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Original Article

Effect of Intravenous Ondansetron on Spinal Anaesthesia-Induced Hypotension During Caesarean Section

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ABSTRACT

Background: Spinal anaesthesia has become the preferred method for elective caesarean sections due to its simplicity, speed, and reliability. However, a significant challenge with this technique is maternal hypotension, which can lead to nausea, vomiting, and decreased cardiac output, necessitating effective preventive measures. Ondansetron, a 5-HT3 receptor antagonist, is commonly used to prevent nausea and vomiting, and recent studies suggest its potential efficacy in reducing hypotension during spinal anaesthesia.

Objective: To compare the frequency of hypotension during spinal anaesthesia for elective caesarean delivery between two groups: one receiving intravenous ondansetron and the other receiving normal saline as a placebo.

Methods: This randomized controlled trial was conducted at the Department of Anaesthesia, Combined Military Hospital Sialkot, over six months (May 6, 2016, to November 6, 2016). A total of 60 pregnant women scheduled for elective caesarean delivery under spinal anaesthesia, aged 18-35 years, classified as ASA I or II, and carrying a singleton pregnancy at 37-42 weeks, were included. Exclusion criteria included contraindications to spinal anaesthesia, history of heart or lung disease, known hypersensitivity to the study medication, diabetes with blood sugar >180 mg/dl, hypertension with blood pressure >160/90 mmHg, morbid obesity, and fetal abnormalities. Participants were randomly assigned to Group A (intervention) receiving 4 mg ondansetron intravenously in 10 ml saline 5 minutes before spinal anaesthesia, or Group B (control) receiving 10 ml saline intravenously. Baseline vitals, including heart rate, mean arterial pressure, systolic and diastolic blood pressure, were recorded. Spinal anaesthesia was administered using a 25-gauge needle with 2.5 ml of hyperbaric 0.5% bupivacaine solution. Hypotension was managed with intravenous bolus of 100 mcg phenylephrine and 100 ml normal saline. Data were analyzed using SPSS version 25.0, with qualitative variables compared using chi-square tests and significance set at $p \leq 0.05$.

Results: The mean age of participants was 27.95±5.68 years, and the mean BMI was 24.12±3.30 kg/m². Baseline systolic blood pressure averaged 129.00±11.24 mmHg, diastolic blood pressure 71.67±6.99 mmHg, and mean arterial pressure 114.67±7.93 mmHg. In Group A, 8 out of 30 participants (26.7%) experienced hypotension compared to 17 out of 30 participants (56.7%) in Group B (p=0.036). Stratification by age revealed a significant difference in hypotension incidence in participants >26 years (p=0.028). No significant differences were observed when stratified by BMI <24 kg/m² (p=0.056) and >24 kg/m² (p=0.300).

Conclusion: Administration of 4 mg intravenous ondansetron 5 minutes prior to spinal anaesthesia for elective caesarean delivery significantly reduces the frequency of hypotension compared to placebo, especially in patients older than 26 years. Ondansetron appears to be a practical and cost-effective prophylactic measure against spinal anaesthesia-induced hypotension, warranting further large-scale, multi-centre trials to validate these findings.

Keywords: Ondansetron, hypotension, spinal anaesthesia, caesarean section, maternal health, elective caesarean delivery.

INTRODUCTION

Spinal anaesthesia has become the preferred method for elective caesarean sections due to its simplicity, speed, and reliability. However, a significant challenge with this technique is maternal hypotension, which can lead to nausea, vomiting, and is associated

Journal of Health and Rehabilitation Research 2791-156X JHRR

with decreased cardiac output. Therefore, it is crucial to prevent or promptly treat this condition (1). Common preventive measures include the use of vasopressors, lateral tilt, and fluid preload. Hypotension occurs in 80-90% of caesarean sections performed under spinal anaesthesia, primarily due to reduced systemic vascular resistance from sympathetic blockade, necessitating the use of vasopressor drugs like ephedrine and phenylephrine to prevent maternal hypotension (2,3). Another proposed mechanism involves the Bezold-Jarish reflex (BJR) activation, which is sensitive to serotonin, specifically the 5-HT3 receptors. Blocking these receptors has been shown to reduce hypotension in parturients (4).

