a computer-

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generated randomization list. Randomization was done by means of sealed opaque envelopes in order to provide allocation concealment and avoid selection bias(Clark, 2022). Group A comprised 30 patients treated with dexmedetomidine as the sedative, and Group B comprised 30 patients treated with midazolam. Randomization was done by a third-party practitioner who was not attached to the administration or observation of the sedatives and hence ensured blinding and objectivity of the study.

Intervention Protocol

Sedation in both groups was begun within two hours of initiating mechanical ventilation. Dexmedetomidine was given as a loading dose of 1 microgram per kilogram over ten minutes, followed by maintenance infusion at the rate of 0.2 to 0.7 micrograms per kilogram per hour to patients in Group A. The rate of infusion was titrated according to sedation needs and hemodynamic state of each patient(K. M. Nelson et al., 2020).

For Group B, midazolam was utilized as the sedative agent. The patients received a loading dose of 0.03 to 0.1 milligrams per kilogram followed by a continuous infusion of 0.02 to 0.1 milligrams per kilogram per hour. The rate of infusion was titrated based on the desired level of sedation and patient response. No other sedative agents were administered unless clinically necessary, and rescue sedation or analgesia usage was also recorded.

Sedation Assessment

The degree of sedation was evaluated every hour on the Richmond Agitation-Sedation Scale (RASS). The target was to have a RASS score between -2, which is light sedation, and -3, which is moderate sedation. Any other value than this range was documented, and the infusion of the sedative was altered accordingly(Ki et al., n.d.). The critical care staff and nursing team were educated regarding the use of the RASS scale to achieve consistency and objectivity in sedation evaluation during the study.

Monitoring and Data Collection

All patients were monitored continuously with routine ICU monitoring equipment. Hourly values for vital signs such as heart rate, mean arterial pressure, oxygen saturation, and respiratory rate were collected. Baseline sedation scores were collected, then hourly until extubation or sedation was stopped. Clinical events like bradycardia, hypotension, desaturation, or other adverse effects were watched closely and recorded.

Besides sedation scores and vital signs, information on the duration of mechanical ventilation, time to successful extubation, ICU stay, and total sedative dose received was gathered. Delirium incidence was detected daily by the Confusion Assessment Method for the ICU (CAM-ICU). Additional opioid

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analgesics required and their cumulative dose were also noted to compare the sedatives' opioid-sparing effects.

Component	Description	Group A (Dexmedetomidine)	Group B (Midazolam)
Study Design	Prospective, randomized, controlled clinical trial in ICU patients requiring sedation on mechanical ventilation	30 patients received dexmedetomidine via loading dose + maintenance infusion	30 patients received midazolam via loading dose + maintenance infusion
Population & Randomization	Adult ICU patients (age 18–65), hemodynamically stable, RASS -2 to -3 target; excluded severe organ dysfunction or psychiatric issues	Randomized via sealed envelopes; intervention by blinded personnel	Same method
Intervention Protocol	Sedation initiated within 2 hours of intubation; dose titrated based on sedation level and vitals	Loading: 1 mcg/kg over 10 min → Infusion: 0.2–0.7 mcg/kg/hr	Loading: 0.03–0.1 mg/kg → Infusion: 0.02–0.1 mg/kg/hr
Monitoring & Assessment	Hourly RASS scoring, vitals monitoring, CAM-ICU for delirium, data on extubation, ICU stay, opioid use	RASS, vitals, adverse effects (e.g., bradycardia, hypotension), opioid-sparing evaluated	Same parameters monitored; comparison of efficacy and safety
Statistical Methods	SPSS v25; t-test/Mann-Whitney for continuous variables, Chi-square/Fisher's exact for categorical; significance at $p < 0.05$	Efficacy in achieving RASS -2 to -3, opioid use, adverse events, ICU stay, etc.	Efficacy in achieving RASS -2 to -3, opioid use, adverse events, ICU stay, etc.

