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Original Research Article

Effect of Prophylactic Ondansetrone on Prevention of Spinal Induced Hypotension among Women underwent Elective Cesarean Section

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Abstract

Background: Hypotension is a common side effect after spinal anesthesia which associates with both maternal and fetal morbidity. Many interventions have been suggested to prevent this clinical problem. A commonly used antiemetic, ondansetron, can be used as an alternative to prevent hypotension after spinal anesthesia. The action believed to inhibit Bezold-Jarisch reflex.

Objective: To assess effect of prophylactic ondansetron on spinal anesthesia induced hypotension among women undergoing elective cesarean section at NMCH, Patna, Bihar, from November 2021 to July 2022.

Method: In this prospective study 100 patients with American Society of Anesthesiologists (ASA) status class-II, age≥18 and BMI 18 -30 kg/m^2 who underwent cesarean section under spinal anesthesia were included. Prophylactic group (n=50) receive 4mg ondansetron, while Non-prophylactic group (n=50) did not receive ondansetron. The outcomes of the study were the incidence of hypotension, nausea, vomiting and the need of rescue vasopressor. Comparisons of variables between study groups were done using student t test and Chi square test. Significance was determined at P value <0.05. Table and graph were used to show result of the study.

Result: The incidence of hypotension is 13(26.5%) in prophylactic group compared to non-prophylactic group 36(75% with (p=007). There was a statistically significant difference in mean systolic blood pressure, mean heart rate and mean arterial pressure between the groups at all-time point with p<0.05. The incidence of nausea and vomiting was higher in non-prophylactic group when compared with prophylactic group with (p=0.003 & 0.001) respectively. There was not significant difference in total need of rescue vasopressor between groups (6.1% in prophylactic and 10.4% in non-prophylactic group with (p=0.17).

Conclusion: prophylactic use of 4mg intravenous ondansetron 5 minutes before spinal anesthesia significantly reduces the incidence of hypotension; nausea and vomiting in parturient undergoing elective cesarean section. We recommend the use prophylaxis ondansetron for prevention of spinal anesthesia induced hypotension in parturient undergo elective cesarean section under spinal anesthesia.

Keywords: Prophylactic, intravenous, Bezold-Jarisch reflex, elective cesarean section

Background

Hypotension is a common clinical problem faced by patients on spinal anesthesia and if severe it can lead to both maternal and fetal morbidity. Hypotension for less than two minutes did not affect neonatal neurobehavioral outcomes whereas more than four minutes of maternal hypotension was associated with neonatal neurobehavioral outcomes changes at four up to seven days of life [1].

Pregnant women also exhibit an increased level of sympathetic activity compared to parasympathetic activity. Sympatholysis therefore leads to a higher degree of peripheral vasodilatation and a predominance of parasympathetic activity, consequently reducing the venous return and cardiac pre-load, and resulting in bradycardia, nausea and vomiting. The reduced pre-load in turn results in reduced cardiac output (CO), leading to systemic hypotension. This state is further aggravated by aortocaval compression and Higher sympathetic block proportionally reduces the occurrence of compensatory mechanisms via baroreceptors and increases the risk of cardio inhibitory reflexes such as the Bezold-Jarisch reflex and, ultimately, cardiac arrest and death [2].

The occurrence of hypotension is decrease in vascular resistance caused by sympathetic blockade which in turn causes vasodilatation and finally leads to drop in arterial pressure [3,4]. For the sympathetic blockage the main cause is blockage of nerve pathway by inhibition of Na influx at Na channel that resulted in activation of Bezold Jarisch reflex (BJR), and increased baroreceptor activity may lead to hypotension and bradycardia. BJR is triggered by chemoreceptors and mechanoreceptors which are serotonin sensitive. Serotonin is an additive trigger for BJR in hypovolemic patients [5]. Bezold Jarisch reflex activation can lead to activation ventricular receptor by nociception or stretch that result in decrease HR & MAP [3].

Ondansetron is a serotonin receptor subtype 3 (5-HT3) antagonist. It is commonly used as an antiemetic, working to block 5-HT3 receptors in the GI system and in the chemoreceptor trigger zone of the brain. It has a rapid onset of action. Aside from its central action in the brain, ondansetron will bind to 5-HT3 receptors peripherally, including those within the cardiac ventricles and on the vagus nerve, which help to mediate the BJR Binding these receptors prevents induction of the BJR and decreases parasympathetic dominance, lessening the degree of bradycardia and hypotension brought about by spinal anesthesia [4].

