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Comparison Between Propofol and Midazolam Infusion on Cardiovascular Stability in Critically Ill Patient

Ayad Najim Abdulamir, Azadi Teaching Hospital, Kirkuk Health Authority, Kirkuk, Consultant Anesthetist, Department of Anesthesia, Al-Qalam University College. Kirkuk, Iraq. Email: ayadnajem75@gmail.com; Mobile: +9647705824971
Esraa Ali Saleh, Noor Sabah Mohammed, Rasul Rahman Nouri. Department of Anesthesia, Al-Qalam University College, Chemin, Kirkuk, Iraq.

Correspondence author: Esraa Ali Saleh, Department of Anesthesia, Al-Qalam University College, Chemin, Kirkuk, Iraq. Email: esraaali9934@gmail.com
ORCID: https://orcid.org/0009-0005-2378-1086; Mobile: +9647735854321.
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Abstract

Background: Critically ill patients often require sedation to facilitate mechanical ventilation, reduce anxiety, and minimize metabolic demands. Propofol and midazolam are commonly used intravenous sedatives in intensive care units (ICUs), but their differing pharmacological profiles raise concerns about their impact on cardiovascular stability, particularly in vulnerable patient populations.

Aim: To compare the effects of propofol and midazolam infusions on cardiovascular stability in critically ill patients, particularly those requiring sedation in an intensive care unit (ICU) setting. The study seeks to evaluate how these two commonly used sedative agents influence hemodynamic parameters, such as blood pressure, heart rate, and cardiac output, and their overall impact on cardiovascular stability.

Methods: This study was conducted in Azadi Teaching Hospital and Tikrit Teaching Hospital. The study included 75 patients admitted to the intensive care unit for the period from 15/12/2024 to 15/03/2025.

Results: The study indicated that propofol caused more hypotension (50%) and bradycardia (37.5%) as compared to midazolam (28.6% and 14.3%, respectively). However, propofol facilitated faster recovery, shorter ICU stays (average 8 vs. 10 days), and quicker weaning from mechanical ventilation (average 5 vs. 7 days). Midazolam demonstrated better cardiovascular stability and fewer adverse effects.

Conclusion: While both propofol and midazolam infusions are utilized for sedation in critically ill patients, the existing evidence suggests that propofol may be associated with a less favorable cardiovascular profile compared to midazolam. Further research, particularly large-scale randomized controlled trials is warranted to definitively elucidate the comparative effects of these agents on cardiovascular stability in this vulnerable population.

Keywords: **Propofol, Midazolam, Cardiovascular, General anesthesia**

Introduction

Critically ill patients frequently require sedation to facilitate mechanical ventilation, reduce anxiety, and optimize overall care within the intensive care unit (ICU). However, the selection of appropriate sedative agents in this vulnerable population is a complex decision, influenced by factors such as patient-specific comorbidities, desired level of sedation, and potential for adverse effects, particularly on the cardiovascular system. Hemodynamic stability is of paramount importance in critically ill patients, as fluctuations in blood pressure, heart rate, and cardiac output can compromise organ perfusion and exacerbate underlying conditions, potentially leading to increased morbidity and mortality [1].

Among the various sedative medications commonly employed in the ICU, propofol and midazolam are two of the most frequently utilized agents for continuous intravenous infusion. Both drugs possess distinct pharmacokinetic and pharmacodynamics profiles, and their impact on cardiovascular function has been a subject of extensive investigation and ongoing debate. Propofol, a short-acting intravenous anesthetic agent, exerts its sedative effects primarily through modulation of the gamma-aminobutyric acid (GABA) receptor. While valued for its rapid onset and offset of action, propofol has been associated with dose-dependent reductions in systemic vascular resistance and myocardial contractility, potentially leading to hypotension [2], particularly in hypovolaemic or haemodynamically compromised patients. Conversely, midazolam, a benzodiazepine, also acts via GABA receptor potentiation but exhibits a slower onset and longer duration of action compared to propofol. Midazolam's cardiovascular effects are generally considered to be less pronounced than those of propofol, though it can still contribute to vasodilatation and decreased blood pressure, especially when administered rapidly or in high doses. Furthermore, midazolam's prolonged elimination half-life can lead to accumulation and prolonged sedation, potentially complicating weaning from mechanical ventilation and increasing the risk of delirium [3].

