

## COMPARED EFFECTIVENESS, SAFETY AND COST OF DEXMEDETOMIDINE WITH MIDAZOLAM: A REVIEW

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### *Abstract*

*Dexmedetomidine, an alpha 2 receptor agonist sedative drug, has recently garnered attention as a viable alternative to midazolam, a widely used benzodiazepine for sedation in adult patients. The aim of this study was to conduct a comprehensive comparison of the clinical sedative efficacy, cost-effectiveness, and safety profiles of dexmedetomidine versus midazolam, utilizing a randomized controlled trial design. The search encompassed several databases, including PubMed, Scopus, Web of Knowledge, CINAHL, the United States National Library of Medicine, and Google Scholar for Systematic Reviews, using the keywords 'dexmedetomidine,' 'midazolam,' and 'effectiveness.' The findings revealed that dexmedetomidine demonstrated a more favorable safety profile, with a lower incidence of delirium compared to midazolam. In terms of effectiveness, no significant differences were observed between the two drugs for local sedation. Notably, adult patients treated with dexmedetomidine had a shorter Intensive Care Unit (ICU) stay (7 days) compared to those receiving midazolam (10 days). Similarly, pediatric ICU treatment indicated a shorter duration with dexmedetomidine (20 hours) as opposed to midazolam (38 hours). Regarding cost-effectiveness, dexmedetomidine emerged as a cost-saving option, being approximately 10% cheaper than midazolam for adult ICU patients. These findings collectively highlight the advantages of dexmedetomidine over midazolam, encompassing superior safety, effectiveness, and cost-efficiency, thus providing valuable insights for healthcare practitioners and decision-makers.*

**Keywords:** *Dexmedetomidine, Effectiveness, Midazolam*

### 1. INTRODUCTION

Procedural sedation plays a crucial role in enhancing patient comfort during painful or unpleasant diagnostic and therapeutic procedures, making them more manageable for both patients and physicians. It is often preferred over general anesthesia due to its physiological, financial, and logistical advantages. Among the classic sedatives used for these purposes, midazolam has been a commonly employed choice. While midazolam is believed to induce minimal hemodynamic effects, it carries the potential risk of compromising airway reflexes, causing respiratory depression, and even leading to apnea (Aggarwal et al., 2020). Effective, reliable, and safe sedatives hold significant promise in general medical practice, particularly benefiting patients who may be debilitated, anxious, highly phobic, or uncooperative.

Dexmedetomidine, an alpha 2-adrenergic agonist, represents a relatively newer option for procedural sedation. This medication possesses sedative and anxiolytic properties and is distinguished by its analgesic potential, achieved through a reduction in sympathetic tone. Dexmedetomidine offers a dose-dependent spectrum of effects, ranging from minimal to deep sedation. Importantly, when administered at doses resulting in profound sedation or general anesthesia, the sedation is reversible. Patients can be easily

roused to a lucid state, but if left undisturbed, they gradually return to a state closely resembling natural sleep a unique characteristic among commonly used sedatives.

Notably, dexmedetomidine does not significantly impair respiratory drive, and instances of apnea associated with its use are rare. However, dexmedetomidine has been documented to impair the respiratory response to hypoxia and hypercapnia, potentially impacting the body's ability to adjust to changes in oxygen and carbon dioxide levels, as observed in the study by Azeem et al. (2018). Additionally, dexmedetomidine can induce hemodynamic effects such as hypertension, hypotension, and bradycardia, as reported by Aggarwal et al. (2020). These cardiovascular effects should be carefully considered, especially in patients with preexisting cardiovascular conditions. Despite the growing body of literature comparing the safety and efficacy of midazolam and dexmedetomidine, there remains a lack of systematic reviews that comprehensively synthesize the available evidence.

Therefore, the primary aim of our study was to systematically review the literature to evaluate the effectiveness, safety, and cost-effectiveness of dexmedetomidine and midazolam when used as mono sedatives for conscious, procedural sedation across a broad range of surgical and diagnostic procedures. This review sought to address the following research questions: Does dexmedetomidine produce more effective sedation than midazolam? Is it safer in the perioperative period? And is it more cost-effective? By addressing these questions, we aim to provide valuable insights into the comparative advantages of these sedatives in procedural sedation.

