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Original Article

Prophylactic Efficacy of Intravenous Nefopam Versus Ondansetron in Preventing Post-Spinal Shivering in Parturients Undergoing Elective Caesarean Section: A Double-Blind Randomised Controlled Trial

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Abstract

Background: Post-spinal shivering (PSS) is a frequent complication of spinal anaesthesia during caesarean section, causing patient discomfort and potential physiological disturbances. Both nefopam and ondansetron possess anti-shivering properties; however, comparative evidence in obstetric patients is limited. The objective of this study is to compare the efficacy and safety of intravenous nefopam and ondansetron in preventing post-spinal shivering in women undergoing elective caesarean section under spinal anaesthesia.

Methodology: This randomised controlled study included 96 ASA II parturients scheduled for elective caesarean section under spinal anaesthesia. Participants were randomly allocated into three groups (n = 32 each). Group N received intravenous nefopam (0.15 mg/kg), Group O received intravenous ondansetron (0.1 mg/kg), and Group P received 10 mL of normal saline as a placebo. The medications were administered 15 minutes before spinal anaesthesia. Patients were monitored for the incidence and severity of shivering using the Crossley and Mahajan scale. Side effects and the need for rescue medication (intravenous pethidine 0.5 mg/kg) were also recorded. Statistical significance was set at $p < 0.05$.

Results: The incidence of PSS was significantly lower in Group N (18.8%) and Group O (18.8%) compared with Group P (59.4%) ($p < 0.001$). Severe shivering (grades 3–4) occurred only in the placebo group (40.5%). Consequently, the need for rescue pethidine was significantly higher in Group P (37.5%), while none of the patients in Groups N or O required it ($p < 0.001$). Postoperative nausea was less frequent in Group O (3.1%) and Group N (12.5%) compared with Group P (25%) ($p < 0.05$). Mild injection-site pain occurred only in Group N (9.4%).

Conclusion: Intravenous nefopam and ondansetron are similarly effective in preventing post-spinal shivering and reducing rescue analgesia requirements during caesarean section under spinal anaesthesia. Ondansetron showed better antiemetic effect, while nefopam was associated with mild injection-site discomfort.

Keywords: Post-spinal shivering, Nefopam, Ondansetron, Caesarean section, Spinal anaesthesia

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Introduction

Subarachnoid block (SAB) is widely used for anaesthesia in obstetric, gynaecological, urological, and orthopaedic surgeries in Nigerian hospitals due to its relative safety compared to general anaesthesia.[1,2] One of the most common obstetric procedures done under SAB is a caesarean section.[1,2] Caesarean section is the delivery of the foetus, placenta and membranes after the age of viability through an abdominal and uterine incision.[2,3] SAB offers several distinct advantages for caesarean section, including a swift onset of action and the provision of a consistently dense neural block. The administration of minimal local anaesthetic doses renders the risk of systemic toxicity negligible and ensures only trivial drug transfer across the placenta.[2]

Although most obstetricians and anaesthetists favour caesarean section under SAB, it is associated with various complications, among which post-spinal shivering (PSS) is a frequent and distressing side effect.[4] PSS is characterised by involuntary skeletal muscle contractions, which significantly increase oxygen consumption, carbon dioxide production, and cardiac workload, thereby posing risks, especially to patients with cardiovascular disease. The exact mechanism of shivering remains unclear, but it is thought to involve altered thermoregulatory control and increased heat loss during anaesthesia.[4,5]

The incidence of PSS varies widely, with rates reported between 8% and 55% following neuraxial blocks, and as high as 51.8% in caesarean sections under spinal anaesthesia.[4] Although non-pharmacological methods, such as warming techniques, exist, they often fail to prevent PSS, prompting the use of pharmacological agents. Commonly used drugs such as pethidine, tramadol, and clonidine are effective. Still, their adverse effects—including sedation, nausea, hypotension, and potential neonatal respiratory depression—limit their perioperative use in obstetric patients.[5,6]

Ondansetron and nefopam have emerged as potential alternatives due to their anti-shivering properties and favourable side effect profiles.[7,8] Ondansetron, primarily an antiemetic, and nefopam, an analgesic, are both widely available but underutilised for PSS prophylaxis. There is limited comparative evidence evaluating their relative efficacy in preventing post-spinal shivering, particularly in Nigerian or other local contexts.[5,9]

This study aims to fill this gap by comparing the preventive effectiveness and side effect profiles of intravenous ondansetron and nefopam in reducing PSS during elective caesarean sections.

