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COMPARISON OF DIFFERENT DOSES OF INTRAVENOUS ONDANSETRON AND PLACEBO FOR THE REDUCTION OF SPINAL ANESTHESIA INDUCED HYPOTENSION IN PARTURIENTS UNDERGOING ELECTIVE CESAREAN SECTION – A PROSPECTIVE RANDOMISED STUDY

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Abstract

Background: Hypotension is the most common side effect in spinal anesthesia for cesarean section. 5HT3 receptor antagonist like ondansetron, inhibits the Bezold-Jarish reflex and thereby supposed to prevent spinal-induced hypotension during cesarean section.The aim of our study was to evaluate the effect of two different doses of ondansetron for prevention of hypotension during spinal anesthesia for cesarean section.

Materials and Methods: This prospective study was conducted on 120 parturients undergoing cesarean section under spinal anesthesia.They were divided into three groups of 40 each. Group C received 0.9% normal saline(10ml),Group B received 8 mg ondansetron in normal saline (10ml).Group A received 4 mg ondansetron in normal saline (10ml).All the three drugs were administered 5 min before spinal anesthesia. Incidence of hypotension, vasopressor requirement, and side effects were evaluated.

Results: Incidence of intraoperative hypotension was significantly high in group C(67.5%) as compared to group A(45%) and group B(20%). Significant difference in incidence of hypotension was also found between A and B groups. Total requirement of ephedrine was significantly higher in group C (5.68 ± 4.62mg) as compared to group A (3.14 ± 4.85mg) and B (1.65 ± 3.94mg). This

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was significantly higher in group A when compared with group B. Fall in mean HR, SBP, DBP, MAP was more in group C at different time intervals compared to other two groups.

Conclusions: Ondansetron before spinal anesthesia reduced the incidence of hypotension and requirement of vasopressors in parturients undergoing cesarean section under spinal anesthesia.

Key words: Cesarean section, hypotension, intraoperative ,ondansetron

Introduction

Spinal anesthesia is the most common mode of anesthesia for patients undergoing elective cesarean sections,[1] Though spinal anesthesia is safe and provides effective anesthesia, it can produce unwanted side effects like hypotension and bradycardia. Incidence of spinal anesthesia induced hypotension is 70-80% in obstetric patients which can be detrimental to both fetus and mother.[2] The cause of maternal hypotension is mainly due to sympathectomy resulting in reduction in cardiac output and systemic vascular resistance.[3] Bradycardia and hypotension occurs due to Bezold-Jarisch reflex, which is an inhibitory parasympathetic reflex originating in cardiac sensory receptors caused by decreased filling of the right atrium which stimulate the peripheral serotonin 5-hydroxytryptamine- receptors (5-HT3 type) mediated by serotonin.[4] Recent studies have revealed that 5-HT3 antagonists may abolish the Bezold-Jarisch reflex. Anti emetics like ondansetron a 5-HT receptors antagonist, can prevent bradycardia and hypotension induced by spinal anesthesia. In the literature, ondansetron was used 5 minutes before performing spinal block to prevent hypotension and bradycardia during cesarean section.[6] But the effective dose of ondansetron is still not clear in literature.[7] Our primary aim was to assess the incidence of hypotension. Secondary aim was to assess requirement of vasopressors and any side effects with different doses of ondansetron.

