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Midazolam or propofol added to ketamine: Which combination is better for the reduction of shoulder dislocation in the emergency department?

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Abstract:

OBJECTIVE: Glenohumeral dislocation is the most common type of shoulder dislocation and a leading cause of shoulder instability. Adequate muscle relaxation and pain control are essential for successful reduction. This study compared the effectiveness and safety of ketamine–midazolam (KM) versus ketamine–propofol (KP) for procedural sedation in anterior shoulder dislocations in the emergency department (ED). Effectiveness was evaluated using Ramsay sedation scale (RSS) scores, sedation onset, total procedure and recovery times, and reduction success. Safety was assessed by recording adverse events.

METHODS: This prospective, single-blind, randomized trial included patients ≥18 years presenting to a tertiary ED with anterior shoulder dislocation. Patients were randomized into two groups: KM (ketamine plus midazolam) and KP (ketamine plus propofol). Demographic and clinical characteristics, RSS scores, procedure and recovery times, adverse events, and additional sedation requirements were recorded.

RESULTS: Sixty-four patients were analyzed, 32 in each group. The overall mean RSS score was 4.5 ± 1.0, significantly higher in the KP group ($P < 0.001$). Adverse events were more common in the KM group, including higher rates of respiratory depression ($P = 0.023$) and tachycardia ($P < 0.001$). The mean procedure time was 5.7 ± 4.7 min, and recovery time was 36.3 ± 14.4 min, both significantly shorter in the KP group ($P = 0.025$ and $P < 0.001$, respectively).

CONCLUSION: In the ED, the ketamine–propofol combination appears to be a safe and effective option for procedural sedation and analgesia, particularly in interventions such as shoulder reduction.

Keywords:

Emergency department, ketamine, midazolam, propofol, sedation, shoulder reduction

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Introduction

The shoulder joint, due to its biomechanical characteristics and complex anatomical structure, has the widest range of motion. Since shoulder stability is primarily provided by soft tissues, it carries a high risk of dislocation.[1] Adequate muscle relaxation and pain management play a

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Box-ED Section

What is already known about the topic?

- Shoulder dislocation is a frequent emergency presentation that often necessitates procedural sedation for successful reduction
- Ketamine is widely used because of its dissociative and analgesic properties. It is commonly combined with midazolam or propofol to enhance sedation quality and reduce side effects, although the optimal combination remains uncertain.

What is the conflict on the issue? Has it have importance for readers?

- There is an ongoing debate about whether ketamine should be combined with midazolam or propofol to achieve the safest and most effective procedural sedation
- This question is clinically important because the choice of drug combination directly impacts patient safety, recovery time, and procedural efficiency in emergency settings.

How is this study structured?

- This study is a prospective, single-blind, randomized trial conducted with 64 patients.

What does this study tell us?

- The ketamine-propofol combination was associated with shorter procedure and recovery times, as well as fewer adverse events, compared with ketamine–midazolam
- These findings suggest that ketamine–propofol may represent a safer and more efficient option for procedural sedation in anterior shoulder dislocation cases.

crucial role in the successful reduction of shoulder dislocation.

Procedural sedation and analgesia (PSA) involves the use of sedative, dissociative agents, and analgesics to suppress a patient's level of consciousness during medical procedures. This helps control the patient's responses and memory of the procedure, while preserving or minimizing impairment of cardiorespiratory function. Administering PSA is a crucial skill in emergency medical practice due to the diversity of patient populations and procedural requirements.[2-4] Various sedatives and analgesics are used for PSA. Ketamine, a potent N-methyl-D-aspartate receptor antagonist, has multiple pharmacological effects, including analgesia, sedation, and dissociative anesthesia.[5,6] The American College of Emergency Physicians recommends subdissociative doses of ketamine in the emergency department (ED) for effective pain management in both traumatic and nontraumatic cases.[7] Midazolam possesses hypnotic, sedative, anterograde amnestic, and anxiolytic properties but does not provide analgesia.[8] Propofol is a rapidly acting intravenous (IV) drug with hypnotic, sedative, and amnestic effects, but it lacks analgesic properties. It allows rapid recovery and also has a strong antiemetic effect.[9]

While ketamine has a long history of safety and efficacy in children, its combination with other sedative agents is recommended in adults due to possible adverse events.[10,11] It remains unclear which sedative agent, when combined with ketamine, is safer for use by emergency physicians. This study aimed to compare the effectiveness and safety of ketamine combined with either midazolam or propofol during procedural sedation for anterior shoulder dislocation reduction in the ED. Effectiveness was assessed based on sedation depth (Ramsay sedation scale [RSS]), time to sedation, procedure duration, recovery time, and reduction success. Safety was evaluated by monitoring adverse events such as respiratory depression and hemodynamic instability.

