ORIGINAL ARTICLE

Comparison of Ketamine Plus Dexamethasone Versus Ketamine Alone for Prevention of Severe Shivering After Spinal Anesthesia in Caesarean Section

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Background	Post-anesthetic shivering is a common complication following spinal anesthesia in cesarean sections, increasing oxygen consumption and patient discomfort. While ketamine has demonstrated efficacy in preventing shivering, its use alone may not provide optimal protection. To evaluate the efficacy of combined ketamine and dexamethasone versus ketamine alone in preventing post-spinal shivering during cesarean section.
Patients and Methods	This randomized, double-blind trial included 182 parturients undergoing elective cesarean section under spinal anesthesia, randomly allocated to receive either ketamine 0.25mg/kg (Group K, $n=91$) or ketamine 0.25mg/kg plus dexamethasone 0.1mg/kg (Group KD, $n=91$). Primary outcomes included incidence and severity of shivering. Secondary outcomes included time to onset, duration of shivering, hemodynamic parameters, and adverse effects.
Results	The combination therapy showed significantly lower shivering incidence (20.9% vs 40.7%, $P < 0.001$) and delayed onset (25.7±6.1 vs 18.4±5.2 minutes, $P < 0.001$) compared to ketamine alone. Shivering duration was shorter in the combination group (28.5±7.4 vs 42.3±8.7 minutes, $P < 0.001$). The combination group demonstrated better sedation profile ($P=0.039$) with more patients maintaining cooperative orientation (74.7% vs 57.1%). Hemodynamic parameters remained comparable between groups, and no significant differences were observed in adverse effects.
Conclusions	The addition of dexamethasone to ketamine provides superior prophylaxis against post-spinal shivering in cesarean sections, with delayed onset, shorter duration, and better sedation profile, without increasing adverse effects.
Keywords	Cesarean section; Dexamethasone; Ketamine; Post-anesthetic shivering; Spinal anesthesia. Egyptian Journal of Anaesthesia 2025,

INTRODUCTION

Post-anesthetic shivering during cesarean sections under spinal anesthesia remains a significant challenge in perioperative care, affecting 40-60% of patients. This thermoregulatory response manifests due to central temperature redistribution, vasodilation-induced heat loss, and altered thermoregulatory thresholds [1]. The complications extend beyond patient discomfort, increasing oxygen consumption by 40-120%, carbon dioxide production by 40-60%, and cardiac workload, potentially compromising surgical recovery and maternal-fetal outcomes [2].

Ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, has demonstrated efficacy in preventing shivering through central thermoregulatory modulation and modifies the shivering threshold [3]. Clinical studies have shown that prophylactic ketamine at sub-anesthetic doses (0.25-0.5mg/kg) reduces shivering incidence, though optimal protection remains elusive [3]. The search for enhanced prophylactic strategies has led to investigating adjunct medications that could potentiate ketamine's antishivering effects [4,5].

Dexamethasone, a potent glucocorticoid, presents a promising adjunct through multiple mechanisms. Beyond its established anti-inflammatory properties, dexamethasone influences thermoregulation through prostaglandin suppression and modulation of inflammatory mediators [6]. Recent evidence suggests its potential role in maintaining perioperative temperature homeostasis [7]. The combination of ketamine's NMDA antagonism with dexamethasone's anti-inflammatory and thermoregulatory effects could provide synergistic protection against postspinal shivering. Despite the theoretical benefits, the combined efficacy of ketamine and dexamethasone for shivering prophylaxis remains inadequately investigated. This randomized, double-blind clinical trial evaluated whether adding dexamethasone to ketamine provides superior prophylaxis against post-spinal shivering in cesarean section patients compared to ketamine alone, assessing both efficacy and safety outcomes.

