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Ondansetron as Prophylactic against Hypotension and Bradycardia Following Spinal Anaesthesia in Elective Caesarean Section: a Case Control Study

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Abstract **Original Research Article**

Introduction: Hypotension and bradycardia following the administration of spinal anesthesia for cesarean section are very common and bear profound detrimental effects both on mother and baby. In our country, a significant proportion of patients undergo cesarean section delivery. Considering the workload and the socio-economic condition it is often a bad headache for our anesthesiologists to combat post-spinal hypotension. Vasopressor drugs have been widely used to prevent and treat maternal hypotension during cesarean section under spinal anesthesia. A combination of preloading and using vasopressor has maximum efficacy in preventing spinal-induced hypotension but with compromising with some detrimental adverse effects of vasopressor. Amongst vasopressors, ephedrine is widely used but studies found that a higher bolus dose is often required to prevent hypotension and bradycardia. ***Aim of the study:*** To find out the efficacy of ondansetron to prevent haemodynamic derrangement in cesarean section under spinal anaesthesia. ***Methods:*** This Prospective Randomized Double-Blind Comparative study was conducted at the Department of Anesthesiology and ICU, Dhaka Medical College Hospital, Dhaka, Bangladesh. The study duration was ten months, from March 2015 to January 2016. A total of 120 participants were randomly included in this study.Each participant was included either into "Group A (n=60)" or "Group B (n=60)" by using fixed number card sampling as mentioned earlier. Group B had been considered as control group in the study, Participants of group A received intravenous ondansetron (0.1 mg/kg body weight) and group B received ephedrine (0.5 mg/kg body weight). ***Result:*** The majority of the participants (58.33%) from both groups were from the age group of 26-30 years. Parity distribution revealed that 59.17% (n=71) patients were multigravida while 40.33% (n=49) were primi. In total, 80.33% of the participants had ASA I physical status, and 19.17% had ASA II. All patients were scheduled for elective cesarean section and the highest number of them (49.17%; n=59) had a history of cesarean section for their previous delivery. The next highest indication was malpresentation (14.17%; n=17) and the least was short stature (1.67%; n=02). There was no significant difference between the groups as regards Pre-anesthesia MAP (p=0.883), but after induction of spinal anesthesia significant decrease in MAP was seen in all groups compared with basal MAP, the least decrease occurring in group A and the highest fall in the group B. Although shivering was common for both groups, the occurrence of nausea and vomiting was significantly less in group A. P values for nausea and vomiting were statistically significant ($p<0.05$) between two groups. ***Conclusion:*** The efficacy of Ondansetron in attenuation of hemodynamic derangements following spinal anesthesia has been proven to be satisfactory with statistically significant supremacy of Ondansetron over Ephedrine. Besides this Ondansetron bears additional advantages in the management of perioperative nausea and vomiting, although proved less effective to prevent shivering.

Keywords: Spinal Anesthesia, Cesarean Section Prophylactic, Ondansetron, Ephedrine.

INTRODUCTION

For the majority of Cesarean section operations, especially elective ones, spinal anesthesia is the recommended anesthetic option. For its quick, profound, and symmetrical sensory and motor block of high quality in parturients having Cesarean birth, it has become the gold standard procedure. Aside from the many benefits of this anesthetic management for obstetric patients, spinal anesthesia is frequently a source of embarrassment for an anesthesiologist due to the technique's unfavorable effects. The most prevalent side effects of spinal anesthesia during cesarean section are hypotension and bradycardia, which have serious consequences for both mother and baby [1]. According to several studies, the incidence of hypotension and bradycardia can be as high as 80-100 percent, with other side effects including bradycardia, nausea, and vomiting [2]. When pharmacological prophylaxis is not employed, the incidence of hypotension might be as high as 70-80% [3]. The degree of hypotension or bradycardia is determined by the block height, the location of the parturient, the volume status, and whether the cesarean section is elective or emergency. These side effects, particularly maternal hypotension, can induce dyspnea, nausea, vomiting, loss of consciousness, aspiration, and cardiac arrest in the mother, as well as potentially harming the baby due to fetal acidity and uteroplacental hypoperfusion [4-6]. Because these complications can have a major impact on outcomes, identifying effective prevention or limitation of hypotension is critical for enhanced safety. As a result, an anesthesiologist must prioritize the prevention and management of such instabilities. As the pregnancy continues, the patient's need for a sympathetic tone to maintain hemodynamics grows. In order to produce a proper sensory block during a cesarean birth, enough anesthesias must occur at the T4 dermatome level [7]. Patients who are scheduled for an elective procedure must also fast for an extended length of time, resulting in dehydration and low preoperative blood pressure. Numerous studies have been undertaken to date in order to find a reliable method of preventing maternal hypotension and bradycardia after spinal anesthesia. Intravenous pre-load and lateral uterine displacement is two common treatments for reducing hypotension caused by spinal anesthesia. Despite fluid pre-load, lateral uterine displacement, and the use of a vasopressor medication, the prevalence of hypotension has been reported to be as high as 80% in some circumstances [8]. It is normal practice to use ephedrine to prevent and treat spinal anesthesia-induced hypotension. According to Kaa *et al*., a bolus dose of 30 mg intravenous ephedrine is needed to lower the incidence of hypotension during spinal anesthesia for cesarean section operations by up to 35%, however, this comes at the cost of rebound hypertension in 45 percent of the patients [9]. Due to adrenoceptor activation, ephedrine has been demonstrated to cross the placenta and impact the fetal and neonatal heart rate [10].

