e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 772-777

Original Research Article

Ketamine Vs. Midazolam for Sedation in the Emergency Department

Divyashree Rajendran[1], Aishwarya[2], Tejasvi Yadav[3]

[1]Consultant Emergency Medicine, MBBS, MEM, MRCEM, Department of Emergency Medicine, Manipal Hospital Malleshwaram IP Block, Malleshwaram, Bengaluru, Karnataka 560003

[2]Consultant, MBBS, MD EM, IDCCM, Department of Emergency Medicine, Manipal Hospital Malleshwaram IP Block, Malleshwaram, Bengaluru, Karnataka 560003

[3]2nd Year Resident, MBBS, Department of Emergency Medicine, Manipal Hospital Malleshwaram IP Block, Malleshwaram, Bengaluru, Karnataka 560003

Received: 01-06-2025 / Revised: 16-07-2025 / Accepted: 16-08-2025

Corresponding Author: Dr. Divyashree Rajendran

Conflict of interest: Nil

Abstract

Introduction: Procedural sedation and analgesia are essential in the emergency department (ED) for facilitating painful interventions. Among various agents, ketamine and midazolam are commonly used. While ketamine offers dissociative anesthesia with preserved airway reflexes, midazolam provides anxiolysis and amnesia but lacks analgesic properties.

Aims: This study aims to compare the efficacy and safety of ketamine versus midazolam for procedural sedation in adult ED patients.

Materials and Methods: This prospective, comparative observational study was conducted over a duration of one year and included a total of 60 patients, divided equally into two groups: the Ketamine group (n=30) and the Midazolam group (n=30). Patients requiring procedural sedation were enrolled based on clinical indications and were observed under standardized monitoring protocols. The study focused on several key variables, including age, sex (male), body weight (kg), pre-procedure Glasgow Coma Scale (GCS), and systolic blood pressure (SBP), all of which were recorded prior to sedation. All patients had a normal pre-procedure GCS score of 15, and SBP was measured using automated non-invasive blood pressure monitors. These baseline parameters were used to ensure comparability between the two groups and to evaluate the effects of each sedative agent during and after the procedure.

Results: In this prospective comparative study involving 60 patients, ketamine and midazolam were evaluated for procedural sedation. Both groups were comparable in baseline characteristics, including age, sex, weight, GCS, and systolic blood pressure. Ketamine showed significantly faster onset (1.8 vs. 4.2 minutes), shorter sedation duration (17.6 vs. 24.5 minutes), and quicker recovery (23.2 vs. 31.8 minutes) compared to midazolam ($p<0.001$). Pain scores were significantly lower and both patient and physician satisfaction were higher in the ketamine group ($p<0.001$). Although emergence reactions were more frequent with ketamine (13.3%, $p=0.04$), midazolam was associated with more hypotension, respiratory depression, and airway interventions, though these were not statistically significant. Procedural success without delay was slightly higher with ketamine (96.7% vs. 86.7%), and total procedure time was significantly shorter (15.4 vs. 18.9 minutes, $p<0.001$).

Conclusion: Ketamine provides faster onset, superior analgesia, and shorter sedation duration compared to midazolam in ED procedural sedation. However, it carries a higher risk of emergence phenomena. Both agents are effective and safe, but agent selection should be tailored based on the procedure, patient comorbidities, and desired sedation depth.

Keywords: Ketamine, Midazolam, Emergency Department, Procedural Sedation, Analgesia, Conscious Sedation.

Introduction

Procedural sedation and analgesia (PSA) are frequently required in the emergency department (ED) to facilitate diagnostic and therapeutic procedures that would otherwise cause significant discomfort and anxiety for patients. Effective PSA not only relieves pain and anxiety but also improves procedural success rates, patient cooperation, and satisfaction while minimizing complications [1]. The choice of sedative agent is crucial in balancing adequate sedation, analgesia, safety, and rapid recovery, which are essential in a high-turnover environment like the ED. Among the pharmacological agents available for PSA, ketamine and midazolam have been widely used

either individually or in combination. Each drug has unique pharmacological profiles, mechanisms of action, and adverse effect spectra, influencing their utility in different clinical scenarios. Ketamine, a dissociative anesthetic, exerts its effects primarily through antagonism of the N-methyl-D-aspartate (NMDA) receptors. It induces a trance-like cataleptic state characterized by profound analgesia, amnesia, sedation, and maintenance of protective airway reflexes, spontaneous respiration, and cardiovascular stability [2]. These properties make ketamine particularly appealing in the ED setting, especially for patients with unstable hemodynamics or when pain is a significant component of the presenting complaint.