## **2. LITERATURE REVIEW**

Moore et al. (2022) in the study of 103 ventilated critically ill patients, Dexmedetomidine (DEX) was compared to usual-care sedation. More usual care patients received midazolam (57.7% vs. 33.3%;  $p=0.01$ ) at higher doses (0.46 [0.20–0.93] vs. 0.14 [0.08–0.38] mg/kg/day;  $p<0.01$ ). However, the plasma levels of stress hormones—adrenaline (0.32 [0.26–0.4] vs. 0.38 [0.31–0.48]), noradrenaline (4.27 [3.12–5.85] vs. 6.2 [4.6–8.5]), adrenocorticotropic hormone (17.1 [15.1–19.5] vs. 18.1 [15.9–20.5]), and cortisol (515 [409–648] vs. 618 [491–776])—showed no significant differences between the DEX and usual care groups. Furthermore, no significant differences were observed in other tested biomarkers or physiological parameters. Sensitivity analysis revealed no age or sepsis-related effects. In conclusion, initial sedation with DEX in ventilated critically ill adults did not yield significant differences in physiological or blood-borne stress biomarkers compared to usual care sedation.

According to (Vuković et al., 2022) randomized controlled trial, MDZ patients experienced desaturation events at a rate of 44%, while DEX patients had a lower rate of 12.7%. DEX effectively resolved desaturation events with supplemental oxygen, while 28% of MDZ desaturated patients needed further support, including chin lifts and jaw thrust maneuvers. Moreover, 76% of MDZ patients snored compared to 49% of DEX patients. DEX significantly reduced the likelihood of coughing by about 4.5 times, with coughing occurring in 14.5% of DEX patients versus 42.1% of MDZ patients. Moreover, DEX proves superior to MDZ in anesthesiology and surgery due to its reduced airway complications, increased patient comfort, fewer intraoperative issues, and minimal respiratory depressant effects. MDZ can lead to paradoxical reactions like confusion, violent behavior, and restlessness, and it also resulted in more instances of restlessness

and coughing compared to DEX. This study recommends the preference of DEX over MDZ for sedation management in transurethral resections of the prostate and bladder (TURB/TURP) under spinal anesthesia.

In a cost-minimization analysis by Aggarwal et al. (2020) in the United States, the per-patient costs for dexmedetomidine, propofol, and midazolam were \$21,115, \$27,073, and \$27,603, respectively. Dexmedetomidine resulted in savings of \$5,958 per patient compared to propofol and \$6,487 compared to midazolam. These savings were primarily due to shorter ICU stays, decreased monitoring and management requirements, and a lower incidence of adverse events. The minimum cost savings were associated with a 0.83-day reduction in ICU length of stay for dexmedetomidine patients (1.90 days in the base case analysis, 2.73 days in sensitivity analysis). The maximum cost savings were linked to a 1.23-day reduction in ICU length of stay for midazolam patients (3.00 days vs. 4.23 days). Additionally, compared to midazolam, dexmedetomidine also led to cost reductions related to mechanical ventilation (MV).

While J. Kim et al. (2021) found that dexmedetomidine demonstrated superior safety compared to midazolam, with a lower incidence of desaturation events (56.3% vs. 68.5%) and a lower proportion of patients with a Ramsay Sedation Scale (RSS) score of less than 3 (77.1% vs. 81.5%). However, the procedure duration was longer for dexmedetomidine (31.5 minutes) compared to midazolam (26.2 minutes). Interestingly, there were no instances of hypotension with dexmedetomidine, whereas one patient experienced hypotension with midazolam. The bronchoscopy score was also better with dexmedetomidine. Nevertheless, two dexmedetomidine patients experienced bradycardia (<50x/minute), while no midazolam patients did. In conclusion, while dexmedetomidine did not outperform midazolam in terms of desaturation events, it did result in fewer instances of coughing during the procedure.

In the study by Y. Zhou et al. (2022), the utilization of dexmedetomidine was linked to several advantages, including quicker recovery, earlier extubation, shorter weaning periods, more time maintained at the target sedation level, reduced fentanyl usage, and a lower incidence of delirium when compared to using midazolam alone, all without an increase in side effects. Moreover, when midazolam and dexmedetomidine were sequentially administered, it resulted in shorter recovery and extubation times, as well as reduced fentanyl doses when compared to patients treated with a sequential combination of midazolam and propofol.

