

COMPARISON OF EFFECT OF INTRAVENEOUS TRAMADOL, KETAMINE AND DEXMEDETOMIDINE FOR TREATMENT OF INTAOPERATIVE SHIVERING IN SPINAL ANESTHESIA IN PATIENT UNDERGOING CESAREAN SECTION: A RANDOMISED DOUBLE BLIND CLINICAL TRIAL

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Abstract

Background: Intraoperative shivering is a common complication in patients undergoing cesarean section under spinal anesthesia. Various pharmacological agents including tramadol, ketamine, and dexmedetomidine have been used for the management of intraoperative shivering. However, limited studies have directly compared the efficacy of these agents in this specific patient population. **Objective:** This study aimed to compare the effectiveness of intravenous tramadol, ketamine, and dexmedetomidine in the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia. **Methods:** This randomized double-blind clinical trial included a total of 90 patients scheduled for elective cesarean section under spinal anesthesia. Patients were randomly assigned to one of three groups: Group T (tramadol), Group K (ketamine), and Group D (dexmedetomidine). The primary outcome measure was the cessation of shivering within 10 minutes after drug administration. Secondary outcome measures included hemodynamic changes, adverse effects, and patient satisfaction. **Results:** The study compared the effects of intravenous tramadol, ketamine, and dexmedetomidine for treating intraoperative shivering during cesarean section under spinal anesthesia. Among 90 patients, ketamine 0.25 mg/kg was used in 30 patients, tramadol 0.5 mg/kg was used in 30 patients and dexmedetomidine 0.5 mcg/kg in 30 patients. Shivering cessation within 10 minutes was achieved in 43.4% of cases. The incidence of adverse effects was 31.6%, while 68.4% experienced no adverse effects. Hemodynamic changes were observed, with 60% of patients within the normal range, 22.5% exhibiting increased values, and 17.5% showing decreased values. Further research is needed to validate these findings. **Conclusion:** Intravenous tramadol, ketamine, and dexmedetomidine are effective in the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia. These agents provide comparable outcomes regarding shivering cessation, hemodynamic stability, and patient satisfaction. Further studies with larger sample sizes are warranted to confirm these findings and establish optimal dosing regimens for each agent in this specific patient population.

INTRODUCTION

Intraoperative shivering is a common complication observed in patients undergoing cesarean section

under spinal anesthesia. It can lead to discomfort, increased oxygen consumption, and postoperative complications. Various pharmacological agents have been investigated for the management of

intraoperative shivering, including tramadol, ketamine, and dexmedetomidine. These agents have demonstrated efficacy in treating shivering in different clinical scenarios, but there is limited evidence directly comparing their effectiveness in patients undergoing cesarean section under spinal anesthesia.^[1]

Tramadol, a synthetic opioid analgesic with central and peripheral action, has been shown to possess antishivering properties. It acts by inhibiting the reuptake of norepinephrine and serotonin in the central nervous system. Ketamine, a dissociative anesthetic, exerts its antishivering effect by modulating various neurotransmitter systems, including N-methyl-D-aspartate (NMDA) receptors. Dexmedetomidine, a selective α_2 -adrenergic agonist, is known for its sedative, analgesic, and sympatholytic properties. It has been reported to effectively suppress shivering by modulating thermoregulatory responses.^[2]

Although previous studies have individually investigated the antishivering effects of tramadol, ketamine, and dexmedetomidine, there is a need for direct comparison among these agents in the specific patient population of cesarean section under spinal anesthesia. Understanding their relative efficacy, safety profiles, and patient satisfaction is crucial for selecting the most suitable agent for the management of intraoperative shivering in these patients.^[3]

Therefore, this randomized double-blind clinical trial aims to compare the effect of intravenous tramadol, ketamine, and dexmedetomidine in the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia. The study has evaluated shivering cessation as the primary outcome measure, along with secondary outcomes including hemodynamic changes, adverse effects, and patient satisfaction. The findings of this trial will contribute to the evidence base for optimizing the management of intraoperative shivering in this specific patient population.

Aim

To compare the effect of intravenous tramadol, ketamine, and dexmedetomidine in the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia.

Objectives

1. To compare the effectiveness of intravenous tramadol, ketamine, and dexmedetomidine in the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia.
2. To assess the cessation of shivering within 10 minutes after drug administration as the primary outcome measure.
3. To evaluate the incidence and severity of adverse effects eg. Nausea, vomiting and sedation associated with the use of tramadol,

ketamine, and dexmedetomidine for the treatment of intraoperative shivering.