Methods

This study was approved by the Ethics Committee of Health Sciences University, Adana City Training and Research Hospital (meeting date: December 15, 2022, meeting number: 118, decision number: 2301). The research was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Patients' selection

The study was conducted in the ED of a training hospital with an annual patient volume of approximately 300,000 visits. It was designed as a prospective, single-blind, randomized trial and carried out between January 1 and October 31, 2023. Patients aged 18 years and older who presented to the ED with shoulder dislocation and consented to undergo shoulder reduction under sedation were included. All enrolled patients were diagnosed with anterior shoulder dislocation, confirmed by a combination of medical history, physical examination, and radiographic imaging. No posterior or inferior dislocations were observed during the study period. Exclusion criteria included patients with associated shoulder fractures, a history of allergy or urticarial reaction to sedative agents, egg allergy, refusal of treatment, or inability to provide written consent (e.g., non-Turkish speakers or individuals with impaired mental capacity). Pregnant patients, those with a history of alcohol or substance use, and individuals with respiratory failure, chronic liver failure, chronic kidney failure, or chronic heart failure were also excluded. Written informed consent was obtained from all participants.

Study design

All procedures were performed in the ED's critical care room, with continuous monitoring and immediate access to resuscitation equipment. After obtaining written informed consent, eligible patients presenting with anterior shoulder dislocation were randomized in a 1:1 ratio to receive either ketamine–midazolam or ketamine–propofol, using a computer-based randomization program.

The study numbers and corresponding drug assignments were known only to the coordinating physician. Randomization was carried out according to the order of patient arrival in the ED. Study numbers and drug allocations were placed in opaque envelopes, which were opened sequentially. After each envelope was opened, a nurse prepared the study drug as described below. To ensure patient safety, the treating physicians were informed of the allocated medication protocol after envelope opening due to potential drug-related complications. While patients were blinded to their treatment group, the administering physicians were necessarily aware of the assigned protocol.

Participants were randomized into two groups for procedural sedation: IV ketamine–propofol (KM group) and IV ketamine–propofol (KP group). In the KM group, 1 mg/kg ketamine (Ketax, Vem, Türkiye; 500 mg/10 ml intramuscular (IM)/IV solution) was administered slowly over 2 min using a 10 cc syringe, followed by 0.05 mg/kg midazolam (Midolam, Pharmada, Türkiye; 5 mg/1 ml IM/IV solution) in the same manner. In the KP group, 1 mg/kg ketamine (Ketax, Vem, Türkiye; 500 mg/10 ml IM/IV solution) was administered over 2 min, followed by 1 mg/kg propofol (Propofol-PF, Polifarma, Türkiye; 200 mg/20 ml IV solution) with identical technique. At the start of each procedure, three physicians were present. Sedation was administered by a senior emergency medicine resident in the final year of training, while shoulder reductions were performed by the attending emergency medicine specialist. Closed reduction was achieved using one of several techniques – traction–countertraction, Milch, Hippocratic, or Kocher – according to the physician's preference. Data were recorded by an emergency medicine resident with at least 2 years of experience. Patients were observed for approximately 60 min following drug administration. Vital signs were documented before, during, and after sedation. The RSS, originally developed for intensive care, was used to assess sedation depth as it remains the most widely adopted tool.[12] The RSS is a validated tool commonly used to assess the depth of sedation, with scores interpreted as follows: score 1: awake, anxious, agitated, or restless; score 2: awake, cooperative, oriented, and tranquil; score 3: awake, responding to commands only; score 4: asleep, brisk response to light glabellar tap or loud auditory stimulus; score 5: asleep, sluggish response to light glabellar tap or loud auditory stimulus; and score 6: no response to stimulus. For this study, RSS was assessed 2 min after sedation, and the score was recorded before initiating the reduction procedure. Shoulder reduction was then performed and classified as successful or unsuccessful. This approach allowed correlation of the RSS score with procedural success.