There is a study by Jakob et al. (2012) published in JAMA which found that dexmedetomidine was not inferior to midazolam and propofol in maintaining mild to moderate sedation among ICU patients receiving prolonged mechanical ventilation, with similar sedation ratios. Dexmedetomidine resulted in a shorter median duration of mechanical ventilation compared to midazolam, though not significantly different from propofol. Furthermore, dexmedetomidine improved patients' ability to communicate pain when compared to both midazolam and propofol, as indicated by VAS scores. However, it was associated with a higher incidence of hypotension and bradycardia. Overall, the study suggests that dexmedetomidine may be a viable alternative to midazolam and propofol for sedation in these patients, offering potential benefits such as reduced ventilation duration and improved pain communication, albeit with increased side effects. ICU and hospital length of stay and mortality rates remained similar across the sedation methods.

Then, J.-Y. Kim et al. (2022) study comparing midazolam (MDZ) and dexmedetomidine (DEX) for intravenous sedation during third molar extraction, it was found that heart rate vital signs remained more consistently normal with MDZ compared to DEX (49.3% vs. 22.7%,  $P=0.001$ ), although heart rate was higher with MDZ ( $P=0.000$ ). The cost analysis revealed that DEX was associated with higher fees compared to MDZ (USD  $29.27\pm 0.00$  vs.  $0.37\pm 0.04$  USD,  $P=0.000$ ), making MDZ a more economical option. Interestingly, there were no significant differences observed in the Observer Rating of Alertness/Sedation Scale (OAAS), level of amnesia, or patient satisfaction between the two groups. However, Bispectral Index (BIS) values were lower in the MDZ group both 5 minutes after sedation administration and at the time of local anesthesia. In summary, DEX exhibited better stability in vital signs, whereas MDZ proved to be the more cost-effective choice. These findings provide valuable insights for healthcare providers when selecting the appropriate sedative for similar procedures.

In their meta-analysis, W.-J. Zhou et al. (2021) compared the efficacy and safety of midazolam (MDZ) and dexmedetomidine (DEX) in critically ill patients. Dexmedetomidine, a highly selective central alpha-2 adrenergic agonist, is known for its mild sedation, analgesia, and sleep-inducing properties, with the added benefit of reducing the incidence of delirium and promoting earlier extubation and discharge from the ICU. However, it is associated with common side effects such as bradycardia and hypotension. On the other hand, midazolam has historically been preferred for initial sedation in critically ill patients, offering effective sedation and amnesia in mechanically ventilated individuals. Nevertheless, midazolam is linked to a higher risk of delirium and prolonged extubation. In summary, dexmedetomidine is recommended for critically ill patients who require minimal sedation with a low risk of delirium and quicker extubation, but its use should be monitored for potential hypotensive and bradycardic effects. Midazolam remains a suitable choice for patients with a limited timeframe for ventilator discontinuation.

A study by Wang et al. (2020) comparing dexmedetomidine and midazolam for sedation in post-oral and maxillofacial surgery patients with retained tracheal intubation, both drugs were found effective in providing sedation while using opioids for analgesia. Dexmedetomidine potentially had some analgesic effects, possibly reducing the need for opioids. Notably, the dexmedetomidine group had a higher incidence of bradycardia but a reduced risk of respiratory depression compared to the midazolam group. Additionally, dexmedetomidine significantly lowered the occurrence of delirium in ICU patients. However, the assessment of patient sedation must consider factors beyond comfort, including resource utilization and mortality. Long-term cognitive and psychological effects, as well as overall recovery, should be assessed for a comprehensive understanding of patient prognosis. Clinically, it's vital to manage drug-related side effects while minimizing patient discomfort to ensure a safe recovery period, although these aspects warrant further discussion.

Salem et al. (2022) in their study, compared intranasal sedatives, midazolam (IN MDZ) and dexmedetomidine (DEX), in pediatric patients with high dental fear, sedation with IN MDZ resulted in more satisfactory overall behavior in very anxious pediatric dental patients. Despite initial uncooperative behavior, the psychological status of the study participants approached the average level and was not associated with sedation failure. Similarly, in Panda et al. (2021) study comparing intranasal dexmedetomidine and midazolam for sedation during transthoracic echocardiography (TTE) in pediatric

patients, both sedatives were deemed safe and effective for TTE sedation. Intranasal midazolam was found to have a relatively faster onset of action, higher scores in terms of sonographers' and parental satisfaction, but had longer sedation time, wake time, and total duration compared to intranasal dexmedetomidine.