Primary and Secondary Outcomes

The main result of the study was the capacity of each sedative drug to sustain the target RASS level of sedation on mechanical ventilation. The secondary outcomes were mechanical ventilation duration, extubation time, delirium incidence, hemodynamic stability, rescue sedation requirement, total sedative use, opioid use, and ICU stay. The safety profile of each agent was also determined by observing for adverse events, specifically cardiovascular instability like hypotension and bradycardia.

Statistical Analysis

All data gathered were keyed into and analyzed with the Statistical Package for Social Sciences (SPSS) version 25.0. Continuous data like age, sedation scores, ventilation duration, and ICU stay length were presented as mean ± standard deviation and tested using the independent Student's t-test or Mann–Whitney U test based on normality of data distribution. The categorical variables, such as the occurrence of delirium or adverse events, were reported as frequencies and percentages and tested with the Chi-square test or Fisher's exact test when necessary(Xiao et al., n.d.). A p-value below 0.05 was used to determine the significance of all tests.

Results

1. Baseline Characteristics of Study Population

A total of 60 patients were enrolled in the final analysis, and 30 patients were in Group A (dexmedetomidine) and Group B (midazolam). Both groups were statistically similar in demographic and clinical characteristics at baseline, so that the groups were uniform and there was no significant pre-treatment bias.

In Group A, the age of the patients was 54.3 ± 10.2 years, whereas in Group B it was 53.6 ± 9.8 years ($p = 0.72$) and revealed no statistically significant difference in age. The gender distribution was also

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equal with 18 men and 12 women in Group A, and 17 men and 13 women in Group B (p = 0.79). The weight of the patients averaged 67.4 ± 8.1 kg in Group A and 66.9 ± 7.5 kg in Group B (p = 0.85). The clinical reasons for ICU admission—namely, sepsis, trauma, and post-operative management—were identical in both groups so that the basic conditions did not affect the results unevenly.

The average Acute Physiology and Chronic Health Evaluation II (APACHE II) score on admission to the ICU was 16.8 ± 4.3 in Group A and 17.1 ± 4.6 in Group B (p = 0.84), which shows that illness severity was also similar between the groups.

2. Sedation Quality and Target RASS Achievement

The main outcome measure of this research was the sustenance of the desired Richmond Agitation-Sedation Scale (RASS) score of between -2 (light sedation) and -3 (moderate sedation). The target RASS range was attained by both groups, but dexmedetomidine was significantly more efficient in sustaining sedation in the desired range throughout the overall duration of mechanical ventilation.

Group A sustained the target RASS level for a mean duration of 85.2% ± 7.3% of the sedation period, while Group B patients sustained it for 74.1% ± 9.6% of the time. The difference was significant at $p < 0.01$, suggesting a more stable and controllable sedation profile with dexmedetomidine.

Furthermore, over-sedation episodes (RASS ≤ -4) were fewer in the dexmedetomidine group, at 3.2% of sedation hours, compared to 11.6% in the midazolam group (p = 0.03). Patients in the dexmedetomidine group were also described by nurses as being more arousable and responsive while sedated, enabling improved monitoring and interaction with patients.

Outcome Measure	Group A (Dexmedetomidine)	Group B (Midazolam)	p-value
Target RASS Maintenance (%)	85.2% ± 7.3%	74.1% ± 9.6%	< 0.01
Duration of Mechanical Ventilation	62.3 ± 11.4 hours	78.5 ± 13.7 hours	0.002
Time to Extubation Post-Sedation	4.5 ± 1.1 hours	7.2 ± 1.8 hours	< 0.001
ICU Delirium Incidence	13.3% (4 patients)	33.3% (10 patients)	0.04
Morphine Equivalent Dose (mg)	98.6 ± 25.3 mg	137.4 ± 31.1 mg	0.001

3. Duration of Mechanical Ventilation

The time of mechanical ventilation was considerably less in Group A than in Group B. It was 62.3 ± 11.4 hours in Group A and 78.5 ± 13.7 hours (p = 0.002) in Group B. This reflects that dexmedetomidine helped in quicker clinical recovery and sooner extubation readiness.