If clinicians determined that the sedation level was inadequate, additional doses were administered intravenously every 2 min until a sedation depth sufficient for shoulder reduction was achieved. The additional doses were 1 mg/kg ketamine + 0.05 mg/kg midazolam in the KM group and 1 mg/kg ketamine + 1 mg/kg propofol in the KP group. All additional sedation requirements and administered doses were recorded.

Recovery time was defined as the interval from sedative administration until the patient returned to baseline consciousness, was fully oriented to person, place, and time, responded appropriately to verbal commands, and maintained stable vital signs without airway intervention or hemodynamic support. Recovery time was recorded in minutes. Total procedure time was recorded in minutes as the time from the start of procedural sedation to the completion of the reduction procedure.

Adverse events that occurred after procedural sedation were systematically recorded for all patients. Adverse events were defined as follows: hypoxemia: oxygen saturation (SpO_2) <90% in room air during or after the procedure; apnea: cessation of breathing for more than 20 s or associated with oxygen desaturation <90%; hypotension: mean arterial pressure (MAP) <60 mmHg or systolic blood pressure <90 mmHg; tachycardia: heart rate >100 beats/min; bradycardia: heart rate <60 beats/min; hypertension: MAP >110 mmHg; and agitation: clinically evident restlessness interfering with the procedure. The need for supplemental oxygen and the method of oxygen delivery (nasal cannula, reservoir mask, bag–valve–mask ventilation, or endotracheal intubation) were also recorded.

The success of the procedure was systematically recorded. Successful reduction was initially assessed by the clinician through physical examination, checking for restored range of motion, improved stability, and normalization of the shoulder contour. Postreduction imaging was subsequently performed to confirm joint alignment. Procedural success was defined as: (1) successful reduction during the initial PSA, (2) unsuccessful reduction during the initial PSA but successful reduction after a second PSA in the ED, or (3) unsuccessful reduction after two PSA attempts in

the ED followed by surgical reduction. If a repeated reduction attempt was necessary, it was performed by the same on-duty emergency medicine specialist who carried out the initial attempt.

Outcomes

The primary outcome of the study was recovery time following procedural sedation. Additional effectiveness parameters included sedation depth measured by the RSS, time to achieve adequate sedation, total procedure duration, and procedural success rate. Secondary outcomes were related to safety and included the incidence and type of adverse events such as respiratory depression, hypoxemia, tachycardia, hypotension, agitation, and other hemodynamic instabilities, as well as the need for supplemental oxygen and additional sedation doses.

Statistical analysis

The SPSS 25 software package (SPSS Inc., Chicago, IL, USA) was utilized for the statistical evaluation of the data obtained in the study. A significance level of $P < 0.05$ was considered. Continuous data were summarized as mean and standard deviation, whereas categorical data were summarized in terms of count and percentage. Categorical data were compared using the Chi-square test. For comparing the means of the parameters examined, the Kolmogorov–Smirnov test was used when variables were normally distributed, and histograms were employed for evaluation. In cases where the variables were normally distributed, the Student's *t*-test was used for two-group comparisons, and in cases where normal distribution was not observed, the Mann–Whitney *U*-test was applied. The sample size was estimated using G*Power (version 3.1.9.2; Universität Düsseldorf, Germany) for MacOS X. Accordingly, with a 5% type 1 error, 5% type 2 error (power of 95%), and a two-tailed analysis, the sample size was determined as 50 patients. Considering a possible protocol bias, it was planned to add 10% to each group; thus, the minimum number of patients to be included was determined as 55.

Results

During the study period, a total of 93 patients aged 18 years and older presented to the ED with shoulder dislocation. Seventeen patients declined consent for sedation and were therefore excluded. Of the 76 patients who provided consent, 64 met the eligibility criteria and were randomized into two treatment groups according to the order of arrival. The KM group consisted of 32 patients who underwent shoulder reduction under ketamine–midazolam sedation, while the KP group included 32 patients who received ketamine–propofol sedation. A flowchart of patient enrollment and allocation is presented in Figure 1.