PATIENTS AND METHODS

Study Design This randomized, double-blind controlled trial was conducted in New Valley University Hospital over six months. Ethical approval was obtained from the Medical and Nursing Ethics Committee (MNVREC) of New Valley University (Approval No. 20240930010). Written informed consent was obtained from all participants prior to enrollment. This study was conducted in accordance with the principles of the Declaration of Helsinki [8].

Eligibility Criteria

Inclusion Criteria:

- 1. Female patients aged 18-40 years.
- 2. Scheduled for elective cesarean section under spinal anesthesia.
- 3. American Society of Anesthesiologists (ASA) physical status I or II.
- 4. Body Mass Index (BMI) 18.5-35kg/m².
- 5. Singleton pregnancy at term (37-40 weeks gestation).

Exclusion Criteria:

1. Known allergy or contraindication to ketamine or dexamethasone.

- 2. Severe cardiovascular, hepatic, or renal diseases.
- 3. History of psychiatric disorders.
- 4. Pre-existing neurological disorders.
- 5. Medications affecting thermoregulation
- 6. Preeclampsia or eclampsia.
- 7. Fever or infection.
- 8. Contraindications to spinal anesthesia.
- 9. Adverse effect of drugs such as sedation, hallucination and tachycardia.

Grouping

Group K (Ketamine Alone):

- Received ketamine 0.25mg/kg IV.
- Followed by normal saline (matching volume).
- Total volume made up to 10mL with normal saline.
- Administered immediately post-spinal anesthesia.
- Given as slow IV injection over 1 minute.

Group KD (Ketamine plus Dexamethasone):

- Received ketamine 0.25mg/kg IV.
- Plus dexamethasone 0.1mg/kg IV.
- Total volume made up to 10mL with normal saline.
- Administered immediately post-spinal anesthesia.
- Given as slow IV injection over 1 minute.

Randomization and Blinding

Randomization was performed using a computergenerated random number sequence with variable block sizes (4 and 6) to ensure equal allocation (1:1 ratio) between groups. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes that were opened only after patient enrollment by an independent research coordinator who managed the randomization process but was not involved in patient care or data collection. The study followed a double-blind design where medications were prepared by an anesthesiologist not involved in patient care or assessment. Both study medications were diluted to identical volumes in identical syringes to maintain blinding of healthcare providers and patients. The randomization code was kept secure and only broken after completion of data analysis.

Anesthetic Management All patients received standardized spinal anesthesia. After establishing standard monitoring (ECG, SpO2, NIBP) and securing 18G IV access, patients were preloaded with Ringer's lactate (10mL/kg). Spinal anesthesia was performed at L3-L4 interspace using 12.5mg hyperbaric bupivacaine (2.5mL). Operating room temperature was maintained at $24\pm1^{\circ}$ C, and all IV fluids were warmed to 37° C. Left lateral tilt position was maintained to prevent aortocaval compression.

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All patients were observed for shivering. Once shivering occurred—after delivery of the fetus—patients received either ketamine 0.25 mg/kg (Group K, n=91) or ketamine 0.25 mg/kg plus dexamethasone 0.1 mg/kg(Group KD, n=91). Patients were monitored for shivering until the end of the operation and for 180 minutes postoperatively. If shivering did not respond to the study drugs, patients received intravenous pethidine (0.5 mg/kg) and were excluded from the study. A warm blanket was also provided postoperatively.

To clarify, the study drugs were administered only after the delivery of the fetus, so they could not have impacted neonatal outcomes. However, APGAR scores at the 1st and 10th minutes were routinely recorded for all newborns as part of the standard obstetric care and to supplement the demographic data of the study population. These scores were not used to evaluate drug safety but were included to ensure a complete clinical profile. Fetal monitoring was performed using the APGAR score, a standardized assessment tool for newborns immediately after delivery. The APGAR score includes five components: (1) color, (2) heart rate, (3) reflexes, (4) muscle tone, and (5) respiration. Each component was scored from 0 to 2, for a total score ranging from 0 to 10. A score of 7 to 10 at 5 minutes was considered normal, 4 to 6 intermediate, and 0 to 3 low.