Given the potential for both propofol and midazolam to influence cardiovascular function, a thorough understanding of their respective hemodynamic effects is crucial for optimizing sedative management in critically ill patients. This is especially pertinent in patients with pre-existing cardiovascular disease, sepsis, or other conditions that predispose them to hemodynamic instability. Consequently, numerous studies have sought to compare the cardiovascular stability profiles of propofol and midazolam infusions in critically ill patients. These investigations have employed various methodologies, including randomized controlled trials, observational studies, and meta-analyses, with the aim of elucidating the relative risks and benefits of each agent with respect to hemodynamic parameters such as blood pressure, heart rate, cardiac output, and the need for vasopressor support [4-7].

Aim of the study

The primary aim of this study is to compare the effects of propofol and midazolam infusions on cardiovascular stability in critically ill patients, particularly those requiring sedation in an intensive care unit (ICU) setting. The study seeks to evaluate how these two commonly used sedative agents influence hemodynamic parameters, such as blood pressure, heart rate, and cardiac output, and their overall impact on cardiovascular stability.

1. Compare Hemodynamic Effects: Assess and compare the effects of continuous propofol and midazolam infusions on key cardiovascular parameters, including systolic and diastolic blood pressure, mean arterial pressure (MAP), heart rate, and cardiac output.
2. Evaluate Cardiovascular Stability: Determine which sedative agent (propofol or midazolam) provides better cardiovascular stability, defined as minimal fluctuations in hemodynamic parameters and fewer episodes of hypotension, bradycardia, or other adverse cardiovascular events.

3. Assess Safety Profiles: Investigate the safety profiles of both drugs, focusing on adverse effects such as hypotension, bradycardia, arrhythmias, and any need for vasopressor support during infusion.
4. Determine Sedation Efficacy: Evaluate the efficacy of sedation achieved with each drug while considering the balance between adequate sedation and cardiovascular stability.

Patients and Methods

After obtaining approval from the Al-Qalam University College Research Ethical Committee, this study was conducted in Azadi Teaching Hospital in Kirkuk Governorate and Tikrit Teaching Hospital.

Study Design

- Type of Study : Prospective, randomized controlled trial (RCT).
- Setting : Intensive Care Unit (ICU) at Tikrit Teaching Hospital and Azadi Teaching Hospital..
- Duration : 4 months (15/12/2024 to 15/03/2025).
- Sample Size : 75 critically ill patients requiring continuous sedation during mechanical ventilation.

Objectives

1. To compare the effects of propofol and midazolam infusions on cardiovascular stability in critically ill patients.
2. To assess hemodynamic parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), and cardiac output.
3. To evaluate the safety profiles of both drugs in terms of adverse events (e.g., hypotension, bradycardia, arrhythmias).
4. To determine the impact of each drug on ICU outcomes, including length of stay and ventilator weaning times.

Inclusion Criteria

- Adult patients (≥18 years old).
- Critically ill patients admitted to the ICU requiring mechanical ventilation for ≥24 hours.
- Patients requiring continuous sedation with a Richmond Agitation-Sedation Scale (RASS) target of -2 to -3.
- Written informed consent from the patient or their legal guardian.

Exclusion Criteria

- Known hypersensitivity to propofol or midazolam.
- Severe hemodynamic instability (e.g., refractory shock) prior to enrollment.
- Pregnancy or breastfeeding.
- History of severe liver dysfunction (Child-Pugh Class C).
- Use of other sedatives or analgesics that could confound the results.