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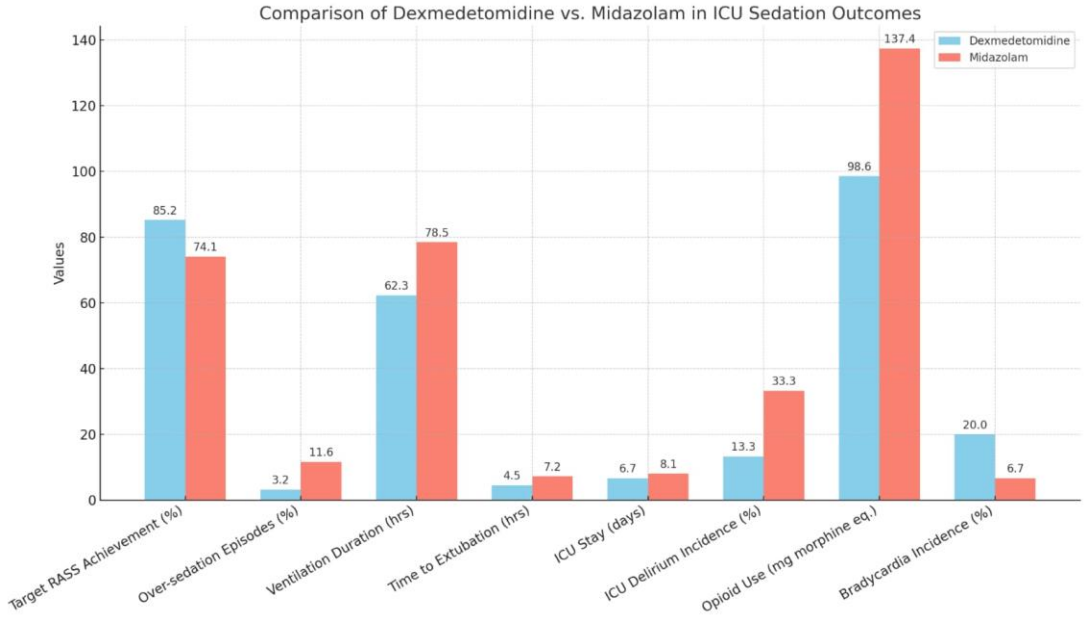

Early weaning and effective extubation were aided by the arousability of the sedative and the absence of significant respiratory depression. This variation also implies that dexmedetomidine has the potential to aid ventilator weaning protocols better compared to midazolam.

4. Extubation Time after Sedation

After sedative discontinuation, Group A patients were extubated faster than Group B patients. Average time to successful extubation following discontinuation of sedative infusion was 4.5 ± 1.1 hours in the dexmedetomidine group versus 7.2 ± 1.8 hours in the midazolam group. This was a statistically significant difference ($p < 0.001$), further lending strength to the better pharmacodynamic profile of dexmedetomidine, specifically its more rapid context-sensitive half-time and less residual sedation.

5. Length of ICU Stay

ICU stay was also a significant clinical outcome. ICU stay in Group A was significantly less than in Group B. ICU stay averaged 6.7 ± 1.9 days in the dexmedetomidine group, whereas the patients in the midazolam group had an average ICU stay of 8.1 ± 2.3 days ($p = 0.01$). The shorter ICU stay in the dexmedetomidine group was probably due to earlier extubation, fewer complications related to sedation, and more favorable overall recovery dynamics.

6. Incidence of ICU Delirium

Delirium is a frequent and severe ICU sedation complication. In this research, the delirium incidence, evaluated with the Confusion Assessment Method for the ICU (CAM-ICU), was considerably lower in the dexmedetomidine group. Delirium was only developed by 4 patients (13.3%) in Group A and by 10 patients (33.3%) in Group B ($p = 0.04$). These observations concur with earlier research indicating that dexmedetomidine is linked to less sedation-related delirium, potentially because of its distinct mode of action and its ability to maintain normal sleep architecture.