Data Collection

1. Baseline Parameters:

- Demographic data.
- Vital signs.
- Core temperature.
- Laboratory values.

2. Intraoperative Monitoring:

- Vital signs every 5 minutes.
- Temperature every 15 minutes.
- Shivering assessment every 15 minutes.
- Sedation scores every 30 minutes.

3. Data Recording Tools:

- Standardized case report forms.
- Electronic data capture system.
- Quality control checks for data accuracy.

Assessment Scales

Shivering and sedation were assessed by an anesthesiologist blinded to group allocation.

Shivering Assessment: Shivering was evaluated using a standardized 4-point scale [9]:

• Grade 0: No shivering.

• Grade 1: Mild fasciculations of face or neck, peripheries.

• Grade 2: Visible tremor involving more than one muscle group.

• Grade 3: Gross muscular activity involving the entire body.

Shivering assessments were performed at baseline, immediately after spinal anesthesia, and then every 15 minutes for 180 minutes postoperatively.

Sedation Assessment: Sedation was evaluated using the Ramsay Sedation Scale (RSS) [10]:

- Score 1: Anxious, agitated, or restless.
- Score 2: Cooperative, oriented, and tranquil.
- Score 3: Responsive to commands only.

• Score 4: Exhibiting brisk response to light glabellar tap or loud auditory stimulus.

• Score 5: Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus.

• Score 6: Unresponsive.

Sedation scores were recorded at baseline and every 30 minutes for 180 minutes postoperatively. For safety monitoring, any patient reaching scores of 5 or 6 would trigger immediate clinical intervention.

Management of complication

An anesthesiologist blinded to group allocation using a standardized adverse effects form recorded all adverse effects. For any adverse effect with severity grade ≥ 2 , a protocol for immediate management was in place. This included administration of ondansetron 4mg IV for nausea/ vomiting, midazolam 1-2mg IV for severe emergence reactions or hallucinations, and diphenhydramine 25mg IV for significant pruritus or allergic reactions. Blood glucose levels >180mg/dL were managed according to our institutional protocol for perioperative hyperglycemia. All adverse effects were followed until resolution or hospital discharge, whichever occurred first.

Sample Size

The sample size was calculated using G*Power software (version 3.1.9.7), based on findings from Saheban Maleki *et al.*, 2021 [5]. Assuming a shivering incidence of 40% in the ketamine group and 20% in the combination group, with an alpha error of 0.05 and power of 80%, 83 patients per group were required. The final sample size was set at 91 patients per group to account for potential dropouts (10%).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics (version 25) and GraphPad Prism (version 9.0). Normality of data distribution was assessed using the Shapiro-Wilk test and Q-Q plots visual inspection. Continuous data were expressed as mean±standard deviation or median (interquartile range) as appropriate, while categorical data were presented as frequencies and percentages. Between-group comparisons for continuous variables were performed using independent *t*-test for normally distributed data or Mann-Whitney *U* test for non-parametric data. Categorical variables were analyzed using Chi-square test or Fisher's exact test as appropriate. Repeated measures were analyzed using mixed-effects model analysis. A *P*-value <0.05 was considered statistically significant, and 95% confidence intervals were reported where appropriate.

RESULTS

Figure (1) illustrates the participant flow. A total of 200 patients were assessed for eligibility, of whom 18 were excluded—10 did not meet the inclusion criteria, 5 declined to participate, and 3 were excluded for other reasons. The remaining 182 patients were randomly allocated into two equal groups (n=91 each).

Table (1) shows the demographic and baseline characteristics of the study participants. There were no significant differences between the ketamine alone and

ketamine plus dexamethasone groups regarding age, BMI, parity distribution, or gestational age (P>0.05).