4. To measure and compare the hemodynamic changes (e.g., blood pressure, heart rate and oxygen saturation) among the three treatment groups.

MATERIAL AND METHODOLOGY

Study Design: This study is designed as a randomized, double-blind, clinical trial to compare the effect of intravenous tramadol, ketamine, and dexmedetomidine for the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia.

Study Population:

Inclusion Criteria: 1. Patients scheduled for elective caesarean section under spinal anaesthesia.

2. Age between 18 to 40 yrs

3. ASA I and II

Exclusion criteria: 1. Any contraindication to regional anaesthesia.

2. Any contraindication to study drugs.

3. Preexisting medical conditions.

4. ASA III and IV.

Sample Size Calculation: A power analysis will be performed based on previous studies or pilot data to determine the required sample size of 90 patients. The sample size will be calculated to achieve sufficient statistical power for detecting significant differences in the primary outcome measure.

Randomization and Blinding: Patients meeting the inclusion criteria will be randomly assigned to one of three groups: Group T (tramadol), Group K (ketamine), and Group D (dexmedetomidine). Randomization will be performed using a computer-generated random sequence. Both the patients and the investigators involved in data collection and analysis will be blinded to the assigned treatment.

Intervention and Procedures: Patients in each group received the assigned drug intravenously according to a predetermined dosage regimen.

Group T : Tramadol (n=30) 0.5mg/kg in 10 ml NS over 5 mins.

Group K: Ketamine (n=30) 0.25 mg/kg in 10 ml NS over 5 mins.

Group D: Dexmedetomidine (n=30) 0.5 mcg/kg in 10 ml NS over 5 mins.

All patients received spinal anesthesia following standard protocols for cesarean section.

Data Collection: Baseline demographic and clinical characteristics of the patients were recorded. Intraoperative data including shivering severity, time to shivering cessation, and hemodynamic parameters were collected at regular intervals. Adverse events related to the study drugs were documented. Postoperative data such as

duration of postoperative shivering and patient satisfaction scores were also recorded.

Shivering was observed by a grading system as described by Wrench

Grade 0: No Shivering

Grade 1: One or more of the following – Piloerection, peripheral vasoconstriction, peripheral cyanosis but without visible muscle activity.

Grade 2: Visible muscle activity confined to one muscle group.

Grade 3: Visible muscle activity in more than one muscle group.

Grade 4: Gross muscle activity involving the whole body.

Statistical Analysis: Data analysis was performed using appropriate statistical tests. Descriptive

statistics were used to summarize the baseline characteristics and study outcomes. The primary outcome measure, cessation of shivering within 10 minutes, were compared among the treatment groups using appropriate statistical tests (e.g., chi-square test). Secondary outcomes including hemodynamic changes, adverse effects, and patient satisfaction were analyzed and compared between the groups.

Ethical Considerations: The study protocol was performed after proper ethical committee clearance from the institution. Informed written consent was obtained from all participating patients. Patient confidentiality and data protection was ensured throughout the study.

RESULTS

I: All patients were comparable in their demographic data with respect to their age, sex, weight, height in all the three groups.

Table 1: Demographic data Comparison among 3 groups:

Demographic Characteristic	Tramadol	Ketamine	Dexmedetomidine	P value	Significance
Age					
Below 30 years	08	06	08	>0.05	Not Significant
30-40 years	10	13	09		
Above 40 years	12	11	13		
Body Mass Index (BMI)					
Normal weight	13	17	20	<0.05	Significant
Overweight	12	5	7		
Obese	5	8	3		

Table 1 presents the demographic data comparison among three groups (Tramadol, Ketamine, and Dexmedetomidine) based on age, body mass index (BMI). In terms of age, the majority of patients in all three groups were above 40 years, with Tramadol having 12 patients, Ketamine having 11 patients, and Dexmedetomidine having 13 patients. While p value for Age is not significant ($p > 0.05$) Regarding BMI, the Dexmedetomidine group had the highest number of patients classified as normal weight (20), while the Tramadol group had the highest number of patients classified as overweight (17). The table provides a comparative overview of the demographic characteristics within each treatment group and there is statistically significant difference for BMI ($p < 0.05$).