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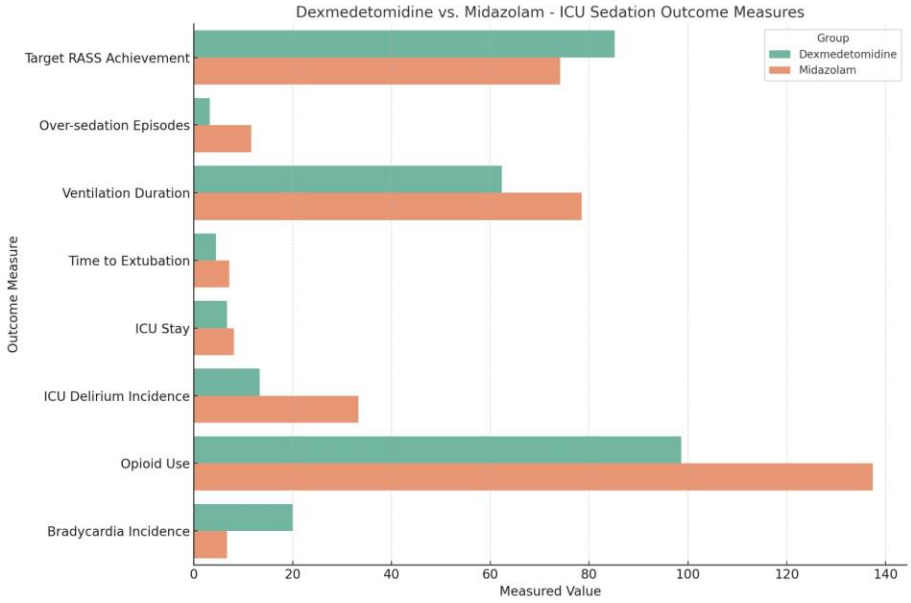

7. Opioid-Sparing Effects

The patients in the dexmedetomidine group needed much less opioid analgesia in the course of their ICU admission. The average cumulative dose of morphine equivalents given was 98.6 ± 25.3 mg in Group A, as opposed to 137.4 ± 31.1 mg in Group B ($p = 0.001$). The opioid-sparing quality of dexmedetomidine not only decreases the chances of opioid-induced side effects like constipation, nausea, and respiratory depression but also adds to improved post-extubation pain control and recovery.

8. Hemodynamic Changes and Adverse Events

While dexmedetomidine was effective in recovery and sedation, it was seen to cause a greater incidence of bradycardia. In Group A, 6 patients (20%) developed severe bradycardia (heart rate < 50 bpm) versus 2 patients (6.7%) in Group B ($p = 0.04$). Such events were usually mild and reversible with temporary lowering of infusion rate or intravenous fluids.

Hypotension (MAP < 65 mmHg) was also found to be more common in Group A (5 patients, 16.7%) compared to Group B (3 patients, 10%), though the difference was not statistically significant ($p = 0.41$). Severe hypotension and cardiac arrest were not found in either group.

Notably, no instances of serious respiratory depression or desaturation were reported from either drug. No patient needed to be re-intubated because of complications related to sedatives. Both drugs were generally well tolerated but necessitating close monitoring of hemodynamics during dexmedetomidine infusion remains essential.

Conclusion of Results

In conclusion, dexmedetomidine showed better performance compared to midazolam across various areas, such as sedation quality, shorter ventilation time, quicker extubation, shorter ICU stay, reduced incidence of delirium, and opioid-sparing. Although dexmedetomidine was found to have a greater incidence of bradycardia, overall safety and clinical outcomes indicate that it is a better and more desirable choice for sedation in mechanically ventilated ICU patients under anesthesia-related treatment.