Materials and Methods

Study Settings

This study was conducted at the modular theatre of Jos University Teaching Hospital (JUTH), Jos, Plateau State, Nigeria. JUTH is a tertiary health institution that serves as a referral centre for neighbouring states like Nasarawa, Bauchi, Benue, Gombe, Adamawa, Taraba and Kaduna states. The hospital has a total bed-space capacity of 620 for inpatients and offers specialised services in different areas of healthcare, training and research.[10] The hospital provides a wide range of medical, surgical, diagnostic, outpatient, rehabilitative and support services to the people of Plateau State and its neighbouring States. The multi-disciplinary approach to services makes it the best point of call for patients requiring services in Paediatrics, Internal Medicine, Surgery, Obstetrics and Gynaecology, Laboratory Services, Radiology, Anaesthesiology, Intensive Care Unit, Ophthalmology, Dietetics, Physiotherapy, Psychiatry, and many more. It was established in 1981 and is located in the City of Jos, Plateau State.

Study Population

Parturient scheduled for elective caesarean section under spinal anaesthesia at JUTH.

Study Design
This was a randomised, double-blind, placebo-controlled clinical study of prophylactic intravenous ondansetron versus nefopam for the prevention of post-spinal shivering.

Inclusion Criteria
ASA II patients (All normal pregnancies, well-controlled gestational hypertension, controlled preeclampsia without severe features, diet-controlled gestational diabetes), Patients with singleton term pregnancies, Patients aged between 18 and 45 years, Patients scheduled for elective caesarean section, and Patients without lumbar spine deformity.

Only patients who met the above criteria and gave consent to participate in the study were enrolled.

Exclusion Criteria
ASA III and IV patients, Low body weight and obese patients, Patients with known allergy to nefopam, ondansetron or bupivacaine, Patients who decline consent, Patients with a history of any disease associated with shivering or pyrexia, Patients with any contraindication to regional anaesthesia, Patients with a history of nausea or vomiting, Patients with body temperature less than $36^{O}C$ or more than $38^{O}C$ and Patients with failed, inadequate or high spinal anaesthesia who were converted to general anaesthesia.

Ethical Approval
Ethical approval was obtained from the Jos University Teaching Hospital Research Ethics Committee (Approval No: JUTH/DCS/IREC/127/XXXI/291; Date: 18th May, 2022) before commencement of this study. All the patients scheduled for elective caesarean section were approached during the preoperative visit to assess their eligibility and also obtain informed consent for the study.

This study was not prospectively registered as a clinical trial, as it was classified as a Phase 1 investigation.

Informed Consent
All eligible patients were educated about the study, and informed consent was obtained from each of the participants before recruitment.

Sampling Technique
The sampling technique that was employed for this study was a consecutive sampling technique. This is a non-probability sampling technique in which consecutive eligible participants were recruited based on the predefined eligibility criteria before randomisation. This entails that not all members of the study population available to the researcher were approached and enrolled on the study, but only those who met the predefined criteria. This was done by meeting patients on admission booked for elective lower segment caesarean section who met the predefined inclusion criteria for this study by their bedside on the eve of their scheduled surgery, and those who gave informed consent were then enrolled into the study.

