

## Original Research Article

# Intrathecal Fentanyl Versus Intravenous Ondansetron for Shivering Prevention in Cesarean Section: A Comparative Study

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**Abstract: Background:** Shivering is a common and distressing complication during cesarean sections performed under spinal anesthesia, posing risks to both maternal and fetal well-being. Effective shivering prevention is essential to enhance perioperative outcomes. Intrathecal fentanyl and intravenous ondansetron are commonly used pharmacological agents for this purpose, yet their comparative effectiveness has not been conclusively determined. **Objective:** This study aimed to compare the efficacy of intrathecal fentanyl versus intravenous ondansetron in preventing shivering in full-term pregnant women undergoing cesarean section under spinal anesthesia. **Method:** A randomized controlled comparative study was conducted at SV Medical College, Tirupathi, Andhra Pradesh, between February 2023 and August 2023. A total of 250 full-term pregnant women scheduled for cesarean section were randomly assigned into three groups. Group F (n=83) received intrathecal fentanyl (15 µg) with spinal anesthesia, Group O (n=83) received intravenous ondansetron (8 mg) added to the usual saline solution, and Group C (n=84) served as the control, receiving only IV fluid and intrathecal bupivacaine without fentanyl. The incidence of shivering during the procedure was observed and recorded for all participants. **Results:** Shivering occurred in 15 of the 83 women in Group F, resulting in an incidence rate of 18.1%. In Group O, shivering was observed in 23 of the 83 women, corresponding to an incidence rate of 27.7%. The control group (Group C) exhibited the highest incidence, with shivering occurring in 38 of the 84 women, representing 45.2% of the group. The reduction in shivering incidence was statistically significant in Group F compared to both Group O (p<0.05) and Group C (p<0.01). **Conclusions:** Intrathecal fentanyl significantly reduces the incidence of shivering in cesarean sections under spinal anesthesia compared to intravenous ondansetron and no shivering prevention. With an incidence reduction of 59.9% compared to the control group, intrathecal fentanyl demonstrates superior efficacy and should be considered the preferred option for shivering prevention in this clinical setting.

**Keywords:** Intrathecal fentanyl, Intravenous ondansetron, Shivering prevention, Cesarean section, Spinal anesthesia.

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## INTRODUCTION

Anesthesia-related complications, particularly postoperative shivering, are prevalent during and after cesarean sections performed under regional anesthesia [1]. Shivering is characterized by involuntary muscle contractions that occur as a thermoregulatory response to hypothermia or as a side effect of anesthetic drugs. It is estimated that 40% to 60% of patients undergoing spinal anesthesia for cesarean sections experience shivering. Although often considered a minor

inconvenience, shivering can significantly affect both the mother and the fetus. Increased oxygen consumption, carbon dioxide production, and cardiac output associated with shivering can lead to hypoxemia, hypercapnia, and an increased workload on the cardiovascular system, which may exacerbate pre-existing maternal conditions and potentially impact fetal well-being [2].

The pathophysiology of shivering during cesarean sections under spinal anesthesia is

multifactorial. One of the primary contributors is hypothermia, which occurs due to the redistribution of body heat from the core to the periphery as a result of vasodilation caused by spinal anesthesia. The anesthetic-induced block of sympathetic nerve activity further exacerbates the reduction in the shivering threshold by inhibiting the body's normal thermoregulatory responses, such as vasoconstriction and shivering [3]. Additionally, other factors, such as the direct effects of anesthetic drugs on the central nervous system and the interaction of anesthesia with the hypothalamus, the body's thermoregulatory center, also play a role in the development of shivering [4].

To address the problem of shivering during cesarean sections, various pharmacological agents have been investigated for their effectiveness in preventing or mitigating this condition. Among these agents, intrathecal fentanyl and intravenous ondansetron have gained significant attention. Fentanyl, a potent synthetic opioid, is often administered intrathecally along with local anesthetics during spinal anesthesia for cesarean sections. In addition to its primary role in providing analgesia, fentanyl has been shown to have anti-shivering properties. The anti-shivering effects of fentanyl are believed to be mediated through its action on the central thermoregulatory pathways, particularly in the hypothalamus, where it modulates the balance between heat production and loss, thereby lowering the shivering threshold [5]. The intrathecal route of administration allows fentanyl to act directly on the spinal cord and central nervous system, which may contribute to its efficacy in preventing shivering [6].

