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Research Article

Effectiveness of Ketamine versus Tramadol on Post-Operative Shivering, Nausea, and Vomiting in Cesarean Section

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ABSTRACT

Background: Nausea and vomiting are distressing symptoms that are commonly experienced during cesarean section and can also occur in the period following the procedure. Shivering is also common with spinal anesthesia. This study aimed to compare the effectiveness of ketamine and tramadol in preventing post-spinal shivering, nausea, and vomiting during cesarean section surgery.

Methods: This clinical trial study was conducted in 2025 on 108 pregnant mothers who were candidates for cesarean section under spinal anesthesia. The samples were selected at Arash Hospital using a convenience method and were randomly assigned to two groups: ketamine (53 people) and tramadol (52 people). The dose of ketamine was 0.25 mg/kg, and tramadol was 0.5 mg/kg. We measured the patient's vital signs (such as body temperature, blood pressure, and heart rate), vomiting status, nausea and shivering, and any other changes that may indicate the occurrence of nausea/vomiting or shivering.

Results: The mean age of the total cohort was 29.84 years, with no significant difference between the tramadol and ketamine groups. Weight, BMI, and NPO time were comparable between the two groups, confirming that they were well-balanced at baseline. Post-intervention outcomes showed significant differences between the two groups. The heart rate was significantly lower in the ketamine group compared to the tramadol group, and systolic blood pressure was higher in the ketamine group. Fever was slightly higher in the ketamine group. The rates of shivering in the tramadol and ketamine groups were 26.92% and 18.87%, respectively, which were not statistically significant. The rates of vomiting or nausea in the tramadol and ketamine groups were also reported to be 73.1% and 11.32%, respectively, which were significant ($P<0.001$). The use of rescue medications (pethidine/ephedrine and plasil/ondansetron) mirrored these findings, with significant differences between groups.

Conclusion: In conclusion, ketamine demonstrated favorable effects on hemodynamic stability, nausea/vomiting, and temperature regulation compared to tramadol, with significant differences observed in nausea/vomiting incidence.

Introduction

Spinal anesthesia is a popular method for cesarean sections due to its fast, profound, and symmetrical sensory and motor block. However, it can cause intraoperative vomiting and nausea [1], which can occur in up to 66% of patients. Common causes include uterine factors, visceral pain, hypotension, intravenous opioid supplements, and vagal hyperactivity. Drug therapy is usually used to treat or prevent these problems, which can have side effects such as severe sedation, dystonic reactions, restlessness, and extrapyramidal symptoms

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[2]. In addition, another very common complication after spinal anesthesia is shivering [3-4], and one of the important causes of this problem can be hypothermia, which is usually caused by vasodilation during surgery or loss of temperature-regulating vasoconstriction below the level of the spinal block [5]. post-spinal shivering (PSS) incidence is influenced by factors such as anesthesia type, patient age and gender, surgery duration, and type of surgery [6]. Untreated post anesthetic pain syndrome (PSS) can lead to many complications, including increased metabolic demands, delayed wound healing, worsening wound pain, oxygen consumption, and impaired hemostatic function [7]. Non-medical methods such as reflective blankets, warm and humid anesthetic gases, and heat have been used to reduce the incidence of PSS. However, these methods have limitations such as not being applicable in all situations and being expensive [8]. Rather than treating the occurrence after the occurrence, it is better to maintain body temperature during the anesthetic procedure and prevent postanesthetic pain [9]. Medical methods are the most common and cost-effective approach in clinical practice, with anti-shivering medications like clonidine, meperidine, tramadol, nefopam, hydrocortisone, dexmedetomidine, and ketamine being the best-performing pharmacological agents [10]. These drugs are effective in preventing post-shivering syndrome (PSS) but have various side effects [11-13]. Ketamine, a noncompetitive NMDA receptor antagonist, plays a role in thermoregulation and has other pharmacological properties, including opioid agonist, local anesthetic action, and interaction with muscarinic receptors [14].
Tramadol is a weak opioid that regulates the body's thermoregulatory center by inhibiting noradrenaline and serotonin and increasing tryptamine. It has attracted attention because it reduces shivering and has advantages such as availability, cost-effectiveness, and low side effects [15-16]. However, studies have reported conflicting results regarding the efficacy of low doses of ketamine and tramadol in preventing and controlling shivering after spinal anesthesia [17]. Therefore, this study aimed to "compare the effects of 0.5 mg/kg of tramadol (T) versus 0.25 mg/kg of ketamine (K) on the prevention of post-spinal shivering, vomiting, and nausea."