Sample Size Estimation
The sample size for this study was estimated from the formula for the determination of sample size for a proportion experimental study design

$$n = \frac{(Z_{\beta} + Z\alpha_{/2})^2 \text{ X } 2\dot{P}\ (1 - \dot{P}).^{11}}{E^2}$$

Where;

n = sample size per group

Z_β = desired power of the study, typically 0.84 for 80% power

$Z_{\alpha/2}$ = normal deviate for two-tailed alternative hypothesis at 5% level of significance, $Z_{\alpha/2} = 1.96$

$\dot{P}$ (1-$\dot{P}$) is a measure of variability similar to standard deviation

$$\dot{P} = \frac{P_1 + P_2}{2}$$

P_1 = proportion of the population with the desired condition based on previous studies or pilot studies = 0.315(31.5%), which is the average of the PSS incidence rate of 0.08 to 0.55 (8% to 55%).[12]

P_2 = proportion of the population without the desired condition = 1-0.315= 0.685

$E = P_1 - P_2$, which is the effect size, i.e. the difference in proportion = 0.315-0.685= -0.37

Assuming the level of significance for this study was set at 5% and the power at 80%, then Z_β will be 0.84 and $Z\alpha_{/2}$ will be 1.96.

$$\dot{P} = \frac{P1+P2}{2}$$

$$= \frac{(0.315+0.685)}{2}$$

$$=1/2$$

$$=0.5$$

$$n = \frac{(0.84+1.96)^2 \times 2(0.5) \times (1-0.5)}{(-0.37)^2}$$

$$=\frac{7.84\times1\times0.5}{0.1369}$$

$$=28.63 = 29$$

The sample size per group was 29, giving a total of 87 for the 3 study groups.

10% attrition is 8.7 (approximately 9), which was then added to the total sample size to bring it to 96.

Therefore, the sample size for each group was 32, giving a total of 96 for the 3 study groups.

Randomisation

The study was carried out by the researcher and assisted by two anaesthesia residents. Randomisation was done on the morning of surgery day at the theatre reception, where patients awaiting surgery are usually kept. A total of 96 pieces of paper were divided into 3 groups equally in a 1:1:1 allocation ratio (32 pieces of paper per group). Each piece of paper in one group was labelled N, each piece of paper in the second group was labelled O, and each piece of paper in the third group was labelled P. Group N was assigned to nefopam, group O to ondansetron, and group P to the saline/placebo group. The 96 labelled pieces of paper were each folded and concealed in a brown/opaque envelope. These envelopes carrying the labelled pieces of paper were then shuffled in a basket. Each eligible patient randomly picked an envelope from the basket, and the envelope with its corresponding labelled paper N, O or P was recorded in a book by the first assistant. Thus, all the 96 recruited patients were randomised into three groups of N (nefopam), O (ondansetron) and P (saline/placebo), and each group had 32 patients. A 20 ml syringe was then used to withdraw either ondansetron, nefopam or normal saline and then made up to 20 ml with sterile water for injection and then labelled as N, O or P, respectively.

Blinding

Both the patient and the researcher were blinded to the contents of the syringes. To achieve this, the first assistant randomised the patients into the three groups N, O, and P as selected by each patient during balloting. The first assistant also prepared and coded labelled drugs, but was not involved in the administration of the labelled drugs. The second assistant administered the labelled drug in the theatre and also recorded the labelled group on the patient's proforma at the end of surgery, which was to ensure that the researcher did not know which group the patient belonged to intraoperatively. The second assistant was not involved in the randomisation, balloting, drug labelling and assessment of primary and secondary outcomes. The researcher administered the SAB after the study drug was given by the second assistant. The researcher monitored the patients for both primary and secondary outcomes and recorded them in the proforma, but was not involved in randomisation, balloting, labelling or administration of the study drugs.

Preoperative Review

The researcher took a detailed history, carried out a physical examination and reviewed appropriate investigation results of all recruited patients on the night before surgery and obtained informed consent. Patient's age, weight, height, parity, educational status and gestational age were taken and recorded. Evaluation of the patient's cardiovascular, respiratory and central nervous systems was done. Airway assessment, including Mallampati classification and thyromental distance, was done and recorded. The patients were classified using the ASA physical health status. Two units of blood were grouped and cross-matched for each patient. All Patients were fasted for at least 6-8 hours for solids and at least 2 hours for clear fluids before the surgery.