Discussion

Successful sedation is an important part of the care for critically ill patients who are being mechanically ventilated in the ICU. Sedation not only allows for ventilator synchrony and procedural tolerance, but it also relieves the psychological discomfort of ICU stay(Mandal et al., 2023). The selection of sedative drugs can significantly affect short-term in-hospital outcomes and long-term outcome. The purpose of this study was to compare the efficacy and safety of two frequently employed sedative drugs—dexmedetomidine and midazolam—to achieve and sustain target levels of sedation in mechanically ventilated patients in Lady Reading Hospital,

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Peshawar. The findings of the randomized controlled trial reveal that dexmedetomidine is superior to midazolam in several clinically important aspects such as sedation quality, duration of mechanical ventilation, extubation time, length of ICU stay, opioid-sparing, and incidence of ICU delirium.

The results of this study are in agreement with previous studies indicating that dexmedetomidine has special benefits compared to standard benzodiazepines in ICU sedation regimes(Møller et al., 2022). Dexmedetomidine is an ultra-selective alpha-2 adrenergic receptor agonist that causes sedation by acting in the locus coeruleus, which closely follows normal patterns of sleep. In contrast to midazolam, which is a gamma-aminobutyric acid (GABA) receptor agonist with deep hypnosis and amnesia, dexmedetomidine delivers cooperative or arousable sedation. This type of sedation enables patients to be relaxed and still responsive, making neurological examination easier, eliminating the risk of over-sedation, and also making early mobilization a possibility in the ICU(Francis, 2021).

The most important finding of this study was that dexmedetomidine could sustain the desired target Richmond Agitation-Sedation Scale (RASS) range more reliably than midazolam. Dexmedetomidine patients spent more of their sedation period in the desired RASS range of -2 to -3. This finding suggests greater control of the sedation depth and reduced under- or over-sedation episodes(Burton, 2023). Over-sedation, also significantly increased in the midazolam group, can cause delay in extubation, prolong length of stay in ICU, and raise the rate of delirium. Sedative profile of dexmedetomidine, where frequent arousability of the patient without agitation is possible, appears to provide a more physiologically sound choice for sedation in ICU.

Another key result was the much reduced ventilation duration with mechanical ventilation in the dexmedetomidine group(Chen et al., 2020). These patients were ventilated for fewer hours and also had a faster course to successful extubation after the cessation of sedation. This benefit can be attributed to the minimal residual effects of dexmedetomidine and its action of not causing respiratory depression, one of the side effects of benzodiazepines. Midazolam, however, has an increased context-sensitive half-time and a higher risk for accumulation, particularly in patients with liver disease, which is prevalent in critically ill patients. These pharmacokinetic phenomena may be responsible for the delayed extubation in the midazolam group(Editors et al., 2024).

Reduced mechanical ventilation time equates to a number of significant advantages, such as decreased ventilator-associated pneumonia risk, fewer ICU days, decreased antibiotic use, and lower healthcare costs. In this study, ICU stay was also significantly less in the dexmedetomidine group. This supports the concept that earlier recovery and mobilization with lighter and more sensitive sedation can result in sooner ICU discharge. These advantages are particularly valuable in the context of resource-poor environments like Pakistan, where ICU beds tend to be in high demand.

Another concern in ICU care that is being explored is the effect of sedation on delirium. Delirium is linked to increased mortality, longer stay in the ICU, and permanent cognitive impairment. In our analysis, the incidence of delirium in the ICU was significantly reduced in the dexmedetomidine group versus the midazolam group. Multiple trials, including the M. This is probably because of its non-GABAergic action, its maintenance of sleep structure, and avoidance of deep sedation. Its preservation of sleep structure and maintenance of a lighter level of sedation and interaction with caregivers prevent the sensory deprivation and disorientation that usually lead to ICU delirium.

Another advantage seen with dexmedetomidine was its opioid-sparing property. Those in the dexmedetomidine group received much less opioid analgesia during their stay in the ICU.