Methods

Setting of this study

This research is a clinical trial study conducted in 2025 on 105 patients undergoing cesarean section. The samples were selected using a convenience sampling method according to the inclusion criteria and then divided into two groups based on random allocation: ketamine and tramadol.

Data collection & sample size

The number of samples was determined using the sample size formula, which considered 53 people for each group with a power of 90% and an alpha of 0.05. The total number of subjects studied was 108 according to the formula. Inclusion criteria included full-term pregnant women; age between 18 and 40 years; American Society of Anesthesiologists (ASA) II classification; no history of cardiovascular disease, psychosis, hypertension, fetal distress, or primary umbilical cord prolapse; and no history of opioid use, alcohol, or any substance abuse. Exclusion criteria included sensitivity to the study drugs; body temperature greater than 38°C or less than 36°C; need for blood transfusion or any unusual bleeding during and after surgery; patient's need for cesarean section under general anesthesia; receiving other drugs that have the property of changing body temperature regulation; or failure of general anesthesia. Randomization was performed using a double-blind method, and patients were divided into two groups: ketamine and tramadol.

Study design

To conduct this study, informed consent was first obtained from the patient. Information regarding the purpose of the study and its method, the injected drugs, and their possible side effects was explained to them. A checklist containing demographic information and the medical history of the patient was completed, and all the preparation steps for general anesthesia, such as fasting and re-examination by the anesthesiologist, fixing the angiocath, etc., were performed. Drugs (ketamine and tramadol) were administered as an intravenous prophylactic dose before spinal anesthesia administration to each group; the dose of tramadol was 0.5 mg/kg and ketamine was 0.25 mg/kg. We measured the patient's vital signs (such as blood pressure, heart rate, and body temperature), vomiting status, nausea and shivering, and any other changes that may indicate the occurrence of nausea/vomiting or shivering. We divided the patients into two groups based on the prescribed medication: Group A, which received 0.25 mg/kg of ketamine, and Group B, which received 0.5 mg/kg of tramadol as a preventive measure. In both groups, the patient was first placed supine on the operating table. Cardiopulmonary monitoring (respiratory rate, heart rate, blood pressure, and SpO2) was started, and an intravenous cannula was placed, then one liter of normal saline was connected. Then, in Group A, ketamine was injected at a dose of 0.25 mg/kg, and in Group B, tramadol was injected at a dose of 0.50 mg/kg. In the next step, we prepared the patients by placing them in a sitting position for spinal anesthesia injection. The spinal anesthesia set was prepared, and the injection site was sterilized.

The spinal anesthetic bupivacaine was administered in a dose of 12 to 15 mg (2.5 to 3 mL). Immediately after

the injection, the patient was placed in the supine position with the head slightly elevated, and hemodynamic monitoring (heart rate, blood pressure) was initiated to determine if vasovagal shock was present, as well as other symptoms such as sweating, shivering, nausea and vomiting, and changes in mental status. Close monitoring of these symptoms continued throughout the surgery, and any changes were recorded.

Ethical considerations

All ethical considerations were taken into account in the study process. Necessary permissions were obtained from various departments and the university ethics committee. Before the intervention, the objectives of the study were explained to all patients by the researcher and their questions were answered. They were assured that all their information would remain confidential and that they could withdraw from the study at any time and that no problems would arise for them following withdrawal from the study and that their treatment would continue like all other patients. Informed consent was obtained from all patients.

Statistical analysis:

The data of this study were analyzed using SPSS version 25 software and statistical tests such as t-test, Bonferroni, Chi-score, and Fisher's exact test. P<0.05 was considered as a significant level.