In Mahmoud & Mason (2015) review of dexmedetomidine, higher doses of intranasal DEX (2 µg kg<sup>-1</sup>) were compared to 0.5 mg of oral midazolam, revealing that intranasal DEX led to a more rapid onset of sedation without a demonstrable difference in the state of induction, emergence, and recovery. Likewise, in Gulla et al.'s 2021 study comparing Dexmedetomidine and Midazolam for sedation in mechanically ventilated children, 49 children receiving intensive care in ICU levels 4 or 5 at the PSCH Hospital were divided into two groups. The results indicated no significant difference in ICU length of stay between the Midazolam and Dexmedetomidine groups. Children receiving Midazolam had an average ICU stay of 38 hours, while those receiving Dexmedetomidine had an average stay of 20 hours, with percentages of 56.5% for DEX and 67.3% for MDZ. The p-value difference was less than 0.05 (not significant). In summary, while there was a 20-hour difference in ICU length of stay favoring DEX over MDZ, the study did not find significant differences in the efficacy of the two sedative drugs. These studies collectively highlight the effectiveness and safety of both intranasal midazolam and dexmedetomidine in different pediatric clinical settings, emphasizing their suitability based on specific sedation requirements and patient characteristics.

In the study by Lachaine & Beauchemin (2012) evaluating the economic aspects of dexmedetomidine versus midazolam for sedation in the intensive care unit, it was found that while median drug costs were higher for dexmedetomidine per patient, the average expenses related to mechanical ventilation and delirium management were lower with dexmedetomidine compared to midazolam. Consequently, the overall cost per patient favored dexmedetomidine, which was confirmed through deterministic sensitivity analysis. In conclusion, the use of dexmedetomidine was generally preferred over midazolam due to its favorable clinical outcomes and cost-effectiveness, as it was associated with lower costs, reduced incidence of delirium, and shorter duration of artificial ventilation. On the other hand, Li et al. (2022) conducted a study involving 530 children to assess sedation with dexmedetomidine-midazolam for magnetic resonance imaging (MRI). The results showed high success rates of sedation, with 95.3% for the initial regimen and 97.7% with a rescue dose of intranasal dexmedetomidine. The sedation onset time averaged 10 minutes, and it was noted that onset time increased with age. Waking and emptying times correlated with the duration of the procedure. Importantly, no cases of oxygen deprivation or drug intervention due to cardiovascular instability were observed. Additionally, a history of previous sedation failure was identified as a significant risk factor for subsequent sedation failure in the multivariate logistic regression model. This study suggests that combining buccal midazolam with intranasal dexmedetomidine can provide a safe and effective sedation regimen for short-duration MRI in children aged 1 month to 10 years.

In Azeem et al. (2018), double-blinded clinical trial comparing dexmedetomidine to morphine and midazolam in preventing and treating delirium after adult cardiac surgery, Group A (administered dexmedetomidine diluted in 5% dextrose via a separate line and marked infusion device) exhibited several advantages. This included a shorter duration of mechanical ventilation, significantly reduced ICU stay (P = 0.038), and a lower risk of postoperative delirium compared to Group B, which received morphine and

midazolam. Group A also demonstrated a statistically significant reduction in heart rate values 4 hours after ICU admission without significant bradycardia and lower consumption of fentanyl after surgery. While the use of dexmedetomidine versus morphine and midazolam didn't significantly reduce the incidence of postoperative delirium, CRP levels, intubation duration, or ventilation duration, it proved to be a promising approach for improving post-cardiac surgery outcomes. The researchers suggested conducting a larger, double-blind randomized controlled trial with additional markers of inflammation and a broader patient age range to further investigate this approach's effectiveness and safety, along with cost-effectiveness and quality-of-life analysis.

In the randomized clinical trial conducted by Kawazoe et al. (2017), out of 203 screened patients, 201 were randomized for the study, with a mean age of 69 years (SD, 14 years) and 63% being male. The study found that mortality at 28 days did not significantly differ between the dexmedetomidine group and the control group (19 patients [22.8%] vs. 28 patients [30.8%]; hazard ratio, 0.69; 95% CI, 0.38–1.22;  $P = 0.20$ ). Likewise, the number of ventilator-free days at 28 days did not show a significant difference between the two groups (dexmedetomidine group: median, 20 [interquartile range, 5–24] days; control group: median, 18 [interquartile range, 0.5–23] days;  $P = 0.20$ ). However, the dexmedetomidine group did exhibit significantly higher levels of well-controlled sedation during mechanical ventilation (ranging from 17% to 58% vs. 20% to 39%;  $P = 0.01$ ). Overall, the use of dexmedetomidine in patients requiring mechanical ventilation did not result in a statistically significant increase in mortality or ventilator-free days. However, it's important to note that this study may be underpowered for assessing mortality, and further research may be warranted to provide a more comprehensive evaluation.