Methods

After obtaining approval from the institutional ethical committee and informed consent, this prospective randomized double blind study was conducted on 120 full-term parturients, age 18–40 years, ASA I and II posted for elective cesarean sections under spinal anesthesia. Parturients having history of allergy to ondansetron or local anesthetic, obesity, pregnancy induced hypertension, or any other associated comorbid conditions were excluded from the study.All the parturients were randomly assigned in to three groups using computer generated randomization chart, receiving normal saline 10 ml (Group C), or ondansetron 4 mg diluted in normal saline up to 10ml (Group A), or 8 mg diluted in normal saline up to 10 ml (Group B).The selected patients underwent a pre-anesthetic check-up a day prior to surgery. Peripheral 18-gauge IV cannula was inserted and inj. ranitidine (1 mg/kg) IV, inj. metoclopramide (0.2 mg/kg) IV was administered. Ringer lactate 10 mL/kg was infused over 30 min before spinal anesthesia. In the operating room baseline HR, SBP, DBP, and MAP were recorded. The study drug was given 5 min before the sub-arachnoid block. Spinal anesthesia was performed with a 25-G Quincke spinal needle in the left lateral position at L3-4 or L4-5 in a dose of 2 ml 0.5% hyperbaric bupivacaine. Sensory block was assessed using pin prick technique in mid clavicular line bilaterally at 1 min interval while motor block was assessed using Modified Bromage score and surgery was allowed when the block height T6 was achieved. Hemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO2) were recorded at the time of spinal block (0 min) and at 2-min interval up to 20

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min, followed by 5-min interval upto 30 min or till the end of surgery.Hypotension was defined as a fall in SBP >20% of baseline and was treated with inj. ephedrine 6 mg intravenously. Bradycardia was defined as HR <50 beats/min and was treated with inj. atropine 0.6 mg intravenously. The incidence of hypotension and requirement of ephedrine were recorded. Patients were also assessed for the presence of nausea, vomiting, and shivering. Shivering was treated with inj. tramadol 25 mg IV. Demographic characteristics like age, weight, height, gestation week, time from spinal anesthesia to delivery, duration of surgery and APGAR score of the baby at 1 min were recorded.The primary outcome of this study was the incidence of maternal hypotension in all three groups while secondary outcomes were total dose of ephedrine requirement and adverse effects .

Results

120 parturients were included in the study,consisting 40 in each group. All the three groups were found to be statistically comparable with regard to demographic variables and baseline parameters.(table 1)

Table 1: Comparison of demographics, obstetric data and neonatal outcome

Demographic variables	Group A	Group B	Group C	P value
Age (year)	28.27 ± 4.10	26.60 ± 3.59	27.70 ± 3.98	0.312
Height (cm)	153.73 ± 2.08	154.73 ± 3.71	153.52 ± 2.12	0.423
Weight (kg)	68.62 ± 5.11	69.33 ±3.66	69.12 ± 3.69	0.116
Gestation week	37.12± 0.45	37.58± 0.43	36.97± 0.84	0.241
Duration of surgery (min)	34.52± 5.62	33.87± 4.85	34.14± 5.11	0.225
Time from S/A to delivery(min)	5.96± 0.8	6.1 0±.55	6.21± 0.38	0.282
APGAR at 1 min	8.12± 0.65	8.24 ± 0,45	8.14± 0.39	0.249

Incidence of intraoperative hypotension was significantly high in group C(67%) as compared to group A (45%) and group B(20%). Incidence of hypotension was also statistically significant between A and B groups. Total requirement of ephedrine was significantly higher in group C (5.68± 4.62mg)as compared to group A (3.14± 4.85mg) and group B (1.65± 3.94mg). It was found to be significantly higher in group A when compared with group B.(table 2)

Table 2: Comparison of incidence of hypotension and requirement of ephedrine in different groups

Variables	Group A	Group B	Group C	P value
Hypotension (n/%)	18(45%)	8(20%)	27(67.5%)	<0.05
Total dose of ephedrine (mg)	3.14± 4.85	1.65± 3.94	5.68± 4.62	<0.05

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Table 3: Comparison of incidence of side effects

Adverse Effect	Group A	Group B	Group C
Nausea	3(7.5%)	2(5%)	14(35%)
Vomiting	1(2.5%)	1(2.5%)	9(22.5%)
Shivering	0	0	4(10%)

Table 3 shows that the incidence of nausea (35%), vomiting (22.5%) and shivering (10%) was significantly higher in group C as compared to group A and group B.