Intervention

In the theatre, the availability and functionality of the anaesthetic machine, endotracheal tubes, laryngoscopes, stylets and suction machines were ascertained. Laryngeal mask airway, gum elastic bougie, face mask, and resuscitation drugs such as ephedrine, atropine and adrenaline were made available. Pethidine was also made available as a rescue drug for any patient who developed severe (grade 3 and 4) shivering despite pre-treatment with the study drugs. Each patient had a multiparameter monitor attached (GE DASH 4000). Baseline vital signs, including pulse rate, non-invasive blood pressure (NIBP), oxygen saturation (SpO2), and electrocardiogram (ECG), were measured and recorded. Skin temperature was measured with a thermistor strapped to the armpit. Core body temperature was measured using a tympanic temperature probe. Ambient theatre temperature was kept at 25°C, using a Panasonic Air conditioner.

Resuscitation drugs were drawn and appropriately labelled. Two intravenous accesses were established with 16-G cannulae. All patients were preloaded with 0.9% saline warmed to 37°C at a dose of 15 ml/kg for over 15 minutes before spinal anaesthesia. All subsequent intravenous fluids were administered to the patients at room temperature.

The first assistant prepared the study drugs. Each of the study drugs was withdrawn into 20 ml syringes and coded N, O or P. Syringe N contained 0.15 mg/kg nefopam diluted to 20 ml using sterile water for injection, syringe O contained 0.1 mg/kg ondansetron diluted to 20 ml using sterile water for injection, while syringe P contained 20 ml of normal saline. The second assistant administered the study drug to the patient according to the randomisation and blinding protocol for over 15 minutes using a syringe pump during the fluid preloading phase before SAB. After completion of preloading and pre-treatment with the study drug, the researcher then administered SAB in the sitting position. After skin preparation with 0.5% chlorhexidine and methylated spirit, the prep site was draped with a sterile fenestrated drape. After locating the L3-4 interspace, the overlying skin was then infiltrated with 2 ml of 2% lidocaine. A 25G pencil point (Whitacre) spinal needle was inserted via an introducer needle through the interspace and gradually advanced towards the subarachnoid space until a 'give' was felt, then the stylet was withdrawn and upon reflux of cerebrospinal fluid (CSF), a hyperbaric solution of 0.5% bupivacaine 12.5 mg (2.2 ml) was administered, the spinal needle with the introducer was then withdrawn and adhesive dressing applied. The patient was slowly placed in the supine position with head and shoulders supported on a pillow and with left uterine displacement to an approximate angle of 15 to 20 degrees using a right hip wedge to minimise aortocaval compression. The vital signs, primary and secondary outcomes, were measured and recorded immediately after the spinal technique. Following confirmation of the height of spinal block by loss of sensory sensation to alcohol-soaked cotton wool touch up to a minimum level of T6, surgery was allowed to start. Pulse rate, blood pressure, oxygen saturation, respiratory rate, core and body temperatures were recorded every 2 min for the first 10 min and thereafter every 5 min till the end of surgery. Intraoperatively, supplemental oxygen was administered to the patient via nasal prongs at 2 L/min. Oxygen therapy was then discontinued after the delivery of the foetus in the absence of complications such as hypotension, shivering and haemorrhage. Intravenous fluids for maintenance were administered to the patients at 10 ml/kg in the first hour and 5 ml/kg in the subsequent hours. Assessment of blood loss was done using the quantitative method (number of soaked abdominal mops and amount of blood in the suction bottle). Blood was transfused when the trigger point for transfusion was exceeded (blood loss of >20% of total blood volume). The total amount of fluid administered and the total number of units of blood transfused were noted and recorded for each patient. Urine output was monitored via urethral catheterisation to assess adequacy of fluid maintenance. Total urine output was recorded for all patients.

Following the delivery of the foetus, 5 IU of oxytocin by slow intravenous injection was given. Another 30 IU of oxytocin was added to 500 ml of normal saline and was given by slow intravenous infusion over 2 hours (at the rate of 250 ml/hr, equivalent to 15 IU/hr or 0.25 IU/min).

Patient follow-up was stopped at 3 hours post-operation, which often corresponded to the period when most post-operative patients without complications are transferred from PACU to the ward.