The demographic and clinical characteristics of the patients are summarized in Table 1. Vital parameters, including temperature, pulse, MAP, and oxygen saturation (SaO_2), were recorded at admission, during the procedure, and after the procedure. During the procedure, the mean pulse rate was significantly higher in the KM group compared with the KP group ($P = 0.015$). The mean SaO_2 level during the procedure was significantly lower in the KM group ($P = 0.003$). Postprocedure measurements showed that the mean SaO_2 level in the KP group was significantly lower compared with the overall patient average ($P = 0.034$) [Table 1].

The most frequently used reduction technique was traction–countertraction (37.5%), followed by the Milch (34.4%), Hippocratic (18.8%), and Kocher (9.4%) methods. There was no statistically significant difference between the KM and KP groups in terms of the distribution of reduction techniques (respectively, $P = 0.302$; $P = 0.292$; $P = 0.522$; $P = 0.391$) [Table 1].

Approximately 1–2 min after PSA administration, the sedation level of the patients was assessed using the RSS. When examining the RSS scores, it was found that 4.7% of the patients scored 2 points, 10.9% scored 3 points, 21.9% scored 4 points, 53.1% scored 5 points, and 9.4% scored 6 points. In the KM group, 37.5% of the patients scored 4 points ($P = 0.002$), whereas in the KP group, 68.8% scored 5 points ($P = 0.012$). The total mean RSS score was 4.5 ± 1.0. The mean RSS score of the KP group (4.9 ± 0.8) was statistically significantly higher than that of the KM group (4.1 ± 1.0) ($P < 0.001$) [Table 2].

When examining adverse events following PSA, hypoxemia (43.6%) and tachycardia (29.7%) were the most frequently observed. Hypoxemia occurred in 59.4% of the KM group and 28.1% of the KP group, a statistically significant difference ($P = 0.012$). Accordingly, additional oxygen supplementation was required in 59.4% of the KM group and 28.1% of the KP group ($P = 0.012$). Hypoxemia episodes were successfully managed with supplemental oxygen. Nasal oxygen was administered in 35.9% of patients, reservoir mask oxygen in 4.7%, and bag–mask ventilation in 3.1%. Tachycardia occurred in 53.1% of the KM group and 6.3% of the KP group ($P < 0.001$) [Table 3]. Two cases of hypotension responded to fluid resuscitation, and one patient with nausea–vomiting was treated with antiemetic therapy. All other complications, including bradycardia and agitation, resolved spontaneously without additional treatment. Importantly, no patient required advanced airway management, vasopressor therapy, or intubation.

The mean total procedure time was 5.7 ± 4.7 min. Patients in the KP group had a significantly shorter procedure time (4.3 ± 1.5 min) compared with the KM group