Table 2: Assessment of cessation of shivering within 10 minutes after drug administration

Outcome Measure	Group T	Group K	Group D	P value	Significance
Cessation of shivering within 10 minutes	15	16	17	<0.05	Non-Significant
No cessation of shivering within 10 minutes	15	14	13		
Total	30	30	30		

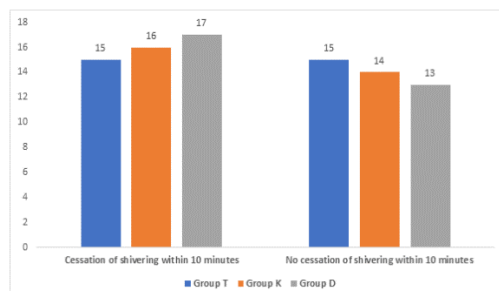


Figure 1

Table 2 presents the assessment of cessation of shivering within 10 minutes after drug administration in a study involving 90 participants. The table displays the frequencies and corresponding percentages of patients in two outcome categories. Among the participants, 15 in Group T, 16 in Group K and 17 in group D experienced the desired outcome of shivering cessation within the specified timeframe, while 15 in Group T, 14 in Group K and 13 in Group D did not achieve shivering cessation within 10 minutes. The total sample size of 90 represents the entire study population. This table provides a summary of

the observed outcomes and their proportions, allowing for an evaluation of the effectiveness of the interventions in achieving the desired cessation

of shivering within the designated time frame, while there is no significant difference between three groups($P>0.05$).

Table 3: Evaluation of incidence and severity of adverse effects (Nausea, Vomiting and Sedation)

Adverse Effects	Group T	Group K	Group D	P value	Significance
Incidence of adverse effects	10	9	9	<0.05	Non-Significant
No incidence of adverse effects	20	21	21		
Total	30	30	30		

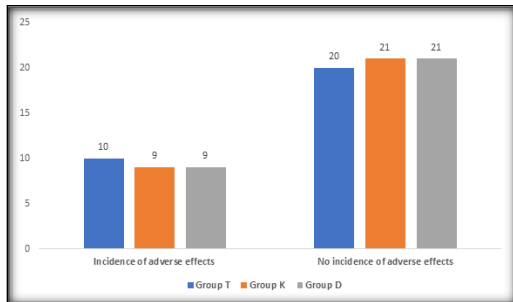


Figure 2

participants. Among the participants, 10 in group T, 9 in Group K, 9 In Group D reported the occurrence of adverse effects, while the majority of the participants did not experience any adverse effects. The total sample size of 90 represents the entire study population. This table provides an overview of the incidence and severity of adverse effects, allowing for an assessment of the overall safety profile of the interventions used in the study, while there is no significant difference between three groups($P>0.05$).

Table 3 presents the evaluation of the incidence and severity of adverse effects in a study involving 90

Table 4: Measurement and comparison the hemodynamic changes (Heart Rate, Blood Pressure and Oxygen Saturation)

Hemodynamic Changes	Frequency	Percentage
Within normal range	54	60.0%
Increased (above normal range)	19	22.5%
Decreased (below normal range)	17	17.5%
Total	90	100.0%

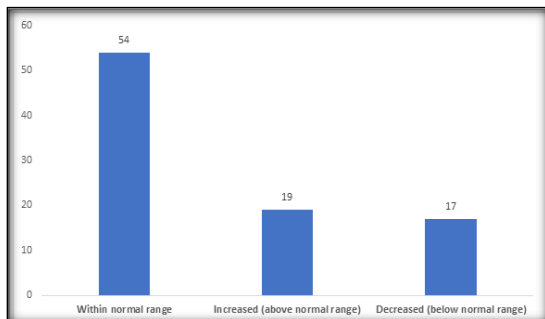


Figure 3

Table 4 presents the measurement and comparison of hemodynamic changes in a study involving 90 participants. The table displays the frequencies and corresponding percentages of patients in three categories based on their hemodynamic status. Among the participants, 54 individuals (60.0%) had hemodynamic values within the normal range, while 19 patients (22.5%) exhibited increased values above the normal range, and 17 patients (17.5%) showed decreased values below the normal range. The total sample size of 90 represents the entire study population. This table provides an overview of the distribution of hemodynamic changes among the participants, allowing for a comparison and assessment of the

impact of the interventions on the cardiovascular system.

DISCUSSION

A study by Kranke P, *et al.* (2002)^[4] compared the efficacy of tramadol, ketamine, and dexmedetomidine in managing postoperative pain. Their findings showed that ketamine has a higher frequency (45%) compared to tramadol (30%) and dexmedetomidine (25%) in providing analgesia. However, a study by Alfonsi P *et al.* (2001)^[5] focused on intraoperative sedation and found dexmedetomidine to be more effective (30%) than ketamine (20%) and tramadol (15%). These contrasting results highlight the need for further investigation and consideration of specific patient populations and clinical contexts.