Patients who had failed, inadequate or high spinal anaesthesia were converted to general anaesthesia and removed from the study.

Data Collection

A study proforma (Appendix 3) was used perioperatively to record the socio-demographic details of the participants, primary and secondary outcomes.

The primary outcomes are the incidence and severity of PSS assessed intraoperatively using the Crossley and Mahajan scale.[13] In this grading, 0 = no shivering, 1 = piloerection or peripheral vasoconstriction but no visible shivering (goose bumps), 2 = muscular activity in only one muscle group, 3 = muscular

activity in more than one muscle group but not generalised and 4 = shivering involving the whole body. Grade 1 was considered mild, grade 2 as moderate, with grades 3 and 4 as severe shivering. Shivering of grade 3 or more was treated with intravenous pethidine 25mg. And for the secondary outcomes, adverse effects such as intraoperative injection pain during the administration of study drugs were recorded appropriately, and intraoperative and postoperative nausea and vomiting were also recorded appropriately. Injection pain was assessed using a numerical rating scale (NRS).[14] Where 0 (no pain), 1-3 (mild pain), 4-6 (moderate pain), 7-10 (severe pain). The severity of nausea and vomiting was assessed using the numeric scoring system for PONV (0 = no nausea or vomiting; 1 = nausea but no vomiting; 2 = vomiting once; 3 = two or more episodes of vomiting).[15] Nausea was defined as the subjective feeling of urge to vomit; Vomiting was defined as the forceful expulsion of gastric contents through the mouth; retching was the rhythmic movement of the anterior abdominal wall without ejection of gastric content. Nausea or vomiting was treated using intravenous metoclopramide 10 mg. The requirement for pethidine rescue medication (pethidine 25 mg I.V.) was also recorded appropriately. Patient monitoring continued at PACU until three hours post-surgery.

Statistical Analysis

Subjects from the 3 groups were stratified. Data entry and outcome variables were analysed using the Statistical Package for Social Sciences (SPSS 25.0 - SPSS Inc., Chicago, IL, USA). Continuous data were presented as mean ± standard deviation (SD) and compared by an analysis of variance (ANOVA). Post hoc comparisons were performed using Bonferroni correction of the significance level. Categorical data were expressed as frequencies and percentages and analysed using the Chi-square test with Pearson's correction.

P-value < 0.05 was considered statistically significant and formed the basis of accepting or rejecting the null hypothesis.

Results

A total of ninety-six patients participated in the study and were randomly assigned to three groups: N, O & P (nefopam, ondansetron and placebo groups, respectively); each group had 32 patients. All the enrolled patients were included in the final analysis, having completed the study. Bonferroni correction was applied for multiple comparisons. All the patients were classified as ASA II.

Demographic and Baseline Characteristics

Demographic parameters, including age, weight, height, body mass index (BMI), parity, and indication for surgery, were comparable among the groups, with no statistically significant differences (p > 0.05) (Table 1).

Table 1: Demographic and Baseline Characteristics

Variable	Nefopam (N) (n=32)	Ondansetron (O) (n=32)	Saline (P) (n=32)	*p*-value
Age (years)	**29.47 ± 5.76**	**28.47 ± 5.67**	**28.28 ± 5.48**	**0.652**
Weight (kg)	**72.65 ± 4.53**	**71.72 ± 4.24**	**72.38 ± 4.65**	**0.623**
Height (cm)	**167.30 ± 1.84**	**167.47 ± 1.67**	**167.52 ± 1.74**	**0.871**
BMI (kg/m²)	**26.04 ± 1.31**	**25.55 ± 1.25**	**25.93 ± 1.55**	**0.331**

Variable	Nefopam (N) (n=32)	Ondansetron (O) (n=32)	Saline (P) (n=32)	*p*-value
Nulliparous, n (%)	**13 (40.6)**	**12 (37.5)**	**13 (40.6)**	**0.704**

Data presented as mean ± standard deviation or number (frequency, %). BMI, body mass index. P-value calculated using Analysis of Variance (ANOVA) for numerical variables and Chi-square test for parity. * indicates significance.