We have commonly used ondansetron as anti-emetic in obstetric anesthesia for prevention or treatment of nausea and vomiting.

Material and Methods

This prospective study was conducted at Nalanda Medical College and Hospital, Patna, Bihar from November 2021 to July 2022. Total 100 cases included in the study, 3 participant were lost, two of them from non- prophylactic and one parturient from prophylactic group.

Inclusion Criteria

- Elective caesarean section under spinal anesthesia.
- ASA class II

- Age > 18 years
- BMI 18 -30 kg/m2

Exclusion criteria

- Mother on anti serotogenic medication or migraine headache
- Known allergy to LAs/opioids/non-steroidal anti-inflammatory drugs
- mothers with Preoperative hypotension or hypertension
- mothers with diabetes mellitus
- mothers with Cardiovascular disease
- mother with pulmonary disease
- mother with renal or liver disease
- Body mass index < 18 or >30Kg/m2
- Failed spinal block
- Hypersensitive for ondansetron
- Mother with neurologic problem
- Mothers with bleeding disorder (placenta previa, abraption and any bleeding disorder)
- Mother with major bleeding intra operatively

Data processing and analysis

Data was coded and then entered and cleaned using Epi Info version 7 and exported to Statistical package for Social Sciences (SPSS) software version 20.0. Using SPSS Numeric have been described in terms of mean ± SD for symmetric and median (Interquartile range) for asymmetric numeric data. Comparison of numerical variables between study groups was done using unpaired student t- test and Manny Whitney U test for symmetric and asymmetric data respectively. Frequency and percentage has been used to describe categorical variable and statistical difference between groups was tested using Chi square. Significance was determined at P value <0.05 .The result is presented by using text, tables, charts and graphs.

Results

One hundred parturient were enrolled in this study three participant were lost, two of them from non- prophylactic and one parturient from prophylactic group. There was no significant difference among the two groups with regard to age, BMI, duration of surgery, mean time from SA to delivery of the fetus (min), Intra operative fluid(ml), Estimated intra operative blood loss(ml), weight of baby(kg), oxytocin(IU) used and level of blocks (p value > 0.05).

Table 1: Socio demographic characteristics and clinical characteristics:

	Prophylactic group(n=49)	**Non-prophylactic group(n=48)**	**p-value**
Age (years)	31.36 ± 5.149	29.72 ±5.077	0.719
Body Mass Index(kg/m2)	23.75 ± 2.974	23.70 ± 2.739	0.935
L2-L3/L3/L4	6 (10.2)/43 (89.8%)	8/ (16.7%)/40 (83.3%)	0.652
Gravidity (weeks)	3±1.32	3 ±1.43	0.982
Base line systolic blood pressure	126.61±13.017	123.12 ±16.964	0.067
Base line diastolic blood pressure	76.98 ± 10.615	80.72 ±11.572	0.438
Base line mean arterial blood pressure	89.39 ±11.987	94.05 ±11.462	0.259
Base Line Heart Rate(bpm)	90.45 ± 10.727	88.10 ±11.567	0.767
Weight of delivered baby(kg)	2.7 ±1,67	2.8 ±1.47	0.243
Gravidity: One	11 (22.45%)	13 (27.1%)	
Two	13 (26.5%)	14(29.2%)	0.736
Three	12 (24.5%)	12 (25%)	
Above	13 (26.55%)	9 (18.7%)	

Blood loss (ml)	328.63± 81	332.63 ± 70.68	0.381
Dose of bupivacaine in mg 10/12.5	21(42.85) / 28(57.15%)	25 (52.1%) / 23 (47.9%)	0.343
Level of Block T4-T5	11(22.5%)	13 (27%)	
T6-T7	24(48.98%)	19 (39.6%)	0.756
T8-T9	14(28.52%)	16 (33.4%)	
Amount of intra-op fluid used	2.003 ± 0.38	2.083 ± 0.33	0.900
Dose of oxytocin(IU)	37.14 ±2.16	36.17 ± 2.14	0.089
skin incision to delivery(min)	4.90 ± 1.74)	5.25±1.446	0.059
Duration of surgery(min)	40.95± 8.3	38.9 ± 6	0.444

Values are presented as: number (%):chi-square test, mean ±standard division: independent T test and $p < 0.05$ is statistically significant

The occurrence of spinal anesthesia induced hypotension analyzed by using chi square test shows there was statically significant lower incidence in patient receiving prophylactic ondansetron. The proportions of patients with hypotension is lower 13(26.5%) in prophylactic group compared to non- prophylactic group 36(75%) with an X^2 (1, N= 97) =9.842 P=0.007.