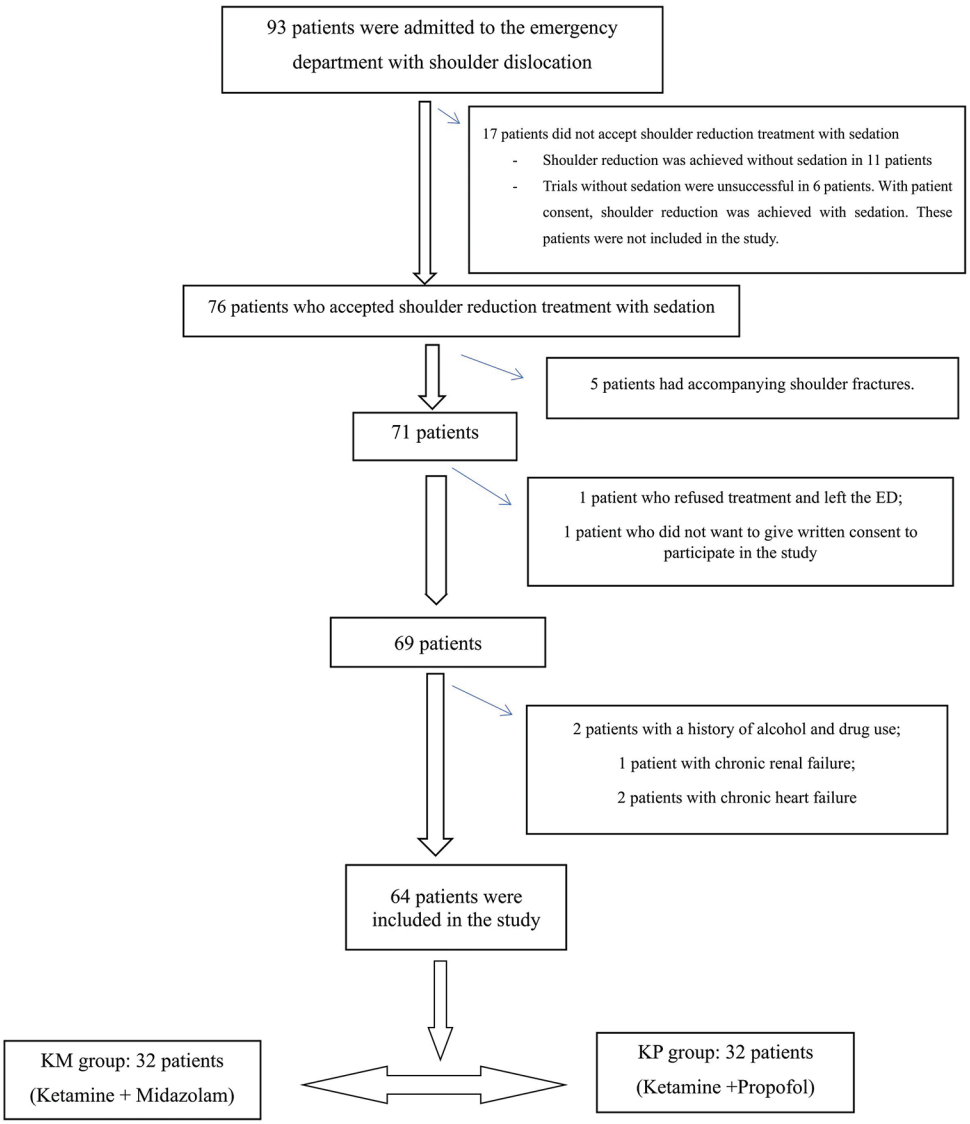

Figure 1: Flow chart of the patients included in the study

(7.0 ± 6.2 min; $P = 0.025$). The mean recovery time was 36.3 ± 14.4 min. Recovery time was significantly shorter in the KP group (26.3 ± 7.4 min) than in the KM group (46.4 ± 12.5 min) [Table 4].

An additional sedation dose was required in 15.6% of patients, with no statistically significant difference between the two groups ($P = 0.491$) [Table 4]. Among patients with an RSS score of 2–3, 80% ($n = 8$) required additional sedation, whereas only 3.7% ($n = 2$) of those with an RSS score ≥4 required it. An RSS score below 4 was statistically significantly associated with the need for additional sedation ($P < 0.001$).

Shoulder reduction was successful on the first attempt in 90.6% of patients and on the second attempt in 9.4%. There was no statistically significant difference between the two groups regarding reduction success ($P = 0.491$). None of the patients required surgical reduction [Table 4].

Discussion

Shoulder dislocation is the most common major joint dislocation and requires effective reduction to restore function and minimize complications. Adequate analgesia and sedation are essential for successful reduction in the ED. In this study, the efficacy of combinations of KM and KP in ED patients undergoing sedation for anterior shoulder reduction using PSA was compared. The study results indicate that the KP group showed shorter total procedure and recovery times, reducing the risk of respiratory depression and tachycardia.