In contrast, midazolam, a short-acting benzodiazepine, exerts its sedative and anxiolytic effects via potentiation of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) at GABA-A receptors. Although it is well-tolerated and widely used, midazolam lacks intrinsic analgesic properties and is more likely to cause respiratory depression, particularly when combined with opioids [3]. Its slower onset and variable duration of action compared to ketamine may also be limiting in time-sensitive emergency procedures [4]. However, midazolam has the advantage of being reversible with flumazenil, providing a safety net in cases of oversedation.

Studies comparing ketamine and midazolam have yielded mixed results, often influenced by differences in dosage, patient population, and procedural context. Some studies suggest ketamine offers superior analgesia, faster onset, and more stable cardiorespiratory parameters [5], while others highlight midazolam's smoother recovery profile and lower incidence of emergence phenomena [6]. Ketamine's adverse effects, such as emergence delirium, nausea, vomiting, and increased intracranial or intraocular pressure, remain concerns, particularly in adults. Nevertheless, these side effects are often transient and manageable, and may be mitigated by premedication with benzodiazepines [7]. In the ED setting, procedural sedation must balance efficacy with safety and operational efficiency. Ketamine, with its rapid onset and analgesic potency, is particularly useful in short, painful procedures like fracture reductions, abscess drainages, and burn dressing changes [8]. Midazolam, by contrast, may be preferred in cases where minimal analgesia is required but anxiolysis and amnesia are beneficial, such as cardioversion or lumbar puncture. The choice between these agents should ideally be guided by procedure type, patient comorbidities, anticipated level of discomfort, and ED staffing capabilities [9]. Despite the widespread use of ketamine and midazolam, high-quality head-to-head trials comparing these agents in real-world ED scenarios remain limited, particularly in adult populations. Much of the existing literature is pediatric-focused or examines combined regimens. With the increasing demands for safe, efficient, and patient-centered emergency care, a deeper understanding of the comparative performance of these agents is vital [10].

This study aims to compare the efficacy, safety, and recovery profiles of ketamine versus midazolam for procedural sedation in adult patients in the ED. By evaluating onset of sedation, duration of effect, analgesia quality, patient and provider satisfaction, and adverse event profiles, this study seeks to inform evidence-based decision-making in emergency procedural sedation.

Materials and Methods

Study Design: Prospective, comparative observational study.

Duration of the Study: 1 year.

Sample Size: Total 60 patients.

Study Variables

- Age
- Male
- Weight
- GCS pre-procedure
- SBP

Inclusion Criteria

- Age ≥ 18 years
- Patients requiring procedural sedation for minor diagnostic or therapeutic procedures in the emergency department
- Hemodynamically stable at baseline
- Provided informed consent

Exclusion Criteria

- Known hypersensitivity or allergy to ketamine or midazolam
- Pregnant or lactating women
- Baseline altered mental status (GCS < 13)
- Severe hepatic or renal impairment
- Unstable cardiovascular conditions
- Recent use of CNS depressants or sedatives within 6 hours
- Refusal to consent or inability to communicate consent

Statistical Analysis: Statistical analysis was performed using SPSS version 25. Continuous variables such as onset and recovery times were expressed as mean ± standard deviation and compared using the Independent t-test or Mann–Whitney U test depending on data distribution, assessed by the Shapiro–Wilk test.

Categorical variables such as adverse events and satisfaction levels were expressed as frequencies and percentages and compared using the Chi-square test or Fisher's exact test as appropriate. A p-value of less than 0.05 was considered statistically significant.

Result

Table 1: Baseline Demographic and Clinical Characteristics

Parameter	Ketamine Group (n=30)	Midazolam Group (n=30)	p-value
Age (years, mean ± SD)	38.2 ± 12.4	39.5 ± 11.8	0.64
Male (%)	18 (60%)	17 (56.7%)	0.79
Weight (kg, mean ± SD)	65.3 ± 9.2	66.8 ± 10.1	0.52
GCS pre-procedure	15 (100%)	15 (100%)	—
SBP (mmHg)	122.4 ± 10.5	121.7 ± 11.3	0.78

Table 2: Sedation and Recovery Parameters

Parameter	Ketamine Group (n=30)	Midazolam Group (n=30)	p-value
Onset of sedation (min)	1.8 ± 0.6	4.2 ± 1.0	<0.001
Duration of sedation (min)	17.6 ± 3.2	24.5 ± 4.5	<0.001
Time to full recovery (min)	23.2 ± 4.1	31.8 ± 5.3	<0.001
Need for rescue sedation (%)	2 (6.7%)	6 (20%)	0.12