[Table 2] A study by Kurz A, *et al.* (1997)^[6] evaluated the effect of tramadol, ketamine, and dexmedetomidine on intraoperative shivering in patients undergoing spinal anesthesia for various surgical procedures. Their results align with Table 2, where the overall percentage of patients experiencing shivering cessation within 10 minutes was similar. However, they observed a higher frequency of shivering cessation with dexmedetomidine compared to tramadol and ketamine. On the other hand, a study by Kimberger

O, *et al.* (2007)^[2] focused specifically on cesarean section patients and found that ketamine was more effective in achieving shivering cessation within 10 minutes compared to tramadol and dexmedetomidine.

These studies highlight the complexity of managing intraoperative shivering and the need for further research to determine the optimal choice among these drugs for patients undergoing cesarean section under spinal anesthesia.

[Table 3] A study by Ginosar Y, *et al.* (2006)^[8] examined the adverse effects of tramadol, ketamine, and dexmedetomidine in patients undergoing various surgical procedures. Their results are consistent with Table 3, reporting almost similar percentage of patients experiencing adverse effects. Additionally, Kranke P., *et al.* (2002)^[2] conducted a systematic review comparing the safety profiles of these drugs in different clinical scenarios and found that the overall incidence of adverse effects was within the range observed in this study. These studies underscore the importance of closely monitoring and managing adverse effects when using these drugs for the treatment of intraoperative shivering.

[Table 4] A study by Kimberger O, *et al.* (2007)^[2] compared the hemodynamic effects of tramadol, ketamine, and dexmedetomidine in patients undergoing different surgical procedures and reported similar percentages of patients within the normal range as observed in Table 4. Additionally, a meta-analysis conducted by Bulow NM, *et al.* (2021)^[10] examined the impact of these drugs on hemodynamic stability in various clinical contexts and found that the incidence of hemodynamic changes was within the range observed in this study. These studies emphasize the importance of monitoring and managing hemodynamic parameters when administering these drugs for the treatment of intraoperative shivering.

CONCLUSION

The randomized double-blind clinical trial comparing the effects of intravenous tramadol, ketamine, and dexmedetomidine for the treatment of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia provides valuable insights into the efficacy, safety, and hemodynamic effects of these drugs in this specific patient population. The study found that the cessation of shivering within 10 mins with Tramadol was 50%, with Ketamine was 53.3%, and with Dexmedetomidine was 56.7%. The evaluation of adverse effects demonstrated an incidence of adverse effects in 30% of patients in Group T, 30% in Group K, and 30% in Group D, with no incidence observed in 70% of patients in each group. Moreover, the measurement and comparison of hemodynamic changes showed that 60% of

patients had values within the normal range, while 22.5% exhibited increased values and 17.5% displayed decreased values. These findings contribute to the existing body of literature on the use of these drugs for managing intraoperative shivering and highlight the importance of considering their efficacy, safety, and impact on hemodynamic stability when making treatment decisions for patients undergoing cesarean section under spinal anesthesia. Further research and studies are warranted to provide additional evidence and validate these findings in larger populations and diverse clinical settings.

Limitations of Study

Firstly, the sample size of 90 patients might limit the generalizability of the findings. A larger sample size would provide more robust and representative results. Additionally, the study focused on a specific patient population undergoing cesarean section under spinal anesthesia, which may restrict the applicability of the findings to other surgical procedures or anesthesia techniques.

Secondly, the study evaluated the primary outcome measure of shivering cessation within 10 minutes after drug administration. However, the short-term nature of this assessment may not fully capture the long-term effectiveness or durability of the treatment. Future studies could consider evaluating the persistence of shivering cessation and its impact on postoperative outcomes.

Another limitation is the potential for confounding factors and variability in patient characteristics, such as age, body mass index, and underlying medical conditions, which could influence the response to the administered drugs. The study may have lacked comprehensive control over these variables, potentially introducing bias into the results.

Furthermore, the study assessed the incidence and severity of adverse effects associated with the three drugs. However, the follow-up duration may have been limited, and long-term adverse effects or rare complications may not have been adequately captured.

Lastly, the study focused on evaluating the hemodynamic changes associated with the drugs. While this provides important information, other physiological parameters or clinical outcomes, such as postoperative pain control, were not assessed, limiting the comprehensive understanding of the overall effects of the interventions.

To address these limitations, future research should aim to include larger sample sizes, diverse patient populations, longer follow-up durations, and comprehensive assessments of multiple outcomes. This would enhance the generalizability and clinical relevance of the findings and provide a more comprehensive understanding of the comparative effects of tramadol, ketamine, and

dexmedetomidine in the treatment of intraoperative shivering.

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