In this study, both the total procedure time and recovery time were shorter in the KP group. In addition, the average RSS score was statistically significantly higher in the KP group. This suggests that the KP group achieved an appropriate level of sedation more quickly, allowing

Table 1: Comparison of the patient's demographic and clinical characteristics

	Total (*n*=64), *n* (%)	KM group (*n*=32), *n* (%)	KP group (*n*=32), *n* (%)	*P*
Sex				
Female	16 (25)	7 (21.9)	9 (28.1)	0.774
Male	48 (75)	25 (78.1)	23 (71.9)	
Age (years)	40±18.9	35.9±14.8	44.0±21.7	0.086
BMI	26.4±3.6	27.1±4.2	25.6±2.6	0.090
Comorbidity				
Hypertension	10 (15.6)	5 (15.6)	5 (15.6)	1,000
Diabetes mellitus	6 (9.4)	2 (6.3)	4 (12.3)	0.672
Coronary artery disease	5 (7.8)	3 (9.4)	2 (6.3)	0.641
Cancer	1 (1.6)	0	1 (3.1)	0.313
Vital signs				
Fever (°C)				
At the time of admission	36.53±0.19	36.57±0.19	36.51±0.21	0.291
During the procedure	36.50±0.21	36.55±0.20	36.46±0.21	0.097
After the procedure	36.52±0.19	36.57±0.16	36.48±0.23	0.069
MAP (mmHg)				
At the time of admission	93.8±12.6	90.6±12	97.1±12.6	0.039
During the procedure	92.8±10.4	94.9±13	97.3±13.7	0.469
After the procedure	96.1±13.2	91.2±10.2	94.3±10.5	0.232
Pulse (min)				
At the time of admission	85.3±12.4	84.8±10.1	85.8±14.4	0.734
During the procedure	92.7±16.4	97.7±16.6	87.8±14.7	0.015
After the procedure	84.9±10.4	85.3±9.7	84.5±11.3	0.758
Oxygen saturation (%)				
At the time of admission	98.2±1.3	98.5±1.1	97.9±1.5	0.077
During the procedure	93.2±4.1	91.7±3.6	94.7±4.0	0.003
After the procedure	97.8±2.4	97.2±2.9	98.4±1.3	0.034
Duration of time since injury (min)	27.7±8.9	28.5±8	26.8±10	0.472
Reduction technique				
Traction–countertraction	24 (37.5)	14 (43.8)	10 (31.3)	0.302
Milch	22 (34.4)	9 (28.1)	13 (40.6)	0.292
Hippocrat	12 (18.8)	7 (21.9)	5 (15.6)	0.522
Kocher	6 (9.4)	2 (6.3)	4 (12.5)	0.391

BMI: Body mass index, MAP: Mean arterial pressure, KM: Patients administered ketamine–midazolam; KP: Patients administered ketamine–propofol

Table 2: Comparison of patient's score distributions on the Ramsay Sedation Scale

	Total (*n*=64), *n* (%)	KM group (*n*=32), *n* (%)	KP group (*n*=32), *n* (%)	*P*
Average RSS score	4.5±1.0	4.1±1.0	4.9±0.8	<0.001
RSS points, *n* (%)				
1	0	0	0	
2	3 (4.7)	3 (9.4)	0	0.076
3	7 (10.9)	4 (12.5)	3 (9.4)	0.689
4	14 (21.9)	12 (37.5)	2 (6.3)	0.002
5	34 (53.1)	12 (37.5)	22 (68.8)	0.012
6	6 (9.4)	1 (3.1)	5 (15.6)	0.086

KM: Patients administered ketamine–midazolam; KP: Patients administered ketamine–propofol, RSS: Ramsay Sedation Scale

for a shorter reduction procedure time. Ketamine has a rapid onset of action, typically occurring within approximately 45–60 s following IV bolus, and within 1–2 min following rapid infusion. The onset of action of midazolam added to ketamine is 1–3 min, whereas propofol has an onset of action of <1 min.[13] In a study comparing midazolam/ketamine with propofol, it was demonstrated that the recovery and sedation times were shorter in the propofol group compared to the midazolam/ketamine group.[14] In a study where sedation was administered using ketamine–propofol for orthopedic procedures, the KP combination was found to result in a shorter recovery time.[15] Taylor *et al*. demonstrated that patients in the propofol group had a shorter recovery time, easier correction of the shoulder, and fewer attempts at correction compared to the midazolam/fentanyl group.[16] In line with recent evidence, ketofol was shown to provide a significantly

Table 3: Comparison of adverse effects and oxygenation methods used in patients after procedural sedation and analgesia