Ondansetron, a 5-HT3 receptor antagonist, is commonly used to prevent vomiting and nausea triggered by chemotherapy, radiotherapy, and surgery (2). Several studies have demonstrated its effectiveness in reducing hypotension during caesarean sections under spinal anaesthesia. For instance, Ayorinde et al. found that pre-emptive intramuscular ephedrine and phenylephrine reduce the severity of hypotension, while Sahoo et al. showed that intravenous 4 mg ondansetron prior to subarachnoid block reduces the use of vasopressors and hypotension in parturients undergoing caesarean delivery (5,6). However, not all studies agree on these findings. A placebo-controlled study by Marciniak et al. in 2015 found no significant difference between groups receiving intravenous ondansetron and those receiving normal saline as a placebo (7,8).

Given the high incidence of hypotension induced by spinal anaesthesia and its potential morbidity and mortality in parturients, this study aims to contribute to improving the protocol for preventing hypotension. Ondansetron is readily available and cost-effective in our setup. To date, no local study has been carried out on ondansetron use to prevent hypotension. This study compares the frequency of hypotension induced by spinal anaesthesia for elective caesarean section between groups receiving intravenous ondansetron and normal saline as a placebo. The hypothesis is that there is a difference in the frequency of hypotension between patients receiving prophylactic intravenous ondansetron compared to a placebo group during caesarean section under spinal anaesthesia. Patients who met the inclusion criteria were randomly allocated to either the intervention group (Group A) or control group (Group B) by lottery method. Group A received 4 mg of ondansetron intravenously in 10 ml saline solution just 5 minutes before spinal anaesthesia, while Group B received only 10 ml of saline intravenously at the same time.

Prior to spinal anaesthesia, resting heart rate, mean arterial pressure, systolic BP, and diastolic BP were recorded as baseline vitals. Maternal mean arterial pressure, systolic BP, and diastolic BP were measured after 5 minutes of administration of spinal anaesthesia. The patients who developed hypotension were noted, and the hypotension was managed. Statistical tests were applied to compare the occurrence of hypotension among the two groups. This study includes a total of 60 patients, with 30 in each group. The mean age of the patients was 27.95±5.68 years, while the mean BMI was 24.12±3.30 kg/m². The mean systolic blood pressure was 129.00±11.24 mmHg, and the diastolic blood pressure was 71.67±6.99 mmHg, both within normal ranges. The mean arterial pressure was 114.67±7.93 mmHg. In Group A, 8 out of 30 participants experienced hypotension, while 22 did not. In Group B, 17 out of 30 participants experienced hypotension, and 13 did not (p-value = 0.036). Upon stratification by BMI and age, a significant difference in the occurrence of hypotension between the two groups was found (p-value = 0.028) in the age group >26 years. The administration of 4 mg intravenous ondansetron 5 minutes prior to spinal anaesthesia for elective caesarean delivery significantly reduces the frequency of hypotension compared to placebo, with important considerations for study limitations (1-7).

MATERIAL AND METHODS

This randomized controlled trial was conducted at the Department of Anaesthesia, Combined Military Hospital Sialkot, over six months from May 6, 2016, to November 6, 2016, following ethical approval (reference number MCPC/FCPC-2015 dated October 12, 2015). The study adhered to the principles outlined in the Declaration of Helsinki to ensure ethical conduct and patient safety. Written informed consent was obtained from all participants during the pre-anaesthetic checkup visit to maintain confidentiality and privacy.

Participants were pregnant women scheduled for elective caesarean delivery under spinal anaesthesia, aged between 18 and 35 years, with physical status classified as ASA I or ASA II, and carrying a singleton pregnancy at 37-42 weeks as assessed by ultrasonography. Exclusion criteria included contraindications to spinal anaesthesia, history of heart or lung disease, known hypersensitivity or allergy to the study medication, diabetes with blood sugar levels exceeding 180 mg/dl, hypertension with resting blood pressure above 160/90 mmHg, morbid obesity, or fetal abnormalities and intrauterine death.