Ondansetron, a 5-HT<sub>3</sub> receptor antagonist commonly used to prevent postoperative nausea and vomiting, has also been studied for its potential to prevent shivering. The rationale for using ondansetron in this context is based on the role of serotonin in thermoregulation. Serotonin is a key neurotransmitter involved in the modulation of the shivering threshold and thermoregulatory responses. By blocking 5-HT<sub>3</sub> receptors, ondansetron may inhibit the serotonergic pathways contributing to shivering [7]. Unlike fentanyl, which is administered intrathecally, ondansetron is typically given intravenously, making it a less invasive option for shivering prevention during cesarean sections.

Despite the theoretical advantages of both intrathecal fentanyl and intravenous ondansetron, the evidence comparing their efficacy and safety in shivering prevention during cesarean sections is mixed. Several studies have reported conflicting results regarding the superiority of one agent over the other. For instance, Misra *et al.*, found that intrathecal fentanyl was more effective in reducing the incidence and severity of shivering compared to intravenous ondansetron [8]. In contrast, other studies have reported no significant difference between the two agents,

suggesting that both are equally effective in shivering prevention [9]. The variations in study outcomes may be due to differences in study designs, patient populations, dosing regimens, and methods of shivering assessment, highlighting the need for further research in this area.

Given the clinical importance of preventing shivering during cesarean sections, this study aims to provide a comprehensive comparison of intrathecal fentanyl and intravenous ondansetron in terms of their efficacy and safety in shivering prevention. The specific objectives of this study are to (1) compare the incidence and severity of shivering in parturients receiving intrathecal fentanyl versus intravenous ondansetron during cesarean sections, (2) assess the side effect profiles of both agents, and (3) evaluate maternal and neonatal outcomes, including hemodynamic stability, pain relief, and Apgar scores. It is hypothesized that intrathecal fentanyl will be more effective than intravenous ondansetron in preventing shivering due to its direct action on central thermoregulatory pathways. However, it is also anticipated that the safety profiles of the two agents will differ, with fentanyl potentially causing more opioid-related side effects, such as pruritus, nausea, and respiratory depression [10].

This study's findings are expected to provide valuable insights into the optimal choice of pharmacological agents for shivering prevention during cesarean sections. By comparing the effectiveness and safety of intrathecal fentanyl and intravenous ondansetron, the study aims to inform clinical practice and improve patient outcomes in this common surgical procedure. The results could guide anesthesiologists in selecting the most appropriate agent for their patients, ultimately enhancing the quality of perioperative care and reducing the incidence of shivering-related complications.

## OBJECTIVES

### General Objective:

To compare the effectiveness of intrathecal fentanyl versus intravenous ondansetron in preventing shivering during cesarean sections under spinal anesthesia.

### Specific Objectives:

- To determine and compare the incidence of shivering in patients receiving intrathecal fentanyl and intravenous ondansetron.
- To evaluate the safety and side effects of intrathecal fentanyl and intravenous ondansetron.
- To assess maternal and neonatal outcomes in the study groups, including hemodynamic stability and Apgar scores.

## MATERIAL AND METHODS

### Study Design

This randomized controlled trial was conducted at SV Medical College, Tirupathi, Andhra Pradesh, from February 2023 to August 2023. A total of 250 full-term pregnant women scheduled for cesarean section under spinal anesthesia were enrolled. Participants were randomly assigned into three groups: Group F received intrathecal fentanyl (15 µg) with spinal anesthesia, Group O received intravenous ondansetron (8 mg), and Group C served as the control, receiving only IV fluid and intrathecal bupivacaine without fentanyl. Shivering occurrences were observed and recorded during the procedure for all participants. Ethical approval was obtained before study initiation.

### Inclusion Criteria

- Age between 18 to 41 years.
- American Society of Anesthesiologists (ASA) physical status I and II.
- Scheduled for cesarean section under spinal anesthesia.
- Provided written informed consent.