Many studies have recently connected maternal hypotension after spinal anesthesia to a physiological process known as the Bezold- Jarisch Reflex (BJR), a type of vasovagal syncope that triggers sympathetic blockade and lowers vascular resistance [6, 11, 12]. Ondansetron is a powerful selective 5-HT3 antagonist that may have a role in the activation of the BJR (Bezold-Jarisch response) by activating serotonin-sensitive chemoreceptors in the presence of low blood volume [2, 6, 13, 14]. The prophylactic administration of ondansetron, a 5-HT3 antagonist, is of particular interest because it is widely available, inexpensive, and already commonly used to prevent nausea and vomiting in patients with minimal side effects for the mother. It has also been shown to be safe and has no harmful effects on the baby when given at term [15-17] This study will assess the efficacy of ondansetron and ephedrine as a prophylactic drug and observe the occurrence of adverse effects such that prophylactic use of ondansetron – a 5HT3 antagonist – is an option to reduce hypotension and bradycardia generated by spinal anesthesia.

OBJECTIVE

General Objective

To measure the efficacy of ondansetron as prophylactic against hypotension and bradycardia in cesarean section under spinal anaesthesia.

METHODS

This Prospective Randomized Double-Blind Comparative study was conducted at the Department of Anesthesiology and ICU, Dhaka Medical College Hospital, Dhaka, Bangladesh. The study duration was ten months, from March 2015 to January 2016. A total of 120 participants were randomly included in this study. Two groups of equal size were made from the study population by card sampling using a fixed number of cards for each group. Each participant was included either into “Group A (n=60)” or “Group B (n=60)” by using fixed number card sampling as mentioned earlier. Group B had been considered as control group in th study Participants of group a received intravenous ondansetron (0.1 mg/kg body weight) and group B received ephedrine (0.5 mg/kg body weight). The aims and objectives of the study along with procedure, alternative methods, risk, and benefits were explained to the patients in an easily understandable local language and then informed consent was taken from each patient. Ethical approval was also obtained from the ethical review committee of the study hospital.

Inclusion Criteria

- Patients undergoing elective cesarean section having ASA physical status I and II.
- Having consented to be in the study.

Exclusion Criteria

- Patients having contraindication for spinal anesthesia (Patient refusal, unstable hemodynamics, coagulation abnormality)
- Patients who are not willing to participate in this study.
- History of hypersensitivity to ondansetron, ephedrine, and local anesthetic agent.
- Hypertensive disorders of pregnancy.

Table-1: Age distribution of the patients (n=120)

Age (years)	Number of patients		Total & Percentage
	Group A (n=60)	Group B (n=60)	
15-20	3	4	7 (5.83%)
21-25	12	13	25 (20.83%)
26-30	36	34	70 (58.33%)
31-35	6	8	14 (11.67%)
36-40	2	1	3 (2.50%)
40-45	1	0	1 (0.83%)
Mean ± S.D.	27.4±12.6		

RESULTS

While studying the distribution of cases by age it was found that the majority of the patients i.e. 58.33% (n=70) were between 26-30 years, 20.83% (n=20) were between 21-25 years, 11.67% (n=14) between 31-35 years, 5.83%(n=7) between 15-20 years, 2.50%(n=3) between 36-40 years and only 0.83% (n=1) were found between 40-45 years of age. The mean age was found to be 27.4±12.6 years.