In the study conducted by Huang et al. (2022), a total of 151 patients were enrolled, with 77 in the dexmedetomidine group and 74 in the midazolam group. The research found no significant difference in 28-day mortality between the two groups (14.3% vs. 24.3%;  $p = 0.117$ ), as well as no notable distinctions in theta/beta ratio (TBR), delta/alpha ratio (DAR), and the ratio  $(\delta + \theta)/(\alpha + \beta)$  (DTABR) on both day 1 and day 3. However, it was observed that TBR and DTABR increased significantly in the dexmedetomidine group, while DTABR increased significantly in the midazolam group. Furthermore, DAR showed a significant increase on the right side in the dexmedetomidine group (20.4 (11.6–43.3) vs. 35.1 (16.7–65.0),  $p = 0.006$ ), and on both sides in the midazolam group (Left: 19.5 (10.1–35.8) vs. 37.3 (19.3–75.7),  $p = 0.006$ ; Right: 18.9 (10.1–52.3) vs. 39.8 (17.5–99.9),  $p = 0.002$ ). Ultimately, the study concluded that when comparing dexmedetomidine with midazolam in patients with brain injuries, there was no significant difference in 28-day mortality or improvement in qEEG results. Additionally, the length of stay in the ICU, length of stay in the hospital, and complications within 28 days were similar between the two groups.

In summary, multiple studies comparing dexmedetomidine and midazolam for sedation management in various clinical contexts reveal nuanced findings. Dexmedetomidine and midazolam each offer specific advantages and considerations. While dexmedetomidine demonstrates superior safety profiles and potential cost-effectiveness, midazolam remains a viable option, particularly for certain procedures. These studies emphasize the importance of individualized sedation choices, considering patient-specific factors and clinical requirements. The optimal selection between

dexmedetomidine and midazolam should be guided by a comprehensive assessment of the specific clinical scenario and desired sedation goals, with further research needed to provide clearer guidelines for their use.

### **3. RESEARCH METHOD**

The methodology employed for conducting this article review involved a comprehensive literature study. The selected sources were scientific journals comprising original articles published within the past five years, known for their reliability and trustworthiness. These journals encompassed both national and international publications focusing on the comparative analysis of effectiveness, safety, and cost-effectiveness in the utilization of dexmedetomidine and midazolam.

The process of article retrieval commenced with thorough searches across various reputable databases, including Google Scholar, PubMed, Science Direct, SCOPUS, Web of Knowledge, Cinahl, and the United States National Library of Medicine. This search was executed using specific keywords such as "dexmedetomidine," "midazolam," "comparison," "safety," "efficacy," "effectiveness," and "cost-effectiveness." In total, this article review identified 90 papers relevant to the research topic, out of which 18 met the predefined inclusion and exclusion criteria. Out of the 18 chosen journal publications, each directly compared dexmedetomidine and midazolam. These studies involved a varied group of participants, including patients and volunteers, resulting in diverse evaluations of effectiveness, cost, and safety. Among the selected publications, 11 studies concentrated on patients receiving procedural sedation, with the rest involving volunteer subjects. Additionally, three studies explored the cost-effectiveness of dexmedetomidine and midazolam, while others examined various facets of efficacy and safety.

The selection process for studies adhered to specific criteria: inclusion of participants receiving procedural sedation treatment, utilization of interventions such as dexmedetomidine for procedural sedation, and the employment of a randomized controlled clinical trial design. To compare efficacy, the results were primarily based on patient satisfaction scores and pain scores. In cases where outcome measures lacked numerical scoring or assessment, the verbal descriptions provided in the respective studies were employed for analysis.

## **4. RESULT AND DISCUSSION**

### **4.1. Effectiveness**

There were no significant differences between the use of midazolam and the use of dexmedetomidine in the OAAS (Observer Rating of Alertness/Sedation Scale), level of amnesia, or patient satisfaction between the two groups. BIS showed lower values in the MDZ group 5 minutes after sedation administration and at the time of local anesthesia [8]. The use of drugs for local anesthetic purposes does not show significant differences, so the choice between these two drugs in performing local sedation cannot be determined which is better.

