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ORIGINAL ARTICLE

Efficacy of Ondansetron used Prophylactically during Spinal Anesthesia for Elective Caesarean Section

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ABSTRACT

Objective: To record the efficacy of ondansetron used prophylactically during spinal anesthesia for elective caesarean section.

Methodology: During July to December 2022, this study was conducted by using randomized control trial method at Department of Anesthesia of Jinnah Hospital, Lahore, the enrolled 120 cases were those with ASA II and already scheduled to perform cesarean delivery electively and using spinal anesthesia. To know the efficacy of Ondansetron, we divided the participants in Group O and P equally. Intravenous ondansetron was administered in Group O with the dose 0.1 mg/kg, well diluted in 5ml distilled water, whereas our control group receiving 5 ml of normal saline was allotted Group P, in both group Ondansetron and N/S was administered before intrathecal injection. Preloading was performed using Ringer's lactate at 10 ml/kg through an 18G intravenous cannula over 10 minutes. Spinal anesthesia was performed in the sitting position at the L3–L4 interspace using a 25-gauge Quincke needle. A total of 1.5 ml of 0.75% hyperbaric bupivacaine was administered into the subarachnoid space. Patients were then positioned supine with a 15° left lateral tilt to reduce aortocaval compression and optimize cephalad drug spread. Sensory blockade was evaluated using a pinprick test prior to incision. Oxygen was supplemented at 3 L/min via face mask throughout the procedure. By using definition of hypotension "a decrease in mean arterial pressure exceeding 25% from baseline or an absolute MAP <60 mmHg" management included intravenous phenylephrine (50–100 µg) or ephedrine, as appropriate. A heart rate under 50 beats per minute, indicative of bradycardia often associated with hypotension, was treated using 0.5 mg of atropine intravenously.

Results: In the ondansetron group we recorded (33.3%) cases of hypotension and (73.3%) in placebo, showing remarkable reduced hypotensive effect with (p = 0.00011) in Ondansetron group.

Conclusion: Women with intravenous administration of ondansetron as prophylactically recorded with decreased findings of hypotension as compared to those with normal saline.

Keywords: Elective caesarean section, ondansetron, placebo, hypotension.

INTRODUCTION

The preferred choice while elective or emergency cesarean section is performed is spinal anesthesia.[1-3] Sensory block height for cesarean section is above T6 whereas sympathectomy is exceeded 2 to 6 dermatomes above sensory level causing blood to collect in the vessels, peripheral vasodilation, decreased venous return, hypovolemia and deceased cardiac output and finally hypotension.[4-5] Maternal and fetal wellbeing is compromised due to hypotension which needs its timely intervention and control.

The mainstay of preventing spinal anesthesia-induced hypotension traditionally involves increasing intravascular volume through pre-loading with crystalloids or colloids, co-loading, administration of vasopressors, and left lateral positioning.[6,7] However, recent reviews have shown that these measures may not consistently provide reliable protection.[6,7] In cases of reduced left ventricular filling, activation of serotonin (5-HT_3) receptors located on vagal nerve endings can trigger the Bezold-Jarisch reflex,[8,9] a proposed mechanism for profound bradycardia and circulatory collapse following spinal anesthesia. A more recent strategy involves the prophylactic use of ondansetron a highly selective 5-HT_3 receptor antagonist which has shown potential in mitigating spinal anesthesia-induced hypotension.[10] In this regard, a prior investigation demonstrated that administering I/V ondansetron before spinal anesthesia in elderly patients led to a noticeably higher systolic blood pressure at five minutes post-administration. Additionally, both diastolic and MAP remained significantly elevated at the 10th, 15th, and 20th minutes in those who received ondansetron.[10] Another clinical trial highlighted preventive potential of ondansetron in minimizing spinal anesthesia-induced hypotensive episodes among healthy cesarean patients, reporting only 37.5% incidence observed in the ondansetron group, in contrast to 77.5% in the control group.[11]

The rationale of this study is to evaluate the preventive effect of ondansetron on spinal anesthesia-induced hypotension during elective cesarean sections in our local population, aiming to generate region-specific evidence and determine its clinical usefulness as a prophylactic agent in routine obstetric anesthesia practice.

METHODOLOGY

This randomized controlled trial was conducted in the Gynecology and Obstetrics Operation Theatre of Jinnah Hospital, Lahore, over a duration of 6 months i.e. July to December 2022, following approval of the research synopsis by the institutional ethical review board. The study population comprised 120 women already scheduled for performance of elective cesarean delivery. We computed sample size with the help of statistical assumptions of 80% power and a 95% CI, with expected rate of hypotension i.e. 37.5% in those administered ondansetron and 77.5% in women receiving placebo.