There are 12(24.5%) patients in prophylactic group and 28(58.3%) patient in non-prophylactic group who have experienced Nausea (p=0.004*)* and 5(10.2%) patients in prophylactic group and 25(52.1%) patients in non-prophylactic group experience vomiting (p=0.001*)*

Table 2: Incidence of nausea and vomiting distribution in two groups of patients

	Prophylactic group(49)	Non-prophylactic group(48)	p-value
Nausea	12(24.5%)	28(58.3%)	(p=0.004)
Vomiting	5(10.2%)	25(52.1%)	(p=0.001)

There was no statistically significant different in the need for rescue vasopressor between groups in which three (6.1%) in prophylactic and five (10.4%) in non- prophylactic group respectively required vasopressor with p =0.17.

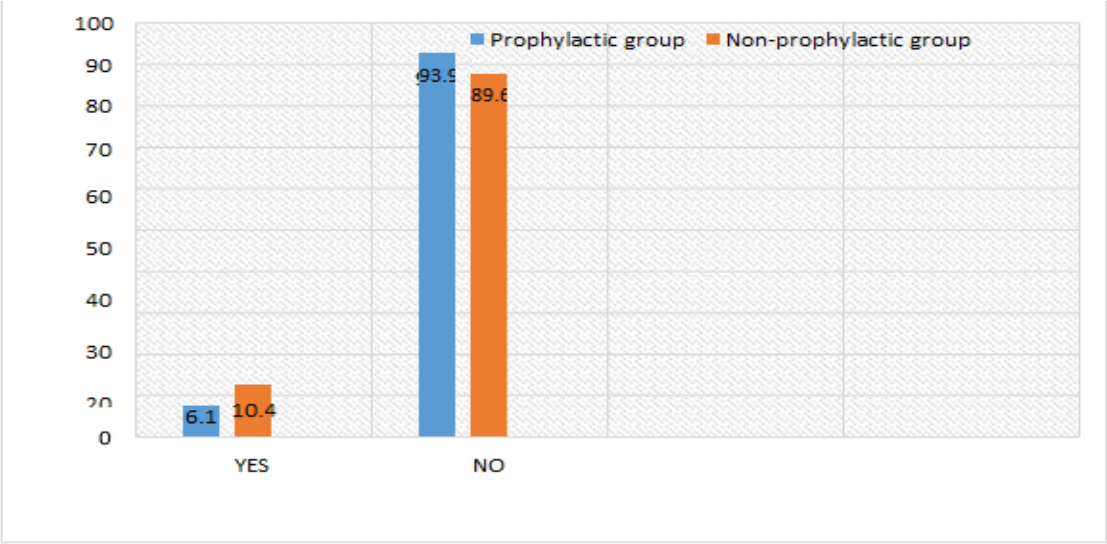

Figure 1: Need of rescue vasopressor between two groups

Intra operative SBP, DBP AND MAP between groups

There is statically significant difference in SBP, DBP and MAP between prophylactic and non-prophylactic group at all point of 5 min interval in span of 50 min. *P* <0.05 was found at all-time intervals.