In the use of sedation for children (Gulla et al., 2021), dividing 49 children who received intensive care in the ICU level 4 or 5 at the PSCH Hospital. The results showed that there was no significant difference between the use of Midazolam and Dexmedetomidine and the length of stay in the ICU. Children who received Midazolam

treatment had an average ICU stay of 38 hours, and children who received Dexmedetomidine had an average ICU stay of 20 hours, if the algorithm (%) is 56.5% (DEX) and 67, 3% (MDZ), has a P value difference of less than 0.05 (not significant) (Gulla et al., 2021).

Based on Zhou's study it was reported that the difference in length of stay in the ICU in patients who received dexmedetomidine and Midazolam was very significant (W.-J. Zhou et al., 2021). Patients receiving midazolam spent longer in the ICU (10 days) compared to patients receiving dexmedetomidine (7 days). In addition, the time to extubation in patients receiving midazolam (7 days) was longer compared to patients receiving dexmedetomidine (4 days). Extubation is the removal of the endotracheal tube after intubation. Extubation has the goal of keeping the endotracheal tube from causing trauma, as well as reducing laryngeal tissue reaction and reducing the risk of post-extubation.

#### 4.2. Safety

According to a study by Zhou et al, 2020 reported that the incidence of delirium in patients who received midazolam was found to be higher compared to patients who received dexmedetomidine, while the incidence of bradycardia in patients who received dexmedetomidine was higher than patients who received midazolam. Delirium is a mental disorder caused by rapid changes in brain function, so that sufferers experience a decrease in their ability to think and concentrate and remember, and even focus. Delirium often causes sufferers to have difficulty sleeping and are often confused.

Another study in brain-injured patients showed that dexmedetomidine could alleviate cerebral ischemic reperfusion injury by increasing  $\alpha_2$ -adrenergic receptors and blocking JNK phosphorylation and caspase activation (Jakob et al., 2012). The use of dexmedetomidine in patients with brain injury did not cause death 28 days lower than the use of midazolam and the EEG results on the use of dexmedetomidine were better.

#### 4.3. Cost Effectiveness

According to a study conducted by Lachaine & Beauchemin (2012), it was shown that the duration of mechanical ventilation was significantly longer with midazolam, compared with those with dexmedetomidine.

**Table 1. Drug Effectiveness Cost**

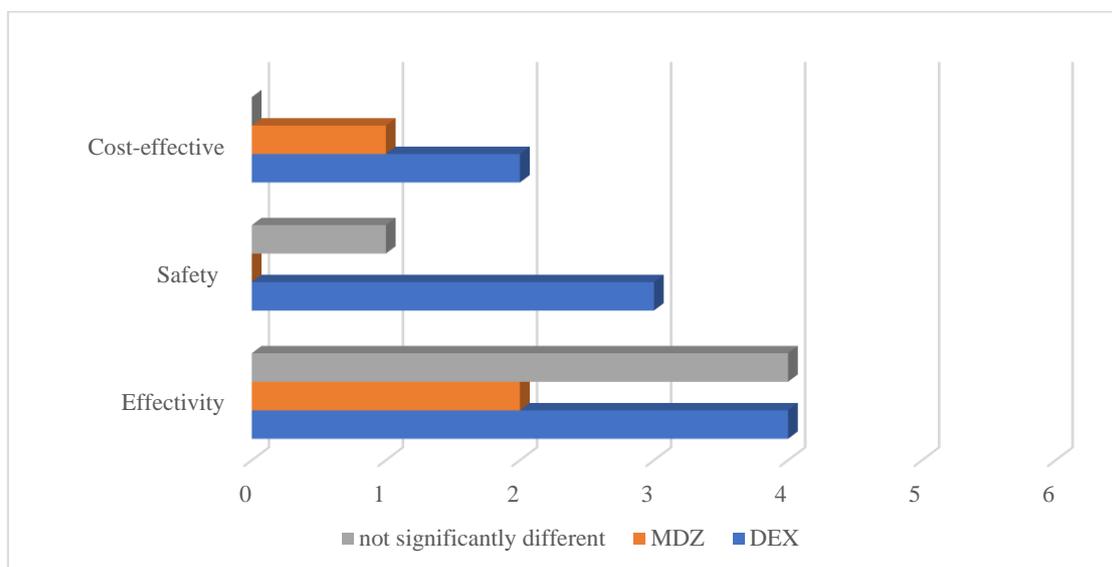
	Dexmedetomidine	Midazolam	Difference
Treatment	IDR 29,522,421	IDR 2,755,530	IDR 26,766,891
Additional therapy	IDR 28,305	IDR 26,928	IDR 1,377
Ventilator	IDR 44,960,886	IDR 68,048,892	(-) IDR 23,088,006
Costs related to delirium	IDR 32,550,597	IDR 46,088,190	(-) IDR 13,537,593
Unwanted reaction	IDR 357,921	IDR 586,755	(-) IDR 210,834
Total cost per patient	IDR 107,438,130	IDR 117,506,295	(-) IDR 10,068,165