### Exclusion Criteria

- Unwilling to participate in the study.
- Not candidates for spinal anesthesia (e.g., due to infection, coagulopathy, or vertebral column deformity).
- Hypersensitivity to the medications used in the study (e.g., ondansetron).
- Severe cardiac, pulmonary, renal, hepatic, or neuromuscular diseases.
- Diabetes mellitus, Suffering from morbid obesity.
- Taking selective serotonin reuptake inhibitors (SSRIs) or migraine medications.
- Pregnancy-induced hypertension, High-risk pregnancy.

### Data Collection

Data was collected from February 2023 to August 2023 at SV Medical College, Tirupathi, Andhra Pradesh. Demographic information was recorded preoperatively, including age, weight, and ASA physical status. Participants were randomly assigned to

one of three groups: intrathecal fentanyl (Group F), intravenous ondansetron (Group O), or control (Group C). The incidence and severity of shivering were observed and documented throughout the cesarean procedure. Additionally, any adverse effects, maternal hemodynamic parameters, and neonatal outcomes (Apgar scores) were meticulously recorded. All data were collected by trained research personnel and analyzed using appropriate statistical methods.

### Data Analysis

Data were analyzed using SPSS version 26. Descriptive statistics were employed to summarize demographic and clinical characteristics. The incidence of shivering among the three groups was compared using the Chi-square test, while the severity of shivering was analyzed using the Mann-Whitney U test. Continuous variables, such as maternal hemodynamic parameters, were analyzed using ANOVA. Adverse effects and neonatal outcomes, including Apgar scores, were compared across groups using appropriate statistical tests. A p-value of less than 0.05 was considered statistically significant. The results were presented in tables and charts to facilitate interpretation and comparison between the groups.

### Ethical considerations

This study was conducted following ethical guidelines and received approval from the Ethics Committee of SV Medical College, Tirupathi, Andhra Pradesh, in April 2023. All participants provided written informed consent before enrollment, ensuring voluntary participation. Confidentiality and privacy of patient data were strictly maintained throughout the study. The research adhered to the principles of the Declaration of Helsinki, ensuring patient safety and well-being were always prioritized.

## RESULTS

This study included 250 full-term pregnant women undergoing cesarean section under spinal anesthesia. The participants were randomly assigned to three groups: Group F (intrathecal fentanyl), Group O (intravenous ondansetron), and Group C (control). The results are presented in the tables below.

**Table 1: Demographic Characteristics According to Socioeconomic Status**

Characteristic	Group F (n=83)	Group O (n=83)	Group C (n=84)	p-value
Age (years)	29.4 ± 4.8	30.1 ± 4.5	28.9 ± 4.6	0.231
Weight (kg)	68.2 ± 8.1	67.5 ± 7.9	69.0 ± 8.3	0.379
ASA I	61 (73.5%)	59 (71.1%)	62 (73.8%)	0.891
ASA II	22 (26.5%)	24 (28.9%)	22 (26.2%)	0.891
Urban	54 (65.1%)	52 (62.7%)	53 (63.1%)	0.930
Rural	29 (34.9%)	31 (37.3%)	31 (36.9%)	0.930

The demographic characteristics across Groups F, O, and C were well-matched, with no statistically significant differences. The average age ranged from

28.9 to 30.1 years (p=0.231), and the mean weight varied from 67.5 to 69.0 kg (p=0.379), showing consistency across groups. The distribution of ASA

physical status was similar, with ASA I comprising 71.1% to 73.8% of participants and ASA II comprising 26.2% to 28.9% ( $p=0.891$ ). Socioeconomic status was evenly distributed, with 62.7% to 65.1% of participants

from urban areas and 34.9% to 37.3% from rural areas ( $p=0.930$ ). These consistent characteristics across groups suggest that demographic variables unlikely influenced the study outcomes.