Table (2) demonstrates the hemodynamic parameters measured at different time points over 180 minutes. Both groups maintained similar body temperature, heart rate, and mean blood pressure profiles throughout the observation period. No statistically significant differences were observed between groups in any of the hemodynamic parameters at any time point (P>0.05).

Table (3) illustrates the distribution of shivering grades at different time points. The ketamine plus dexamethasone group showed significantly lower shivering scores compared to ketamine alone from 15 to 120 minutes post-intervention (P<0.05). The maximum difference was observed at 60 minutes, where 85.7% of patients in the combination group were shivering-free compared to 65.9% in the ketamine-alone group (P<0.001). The antishivering effect gradually diminished after 150 minutes, with no significant differences between groups at 150 and 180 minutes.

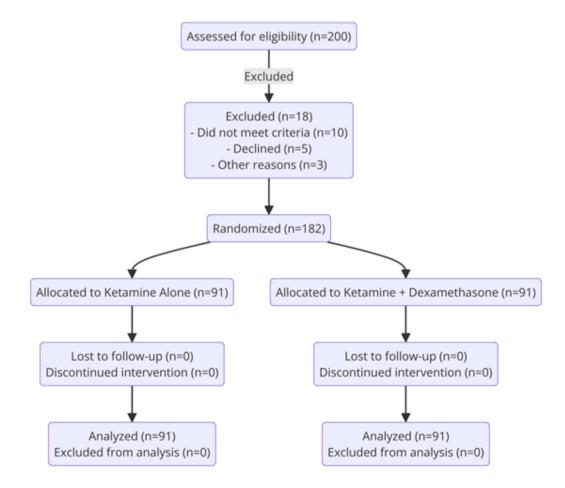


Figure 1: Flow chart of the study.

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Table 1: Demographic and Baseline Characteristics of Study Participants between Ketamine Alone and Ketamine with Dexamethasone:

Ketamine Alone (<i>n</i> =91)	Ketamine+Dexamethasone (<i>n</i> =91)	<i>P</i> -value
30.29±5.38	30.40±5.11	0.889
32.79±4.73	31.04±4.55	0.879
32(35.2%)	34(37.4%)	0.088
35(38.5%)	33(36.3%)	
24(26.3%)	24(26.3%)	
38.02±2.09	38.11±2.18	0.755
8.22±0.57	8.15±0.59	0.465
9.58±0.50	9.55±0.52	0.719
	30.29±5.38 32.79±4.73 32(35.2%) 35(38.5%) 24(26.3%) 38.02±2.09 8.22±0.57	30.29±5.38 30.40±5.11 32.79±4.73 31.04±4.55 32(35.2%) 34(37.4%) 35(38.5%) 33(36.3%) 24(26.3%) 24(26.3%) 38.02±2.09 38.11±2.18 8.22±0.57 8.15±0.59

Values are presented as Mean±SD or Number (%).

Table 2: Hemodynamic Parameters Measurements at Different Time Points between Ketamine Alone and Ketamine with Dexamethasone:

Parameter	Baseline	15min	30min	45min	60min	90min	120min	150min	180min
Body Temperature (°C)									
• Ketamine Alone	36(36-37)	37(36-38)	36(36-38)	36(36-38)	37(36-38)	36(36-37)	36(35-37)	36(35-38)	37(36-38)
• K+D	36(36-37)	37(36-37)	36(36-38)	36(36-37)	37(36-38)	36(35-38)	36(36-38)	36(35-38)	37(35-38)
P value	0.138	0.612	0.758	0.513	0.884	0.618	0.070	1.000	0.712
Heart Rate (be	eats/min)								
• Ketamine Alone	79(64-99)	84(58-107)	77(62-95)	75(62-93)	83(62-104)	82(66-104)	82(64-99)	79(59-95)	83(63-97)
• K+D	79(61-105)	87(66-116)	80(62-98)	77(62-94)	83(61-100)	81(58-100)	82(60-97)	77(48-98)	81(63-101)
P value	0.683	0.113	0.050	0.095	0.987	0.877	0.597	0.670	0.993
Mean blood p	ressure (mmHg))							
• Ketamine Alone	87(72–101)	91(75–104)	88(72–107)	89(75–102)	87(71–109)	86(66–100)	87(73–106)	86(71–100)	94(78–110)
• K+D 88(71–104) 90(70–105) 88(75–100)				88(76–101)	87(73–107)	86(71–103)	85(65–101)	86(69–99)	92(74–109)
P value	0.188	0.154	0.294	0.277	0.586	0.209	0.571	0.637	0.079