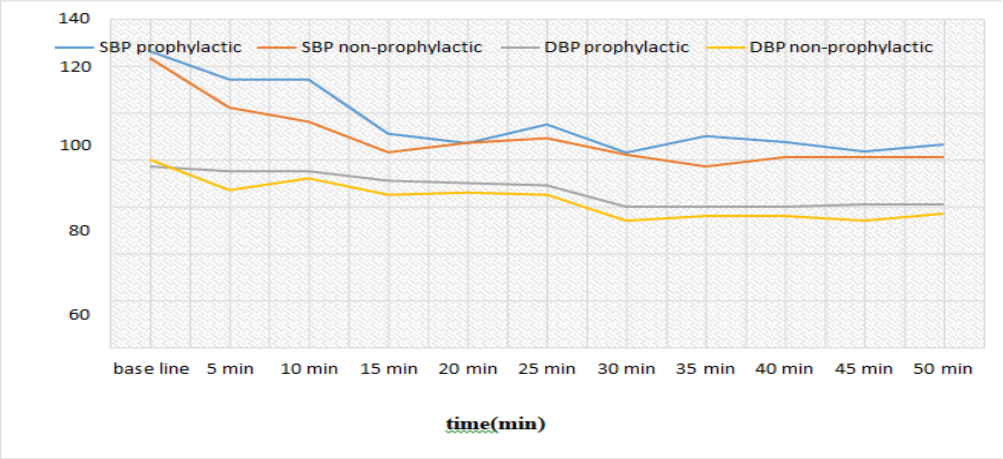

Figure 2: Comparison of systolic and diastolic blood pressure change between two groups

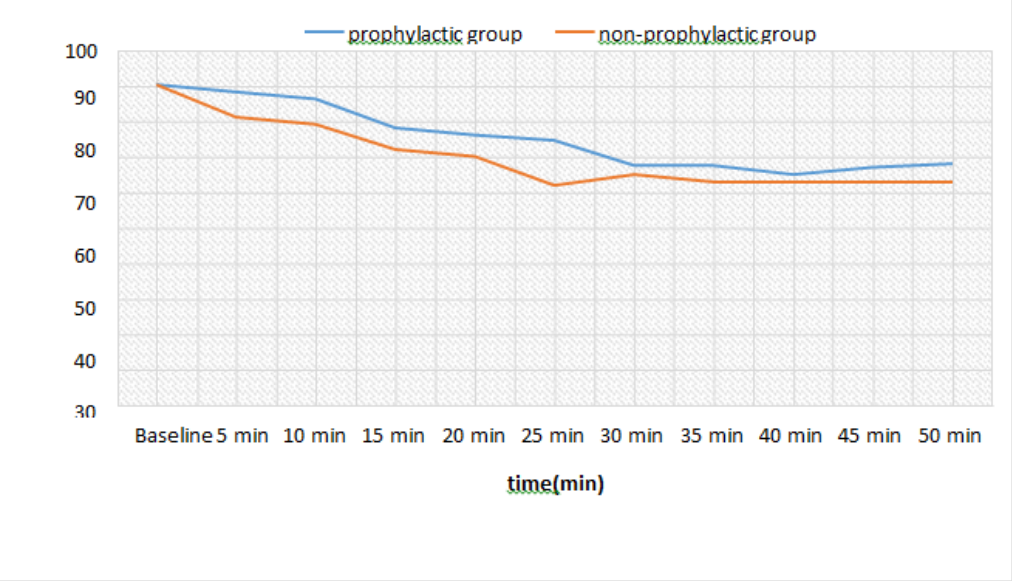

Figure 3: Comparison of mean arterial blood pressure changes between two groups

Discussion

Hemodynamic change after spinal anesthesia have serious complications on both mother as well as fetus because maternal hypotension can lead to decreased placental perfusion that can cause intra uterine fetal hypoxia which is manifested as abnormal fetal heartbeat. One of the important issues regarding anesthesia in pregnant women underwent spinal anesthesia is prevention of spinal induced

hypotension [5,6]. Different techniques and methods are evaluated to prevent the occurrences of spinal induced hypotension Such as preloading or co-loading fluid, administration of atropine prophylaxis, Trendelenburg position and vasopressors [2].Intra venous administration of ondansetron is one of the methods currently used treat severe nausea and vomiting after spinal or general anesthesia because it can block 5HT3 receptor that can cause sympathetic blockage [7].

We assessed the effect of prophylactic ondansetron on spinal anesthesia induced hypotension in 97 parturient who undergone cesarean section. Our study showed statically significant lower incidence of spinal anesthesia induced hypotension in prophylactic 13(26.5%) group compared to non- prophylactic group 36(75%) (p=0.007). The result of this study is in line with study done in Tunisia by Walid Trabelsi *et al*, that assessed Effect of ondansetron on the occurrence of hypotension and on neonatal parameters during spinal anesthesia for elective caesarean section showed that, the incidence of hypotension was 15 (37.5%) in prophylactic and 31 (77.5%) non-prophylactic group ($P < 0.001$) [4].