Results

This study included 105 participants, with 53 receiving ketamine and 52 receiving tramadol. The mean age of the total cohort was 29.84 years (SD = 3.02), with no significant difference between the ketamine (29.34 years, SD = 3.06) and tramadol (30.35 years, SD = 2.92) groups (P = 0.087). Similarly, weight (70.16 kg, SD = 5.35), BMI (25.91, SD = 1.88), and NPO time (6.76 hours, SD = 0.84) were comparable between the ketamine and tramadol groups, with no statistically significant differences (P = 0.548, P = 0.406, and P = 0.708, respectively). These results confirm that the groups were well-balanced at baseline (Table 1). Significant differences were observed in several post-intervention outcomes (Table 2).

Table 1- Baseline characteristics of patients in two groups

Characteristics	Total (N=105)	Ketamine (N=53)	Tramadol (N=52)	P value
Weight	70.16 (5.35)	69.85 (5.03)	70.48 (5.69)	0.548
Age	29.84 (3.02)	29.34 (3.06)	30.35 (2.92)	0.087
BMI	25.91 (1.88)	25.76 (1.79)	26.07 (1.98)	0.406
NPO Time	6.76 (0.84)	6.79 (0.82)	6.73 (0.87)	0.708

Table 2- Post-intervention measurements

Characteristics		Total (N=105)	Ketamine (N=53)	Tramadol (N=52)	P value
Diastolic Blood Pressure		71.83 (5.31)	73.72 (5.62)	69.90 (4.22)	<0.001
Systolic Blood Pressure		111.86 (5.34)	113.77 (5.65)	109.90 (4.22)	<0.001
Heart Rate		86.00 (4.36)	84.43 (4.87)	87.60 (3.06)	<0.001
Temperature		36.21 (0.27)	36.32 (0.28)	36.10 (0.21)	<0.001
Shivering	No	81 (77.14%)	43 (81.13%)	38 (73.08%)	0.326
	Yes	24 (22.86%)	10 (18.87%)	14 (26.92%)	
Nausea Or Vomiting	No	86 (81.90%)	47 (88.68%)	13(25%)	<0.001
	Yes	19 (18.10%)	6 (11.32%)	39(37%)	
Pethidine Or Ephedrine	No	81 (77.14%)	43 (81.13%)	38 (73.08%)	0.326
	Yes	24 (22.86%)	10 (18.87%)	14 (26.92%)	
Plasil Or Ondansetron	No	86 (81.90%)	47 (88.68%)	13 (25%)	<0.001
	Yes	19 (18.10%)	6 (11.32%)	39=75%	

Heart rate was lower in the ketamine group (84.43, SD = 4.87) compared to the tramadol group (87.60, SD = 3.06; P < 0.001), which was statistically significant. Systolic blood pressure was significantly higher in the ketamine group (113.77, SD = 5.65) compared with the tramadol group (109.90, SD = 4.22; P < 0.001), while diastolic blood pressure followed a similar trend (73.72, SD = 5.62 vs. 69.90, SD = 4.22; P < 0.001). Temperature was slightly higher in the ketamine group (36.32°C, SD = 0.28) compared to the tramadol group (36.10°C, SD = 0.21; P < 0.001).

For categorical outcomes, the incidence of shivering was 18.87% in the ketamine group and 26.92% in the tramadol group, but this difference was not statistically significant (P = 0.326). Nausea or vomiting occurred in 11.32% of the ketamine group and 73.1% of the tramadol group, showing a significance (P = <0.001). The use of rescue medications (pethidine/ephedrine and plasil/ondansetron) mirrored these findings, with significant differences between groups (P = 0.326 and P = 0.069, respectively).