Values are presented as Median (Minimum-Maximum).

Figure (2) illustrates the distribution of shivering severity between the ketamine alone and ketamine plus dexamethasone groups. The combination therapy demonstrated superior efficacy in preventing shivering, with 79.1% of patients showing no shivering (Grade 0) compared to 59.3% in the ketamine-alone group. Lower incidences were observed in the combination group across all severity grades: mild shivering (13.2% vs 19.8%), moderate shivering (5.5% vs 13.2%), and severe shivering (2.2% vs 7.7%). The overall difference in shivering grade distribution between groups was statistically significant (P=0.024).

Figure (3) demonstrates the time to onset of shivering between the two treatment groups. The ketamine plus dexamethasone group showed significantly delayed onset of shivering compared to ketamine alone. The median time to onset was longer in the combination group (26.5 minutes) compared to the ketamine-alone group (18.0 minutes). The box plot reveals a wider interquartile range in the combination group (21.2-29.8 minutes) versus the ketamine-alone group (14.8-22.3 minutes), indicating greater variability in onset time. This difference was highly statistically significant (P<0.001).

Time Point	Shivering Grade	Ketamine Alone (<i>n</i> =91)	Ketamine+Dexamethasone (n=91)	P-value
Baseline	Grade 0	91(100%)	91(100%)	-
	Grade 1-3	-	-	-
15 min	Grade 0	72(79.1%)	82(90.1%)	0.034*
	Grade 1	12(13.2%)	7(7.7%)	
	Grade 2	5(5.5%)	2(2.2%)	
	Grade 3	2(2.2%)	0	
30 min	Grade 0	65(71.4%)	79(86.8%)	0.012*
	Grade 1	15(16.5%)	8(8.8%)	
	Grade 2	8(8.8%)	3(3.3%)	
	Grade 3	3(3.3%)	1(1.1%)	
60 min	Grade 0	60(65.9%)	78(85.7%)	< 0.001*
	Grade 1	18(19.8%)	9(9.9%)	
	Grade 2	9(9.9%)	3(3.3%)	
	Grade 3	4(4.4%)	1(1.1%)	
90 min	Grade 0	67(73.6%)	81(89.0%)	0.008*
	Grade 1	15(16.5%)	7(7.7%)	
	Grade 2	7(7.7%)	2(2.2%)	
	Grade 3	2(2.2%)	1(1.1%)	
120 min	Grade 0	75(82.4%)	84(92.3%)	0.042*
	Grade 1	11(12.1%)	5(5.5%)	
	Grade 2	4(4.4%)	2(2.2%)	
	Grade 3	1(1.1%)	0	
150 min	Grade 0	82(90.1%)	87(95.6%)	0.156
	Grade 1	7(7.7%)	4(4.4%)	
	Grade 2	2(2.2%)	0	
	Grade 3	0	0	
180 min	Grade 0	85(93.4%)	89(97.8%)	0.278
	Grade 1	5(5.5%)	2(2.2%)	
	Grade 2	1(1.1%)	0	
	Grade 3	0	0	

Table 3: Shivering Score Distribution at Different Time Points between Ketamine Alone and Ketamine with Dexamethasone:

Values are presented as Number (%); *: Statistically significant (P<0.05).