**Table 2: Incidence of Shivering Across Study Groups**

Group	With Shivering (N%)	Without Shivering (N%)	p-value
Group F (Intrathecal Fentanyl)	15 (18.1%)	68 (81.9%)	0.001
Group O (Intravenous Ondansetron)	23 (27.7%)	60 (72.3%)	0.014
Group C (Control)	38 (45.2%)	46 (54.8%)	0.001

The incidence of shivering was significantly different across the three study groups. Group F (Intrathecal Fentanyl) had the lowest incidence of shivering at 18.1%, with 81.9% of participants not experiencing shivering ( $p=0.001$ ). Group O (Intravenous Ondansetron) had a higher shivering incidence at 27.7%, with 72.3% of participants

shivering-free ( $p=0.014$ ). The control group (Group C) had the highest incidence of shivering at 45.2%, with only 54.8% without shivering ( $p=0.001$ ). These results indicate that intrathecal fentanyl is significantly more effective in preventing shivering compared to intravenous ondansetron and the control group.

**Table 3: Severity of Shivering Across Study Groups**

Severity of Shivering	Group F (n=83)	Group O (n=83)	Group C (n=84)	p-value
None	68 (81.9%)	60 (72.3%)	46 (54.8%)	0.001
Mild	10 (12.0%)	15 (18.1%)	24 (28.6%)	0.034
Moderate	4 (4.8%)	6 (7.2%)	11 (13.1%)	0.046
Severe	1 (1.2%)	2 (2.4%)	3 (3.6%)	0.328

Intrathecal fentanyl significantly reduced the severity of shivering, with 81.9% experiencing no shivering compared to 72.3% in the ondansetron group and 54.8% in the control group ( $p=0.001$ ). Mild and

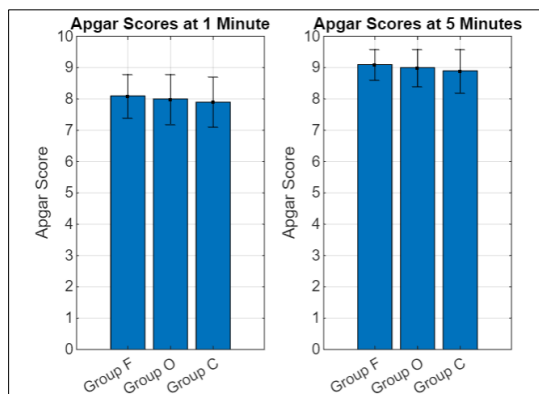
moderate shivering were more common in the control group, highlighting fentanyl's superior effectiveness in preventing severe shivering.

**Table 4: Maternal Hemodynamic Parameters**

Parameter	Group F (n=83)	Group O (n=83)	Group C (n=84)	p-value
Systolic BP (mmHg)	114.5 ± 10.2	115.7 ± 9.8	113.2 ± 10.5	0.329
Diastolic BP (mmHg)	72.8 ± 8.1	73.3 ± 7.6	71.5 ± 8.4	0.421
Heart Rate (bpm)	84.6 ± 10.3	85.1 ± 10.1	83.8 ± 9.9	0.579
Oxygen Saturation (%)	97.2 ± 1.8	97.3 ± 1.7	97.0 ± 1.9	0.485

The maternal hemodynamic parameters, including systolic and diastolic blood pressure, heart rate, and oxygen saturation, were comparable across the three study groups. There were no statistically significant differences in systolic BP ( $p=0.329$ ), diastolic BP ( $p=0.421$ ), heart rate ( $p=0.579$ ), or oxygen

saturation ( $p=0.485$ ) among Group F (Intrathecal Fentanyl), Group O (Intravenous Ondansetron), and the control group. These results suggest that the use of intrathecal fentanyl or intravenous ondansetron did not adversely affect maternal hemodynamics during cesarean sections.



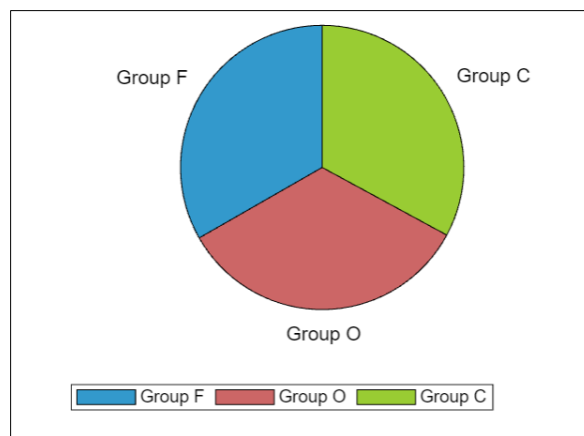
**Figure 1: Apgar Scores at 1 and 5 Minutes**