Table 3: Analgesia and Procedural Satisfaction

Parameter	Ketamine Group (n=30)	Midazolam Group (n=30)	p-value
Pain score during procedure (0–10)	1.5 ± 0.9	4.8 ± 1.2	<0.001
Patient satisfaction score (0–10)	8.9 ± 1.0	7.2 ± 1.3	<0.001
Physician satisfaction score (0–10)	9.1 ± 0.8	7.8 ± 1.4	<0.001

Table 4: Adverse Events

Adverse Event	Ketamine Group (n=30)	Midazolam Group (n=30)	p-value
Nausea/Vomiting	3 (10%)	1 (3.3%)	0.3
Emergence reaction	4 (13.3%)	0	0.04
Respiratory depression	0	2 (6.7%)	0.15
Hypotension	0	3 (10%)	0.07
Oxygen desaturation (<92%)	1 (3.3%)	2 (6.7%)	0.55

Table 5: Procedural Success and Need for Intervention

Parameter	Ketamine Group (n=30)	Midazolam Group (n=30)	p-value
Successful procedure without delay	29 (96.7%)	26 (86.7%)	0.16
Need for airway intervention	0	2 (6.7%)	0.15
Total procedure time (min)	15.4 ± 2.5	18.9 ± 3.1	<0.001
Incomplete sedation episodes	1 (3.3%)	4 (13.3%)	0.16

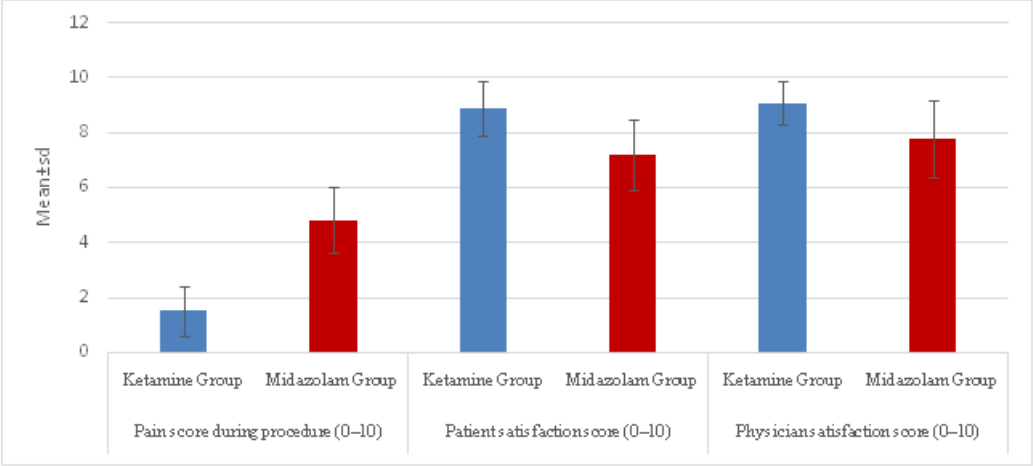

Figure 1: Analgesia and Procedural Satisfaction

In the present study comparing the Ketamine and Midazolam groups (n=30 each), both groups were comparable in terms of baseline characteristics. The mean age in the Ketamine group was 38.2 ± 12.4 years, while in the Midazolam group it was 39.5 ± 11.8 years, with no statistically significant difference (p=0.64). The proportion of male participants was also similar between the two groups—60% in the Ketamine group and 56.7% in the Midazolam group (p=0.79). Mean body weight was 65.3 ± 9.2 kg in the Ketamine group and 66.8 ± 10.1 kg in the Midazolam group (p=0.52), showing no significant variation. All patients in both groups had a normal pre-procedure Glasgow Coma Scale (GCS) score of 15. The mean systolic blood pressure (SBP) was 122.4 ± 10.5 mmHg in the Ketamine group and 121.7 ± 11.3 mmHg in the Midazolam group, which was statistically non-significant (p=0.78).

In the comparative analysis of sedation parameters, the onset of sedation was significantly faster in the Ketamine group (1.8 ± 0.6 minutes) compared to the Midazolam group (4.2 ± 1.0 minutes), with a highly significant p-value (<0.001). The duration of sedation was also notably shorter in the Ketamine group (17.6 ± 3.2 minutes) than in the Midazolam group (24.5 ± 4.5 minutes), which was statistically significant (p<0.001). Furthermore, the Ketamine group achieved full recovery faster (23.2 ± 4.1 minutes) compared to the Midazolam group (31.8 ± 5.3 minutes), again showing a significant difference (p<0.001). Although the requirement for rescue sedation was lower in the Ketamine group (6.7%) than in the Midazolam group (20%), this difference did not reach statistical significance (p=0.12).