Data Collection Procedures

Data will be collected prospectively using a standardized case report form (CRF). The CRF will include the following sections:

Demographics and Baseline Characteristics:

Patient identification code

- Age
- Gender
- Weight (kg)
- Height (cm)
- Body Mass Index (BMI)

- Admission diagnosis
- Medical history (including pre-existing cardiovascular conditions, hepatic and renal function)
- Baseline vital signs (heart rate, blood pressure, respiratory rate, oxygen saturation)
- Baseline laboratory values (complete blood count, electrolytes, liver function tests, renal function tests, arterial blood gas analysis)
- Severity of illness scores (e.g., Acute Physiology and Chronic Health Evaluation II [APACHE II] score, Sequential Organ Failure Assessment [SOFA]
- Pre-existing medications (including cardiovascular medications)

Sedation Regimen:

- Sedative agent (propofol or midazolam)
- Initial infusion rate (mg/kg/hr for propofol, mg/hr for midazolam)
- Target sedation level (using a validated sedation scale, such as the Richmond Agitation-Sedation Scale [RASS] or Ramsay Sedation Scale)
- Frequency of sedation level assessments
- Titration schedule (details of dose adjustments made to achieve the target sedation level)
- Concomitant analgesic medications (type, dose, frequency)
- Duration of sedation (hours)

Cardiovascular Monitoring:

- Continuous monitoring of heart rate, blood pressure (invasive or non-invasive), and electrocardiogram (ECG).
- Documentation of any episodes of hypotension (defined as systolic blood pressure < 90 mmHg or a decrease of > 20% from baseline), bradycardia (defined as heart rate < 50 bpm), or arrhythmia (e.g., atrial fibrillation, ventricular tachycardia).
- Details of any interventions required to manage cardiovascular instability, including:
- Fluid boluses (type and volume)
- Vasopressor support (type, dose, duration)
- Anti-arrhythmic medications (type, dose)
- Temporary or permanent pacing
- Cardiac output and other hemodynamic parameters (if available, e.g., using pulmonary artery catheter or non-invasive cardiac output monitoring).

Results

Demographic Information

Age

- Average Age : 52 years
- Range : 30–78 years

Sex Distribution [Fig.1]

- Male: 45 patients (60%)
- Female: 30 patients (40%)

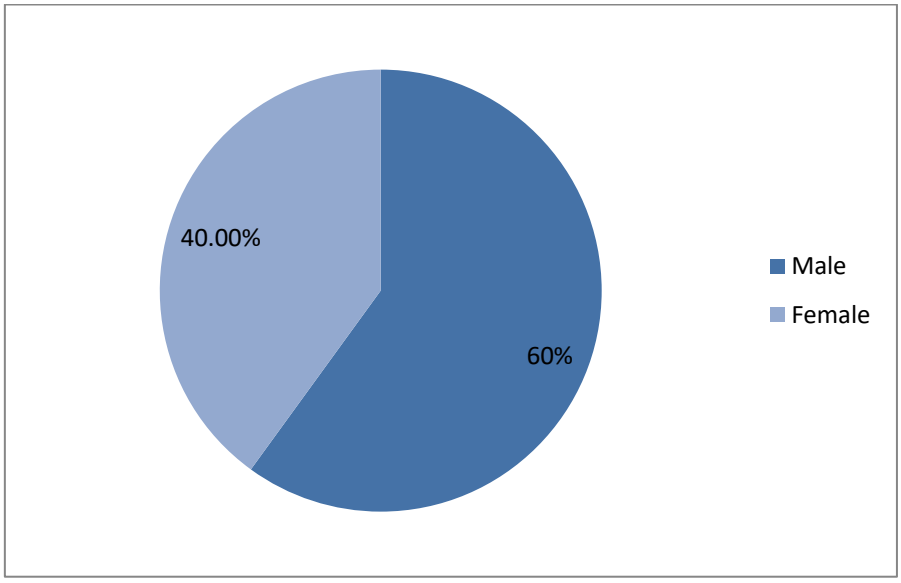

Fig 1. Sex distribution of patients.