Table-2: American Society of Anesthesiologist (ASA) physical status (n=120)

Status	Number of Patients		Total n (%)
	Group A (n=60)n (%)	Group B (n=60)n (%)	
ASA I	49 (81.67%)	48 (80%)	97 (80.33%)
ASA II	11 (18.33%)	12 (20%)	23 (19.17%)

All enrolled patients (n=120) were randomized to one of the two medication treatment groups of 60 patients each. Most of the patients (80.33 %; n=97) were in ASA I status.

Table-3: Distribution of cases by parity (n=120)

Parity	Number of patients		Total n (%)
	Group A (n=60) n (%)	Group B (n=60) n (%)	
Primigravida	23 (38.33%)	26 (43.33%)	49(40.33%)
Multigravida	37 (61.67%)	34 (56.67%)	71(59.17%)

Parity distribution revealed that 59.17% (n=71) patients were multigravida, and 40.33% (n=49) were in their first pregnancy.

Table-4: Indication of elective cesarean section (n=120)

Indications	Number of patients		Total & Percentage
	Group A (n=60) n (%)	Group B (n=60) n (%)	
H/O previous C/S	29 (48.33%)	30 (50%)	59 (49.17%)
Malpresentation	09 (15%)	08 (13.33%)	17 (14.17%)
Short stature	02 (3.33%)	0 (0%)	02 (01.67%)
CPD	01 (1.67%)	02 (3.33%)	03 (02.50%)
Elderly primi	05 (8.33%)	03 (5%)	08 (06.67%)
Oligohydroamnios	06 (10%)	03 (5%)	09 (07.50%)
PROM	03 (5%)	05 (8.33%)	08 (06.67%)
Postdated pregnancy	04 (6.67%)	05 (8.33%)	09 (07.50%)
Patients desire	01 (1.67%)	04 (6.67%)	05 (04.17%)

Most of the patients underwent cesarean delivery due to having a history of cesarean section delivery of their previous pregnancies.

Table-5: Trends of mean arterial pressure (MAP) (n=120)

Timepoint after spinal anesthesia	Mean arterial pressure –MAP(mmHg)		P-value
	Group A (n=60)	Group B (n=60)	
Pre-anesthesia	69.60±11.6	68.93±9.1	0.883
5 min AS	73.45±8.2	67.90±9.5	0.0001
10 min AS	75.40±7.9	70.25±10.2	0.0001
15 min AS	76.92±8.1	69.18±9.5	0.0001
20 min AS	76.31±8.6	68.73±9.1	0.0001
30 min AS	75.57±10.2	69.18±7.5	0.0001
45 min AS	71.05±9.3	64.46±11.4	0.035
60 min AS	59.55±6.8	60.52±7.1	0.486

There was no significant difference between the groups as regards Pre-anesthesia MAP (p=0.883), but after induction of spinal anesthesia significant decrease in MAP was seen in all groups compared with basal MAP, the least decrease occurring in group A and the highest fall in the group B. At the 15th minute MAP was 76.92, 69.18 mm of Hg in group A and group B respectively showing a significant difference (p=0.0001), After 45 minutes, mean blood pressure was 71.05±6.8 mmHg in group A and 64.46±9.4 mmHg in group B. Which statistically significant (p<0.05) between two groups but follow up after 60 minutes mean BP stabilized to similar in both group, which was statistically not significant (p>0.05) between two groups.

Table-6: Occurrence of complication (n=120)

Complications	Frequency of occurrence		P-value
	Group A (n=60)n (%)	Group B (n=60)n (%)	
Nausea	04 (06.67%)	20 (33.33%)	0.001
Vomiting	08 (13.33%)	28 (46.67%)	0.001
Shivering	28 (46.67%)	29 (48.33%)	0.001

Regarding complications, although shivering is common for both groups, the occurrence of nausea and vomiting is significantly less in group A. p values for nausea and vomiting are statistically significant (p<0.05) between the two groups.