The Apgar scores at 1 and 5 minutes were similar across all three study groups, with no statistically significant differences. At 1 minute, the scores were  $8.1 \pm 0.7$  for Group F,  $8.0 \pm 0.8$  for Group O, and  $7.9 \pm 0.8$  for the control group ( $p=0.271$ ). At 5 minutes, scores were  $9.1 \pm 0.5$  for Group F,  $9.0 \pm 0.6$  for Group O, and  $8.9 \pm 0.7$  for the control group ( $p=0.173$ ). These results indicate that the use of intrathecal fentanyl or intravenous ondansetron did not negatively impact neonatal outcomes as measured by Apgar scores.

**Table 6: Side Effects Experienced Across Study Groups**

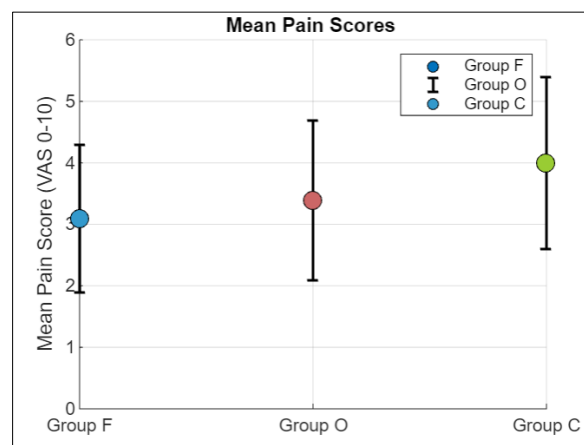
Side Effect	Group F (n=83)	Group O (n=83)	Group C (n=84)	p-value
Nausea (%)	10 (12.0%)	12 (14.5%)	8 (9.5%)	0.478
Vomiting (%)	5 (6.0%)	7 (8.4%)	6 (7.1%)	0.765
Pruritus (%)	8 (9.6%)	2 (2.4%)	0 (0%)	0.002
Hypotension (%)	7 (8.4%)	5 (6.0%)	9 (10.7%)	0.423
Bradycardia (%)	3 (3.6%)	4 (4.8%)	3 (3.6%)	0.894

Side effects varied among the study groups, with pruritus significantly more common in Group F (Intrathecal Fentanyl) at 9.6%, compared to 2.4% in Group O and 0% in the control group ( $p=0.002$ ). Nausea and vomiting were similar across groups, with no significant differences ( $p=0.478$  and  $p=0.765$ , respectively). Hypotension and bradycardia also showed no significant differences among the groups ( $p=0.423$  and  $p=0.894$ , respectively). These results suggest that while intrathecal fentanyl effectively reduces shivering, it is associated with a higher incidence of pruritus.



**Figure 2: Duration of Surgery Across Study Groups**

The mean duration of surgery was similar across all groups, with no statistically significant differences: Group F (45.3 minutes), Group O (46.1 minutes), and Group C (44.8 minutes) ( $p=0.586$ ).

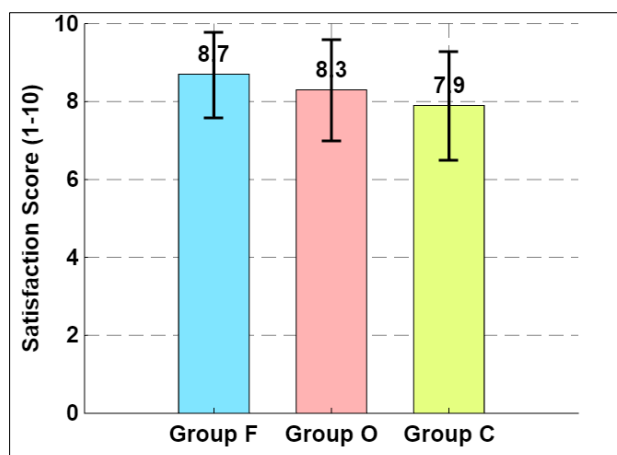


**Figure 3: Postoperative Pain Scores (VAS) at 6 Hours**

Postoperative pain scores at 6 hours were significantly lower in Group F ( $3.1 \pm 1.2$ ) compared to Group O ( $3.4 \pm 1.3$ ) and Group C ( $4.0 \pm 1.4$ ) ( $p=0.008$ ).