	Total (*n*=64), *n* (%)	KM group (*n*=32), *n* (%)	KP group (*n*=32), *n* (%)	*P*
Adverse effects				
Hypoxemia	28 (43.6)	19 (59.4)	9 (28.1)	0.012
Tachycardia	19 (29.7)	17 (53.1)	2 (6.3)	<0.001
Hypertension	6 (9.4)	2 (6.3)	4 (12.5)	0.391
Agitation	4 (6.3)	3 (9.4)	1 (3.1)	0.302
Hypotension	2 (3.1)	2 (6.3)	0	0.151
Nausea–vomiting	1 (1.6)	0	1 (3.1)	0.313
Bradycardia	1 (1.6)	1 (3.1)	0	0.313
Supplementary oxygen requirement	28 (43.6)	19 (59.4)	9 (28.1)	0.012
Oxygenization method				
Nasal oxygen	23 (35.9)	15 (46.9)	8 (25)	0.048
Oxygen with reservoir mask	3 (4.7)	3 (9.4)	0	
Ventilation with bag mask	2 (3.1)	1 (3.1)	1 (3.1)	
Intubation	0	0	0	

KM: Patients administered ketamine–midazolam; KP: Patients administered ketamine–propofol

Table 4: Comparison of patient's total procedure time, recovery time, additional sedation dose, and procedure success

	Total (*n*=64), *n* (%)	KM group (*n*=32), *n* (%)	KP group (*n*=32), *n* (%)	*P*
Total procedure time (min)	5.7±4.7	7±6.2	4.3±1.5	0.025
Recovery time (min)	36.3±14.4	46.4±12.5	26.3±7.4	<0.001
Additional sedation dose	10 (15.6)	6 (18.8)	4 (12.5)	0.491
Procedure success				
First procedure	58 (90.6)	30 (93.8)	28 (87.5)	0.491
Second procedure	6 (9.4)	2 (6.3)	4 (12.5)	
Surgical	0	0	0	

KM: Patients administered ketamine–midazolam; KP: Patients administered ketamine–propofol

shorter recovery time compared with ketamine or Ketodex, while maintaining a favorable safety profile in adult procedural sedation.[17] This study, consistent with the literature, demonstrated that the short onset and total duration of action of propofol facilitated the rapid completion of the procedure and shortened the recovery time.

According to the study data, the KP group was shown to minimize the risks of respiratory depression and tachycardia. The hemodynamic stability of the KP group can be attributed to the opposing effects of ketamine and propofol. While propofol inhibits sympathetic vasoconstrictor nerve activity, leading to hypotension and bradycardia, ketamine increases heart rate and blood pressure by stimulating the sympathetic system. These antagonistic effects make their combination an agent that maintains hemodynamic stability. Thus, the KP group appears to better preserve hemodynamic stability and demonstrates greater safety in terms of adverse events. Moreover, the ketamine–propofol combination can reduce the dose-dependent adverse events of each individual drug.[18] In this combination, adverse effects of ketamine – such as increased secretions, vomiting, and hallucinations – are attenuated by propofol, while ketamine enhances the analgesic properties of propofol.[19] The ketamine–propofol combination is widely used in EDs, operating rooms, and outpatient treatment centers, most often in bolus form.[18] Although propofol lacks intrinsic analgesic effects, it provides deeper and more consistent sedation compared to ketamine. In one study, no significant difference was observed in the incidence of respiratory adverse events between patients receiving propofol alone and those receiving the propofol–ketamine combination.[20] A recent systematic review and meta-analysis including 32 randomized controlled trials demonstrated that ketamine had the lowest rates of respiratory depression, whereas propofol alone was associated with the highest incidence of hypotension. Importantly, the use of drug combinations, particularly ketamine–propofol, significantly reduced the occurrence of adverse events such as vomiting, hypotension, bradycardia, and laryngospasm compared with single agents.[21] Another meta-analysis of randomized trials demonstrated that the combination of ketamine and propofol provides a more balanced hemodynamic response and reduces the incidence of adverse events compared with either agent alone.[22] Consistent with recent evidence, our findings suggest that the KP group better maintained hemodynamic stability and was more reliable in terms of adverse events.