Source : (Aggarwal et al., 2020; Azeem et al., 2018; Gulla et al., 2021; Huang et al., 2022; Jakob et al., 2012; Kawazoe et al., 2017; J.-Y. Kim et al., 2022; J. Kim et al., 2021; Lachaine & Beauchemin, 2012; Li et al., 2022; Mahmoud & Mason, 2015; Moore et al., 2022; Panda et al., 2021; Salem et al., 2022; Vuković et al., 2022; Wang et al., 2020; W.-J. Zhou et al., 2021; Y. Zhou et al., 2022)

According to the table above, in the dexmedetomidine-treated group, because delirium occurred in fewer patients, the duration of mechanical ventilation was shorter, and intervention for hypertension was required in fewer patients (10.6 percentage point difference). As a result, the total cost per patient for dexmedetomidine administration was IDR 107,438,130, approximately IDR 10,068,165 lower than the total cost per patient for midazolam administration, which was IDR 117,506,295.

The results of a previous cost minimization analysis performed in this study indicated that dexmedetomidine is less expensive than midazolam for long-term sedation in the ICU. The results of the reported cost consequence analysis, lead to the same conclusion. Compared with midazolam, dexmedetomidine is associated with a lower incidence of delirium episodes and a shorter median time to extubation, while being a cost-effective alternative. The main drivers of cost savings in the cost minimization and cost consequence studies were the reduction in costs associated with ICU stay and reduction in the cost of mechanical ventilation.

The following is a flowchart for comparing the effectiveness, safety and cost-effectiveness of MDZ vs DEX:



**Figure 1. Comparison of the Effectiveness, Safety and Cost-Effectiveness of The Anti-Sedative Therapy Dexmedetomidine with Midazolam**

In Figure 1, it has been explained that from the value of effectiveness as many as 4 studies found dexmedetomidine to be more effective than midazolam and as many as 2 studies favored midazolam, while there were 4 studies that produced insignificant differences. Then from the safety point of view, treatment with dexmedetomidine has shown that it is safer with 3 supporting studies when compared with midazolam, but there

is 1 study which states that there is no significant difference. And in terms of cost-effectiveness, only a few have explained that 2 studies supporting dexmedetomidine are more cost-effective when compared to midazolam.

## 5. CONCLUSION

The systematic review of available literature has provided valuable insights into the comparative effectiveness, safety, and cost-effectiveness of dexmedetomidine and midazolam for procedural sedation. Dexmedetomidine appears to offer several advantages over midazolam, particularly in terms of shorter Intensive Care Unit (ICU) stays for adult patients. The reduced length of ICU stay not only potentially enhances patient comfort but also contributes to more efficient resource utilization. Additionally, the lower incidence of delirium observed in patients receiving dexmedetomidine suggests a potential improvement in patient safety compared to midazolam. Moreover, the reduced mortality rate among brain-injured patients receiving dexmedetomidine underscores its potential as a safer option in specific clinical scenarios.

Furthermore, the cost-effectiveness aspect cannot be overlooked, with dexmedetomidine emerging as a cost-saving option, approximately 10% cheaper than midazolam for adult ICU patients. This financial advantage could significantly impact healthcare budgets while still maintaining the quality of care. However, it is essential to note that dexmedetomidine does present a higher incidence of bradycardia compared to midazolam, warranting careful patient monitoring and consideration of individual patient factors when making sedation choices. Overall, the findings of this systematic review suggest that dexmedetomidine stands as a promising alternative to midazolam in procedural sedation, offering benefits in terms of patient outcomes, cost-effectiveness, and safety.

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