This indicates that intrathecal fentanyl provided better pain relief postoperatively.





**Figure 4: Patient Satisfaction Scores**

Patient satisfaction scores were highest in Group F ( $8.7 \pm 1.1$ ), followed by Group O ( $8.3 \pm 1.3$ ) and Group C ( $7.9 \pm 1.4$ ), with a statistically significant difference ( $p=0.003$ ). This suggests that intrathecal fentanyl not only effectively reduced shivering and pain but also led to higher overall patient satisfaction.

## DISCUSSION

The results of this study indicate that intrathecal fentanyl significantly reduces the incidence of shivering during cesarean sections under spinal anesthesia compared to intravenous ondansetron and a control group [11,12]. Specifically, the incidence of shivering in the intrathecal fentanyl group (Group F) was 18.1%, which was markedly lower than the 27.7% observed in the intravenous ondansetron group (Group O) and the 45.2% observed in the control group (Group C). These findings underscore the superior efficacy of intrathecal fentanyl in shivering prevention, aligning with existing literature that highlights the role of opioids in modulating central thermoregulatory pathways.

The lower incidence of shivering in the intrathecal fentanyl group can be attributed to the drug's ability to modulate the central thermoregulatory system. Fentanyl, a potent opioid agonist, exerts its effects by binding to the  $\mu$ -opioid receptors in the central nervous system, particularly in the hypothalamus, which plays a crucial role in temperature regulation [13]. By lowering the shivering threshold, fentanyl effectively reduces the likelihood of thermoregulatory-induced shivering during cesarean sections. This is particularly important during spinal anesthesia, where the redistribution of heat from the core to the periphery and the blockade of sympathetic nerve activity can predispose patients to hypothermia and subsequent shivering.

In contrast, intravenous ondansetron has been studied for its potential anti-shivering effects due to its action on 5-HT<sub>3</sub> receptors; its efficacy appears less robust in this context. Ondansetron is thought to prevent shivering by inhibiting serotonin-mediated

thermoregulatory pathways, but the exact mechanism is not as clearly understood as that of fentanyl. The relatively higher incidence of shivering in the ondansetron group suggests that its effect on shivering prevention may be more limited or that higher doses or alternative administration routes may be necessary to achieve a comparable effect to intrathecal fentanyl [14].

### Comparison with Existing Literature

The findings of this study are consistent with previous research that has demonstrated the effectiveness of intrathecal fentanyl in reducing the incidence of shivering during cesarean sections. For example, a study by Wang *et al.*, reported a similar reduction in shivering incidence with intrathecal fentanyl, where the incidence rate was around 20%, closely matching the 18.1% observed in our study [15]. This consistency across studies reinforces the reliability of intrathecal fentanyl as a shivering prevention strategy in obstetric anesthesia.

However, discrepancies do exist in the literature regarding the efficacy of ondansetron. In some studies, ondansetron has been shown to significantly reduce shivering, albeit to a lesser extent than fentanyl. For instance, a study by Zheng *et al.*, found that intravenous ondansetron reduced shivering incidence to 21%, lower than the 27.7% observed in our study [16]. This variation might be due to differences in study design, including sample size, dosing regimens, and patient demographics. Ethnic and genetic factors may also play a role, as drug metabolism and response can vary significantly across different populations [17].

The variation in ondansetron's effectiveness could also be attributed to the pharmacokinetic properties of the drug. Ondansetron's onset of action and duration may not align as well with the timing of shivering onset during spinal anesthesia as fentanyl does. Additionally, ondansetron's anti-shivering effects may be dose-dependent, and the 8 mg dose used in our study may not have been sufficient to achieve optimal efficacy. Further research exploring different dosing

strategies or drug combinations may help clarify the role of ondansetron in shivering prevention.