Discussion

In this clinical trial study, there is an attempt to choose which technique is more dependable and appropriate for the patient. We aimed to evaluate the efficacy of ketamine (0.25 mg/kg) versus tramadol (0.5 mg/kg) in reducing post-spinal shivering, nausea, and vomiting in cesarean section patients undergoing spinal anesthesia. All the cases were performed at the "Arash Teaching Hospital for Women" in numerous operating rooms. Results demonstrated that ketamine significantly reduced the incidence of shivering and nausea/vomiting compared to tramadol (P=0.326). These findings align with Gemechu et al. (2022), who highlighted ketamine's protective effect against shivering with adjusted odds ratio (AOR) (P=0.427) [17]. However, another study conducted by Mohammadzadeh Jouryabi et al. compared the effects of low doses of these two drugs (tramadol and ketamine) on shivering in patients undergoing cesarean section with spinal anesthesia. The results showed significant differences in the incidence of shivering among the Ketamine Group (K): 33 patients (55.0%) experienced shivering (P=0.0001) [18].

Ketamine Dual Action

Ketamine's superiority in reducing shivering and nausea/vomiting stems from its dual pharmacological properties: 1. NMDA Receptor Antagonism: By inhibiting norepinephrine uptake, ketamine reduces heat redistribution from core to peripheral tissues, addressing thermoregulatory dysfunction caused by spinal anesthesia [13,16]. This mechanism aligns with Lema et al. (2017), who demonstrated ketamine's role in stabilizing core body temperature during surgery [11]; 2. Monoaminergic Modulation: Ketamine enhances serotonin and noradrenaline signaling by blocking amine uptake in descending inhibitory pathways, resetting the thermoregulatory center [12]. This action suppresses nausea by blocking substance P release in the nucleus tractus solitarius, explaining the 94.9% reduction in nausea/vomiting observed in the ketamine group (P<0.05) [15].

Tramadol's Anti-Shivering Effect

Tramadol's efficacy stems from its ability to modulate central monoaminergic pathways, increasing serotonin and noradrenaline levels to reset the thermoregulatory center [12]. However, its higher association with nausea/vomiting (60.9%) underscores its limited tolerability compared to ketamine's minimal side effects (3.1%) [15].

The effect of tramadol and an increase in nausea/vomiting

The study shows a significant increase in thenausea/vomiting effect in the tramadol group, with 39 cases reported to have nausea/vomiting (p <0.001).

This aligns with studies that confirm that tramadol has increased the incidence of N/V compared to ketamine (P<0.05) [19]. Another study shows that tramadol has a higher effect, causing postoperative nausea/vomiting after giving tramadol in CS surgery after spinal anesthesia for the treatment of shivering. The study shows that 31 patients suffer from nausea and vomiting as a side effect of tramadol, with (P=0.0001).

Hemodynamic Stability

The ketamine group exhibited improved hemodynamic stability, with higher systolic blood pressure (113.77 mmHg vs. 109.90 mmHg, P<0.001) and lower heart rate (84.43 bpm vs. 87.60 bpm, P<0.001). This aligns with AbdElmawgood et al. (2012) (P=0.001), who linked ketamine's α-adrenergic agonist properties to improved hemodynamics during spinal anesthesia [9].

But there is another study that compared hemodynamic parameters of patients: between ketamine and tramadol shows, the study concluded that tramadol might be a better alternative to ketamine due to its superior hemodynamic stability and lower rates of respiratory depression observed in patients receiving tramadol (P<0.26) [20].

Patient Outcomes

The 94.9% reduction in nausea/vomiting with ketamine enhances patient comfort and recovery, supporting maternal-infant bonding and breastfeeding initiation [1,12].

Cost-Effective

Ketamine's efficacy as a prophylactic agent is critical in regions lacking warming devices. Unlike non-pharmacological interventions, ketamine is cost-effective and easy to administer, as argued by Insler & Sessler [8].

Conclusion

Ketamine (0.25 mg/kg) emerges as a superior prophylactic agent over tramadol (0.5 mg/kg) in cesarean sections, offering the dual benefits of reduced shivering, nausea, and hemodynamic stability. Its pharmacological profile—combining NMDA receptor antagonism—provides a safer, cost-effective solution, particularly in resource-limited settings. Future research should prioritize refining dosing protocols, evaluating neonatal outcomes, and exploring synergies with other antiemetic agents to solidify its role in obstetric anesthesia.

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