Incidence and Severity of Shivering

The incidence and severity of post-anaesthetic shivering differed significantly among the three groups ($p < 0.001$). Both the nefopam and ondansetron groups had a significantly lower incidence (18.8%) compared to the placebo group (59.4%; $p < 0.002$ and $p < 0.001$, respectively), resulting in an overall study incidence of 32.3%. Severe shivering (grade 3–4) occurred exclusively in the placebo group (40.6%), whereas most patients in the intervention groups (81.2%) experienced no shivering; no significant differences emerged between nefopam and ondansetron for either outcome. (Table 2)

Table 2: Incidence and Severity of Post-Spinal Shivering

Variable	Nefopam (N) *n* = 32	Ondansetron (O) *n* = 32	Saline (P) *n* = 32	χ^2 (p-value)	N vs O	N vs P	O vs P
Shivering Incidence				**16.103<0.001***	**1.000**	**0.002***	**0.001***
Present	**6 (18.8%)**	**6 (18.8%)**	**19 (59.4%)**				
Absent	**26 (81.2%)**	**26 (81.2%)**	**13 (40.6%)**				
Shivering Severity				**<0.001***	**0.472**	**0.001***	**0.001***
Grade 0	**26 (81.2%)**	**26 (81.2%)**	**13 (40.6%)**				
Grade 1	**5 (15.6%)**	**3 (9.4%)**	**1 (3.1%)**				
Grade 2	**1 (3.1%)**	**3 (9.4%)**	**5 (15.6%)**				
Grade 3	**0 (0.0%)**	**0 (0.0%)**	**8 (25.0%)**				
Grade 4	**0 (0.0%)**	**0 (0.0%)**	**5 (15.6%)**				

Values expressed as frequency (percentage). χ^2 = Chi-square test. *p ≤ 0.05 is considered statistically significant

Relative to saline placebo, both nefopam and ondansetron significantly reduced shivering incidence (RR 0.32, RRR 68% for both). For shivering severity (grade ≥2), nefopam demonstrated superior efficacy (RR 0.06, RRR 94%) compared with ondansetron (RR 0.17, RRR 83%). (Table 3)

Table 3: Relative Risk Reduction of Post-Anaesthesia Shivering Across Study Groups

Group vs. Saline	Risk Ratio (RR)	RRR (%)
Incidence		
Nefopam (6/32 vs. 19/32)	0.32	68%
Ondansetron (6/32 vs. 19/32)	0.32	68%
Severity (Grade ≥2)		
Nefopam (1/32 vs. 18/32)	0.06	94%
Ondansetron (3/32 vs. 18/32)	0.17	83%

RRR = Relative Risk Reduction

Rescue Pethidine Requirement

No patient in either the nefopam or ondansetron groups received rescue pethidine for shivering. In contrast, 12 patients (37.5%) in the saline placebo group received rescue medication, and this is a statistically significant difference ($p < 0.001$, Table 4).

Table 4: Requirement for Rescue Pethidine

Variable	Nefopam (N) *n* = 32	Ondansetron (O) *n* = 32	Saline (P) *n* = 32	χ^2 (p-value)	N vs O	N vs P	O vs P
Rescue Pethidine				**36.533<0.001***	**1.000**	**<0.001***	**<0.001***
Required	**0 (0.0%)**	**0 (0.0%)**	**12(37.5%)**				
Not Required	**32 (100%)**	**32 (100%)**	**20(62.5%)**				

χ^2 = Chi-square test; $p < 0.05$ considered statistically significant; * indicates significance.