Discussion

Hypotension is the most common complication of spinal anesthesia. The main causes of this spinal induced hypotension are sympathetic blockade with a parasympathetic overactivity, aorto caval compression due to gravid uterus and Bezold-Jarisch reflex. Ondansetron, a $5HT_3$ receptor antagonist, can prevent hypotension and bradycardia by blunting the Bezold-Jarisch reflex,[9] which can provide better maternal and foetal outcome. Different doses of ondansetron has been used for prevention of spinal induced hypotension but ideal dose is still not known in literature.[8] Our study was designed to determine the effect of different doses of ondansetron on prevention of spinal induced hypotension.

The incidence of hypotension and requirement of ephedrine was significantly greater in the saline group as compared to both ondansetron groups. Ondansetron 8mg significantly reduced requirement of ephedrine as compared to group ondansetron 4mg. The incidence of hypotension was also reduced in ondansetron 8mg as compared to ondansetron 4mg. Wang et al.[9] studied dose–response relationship between four doses of ondansetron (2, 4, 6, and 8 mg) for prevention of maternal hypotension. They found that ondansetron 4 mg and 6 mg reduced the incidence of maternal hypotension and vasopressor requirement as compared with ondansetron 2 mg and 8 mg. In our study ondansetron 8 mg was found more effective in reducing the requirement of ephedrine. Similarly Potdar et al.[8] in their study found higher incidence of hypotension and greater requirement of ephedrine in control group in contrary to ondansetron groups. They concluded that 8 mg of ondansetron had no advantage of over 4 mg. Badway et al[11] in their study concluded that the incidence of hypotension and requirement of vasopressor in ondansetron group was less as compared to control group. Karacaer et al.[12] found that there was no significant difference in the incidence of hypotension among the groups. Incidence of hypotension and norepinephrine

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requirement was significantly more in control group compared to ondansetron group. Ortiz-Gomez et al.[13] in their study concluded that the incidence of hypotension in control group and ondansetron group (2, 4, and 8 mg) were similar which was in contradiction to our study findings. Marciniak et al [15] in their study did not find any significant difference in the incidence of hypotension and requirement of vasopressors in the control and ondansetron groups which was in contradiction to our study findings. This may be due to different study population, and sample size.In our study the fall in heart rate after spinal anaesthesia was more in control group compared to ondansetron group. Sahoo T et al.[10] concluded that the fall in heart rate was more in the control group and the difference was statistically significant as compared to ondansetron group. Terkwi et al[14] in their study concluded that the variation in heart rate among the ondansetron groups and control group was not statistically significant.In our study the fall in SBP, DBP and MAP from baseline was found more in saline group compared to ondansetron groups which was similar to study by Badway.[11] Nivatpumin et al [16] found no significant differences in the hemodynamic variables in all the groups which was in contradiction to our study.In our study, the incidence of vomiting was more in saline group which was in agreement with study by Sahoo et al.[10] Studies in literature have demonstrated that ondansetron can significantly reduce the incidence of postoperative nausea and vomiting as also seen in our study. The 5-HT_3 receptor- induced vagal stimulation and 5-HT release in the fourth ventricle are inhibited by ondansetron leading to control of vomiting.

Shivering was found only in 3 patients in the control group which was similar to the study by Badway et al.[11] who also found a higher incidence of shivering in the control group as compared to ondansetron group. Ondansetron has been proved to possess anti-shivering properties, but it may be attributed to its central action by inhibiting serotonin reuptake at the level of the pre-optic anterior hypothalamic region.[17]Further research, should be done to find out optimum dose of ondansetron and timing of ondansetron administration to prevent post spinal hypotension.

Conclusion

Ondansetron (8mg)given 5 min before spinal anesthesia can decrease the incidence of hypotension and requirement of vasopressors in parturients undergoing cesarean section compared to ondansetron 4mg.

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