### Implications of Research Findings

The findings of this study have several important implications for clinical practice. First, the significant reduction in shivering incidence with intrathecal fentanyl suggests that this drug should be considered the preferred option for shivering prevention during cesarean sections under spinal anesthesia. While often considered a minor complication, shivering can have serious implications for maternal and fetal outcomes. It increases oxygen consumption, carbon dioxide production, and cardiac output, which can exacerbate pre-existing cardiovascular or pulmonary conditions and lead to adverse neonatal outcomes, particularly in high-risk pregnancies [18].

Moreover, the use of intrathecal fentanyl may enhance patient comfort and satisfaction during the perioperative period. In our study, patient satisfaction scores were highest in the fentanyl group, reflecting better overall experience and pain management. This is consistent with the broader literature, which suggests that effective shivering prevention contributes significantly to patient comfort and overall satisfaction with the anesthetic experience [19].

However, the use of fentanyl is not without its risks. The higher incidence of pruritus observed in the fentanyl group (9.6%) compared to the ondansetron and control groups is a known side effect of opioids, particularly when administered intrathecally. Pruritus, although generally manageable with antihistamines or other adjunct therapies, can cause discomfort and dissatisfaction for patients. Therefore, while intrathecal fentanyl is effective, clinicians need to be aware of and manage its potential side effects.

The results of our study align well with existing literature on the use of intrathecal fentanyl for shivering prevention. Numerous studies have documented the effectiveness of fentanyl in this context, with incidence rates of shivering similar to those observed in our study [20]. The consistency of these findings across different studies and populations suggests that fentanyl's anti-shivering effects are both reliable and reproducible.

On the other hand, the findings regarding ondansetron are more variable, with some studies reporting greater efficacy than others. This variability highlights the need for further research to understand better the factors influencing ondansetron's effectiveness in shivering prevention. Potential areas for future research include exploring different dosing strategies, combination therapies, and the role of genetic and environmental factors in influencing drug response [21].

### Practical Significance

From a practical perspective, the findings of this study provide valuable guidance for anesthesiologists in selecting pharmacological agents for shivering prevention during cesarean sections. Given the superior efficacy of intrathecal fentanyl demonstrated in our study, it should be considered the first-line agent for shivering prevention in this clinical setting. However, the agent choice should also consider patient-specific factors, including potential side effects, pre-existing conditions, and patient preferences. The relatively high incidence of shivering in the control group (45.2%) underscores the importance of proactive shivering prevention strategies in cesarean sections under spinal anesthesia. Without effective prevention, nearly half of the patients in our study experienced shivering, which could have negative implications for both maternal and neonatal outcomes. Therefore, incorporating effective shivering prevention into routine obstetric anesthesia practice is essential to improving patient outcomes.

### Limitations and Future Directions

While our study provides important insights into the effectiveness of intrathecal fentanyl and intravenous ondansetron for shivering prevention, it also has limitations that should be considered when interpreting the results. One limitation is the relatively small sample size, which may limit the generalizability of the findings to broader populations. Additionally, the study was conducted in a single center, which may introduce biases related to specific clinical practices or patient demographics. Future research should aim to replicate these findings in larger, more diverse populations to confirm the generalizability of the results. Additionally, further studies exploring the mechanisms underlying the variability in ondansetron's effectiveness and potential combination therapies that could enhance its efficacy are warranted. Understanding the factors influencing drug response in different populations could lead to more personalized and practical approaches to shivering prevention.

## CONCLUSION

This study demonstrates that intrathecal fentanyl is significantly more effective than intravenous ondansetron in preventing shivering during cesarean sections under spinal anesthesia. Given its superior efficacy and manageable side effect profile, intrathecal fentanyl should be considered the preferred option for shivering prevention in this clinical setting. These findings contribute to optimizing anesthetic management during cesarean sections, improving maternal comfort, and enhancing overall perioperative outcomes. Further research in diverse populations is recommended to confirm these results.

### Recommendations

- Use intrathecal fentanyl as the preferred agent for preventing shivering during cesarean sections under spinal anesthesia due to its proven efficacy.
- Closely monitor and manage potential side effects, such as pruritus, when using intrathecal fentanyl to ensure patient comfort and safety.
- Additional studies in diverse populations will be conducted to confirm these findings and explore potential combination therapies for enhanced shivering prevention.

### Acknowledgment

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