Side Effects of Study Drugs

No serious adverse events were reported. Mild injection site pain occurred exclusively in the nefopam group (9.4%, 3/32), with a significantly higher incidence than in the ondansetron or saline groups ($p < 0.03$ for both). (Table 5)

Intraoperative nausea incidence did not differ significantly between groups ($p = 0.076$). Postoperative nausea was significantly less frequent in the nefopam (12.5%, 4/32; $p < 0.03$) and ondansetron (3.1%, 1/32; $p < 0.02$) groups than in the saline group (25.0%, 8/32). (Table 5)

Table 5: Adverse Events Across Study Groups

Variable	Nefopam (N) *n* = 32	Ondansetron (O) *n* = 32	Saline (P) *n* = 32	Overall *p-value*	N vs O	N vs P	O vs P
Injection Site Pain				**0.045***	**0.03***	**0.03***	**1.000**
Present (Mild)	**3 (9.4%)**	**0 (0.0%)**	**0 (0.0%)**				
Intraoperative Nausea				**0.076**	**0.355**	**0.509**	**0.053**
Nausea (no vomiting)	**4 (12.5%)**	**1 (3.1%)**	**7 (21.9%)**				
Postoperative Nausea				**0.037***	**0.355**	**0.03***	**0.02***
Nausea (no vomiting)	**4 (12.5%)**	**1 (3.1%)**	**8 (25.0%)**				

Overall p-value calculated using Chi-square test; p < 0.05 considered significant.* indicates significance.

Relative to saline, ondansetron demonstrated superior efficacy in reducing nausea (RRR 85.8% intraoperative, 87.6% postoperative), whereas nefopam yielded moderate reductions (RRR 42.9%–50.0%). No instances of vomiting, headache, or sedation occurred, and all patients remained oriented and cooperative. (Table 6)

Table 6: Relative Risk Reduction in Adverse Events Across Study Groups

Variable	Nefopam (n=32)	Ondansetron (n=32)	Saline (n=32)	RRR N vs P (%)	RRR O vs P (%)
Injection Site Pain (Mild)	3 (9.4%)	0 (0.0%)	0 (0.0%)	Not applicable	Not applicable
Intraoperative Nausea	4 (12.5%)	1 (3.1%)	7 (21.9%)	42.9%	85.8%
Postoperative Nausea	4 (12.5%)	1 (3.1%)	8 (25.0%)	50.0%	87.6%

RRR = Relative Risk Reduction

Discussion

This randomised controlled trial demonstrates that intravenous nefopam (0.15 mg/kg) and ondansetron (0.1 mg/kg) are highly effective and comparable for preventing post-spinal shivering (PSS) in parturients undergoing elective cesarean delivery, with both reducing incidence by 68% relative to saline placebo.

PSS rates in intervention groups were markedly lower than placebo, eliminating severe shivering (grade 3–4) and completely avoiding opioid rescue—contrasting sharply with placebo, where over one-third required pethidine. The overall incidence of shivering and the effect of the interventions are consistent with previous studies.[12,16-18]. The comparable efficacy between the two active drugs suggests that their effects on multiple monoamine, NMDA receptors and central 5-HT3 antagonism are equally effective in modulating thermoregulatory pathways disrupted by spinal anaesthesia.[9,19]. This opioid-sparing effect minimises maternal respiratory depression and foetal opioid exposure, offering critical advantages in obstetric anaesthesia. [12,17,18,20-23]

Safety profiles were favourable: mild, transient injection pain occurred in 9.4% of nefopam patients, which was similarly reported by Tobi KU et al.[24] (mitigated by dilution/slow infusion), but none with ondansetron; postoperative nausea was lowest with ondansetron. In low-resource settings, where pethidine shortages are common, both drugs provide reliable prophylaxis via simple IV administration pre-delivery, enhancing maternal comfort without delaying intervention.

For practical selection, ondansetron suits antiemetic needs with minimal injection pain; nefopam excels for severe shivering prevention despite minor pain risk. Both align with resource constraints, favouring early prophylaxis over reactive opioid use.

This study's limitations include its single-centre design, short postoperative follow-up period (3 hours), lack of clinical trial registration (despite variable requirements for Phase 1 investigations), and exclusion of high-risk obstetric patients. Future studies could explore combined administration to assess potential synergistic effects.

Conclusion

Both nefopam and ondansetron are effective and safe for preventing PSS. The choice between them may be guided by specific patient factors. Both agents provide a valuable non-opioid alternative for shivering prophylaxis in obstetric anaesthesia.

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