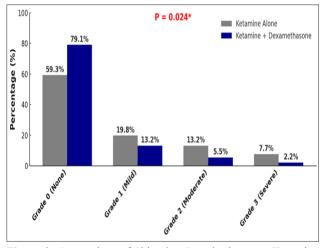


Figure 2: Comparison of Shivering Severity between Ketamine Alone and Ketamine with Dexamethasone.

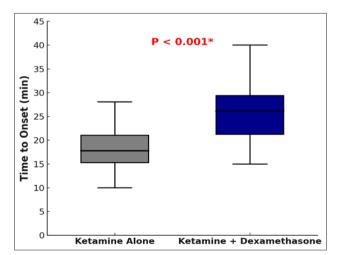


Figure 3: Comparison of Shivering time to onset (min.) between Ketamine Alone and Ketamine with Dexamethasone.

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Figure (4) compares the duration of shivering between the treatment groups. The ketamine plus dexamethasone group demonstrated significantly shorter shivering duration compared to ketamine alone. The median duration in the combination group was 27.0 minutes (IQR: 23.5-33.5 minutes) versus 41.0 minutes (IQR: 35.5-48.5 minutes) in the ketamine-alone group. The difference was highly statistically significant (P<0.001). The narrower box plot in the combination group also suggests more consistent treatment effect compared to ketamine alone.

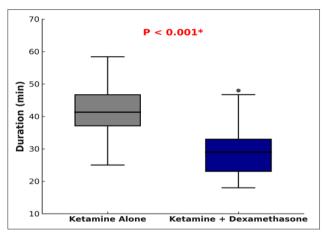


Figure 4: Comparison of shivering duration (min.) between Ketamine Alone and Ketamine with Dexamethasone.

Table (4) presents the incidence of adverse effects between groups. Both treatment regimens demonstrated comparable safety profiles, with no significant differences in the occurrence of nausea, vomiting, hallucinations, dizziness, or pruritus (P>0.05). The overall incidence of adverse effects was low in both groups, indicating good tolerability of both interventions.

The distribution of Ramsay Sedation Scale scores between the two treatment groups. The majority of patients in both groups maintained cooperative and oriented status (Grade 2), with a higher percentage in the ketamine plus dexamethasone group (74.7% vs 57.1%). Lower proportions of agitation (Grade 1) were observed in the combination group (3.3% vs 6.6%). Similarly, fewer patients in the combination group showed increased sedation levels (Grade 3: 16.5% vs 25.3%; Grade 4: 5.5% vs 11.0%). No patients in either group experienced deep sedation (Grades 5-6). The overall difference in sedation score distribution was statistically significant (P=0.039) (Figure 5).

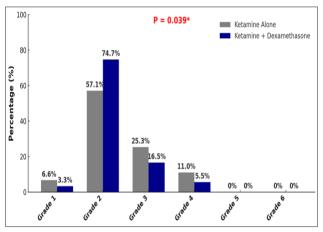


Figure 5: Comparison of sedative score between Ketamine Alone and Ketamine with Dexamethasone.

Table 4: Incidence of Adverse Effects between Ketamine Alone and Ketamine with Dexamethasone:

Adverse Effect	Ketamine Alone (n=91)	Ketamine + Dexamethasone (n=91)	<i>P</i> -value
Nausea	12(13.2%)	14(15.4%)	0.673
Vomiting	8(8.8%)	9(9.9%)	0.792
Hallucinations	3(3.3%)	2(2.2%)	0.651
Dizziness	10(11.0%)	9(9.9%)	0.814
Pruritus	5(5.5%)	6(6.6%)	0.762

Values are presented as Number (%); *: Statistically significant (P<0.05).