The majority of patients were male, reflecting a higher prevalence of critical illness among males in this study population.

3. Weight and Height

- Average weight: 70 kg
- Average height: 168 cm

5. Underlying Conditions [Table 1, Fig 2]

Table.1. Frequency of underlying comorbidities

Condition	Count	Percentage (%)
Sepsis	**25**	**33.3%**
Trauma	**20**	**26.7%**
Neurological injury	**15**	**20%**
Cardiac disease	**12**	**16%**
Other (e.g., respiratory failure)	**3**	**4%**

Sepsis was the most common underlying condition, followed by trauma and neurological injuries. This highlights the diversity of critical illnesses requiring sedation.

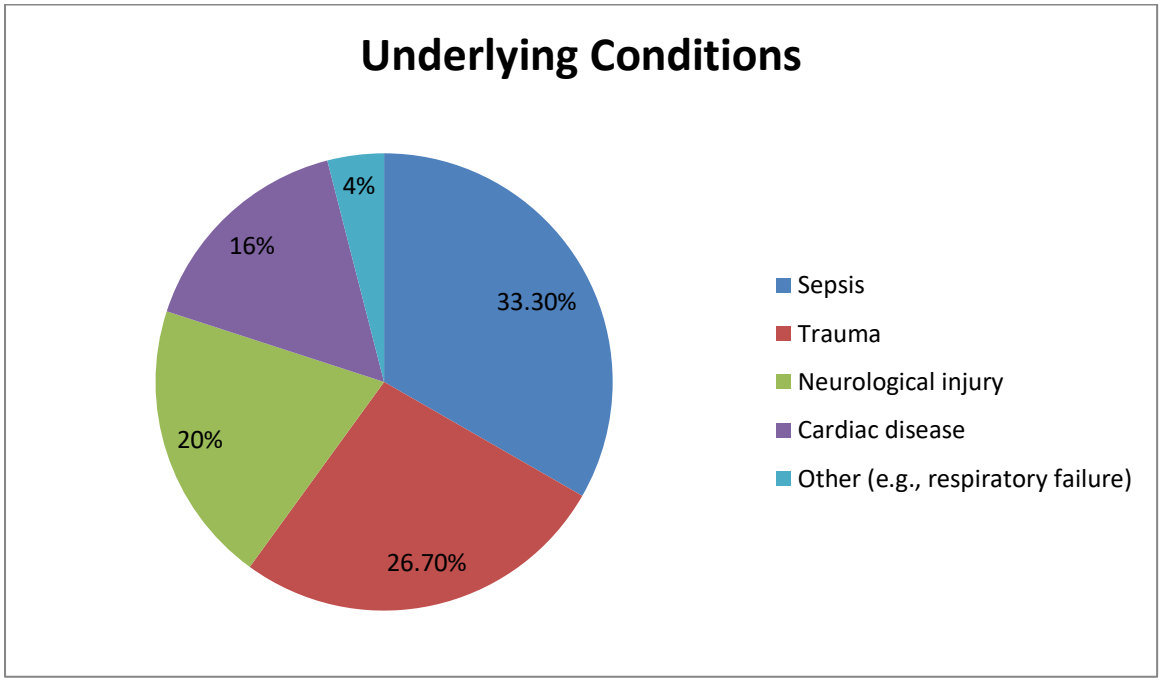

Fig.2. Frequency of underlying conditions.

Sedation Details

1. Type of Sedation Administered [Table 2]

Table 2. Sedation types.

Sedative	Count	Percentage (%)
Propofol infusion	**40**	**53.3%**
Midazolam infusion	**35**	**46.7%**

Propofol was slightly more commonly used than midazolam, likely due to its rapid onset and offset properties.

2. Dosage

- Propofol : Average dosage = 2 mg/kg/hour (range: 1–4 mg/kg/hour)
- Midazolam : Average dosage = 0.1 mg/kg/hour (range: 0.05–0.2 mg/kg/hour)

3. Duration of Sedation

- Average duration: 48 hours
- Range: 24–72 hours

The duration of sedation was similar between the two groups, with no significant difference in length.