A non-probability consecutive sampling technique was employed to select participants who met the inclusion criteria and consented to the study(8). Patients were randomly assigned to either the intervention group (Group A) or the control group (Group B) using a lottery method to minimize selection bias. Group A received 4 mg of ondansetron intravenously in 10 ml saline solution five minutes before spinal anaesthesia, while Group B received 10 ml of saline intravenously at the same time. Blinding was maintained for the patients, but not for the health professionals administering the medication due to the nature of the intervention (9).

Journal of Health and Rehabilitation Research 2791-156X JHRR

In the operating room, patients were connected to a patient monitor to record and monitor pulse rate, ECG, non-invasive blood pressure, and pulse oximetry. Baseline vitals, including resting heart rate, mean arterial pressure, systolic blood pressure, and diastolic blood pressure, were recorded. An 18-gauge venous cannula was placed in a superficial vein of the forearm, and a rapid infusion of 10 ml/kg of normal saline solution was administered approximately five minutes before spinal anaesthesia, which was then reduced to a minimal rate to maintain vein patency (10).

Spinal anaesthesia was administered at the L4-L5 or L3-L4 interspace using a 25-gauge spinal needle with the patient in a sitting position. Patients received 2.5 ml of hyperbaric 0.5% bupivacaine solution intrathecally. Immediately following the intrathecal injection, patients were positioned supine. Maternal mean arterial pressure, systolic blood pressure, and diastolic blood pressure were measured five minutes after spinal anaesthesia administration. Sensory block assessment using the pin-prick method was conducted every five minutes for fifteen minutes. If the sensory level was below T-6, the patient was excluded from the study. Upon achieving T-6 level anaesthesia, surgery commenced.

Hypotension, defined as a significant drop in blood pressure, was managed with intravenous bolus administration of 100 mcg phenylephrine and 100 ml normal saline. The total dose of phenylephrine administered was recorded. Post-surgery, standard postoperative care was provided to all patients. Data collection included patient demographics, baseline vitals, and incidence of hypotension, which were analyzed using SPSS version 25.0. Qualitative variables such as hypotension were expressed as frequencies and percentages, while quantitative variables such as age, BMI, systolic blood pressure, and diastolic blood pressure were expressed as mean ± standard deviation. Comparisons between groups were performed using the chi-square test, with a p-value of ≤ 0.05 considered statistically significant. Stratification by age and BMI was conducted to address potential effect modifiers, and post-stratification chi-square tests were applied to assess differences between groups (1-7).

RESULTS

A total of 60 participants, meeting the inclusion and exclusion criteria, were enrolled in the study and randomly allocated to Group A (intervention) and Group B (control), with 30 participants in each group. The mean age of the patients was 27.95±5.68 years, and the mean BMI was 24.12±3.30 kg/m². The baseline systolic blood pressure was 129.00±11.24 mmHg, and diastolic blood pressure was 71.67±6.99 mmHg. The mean arterial pressure was 114.67±7.93 mmHg, indicating overall good cardiovascular health among the participants.

Table I: Summary of Patient Characteristics and Baseline Vital Parameters

Parameter	Mean Value	Standard Deviation
Age (years)	27.95	5.68
BMI (kg/m²)	24.12	3.30
Systolic Blood Pressure (mmHg)	129.00	11.24
Diastolic Blood Pressure (mmHg)	71.67	6.99
Mean Arterial Pressure (mmHg)	114.67	7.93

The primary outcome measured was the frequency of hypotension in both groups. In Group A (intervention), 8 out of 30 participants experienced hypotension, whereas in Group B (control), 17 out of 30 participants experienced hypotension. This difference was statistically significant (p-value = 0.036), indicating that intravenous ondansetron significantly reduced the incidence of hypotension compared to the placebo.

Table II: Comparison of Hypotension between Intervention (Group A) and Control (Group B) Groups

Variable	Group A (n=30)	Group B (n=30)	p-value
Hypotension	8	17	0.036
No Hypotension	22	13	

To address potential confounding factors, data was stratified by age and BMI. For participants under 26 years, no significant difference in the occurrence of hypotension was observed between the two groups (p-value = 0.439). However, in participants over 26 years, a significant difference in the occurrence of hypotension was found (p-value = 0.028), with the control group showing a higher incidence. For participants with a BMI <24 kg/m², the difference in hypotension incidence was not significant (p-value = 0.056). Similarly, for participants with a BMI >24 kg/m², no significant difference was found (p-value = 0.300).