DISCUSSION

Shivering is a common complication following spinal anesthesia during caesarean sections, often leading to discomfort, increased oxygen consumption, and potential hemodynamic instability [3]. This study compared the effectiveness of ketamine alone versus ketamine combined with dexamethasone in preventing post-spinal anesthesia shivering, and assessed whether adding dexamethasone could improve the sedation profile associated with ketamine. Our findings demonstrated that the ketamine– dexamethasone combination significantly reduced the incidence and severity of shivering compared to ketamine alone. The greatest difference was observed at 60 minutes, with 85.7% of patients in the combination group remaining shivering-free, compared to 65.9% in the ketamine-alone group (P<0.001). The anti-shivering effect persisted until 120 minutes; however, the difference was no longer statistically significant after 150 minutes. Khosravi *et al.*, [11] investigated the effects of Dexamethasone (0.15mg/kg) on postoperative shivering in 200 elective surgical patients. They found that the incidence of postoperative shivering was significantly lower in the dexamethasone group (12%) compared to the control group (31%, P<0.001). This supports our finding that Dexamethasone effectively reduces the incidence and severity of postoperative shivering.

Additionally, Shakya *et al.*, [12] compared ketamine (0.25 mg/kg) and ondansetron (4mg) for shivering prevention after spinal anesthesia in 120 lower abdominal surgery patients. Their findings showed that shivering incidence was 2.5% in the ketamine group, 10% in the ondansetron group, and 42.5% in the normal saline group, indicating that ketamine was superior to ondansetron in preventing shivering. This is consistent with our study, where ketamine significantly delayed the onset of shivering and reduced its severity.

These results align with a study by Meena *et al.*, (2024) [13], who evaluated the effectiveness of prophylactic lowdose intravenous ketamine (0.25mg/kg) in preventing shivering after spinal anesthesia in elective caesarean sections. They reported a significantly lower incidence of shivering in the ketamine group (12.5%) compared to placebo (32.5%) (P=0.030), and a significantly shorter duration of shivering (0.75 ± 2.02min vs. 2.38±3.57min, P=0.014). Similarly, Farooqi *et al.*, (2023) [14] found that ketamine completely prevented shivering in 53.3% of patients versus 0% in the placebo group (P=0.0005).

El-Hafez and Sayed (2019) [15] found that ketamine combined with midazolam was more effective than dexamethasone alone in reducing shivering incidence (10% vs. 33.3%, P<0.05). This suggests that while dexamethasone may be less potent than midazolam when combined with ketamine, it remains more effective than ketamine alone.

Our results showed that the ketamine–dexamethasone group had a significantly delayed onset of shivering (median 26.5min vs. 18.0min, P<0.001). Additionally, the duration of shivering was significantly shorter in the combination group (27.0min vs. 41.0min, P<0.001).

A similar pattern was observed in Sarshivi *et al.*, (2020) [16], where ketamine (0.3 mg/kg) delayed the onset of shivering (41.6 \pm 20.7min) compared to placebo (33.1 \pm 11.7min, *P*<0.05).

CONCLUSIONS

In conclusion, Ketamine and Dexamethasone is more effective than Ketamine alone in preventing post-spinal anesthesia shivering in cesarean section patients. The combination therapy reduced shivering incidence and severity, delayed onset, and shortened duration, while maintaining better sedation control without deep sedation.

LIMITATION

This study has several limitations. First, while pethidine is a widely recognized gold standard for treating postoperative shivering, our study was specifically designed to assess whether the addition of dexamethasone enhances the anti-shivering effect of ketamine. As such, a comparison with pethidine was outside the scope of our primary objective. However, the absence of a gold standard comparator limits broader conclusions and suggests an opportunity for future comparative research. Second, multiple doses of ketamine may be required to optimize its anti-shivering effect while minimizing side effects such as sedation or hallucinations; however, only a single dose was evaluated in this trial. Third, this study was conducted at a single center, which may limit the generalizability of the findings to other clinical settings.

DATA AVAILABILITY STATEMENT

The datasets that were assessed in the present study are available from the corresponding author upon request.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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