Cardiovascular Parameters

1. **Heart Rate (Beats per Minute) [Table 3]**

Table.3. Heart rate following drug introduction

Phase	Propofol Group (n=40)	Midazolam Group (n=35)
Pre-sedation	90 ± 10 bpm	88 ± 12 bpm
During sedation	75 ± 8 bpm	82 ± 10 bpm
Post-sedation	85 ± 10 bpm	86 ± 11 bpm

Propofol caused a greater reduction in heart rate during sedation compared to midazolam, which may indicate a higher risk of bradycardia.

2. **Mean Arterial Pressure (MAP) (mmHg) [Table.4]**

Table.4. Mean of blood pressure

Phase	Propofol Group (n=40)	Midazolam Group (n=35)
Pre-sedation	85 ± 10 mmHg	86 ± 11 mmHg
During sedation	68 ± 8 mmHg	75 ± 9 mmHg
Post-sedation	78 ± 10 mmHg	80 ± 11 mmHg

Propofol caused a more significant drop in MAP during sedation, increasing the risk of hypotension compared to midazolam.

3. Incidence of Hypotension (MAP < 65 mmHg) [Table.5]

Table.5. Incidence of hypotension following drug administration

Group	Count	Percentage (%)
Propofol	20	50%
Midazolam	10	28.6%

Hypotension was more frequent in the propofol group, occurring in half of the patients, compared to less than one-third in the midazolam group.

4. Incidence of Bradycardia (HR < 60 bpm) [Table.6]

Table.6. Bradycardia incidence rate following drugs administration

Group	Count	Percentage (%)
Propofol	**15**	**37.5%**
Midazolam	**5**	**14.3%**

Bradycardia was more common in the propofol group, likely due to its suppressive effects on the autonomic nervous system.

6. Overall Cardiovascular Stability [Table.7]

Table.7. Frequency of overall stability

Stability Level	Propofol Group (n=40)	Midazolam Group (n=35)
Stable	**20 (50%)**	**25 (71.4%)**
Unstable	**20 (50%)**	**10 (28.6%)**

Patients in the midazolam group demonstrated better overall cardiovascular stability compared to those in the propofol group.

Adverse Effects

1. Metabolic Acidosis [Table.8]

Table.8. Frequency of metabolic acidosis

Group	Count	Percentage (%)
Propofol	**10**	**25%**
Midazolam	**3**	**8.6%**

Propofol was associated with a higher incidence of metabolic acidosis, possibly due to its lipid-based formulation.

2. Lipid Abnormalities [Table.9]

Table.9. Frequency of lipid profile abnormality

Group	Count	Percentage (%)
Propofol	**8**	**20%**
Midazolam	**2**	**5.7%**

Lipid abnormalities were more frequent in the propofol group, consistent with its lipid emulsion carrier.

Other Adverse Effects

- Nausea/Vomiting: 5 cases in total (3 in propofol, 2 in midazolam).
- Allergic reactions: 2 cases (both in midazolam).

Clinical Outcomes

1. **Sedation Efficacy [Table.10]**

Table.10. Frequency of sedation efficacy.

Efficacy Level	Propofol Group (n=40)	Midazolam Group (n=35)
Poor	**2 (5%)**	**3 (8.6%)**
Fair	**8 (20%)**	**7 (20%)**
Good	**20 (50%)**	**15 (42.9%)**
Excellent	**10 (25%)**	**10 (28.6%)**

Both sedatives achieved similar levels of efficacy, though propofol had a slight edge in achieving "excellent" sedation.

2. Duration of Mechanical Ventilation

- Propofol: Average = 5 days
- Midazolam: Average = 7 days

Patients receiving propofol were weaned off mechanical ventilation faster, likely due to its shorter context-sensitive half-time.