Eligible participants included women aged between more than 18 and less than 45 years, with ASA physical status II, with a full-term pregnancy and a fasting duration exceeding six hours. Patients were excluded if they declined to give written consent, had known coagulation abnormalities (prothrombin time >1.5), were morbidly obese (body mass index over 40), had any hypertensive disorder such as chronic hypertension, pre-eclampsia, or eclampsia, were administered intraoperative supplemental anesthesia, or were in active labor at the time of inclusion.

Informed consent and prior approval from ethical review board was taken well before the trial and for randomization was done by using table which was computer generated. To know the efficacy of Ondansetron, we divided the participants in Group O and P equally. Intravenous ondansetron was administered in Group O with the dose 0.1 mg/kg, well diluted in 5ml distilled water, whereas our control group receiving 5 ml of normal saline was allotted Group P, in both group Ondansetron and N/S was administered before intrathecal injection.

All patients were preloaded with Ringer's lactate at 10 ml/kg body weight, infused over a 10-minute period through two 18-gauge intravenous cannulas.

The L3–L4 intervertebral space was accessed for spinal anesthesia with the patient maintained in a sitting posture. Spinal anesthesia was achieved by injecting 1.5 ml of 0.75% hyperbaric bupivacaine into the subarachnoid space through a 25G Quincke needle.

Immediately following the spinal injection, patients were repositioned to a supine posture with a 15-degree tilt to the left to improve gravitational spread and minimize aortocaval compression. The sensory block was confirmed by pinprick before incision. Oxygen at 3 L/min was delivered continuously through a face mask during surgery.

Hypotension was operationally defined as a reduction of mean arterial pressure (MAP) by more than 25% from baseline or an absolute MAP reading below 60 mmHg, recorded after the administration of spinal anesthesia. Hemodynamic management included prompt intravenous administration of phenylephrine (50–100 µg) or ephedrine as needed. In cases where hypotension was accompanied by bradycardia defined as a heart rate of fewer than 50 beats per minute 0.5 mg of intravenous atropine was administered. Any additional interventions, including fluid boluses and vasopressor use, were recorded. All perioperative data, such as vital sign trends, hypotension episodes, and therapeutic interventions, were documented using a predesigned structured proforma to ensure uniformity and completeness in data collection.

The collected data were processed and analyzed in SPSS version 19. Quantitative measures like age and BMI were described using mean and standard deviation. Categorical outcomes, including hypotension occurrence, were expressed as frequencies and percentages. Group comparisons were performed using the chi-square test. A p-value of ≤ 0.05 was considered to indicate statistical significance. To explore potential effect modifiers, stratified analysis was carried out based on patient age and BMI categories. Post-stratification chi-square testing was then applied to detect any statistically significant associations within these subgroups.

RESULTS

We recorded Group-O (ondansetron) and Group-P (placebo), with 60 patients each. In terms of age, the majority of patients in both groups were between 18 to 30 years, with 68.33% in Group-O and 70.0% in Group-P. Patients aged 31 to 45 years constituted 31.67% of Group-O and 30.0% of Group-P. The mean age in Group-O was 28.48 ± 4.47 years, and in Group-P, it was 28.43 ± 3.21 years, indicating comparable age distributions. The mean BMI was also similar between the two groups: 28.72 ± 3.11 in Group-O and 29.17 ± 3.13 in Group-P. These findings show that the baseline demographic and clinical characteristics were equitably represented in both groups.

In Group-O (ondansetron), 20 patients (33.33%) developed hypotension, whereas a significantly higher proportion, 44 patients (73.33%), experienced hypotension in Group-P (placebo). Conversely, the number of patients who did not develop hypotension was 40 (66.67%) in Group-O and only 16 (26.67%) in Group-P. The statistically significant p-value (p = 0.000) strongly indicates that ondansetron is substantially more effective than placebo in preventing spinal anesthesia-induced hypotension.

Table 3 provides a stratified analysis of hypotension occurrence across different subgroups based on age and BMI. Among patients aged 18–30 years, hypotension was observed in 28 patients from Group-O and 15 from Group-P, (p=0.006). In the 31–45 years age group, 16 patients in Group-O and 5 in Group-P experienced hypotension(p= 0.0001). When stratified by BMI, for patients with BMI ≤ 30, hypotension occurred in 26 patients of Group-O and 16 of Group-P (p = 0.003), while among those with BMI > 30, 18 patients in Group-O and only 4 in Group-P developed hypotension (p = 0.0004). These stratified findings reinforce the overall observation that ondansetron is associated with a significantly lower risk of hypotension, particularly among older patients and those with higher BMI.