Journal of Health and Rehabilitation Research 2791-156X JHRR

Table III: Stratification of Hypotension by Age and BMI

Stratification Criteria	Group A (n=30)	Group B (n=30)	p-value
Age <26 years			
Hypotension	2	6	0.439
No Hypotension	6	7	
Age >26 years			
Hypotension	6	10	0.028
No Hypotension	14	8	
BMI <24 kg/m²			
Hypotension	2	8	0.056
No Hypotension	10	6	
BMI >24 kg/m²			
Hypotension	5	9	0.300
No Hypotension	8	6	

The findings indicate that the administration of 4 mg intravenous ondansetron five minutes prior to spinal anaesthesia for elective caesarean delivery significantly reduces the frequency of hypotension compared to placebo, particularly in patients older than 26 years. This suggests that ondansetron can be an effective prophylactic measure against spinal anaesthesia-induced hypotension in this demographic.

DISCUSSION

The discussion of this study's findings reveals that the administration of 4 mg intravenous ondansetron significantly reduced the incidence of hypotension during spinal anaesthesia for elective caesarean delivery. The frequency of hypotension in the intervention group was substantially lower than in the control group, indicating that ondansetron effectively mitigates the risk of this common and potentially dangerous side effect. This aligns with previous research, such as the studies by Sahoo et al. and El Khouly et al., which demonstrated similar reductions in hypotension with prophylactic ondansetron administration (11,12,14).

The study's results are particularly noteworthy in the subgroup analysis, where the difference in hypotension incidence was significant in patients over 26 years of age. This suggests that age may be an important factor influencing the effectiveness of ondansetron in preventing hypotension. The findings are corroborated by Mendonça et al., who observed that older patients, particularly those over 60 years, benefitted more from ondansetron in terms of reduced hypotension (13-15). This may be due to age-related changes in the autonomic nervous system and cardiovascular responses, which could amplify the protective effects of ondansetron against hypotension.

While this study adds to the body of evidence supporting ondansetron's use in preventing spinal anaesthesia-induced hypotension, it also highlights some limitations. The single-centre design may limit the generalizability of the findings, as the patient population and clinical practices at Combined Military Hospital Sialkot might differ from other settings. Furthermore, the lack of blinding for healthcare professionals administering the intervention introduces a potential bias in care provision and outcome assessment. Future studies should aim for a multi-centre design and implement double-blind procedures to enhance the robustness and applicability of the results (16,17).

Additionally, this study did not assess the impact of ondansetron on other clinical outcomes, such as heart rate, nausea, and vomiting, which are also critical factors in the perioperative management of caesarean deliveries. Previous studies, including those by Xiao et al. and Gao et al., have indicated that ondansetron might reduce the need for vasopressors and improve overall haemodynamic stability (10,12). Therefore, comprehensive assessments in future research could provide a more holistic understanding of ondansetron's benefits and potential side effects.

Despite these limitations, the study's findings are promising. Ondansetron is readily available and cost-effective, making it a practical option for improving maternal outcomes during caesarean sections. However, the potential side effects, such as ECG changes and cardiovascular complications, must be carefully considered (17,18). Clinicians should weigh the benefits of hypotension prevention against these risks, especially in populations with existing cardiovascular concerns.

CONCLUSION

In conclusion, this study contributes valuable evidence supporting the prophylactic use of ondansetron to reduce hypotension during spinal anaesthesia for elective caesarean sections. The significant reduction in hypotension, particularly among older patients,

suggests that ondansetron can enhance perioperative safety and maternal outcomes. However, further research with larger, multi-centre trials and comprehensive outcome assessments is warranted to validate these findings and refine clinical protocols. The potential benefits must be balanced with a vigilant approach to monitoring and managing any adverse effects associated with ondansetron use (1)(2)(3)(4)(5)(6)(7)(8)(9)(10)(11)(12)(13)(14)(15)(16)(17)(18).

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