This study is in line with study done in Rawalpindi at Family Hospital by Baiq *et al*, on the Use of Ondansetron for Prevention of Spinal Induced Hypotension found that the incidence of hypotension occurred in7.5% cases in prophylactic group compared to 28.3% in non-prophylactic group (p=0.005) [8].

Similarly the study done in India is in line with study done in India by Raghu *et al* that assessed the Effect of ondansetron in the prevention of spinal anesthesia-induced hypotension showed that that the incidence of hypotension occurred in 34(60.7% in prophylactic group compared to 22(39.3%) non-prophylactic group p=0.0359) [9].

In contrary to these results a study done in Poland by owczuk *et al*, found hypotension was observed in 14 (39%) in ondansetron prophylactic group and 15(44%) in none ondansetron prophylactic group (p>0.005) [5]. The observed difference was due to they have used 8 mg of ondansetron as prophylaxis because in dose dependent study in china by Wang *et al* found that those mother who have took 4mg and 6 mg were statistically significant(p<0.005) but those who had taken 2mg and 8mg was not statically significant(p>0.005).

The observed difference was due to they have used 8 mg of ondansetron as prophylaxis but in our study we have used 4 mg ondansetron, because study done by Terkawi *et al* and Wang *et al* showed that those mother who have taken 8 mg ondansetron prophylaxis when compared with control group have no significant effect in prevention of hypotension (p > 0.05) [10,11]. The results of this study shows significant difference in incidence of Nausea and vomiting 24.5% patients in prophylactic group and (58.3%) patient in non-prophylactic group were experience Nausea (p=0.004*) and* 5(10.2%) patients in prophylactic group and 25(52.1%) patients in non-prophylactic group experience vomiting (p=0.001).

The result of this study is in line with study done in Egypt by Nabih *et al*, that compared ondansetron and placebo for the reduction of spinal anesthesia-induced hypotension for elective cesarean section found that the incidence of nausea and vomiting were (12% vs 30%) and (4% vs 18%) in prophylactic and non-prophylactic groups respectively(p=0.02,p=0.031) [12].

The result of this study is in line with study done in china by Wang *et al*, A dose dependent study on ondansetron ,Showed that the incidence of nausea and vomiting were (10.3% vs 33.3%) and (3.4% vs 3.3%)

in prophylactic and non-prophylactic groups respectively (p<0.05) [10].

This finding is also in line with study done in Iran by Hajian *et al*, that assessed on the Efficacy of Intravenous Ondansetron on Hemodynamic Complications in Women Undergoing Spinal Anesthesia for Cesarean Section showed that the incidence of nausea vomiting were 7.8% in prophylactic group and 33.3% in non-prophylactic group(p=0.001) [7].

In this study we found that three (6.1%) patients and 5(10.4%) patients in prophylactic and non- prophylactic group respectively required vasopressor with (p =0.17).The results of this study is in line with study done in Egypt by Rashad *et al* that assessed the Effects of ondansetron on hemodynamic changes for mother undergoing elective cesarean section under spinal anesthesia, found that prophylactic group require lower vasopressor compared to non-prophylactic group [13].

In this study we found that significant difference in intra operative SBP, DBP and MAP between groups. The result of this study is in line with study done in Egypt by Nabih *et al* that compared ondansetron and placebo for the reduction of spinal anesthesia-induced hypotension during elective cesarean found that there is Significant differences in SBP, DBP and MAP were observed between lumber puncture and 2 hours in both groups (P < 0.05) for all comparisons [14].

A study done in Poland by sahoo *et al*, the effect of ondansetron in Reduction of spinal-induced hypotension for parturient undergoing caesarean section showed that, there is significant differences in SBP, DBP and MAP between groups(p<0.05) [15].

The result of this study is in line with study done in china by Wang *et al*, showed that there is significant differences between prophylactic group and non-prophylactic group (p< 0.05) [10].

The observed difference is due to they have used higher dose (15 mg) 0.5% hyperbaric bupivacaine for all parturient compared to 10 mg or 12.5 mg in our study. The other probability may be due to they have used atropine and ephedrine for those mother whose heart rate decreased 20% from base line [16].

Conclusion

The results of this study shows that 4mg ondansetron prophylaxis given intravenously 5 minutes prior to spinal anesthesia is decreased the incidence of spinal induced hypotension, nausea and vomiting for parturient undergoing elective cesarean section.

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