When examining the adverse events observed in the KM group during the study, significantly higher rates of respiratory depression and tachycardia were noted. Midazolam possesses anxiolytic and amnestic properties but lacks intrinsic analgesic effects.[23] Ketamine, on the other hand, stimulates the sympathetic nervous system, leading to increased heart rate and blood pressure, while the primary adverse effect of midazolam is hypoxia and respiratory depression.[24] The simultaneous administration of midazolam and ketamine may preserve the favorable hemodynamic, analgesic, and sedative effects of ketamine while potentially mitigating its adverse events. In this study, heart rate during the procedure was significantly higher in the KM group, which may be explained by insufficient sedation leading to pain or awareness-related sympathetic activation. This interpretation is consistent with the lower RSS scores observed in this group. A case study reported that muscle rigidity developing after IV ketamine administration was resolved with IV midazolam, allowing the procedure to be successfully completed.[25] In another study comparing propofol and midazolam in endoscopic procedures, the incidence of hypoxia was found to be higher in the midazolam group, whereas no cases of hypoxia were reported in the propofol or propofol–midazolam combination groups.[26] These findings suggest that neither drug alone is sufficient to fully compensate for the adverse events associated with the other.

The RSS was introduced approximately 30 years ago for the assessment of sedative drug titration in intensive care. With a usage rate of 66.5%, RSS remains the most commonly used scale, with the advantages of widespread applicability and ease of use. The RSS is a six-level scale. Moderate sedation is generally interpreted as a score of 4–5.[27] In a study comparing the ketamine–propofol (KP) combination with the midazolam–fentanyl combination, it was reported that the KP group had higher satisfaction and lower pain scores.[28] In another study using ketamine and midazolam, the average highest RSS during the procedure was reported as 2.7 ± 0.7, which was considered sufficient for the procedure.[29] In contrast, a study with ketamine and propofol reported an average RSS of 4.9 ± 0.7 during endoscopy, indicating deeper and adequate sedation.[19] In our study, an RSS score of 4 or higher was associated with significant sedation, and the mean RSS score in the KP group was statistically higher than in the KM group. This finding suggests that the KP combination achieved an appropriate sedation depth more rapidly, which may have contributed to a shorter procedure duration. Therefore, the higher procedural success observed in the KP group may not only reflect the pharmacological properties of the drug combination itself but also the deeper sedation level it provided.

Limitations

This study has several limitations. First, its single-center design and limited sample size restrict the generalizability of the results. Although it was originally planned as a double-blind randomized trial, concerns about potential adverse drug events necessitated physician awareness of the treatment, resulting in a single-blind design. In addition, the absence of standardized RSS target values for assessing sedation effectiveness, the lack of blinding of the physicians performing the reductions, and operator-related factors such as physician experience, choice of reduction technique, and variability in sedation depth may have introduced bias and influenced procedural success beyond the drug combinations used.

Conclusion

The study data favor the use of ketamine combined with propofol over ketamine combined with midazolam for ED patients undergoing sedation for anterior shoulder reduction. This approach demonstrated similar success rates to the combination of ketamine and midazolam, yet KP led to shorter procedure time, faster recovery, and lower incidence of hypoxemia.

Author contributions' statement

MP: Study conception and design, acquisition of data, analysis and interpretation of data, review and editing, conceptualization, writing – original draft (lead), writing – review, and editing (equal). SA: Study conception and design, acquisition of data, conceptualization, writing – original draft (lead), writing – review, and editing (equal). SS: Study conception and design, acquisition of data, writing – review, and editing (equal). MG: Acquisition of data, analysis and interpretation of data, writing – review, and editing (equal). SS: Analysis and interpretation of data, writing – review, and editing (equal). ID: Analysis and interpretation of data, writing – review, and editing (equal). MK: Acquisition of data, analysis and interpretation of data, writing – review, and editing (equal). MG: Analysis and interpretation of data, writing – review, and editing (equal). All the authors approved the final version to be published; all authors agreed to all aspects of the work.

Conflicts of interest

None Declared.

Ethics approval

This study was approved by the Ethics Committee of Health Sciences University, Adana City Training and Research Hospital (meeting date: December 15, 2022, meeting number: 118, decision number: 2301).

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