(Donatiello et al., 2022). The analgesic effect of dexmedetomidine is well established and arises from its effect on spinal and supraspinal alpha-2 receptors. Opioid sparing not only decreases the risks of respiratory depression and ileus but also leads to easier recovery, fewer withdrawal phenomena, and lower rates of opioid-induced hyperalgesia.

Although these advantages, dexmedetomidine has some side effects. In the current study, in comparison with midazolam group, bradycardia incidence was much higher in dexmedetomidine group(Motlagh et al., n.d.). While no serious cardiovascular complications were noted, and all bradycardia were reversible with dose adjustment or fluid loading, this

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observation reiterates the need for hemodynamic monitoring close at hand during infusion of dexmedetomidine. Hypotension was also slightly increased in the dexmedetomidine group, though the difference wasn't statistically significant. These cardiovascular effects are due to dexmedetomidine's central sympatholytic effect and are dose-related(Ashraf et al., 2020). Physicians should exercise prudence, particularly when employing loading doses or commencing therapy in patients with compromised cardiac function.

The results of this research have significant implications for ICU sedation practice in Pakistan and other healthcare institutions. Resources in ICUs are limited in most developing countries, and long-term ICU stay can be costly for the healthcare system. An agent such as dexmedetomidine, which allows quicker weaning from mechanical ventilation, early extubation, and fewer ICU days, can enhance ICU turnover and save costs(Buckley et al., 2021). Nonetheless, its somewhat greater expense relative to midazolam could restrict use on a routine basis, and cost analyses must balance the initial cost against downstream savings that will derive from decreased ICU utilization.

In addition, this research contributes to the increasing evidence base for dexmedetomidine as the agent of choice in sedating mechanically ventilated patients. Although midazolam is still commonly used as a result of its affordability and familiarity, its shortcomings—particularly increased risk of delirium, longer extubation time, and increased requirement for opioid supplementation—are reason enough that it should be avoided in most ICU situations. Institutions that plan to apply evidence-based sedation guidelines should consider including dexmedetomidine, especially for patients needing prolonged mechanical ventilation or those at high risk of delirium.

Limitations of the study should be recognized. First, the sample size, while adequate to detect statistically significant differences, was relatively small and confined to one center. Larger multicenter trials would increase the generalizability of the results. Second, although the study was controlled and randomized, blinding was challenging to preserve since the two drugs have unique sedative profiles(Deng et al., 2022). Lastly, long-term results like cognition following ICU discharge were not measured and would be useful in future studies.

Overall, in conclusion, the randomized controlled trial showed that dexmedetomidine is superior to midazolam in achieving target levels of sedation, decreasing mechanical ventilation and ICU stay duration, lowering ICU delirium incidence, and minimizing the need for opioids in mechanically ventilated ICU patients. Dexmedetomidine, though with a greater incidence of bradycardia, was otherwise well-tolerated and clinically better. These results support the preferential utilization of dexmedetomidine compared to midazolam for sedation in the ICU, especially in anesthesia-intensive care of ventilated patients. Incorporation of such evidence into clinical protocols can result in improved patient outcomes and optimal use of ICU resources.

Conclusion

This Lady Reading Hospital, Peshawar, randomized controlled trial reveals that dexmedetomidine is clinically more beneficial than midazolam for sedating mechanically ventilated ICU patients. Dexmedetomidine achieved more stable sedation within the target RASS range, decreased mechanical ventilation duration, decreased ICU stay duration, and decreased ICU-associated delirium incidence significantly. It also showed opioid-sparing activity, leading to improved patient outcomes and better recovery. While dexmedetomidine was linked to an increased incidence of bradycardia, it was otherwise well-tolerated and controlled with proper clinical monitoring. These data highlight the possibility of using dexmedetomidine as a first-line sedative in ICU, especially in patients with the need for extended mechanical ventilation. Integration of dexmedetomidine into ICU sedation practices could not only optimize patient outcomes but also increase the overall effectiveness of critical care provision, particularly in settings with limited resources. Future multicenter studies are suggested to confirm these data and facilitate broad clinical application

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