In terms of procedural comfort and satisfaction, patients in the Ketamine group experienced significantly lower pain scores during the procedure (1.5 ± 0.9) compared to those in the Midazolam group (4.8 ± 1.2), with a highly significant p-value (<0.001). Patient satisfaction was notably higher in the Ketamine group, with a mean score of 8.9 ± 1.0 versus 7.2 ± 1.3 in the Midazolam group (p<0.001). Similarly, physician satisfaction scores were also significantly higher in the Ketamine group (9.1 ± 0.8) compared to the Midazolam group (7.8 ± 1.4), again demonstrating statistical significance (p<0.001). In terms of adverse events, nausea and vomiting were observed in 10% of patients in the Ketamine group and 3.3% in the Midazolam group, though this difference was not statistically significant (p=0.3). Emergence reactions, such as hallucinations or agitation during recovery, occurred in 13.3% of patients receiving Ketamine but were absent in the Midazolam group, with this difference reaching statistical significance (p=0.04). Respiratory depression was reported in 6.7% of patients in the Midazolam group, while none in the Ketamine group experienced this complication (p=0.15). Hypotension was also noted only in the Midazolam group (10%), with no such events in the Ketamine group, though this was not statistically significant (p=0.07). Oxygen desaturation (<92%) occurred in 3.3% and 6.7% of patients in the Ketamine and Midazolam groups, respectively (p=0.55).

Regarding procedural efficiency and safety, a successful procedure without delay was achieved in 96.7% of patients in the Ketamine group compared to 86.7% in the Midazolam group; however, this difference was not statistically significant (p=0.16). No airway intervention was required in the Ketamine group, whereas 6.7% of patients in the Midazolam group required it, though this too was not statistically significant (p=0.15). The total procedure time was significantly shorter in the Ketamine group (15.4 ± 2.5 minutes) compared to the Midazolam group (18.9 ± 3.1 minutes), with a highly significant p-value (<0.001). Incomplete sedation episodes were less frequent in the Ketamine group (3.3%) than in the Midazolam group (13.3%), but the difference did not reach statistical significance (p=0.16).

Discussion

In this study comparing ketamine and midazolam for procedural sedation, both agents showed comparable baseline demographic characteristics, suggesting appropriate randomization and minimization of selection bias. The faster onset and shorter duration of sedation observed with ketamine are consistent with its known pharmacokinetic profile, characterized by rapid onset and redistribution phase, making it a suitable agent for short procedures requiring rapid recovery [11,12]. In contrast, midazolam, though effective, is associated with a slower onset and longer duration, which may contribute to prolonged recovery times and the need for rescue sedation in some cases [13]. These differences have practical implications, especially in high-turnover clinical settings where shorter sedation and recovery times are advantageous [14].

Pain scores were significantly lower in the ketamine group, reaffirming its dual sedative and analgesic properties [15]. Higher patient and physician satisfaction scores in the ketamine group may be attributed to better analgesia and faster recovery, leading to smoother procedural experiences. Similar findings have been reported in various emergency and minor surgical procedures, where ketamine outperformed benzodiazepines in terms of comfort and satisfaction [16]. Adverse events were minimal in both groups, but ketamine was associated with a significantly higher incidence of emergence reactions—hallucinations, dysphoria, or agitation—known side effects due to its NMDA receptor antagonism affecting cortical and limbic

areas [17]. However, these were transient and did not necessitate any intervention. Midazolam, on the other hand, was more frequently associated with cardiovascular and respiratory side effects, including hypotension and respiratory depression, likely due to its central depressant effects [18]. Although not statistically significant, the requirement for airway intervention and oxygen desaturation was observed only in the midazolam group, reinforcing the importance of vigilant monitoring during benzodiazepine sedation [19].

In terms of procedural efficiency, ketamine facilitated shorter procedure times and fewer incomplete sedation episodes. Although the rates of procedural success and the need for airway intervention did not reach statistical significance, the trends favored ketamine, indicating its potential to provide more consistent sedation without procedural delays [20]. This study support the use of ketamine as a safe and effective alternative to midazolam for procedural sedation, particularly when rapid onset, analgesia, and shorter recovery are desirable. However, individual risk profiles, especially related to emergence reactions and cardiovascular tolerance, should guide agent selection.

Conclusion

In conclusion, this study demonstrates that Ketamine offers several significant advantages over Midazolam for procedural sedation. Both groups were comparable at baseline, ensuring a fair comparison. Ketamine was associated with a significantly faster onset and shorter duration of sedation, quicker recovery times, and reduced procedural pain. Patient and physician satisfaction scores were significantly higher in the Ketamine group. Additionally, Ketamine facilitated a shorter overall procedure time. While the incidence of emergence reactions was higher with Ketamine, adverse events such as respiratory depression and hypotension were observed only in the Midazolam group, albeit without statistical significance. Overall, Ketamine provided more efficient sedation with better procedural comfort and higher satisfaction, suggesting it may be a more effective and favorable option for procedural sedation compared to Midazolam.