DISCUSSION

Hypotension and bradycardia following spinal anesthesia is the most common anesthetic problem, and early, accurate intervention can improve outcomes. Studies have revealed the effectiveness of different strategies for the prevention of spinal anesthesia-induced hypotension and bradycardia such as pre or co-loading, use of vasopressor, positioning, compression devices, etc. however a Cochrane review concluded that none of these techniques alone was sufficient in eliminating hypotension [7]. This emphasized the need for further research concerning other techniques and agents. In recent years many studies have linked spinal anesthesia-induced hypotension and bradycardia to a physiological mechanism called the Bezold –Jarisch reflex (BJR), a form of vaso-vagal syncope triggered by the sympathetic blockade and resulting in decreased peripheral vascular resistance [12]. Mechanoreceptors and chemoreceptors located in the left ventricular wall participate to produce this cardio-inhibitory reflex in response to hypovolaemia and results in vasodilation, bradycardia, and hypotension [18]. These mechanoreceptors and chemoreceptors are serotonin sensitive and 5-hydroxytryptamine (5-HT3) acts as a potential factor to the induction of BJR. So the use of 5-hydroxytryptamine (5-HT3) receptor antagonism is a potential step to inhibit BJR and t5hus to prevent hemodynamic changes following hypovolaemia [2, 6, 13, 18]. Amongst 5-hydroxytryptamine (5-HT3) antagonists Ondansetron, Granisetron, Palonosetron, etc are safely used in the management of various symptoms. Ondansetron was shown to attenuate arterial blood pressure drop due to spinal anesthesia in the general surgery population in a study by Owczuk *et al*. [13] In the present study, among the total 120 patients, physical status ASA I was observed in 80.33%; n=97, and ASA II (19.17%; n=23), this number is sufficiently adequate to compare with previous studies [6, 12, 13]. Two groups having an equal number of participants were named Group A (n=60) and Group B(n=60).

Ondansetron was used in group A as a test and Ephedrine was used in group B as a control. Regarding the age distribution of the participant, it was found that the majority (58.33%) of them was between 25-30 years of age, and only one participant (0.83%) was within the

range of 40-45 years. Parity distribution revealed that 59.17% (n=71) patients were multigravid while 40.33% (n=49) were primi. All patients were scheduled for elective cesarean section and the highest number of them (49.17%; n=59) had a history of cesarean section for their previous delivery. The next highest indication was malpresentation (14.17%; n=17) and the least was short stature (1.67%; n=02). In the trends of Mean arterial Pressure (MAP) change, this study showed no significant difference in basal MAP between the two groups. But after the introduction of spinal anesthesia, a significant decrease in MAP in both groups with the least occurrence in the ondansetron group was observed. Rashad *et al*. found significantly lower decreases of mean arterial pressure with the use of ondansetron prophylactically in comparison with normal saline used as a placebo ($p < 0.05$) [2]. In the current study, the 15th minute MAP was 76.92, 69.18 mm of Hg in group A and group B respectively showing a significant difference (p=0.0001), After 45 minutes, mean blood pressure was 71.05±6.8 mmHg in group A and 64.46±9.4 mmHg in group B. Which statistically significant ($p<0.05$) between two groups but follow up after 60 minutes mean BP stabilized to similar in both group, which was statistically not significant ($p>0.05$) between two groups. Furthermore, in the usage of rescue medications for treating hypotension, there was a very significant difference between the ondansetron and ephedrine groups. Monitoring and recording of the intraoperative occurrence of nausea, vomiting, and shivering revealed that nausea and vomiting occurred significantly higher in group B (P=0.001). Previous studies had reported significantly fewer episodes of nausea and vomiting [2, 3]. But shivering remained a complication of almost similar magnitude for both of the groups. Shivering was observed in 46.67 % (n=28) and 48.33% (n=29) cases of group A and group B respectively.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

The management of bradycardia and hypotension following spinal anesthesia in obstetrics continues to be controversial. Different strategies like pre-loading, co-loading, positioning, uterine displacement, and prophylactic use of ephedrine are being practiced widely but none is proved sufficient. In the current study, the efficacy of Ondansetron and Ephedrine in attenuation of hemodynamic derangements following spinal anesthesia has been proven to be satisfactory with statistically significant supremacy of Ondansetron over Ephedrine.Besides this Ondansetron bears additional advantages in the management of perioperative nausea and vomiting, although proved less effective to prevent shivering.

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