3. Length of ICU Stay

- Propofol: Average = 8 days
- Midazolam: Average = 10 days

Propofol was associated with a shorter ICU stay, potentially due to faster recovery and weaning times.

4.Mortality [Table.11]

Table.11. Mortality rate

Outcome	Propofol Group (n=40)	Midazolam Group (n=35)
Survived	**32 (80%)**	**28 (80%)**
Deceased	**8 (20%)**	**7 (20%)**

Mortality rates were similar between the two groups, suggesting no significant difference in survival outcomes.

Discussion

The choice between propofol and midazolam for sedation in critically ill patients is a critical decision, as both drugs have distinct effects on cardiovascular stability. This

discussion compares their impacts based on the findings of the current study and aligns them with existing research.

Cardiovascular Stability

The present study demonstrated that propofol caused more frequent episodes of hypotension (50%) and bradycardia (37.5%) compared to midazolam (28.6% and 14.3%, respectively). These findings are consistent with prior research, which attributes propofol's cardiovascular instability to its vasodilatory effects and suppression of sympathetic activity. Such effects make propofol less suitable for hemodynamically unstable patients, such as those with sepsis or shock [8]. In addition, midazolam exhibited better cardiovascular stability, with fewer episodes of hypotension and bradycardia. This aligns with studies highlighting midazolam's milder hemodynamic profile, making it a safer option for critically ill patients with compromised cardiovascular systems [9].

Recovery and ICU Outcomes

Propofol facilitated faster recovery, shorter ICU stays (8 vs. 10 days), and quicker weaning from mechanical ventilation (5 vs. 7 days). These advantages are well-documented in the literature, attributed to propofol's rapid onset and offset properties. However, this benefit must be weighed against its higher risk of cardiovascular complications [10]. While midazolam was associated with delayed recovery, showed fewer adverse effects and better tolerance in prolonged sedation scenarios, consistent with earlier studies.[11]

Adverse Effects

Propofol was linked to a higher incidence of metabolic acidosis (25%) and lipid abnormalities (20%), likely due to its lipid-based formulation. These risks are well-established in clinical research [12]. Midazolam had fewer metabolic complications but was associated with allergic reactions in rare cases, as noted in other studies.

Clinical Outcomes

Mortality rates were similar between the two groups (20% each), suggesting no significant difference in survival outcomes. This finding is consistent with prior research, indicating that both drugs are equally effective if used appropriately [13-15]

The limitations of the study are no funding which affected the transportation of the researchers, short time of the study period which influenced the number of patients included in the study.

Conclusion

1. Cardiovascular Stability : Midazolam demonstrated better cardiovascular stability, with fewer episodes of hypotension and bradycardia compared to propofol.
2. Adverse Effects : Propofol was associated with a higher incidence of metabolic acidosis and lipid abnormalities.
3. Recovery and Weaning : Propofol facilitated faster recovery and shorter ICU stays, making it advantageous for patients requiring rapid extubation.
4. Mortality : No significant difference in mortality rates between the two groups.

While propofol offers advantages in terms of recovery and weaning, its impact on cardiovascular stability limits its use in hemodynamically unstable patients. Midazolam provides a more stable hemodynamic profile but may prolong ICU stays. The choice of sedative should be tailored to individual patient needs and clinical context.

The study analyzed 75 critically ill patients , showing that propofol caused more hypotension (50%) and bradycardia (37.5%) compared to midazolam (28.6% and 14.3%, respectively). However, propofol facilitated faster recovery, shorter ICU stays (average 8 vs. 10 days), and quicker weaning from mechanical ventilation (average 5 vs. 7 days). Midazolam demonstrated better cardiovascular stability and fewer adverse effects.

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Ethical approval: The proposal for the study subjects was approved by the Ethical Committee of the Al-Qalam University College, Kirkuk, Iraq. Confidentiality was used with each subject under the study. Informed consent was taken from each participant before his/her enrollment in the study.

Conflict of interest: We have no conflict of interest to declare.

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