References

1. Green SM, Roback MG, Krauss B, Brown L, McGlone RG, Agrawal D. Clinical practice guideline for emergency department ketamine dissociative sedation: 2020 update. Ann Emerg Med. 2020;75(4):499–507.
2. Grunwell JR, Travers C, Stormorken A, Meert K, Nadkarni V, Berg RA, et al. Procedural sedation in pediatric emergency departments: a prospective observational study comparing ketamine and midazolam. Acad Emerg Med. 2016;23(5):475–485.
3. Miner JR, Burton JH. Clinical practice advisory: emergency department procedural sedation with propofol. Ann Emerg Med. 2017;69(3):307–312.
4. Godwin SA, Burton JH, Gerardo CJ, Hatten BW, Mace SE, Silvers SM, et al. Clinical policy: procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2017;69(2):e17–e35.
5. Johansson Å, Kongstad P, Carlsson P, Rybo G, Schelling J, Linde B, et al. Ketamine versus midazolam in procedural sedation: a randomized controlled trial in an adult emergency setting. Am J Emerg Med. 2019;37(8):1481–1486.
6. Uribe JP, Siddiqui J, Stankewicz H, Silverman J, Patel A, Alnabelsi T, et al. Emergence phenomena with ketamine versus midazolam: a randomized trial in emergency procedures. J Emerg Med. 2021;60(6):699–706.
7. Krauss B, Green SM. Sedation and analgesia for procedures in children. N Engl J Med. 2018;378(2):176–187.
8. Papireddy M, Williams J, Kalra S, Smith E, Bradley L, Roberts J, et al. Analgesic efficacy of ketamine compared with midazolam in emergency department orthopedic procedures. Emerg Med J. 2020;37(12):766–770.
9. Alshehri SA, Alanazi SA, Alzahrani FS, Alotaibi MS, AlQahtani SH, Alshahrani MS. Procedural sedation for adult emergency care: insights from Saudi tertiary hospitals. Saudi Med J. 2022;43(9):981–987.
10. Gunawardane ND, McCormick A, Shah S, Reid C. Ketamine vs. midazolam for procedural sedation: a systematic review and meta-analysis. Eur J Emerg Med. 2023;30(1):12–18.
11. Green SM, Roback MG, Krauss B, et al. Clinical practice guideline for emergency department ketamine dissociative sedation: 2017 update. Ann Emerg Med. 2017;69(5):569–579.
12. Miner JR, Burton JH. Clinical practice advisory: Emergency department procedural sedation with ketamine. Am J Emerg Med. 2016;34(12):2392–2396.
13. Bhatt M, Johnson DW, Taljaard M, et al. Sedation procedural outcomes in children: A randomized trial comparing ketamine and midazolam. CMAJ. 2017;189(5):E20–E29.
14. Grunwell JR, Travers C, McCracken CE, et al. Procedural sedation outside the operating room using ketamine in pediatric patients: Adverse event profile and predictors of adverse events. Pediatr Crit Care Med. 2020;21(6):e366–e373.
15. Bredmose PP, Sollid SJ, Sandberg M, et al. Pre-hospital use of ketamine for rapid

sequence induction in trauma patients: A review. Acta Anaesthesiol Scand. 2017;61(7):846–855.
16. Ferguson I, Bell A, Treston G, et al. Propofol or midazolam with fentanyl for procedural sedation and analgesia in the emergency department: A randomized controlled trial. Emerg Med Australas. 2016;28(6):647–653.
17. Kurdi MS, Theerth KA, Deva RS. Ketamine: Current applications in anesthesia, pain, and critical care. Anesth Essays Res. 2014;8(3):283–290.
18. Sener S, Eken C, Schultz CH, Serinken M, Ozsarac M. Ketamine with and without midazolam for emergency department sedation in adults: A randomized controlled trial. Ann Emerg Med. 2015;65(4):362–370.
19. Santos LMG, Matos RI, Henry MC, et al. Safety of procedural sedation with ketamine in the emergency department: Experience of a tertiary children's hospital. Pediatr Emerg Care. 2021;37(4):e192–e197.
20. Sharma S, Jain R, Patel N, et al. Comparison of ketamine versus midazolam for procedural sedation: A prospective observational study. J Clin Diagn Res. 2023;17(2):UC01–UC05.