Table 1: Baseline Characteristics Including Age and BMI (n=120)

Characteristic	Group-O (n=60)	Group-P (n=60)
Age (years)		
18–30	41 (68.33%)	42 (70.0%)
31–45	19 (31.67%)	18 (30.0%)
Total	60 (100%)	60 (100%)
Mean ± SD	28.48 ± 4.47	28.43 ± 3.21
BMI (Mean ± SD)	28.72 ± 3.11	29.17 ± 3.13

Table 2: Comparison of Hypotension between Ondansetron and Placebo Groups (n=120)

Hypotension	Group-O (n=60)	%	Group-P (n=60)	%	P value
Yes	20	33.33%	44	73.33%	0.000
No	40	66.67%	16	26.67%	

Table 3: Stratification of Hypotension with Ondansetron vs Placebo

Variable		Group	Yes	No	P-value
Age (years)	18-30	O	28	14	0.006
		P	15	26	
	31-45	O	16	2	0.0001
		P	5	14	
BMI	≤ 30	O	26	12	0.003
		P	16	28	
	> 30	O	18	4	0.0004
		P	4	12	

DISCUSSION

Our study confirmed a notable reduction in spinal anesthesia-induced hypotension with ondansetron (33.3%) compared to placebo (73.3%; p = 0.000), supporting its use as a prophylactic agent during elective cesarean sections. Demographically, our study population was well-balanced between the two groups in terms of age and BMI, minimizing confounding influences. Most participants were aged 18–30 years, with a mean age of approximately 28.5 years, and BMI averages were similar across groups. These findings align with those of El Khouly and Meligy,[12] who also studied a relatively young population (mean age: 20–40 years) and demonstrated that the use of prophylactic ondansetron effectively reduced the incidence of hypotension and minimized heart rate variability during spinal anesthesia for cesarean sections.

Our findings are corroborated by several studies. For instance, Mendonça et al.[13] demonstrated a significant reduction in spinal anesthesia-induced hypotension with the use of ondansetron in non-obstetric surgical patients (27.8% vs. 50%; p = 0.007), further demonstrating the effectiveness of 5-HT_3 antagonism in attenuating spinal-induced hemodynamic instability. Similarly, the trial by Trabelsi et al[14] demonstrated a marked reduction in both hypotension (37.5% vs. 77.5%) and bradycardia (15% vs. 37.5%) with ondansetron, along with better neonatal outcomes higher Apgar scores and more physiological umbilical pH compared to placebo.

Moreover, our findings echo those of Salahat et al[15] who reported significantly fewer incidences of hypotension (22.5% vs. 62.5%), nausea, vomiting, and shivering with prophylactic ondansetron in cesarean patients. These results support the proposed mechanism that ondansetron may attenuate the Bezold-Jarisch reflex by blocking 5-HT_3 receptors, thereby maintaining vascular tone and hemodynamic stability during sympathectomy induced by spinal anesthesia.

Our stratified analysis revealed a more pronounced protective effect in patients with higher BMI and older age, indicating that ondansetron might be particularly beneficial in high-risk subgroups. This trend is supported by exploratory findings from Mendonça et al[13] where ondansetron was more effective in patients aged 60 and above.

Meta-analytical evidence also contributes to the consistency of findings. Zhou et al[16] analyzed 21 RCTs and concluded that

ondansetron significantly reduces intraoperative nausea, vomiting, and bradycardia during cesarean section under spinal anesthesia. Although their results did not show a statistically significant reduction in hypotension overall, this could be attributed to heterogeneity in study protocols and ondansetron dosages. Nevertheless, the observed trend aligns with the majority of individual studies favoring ondansetron.

Supporting this, Sahoo et al[17] and Fattahi et al[18] both reported higher MAP and reduced hypotension in ondansetron groups versus placebo during cesarean sections, further validating the effectiveness of pre-spinal ondansetron. Ranalli et al[19] also observed consistently higher systolic blood pressure and reduced need for vasopressors in the ondansetron group, though the findings did not reach statistical significance.

A key strength of this study lies in its randomized, double-blind methodology and comparatively larger sample size relative to previous research, enhancing its internal validity. Furthermore, detailed stratification and comprehensive statistical analysis allowed for a more nuanced evaluation of ondansetron's effectiveness across different age and BMI categories.

However, there are limitations, the single-center nature of our trial may restrict generalizability to broader populations. Furthermore, we did not measure fetomaternal outcomes regarding side effects including nausea/vomiting, which have shown improvement in other studies. Also, we used a fixed dose (0.1 mg/kg), and future studies should explore the optimal dosing strategy to balance efficacy and safety.

Clinical implications of our findings suggest that routine prophylactic use of ondansetron before spinal anesthesia for cesarean sections may effectively prevent hypotension and reduce the need for vasopressors, particularly in high-risk groups such as those with elevated BMI or advanced maternal age. This intervention is cost-effective, readily available, and carries a low risk of adverse effects.

CONCLUSION

Our findings reinforce the growing body of evidence suggesting that ondansetron is a valuable agent in preventing spinal anesthesia-induced hypotension in obstetric patients. While more multicentric trials in diverse populations are warranted, ondansetron represents a promising adjunct in improving maternal hemodynamic stability and possibly neonatal outcomes during cesarean delivery.

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