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A CLINICAL STUDY ON THE EFFECTS OF ONDANSETRON ON THE DOSE OF VASSOPRESSOR IN SPINAL - INDUCED HYPOTENSION IN CAESAREAN SECTION CASES- A RANDOMISED CONTROLLED TRIAL.

Anaesthesiology

Nilotpal Das Associate Professo Department of Anesthesiology, Gauhati Medical College. *Corresponding Author

Tejwant. Rajkhowa Assistant Professor Department of Anesthesiology, Gauhati Medical College.

Mahbub Alam Post graduate trainee Department of Anesthesiology, Gauhati Medical College.

ABSTRACT

Background: Subarachnoid block is the preferred method of anesthesia for caesarean section, but it is associated with hypotension and bradycardia, which may be deleterious to both parturient and baby. Animal studies suggest that in the presence of decreased blood volume, 5-HT may be an important factor inducing the Bezold Jarisch reflex via 5-HT3 receptors located in intracardiac vagal nerve endings. In this study, we evaluated the effect of ondansetron, as a 5-HT3 receptor antagonist, on the haemodynamic response and required dose of vessopressors following subarachnoid block in parturients undergoing elective caesarean section.

Methods: Hundred parturients scheduled for elective caesarean section were randomly allocated into two groups. Before induction of spinal anaesthesia Group A (n = 50) received normal saline ; Group B (n = 50) received ondansetron , 4mg. Blood pressure, heart rate and vasopressor requirements were assessed.

Results: No significant difference were observed in demographic profile of both the group. Decrease in HR was observed in both the group and the difference is found to be statistically significant at every 3 minutes interval except at 12 mins. Decrease in mean arterial pressure was lower in the group receiving ondansetron. Vasopressor requirement in group B patients were less compared to group A patients.

KEYWORDS

Spinal anaesthesia, Vasopressor, hypotension

INTRODUCTION:

Spinal anesthesia is one of the anesthetic techniques which is being extensively used in Caesarian section cases in present day surgeries. Though spinal anesthesia has a number of advantages over general anesthesia, but the main drawback is the hypotension associated with it. Spinal anesthesia causes hypotension with decrease in cardiac output in general and utero-placental flow in cesarean section cases which may induce fetal morbidity. Spinal anesthesia induces sympathetic block with vasodilatation which causes hypotension. Bradycardia can occur from the shift in cardiac autonomic balance towards parasympathetic system, from activation of left ventricular mechanoreceptor from a sudden decrease in left ventricular volume (Bezold Jarisch reflex) [1]. Animal study suggest that in the presence of decreased blood volume , 5 HT may be an important factor inducing Bezold Jarisch reflex via 5 HT3 receptors located in intracardiac vagal nerve ending . Owczuk et al. observed that intravenous ondansetron attenuated spinal-induced hypotension.[2] Animal studies suggest that 5-HT (serotonin) may be an important factor associated inducing the BJR in the setting of decreased blood volume[4–6]; this effect can be blocked at the 5-HT3 receptor.[3] In this study we will assess the effect of prophylactic preoperative ondansetron 4mg iv as 5 HT 3 receptor antagonist on the hemodynamic response and requirements of vasopressors following spinal anesthesia in Caesarian section in comparison to the cases where ondansetron is not used prophylac tically. Objectives of our study are:

1. To study the effect of ondansetron on the dose of vasopressors in spinal- induced hypotension in c. s cases.
2. To study the effects of prophylactic iv ondansetron on hemodynamic.

METHODOLOGY:

This study was conducted at the Department of Anaesthesiology, Gauhati Medical College , Guwhati, India between 20th August 2016 to 20th February 2017. Institutional ethical committee approval and informed written consent were obtained from all patients. A randomnised controlled trial with non probability sampling method was conducted. A sample size of 100 patients were selected. The selected patients were randomnised into 2 groups one receiving the 4mg ondansetron 5 minutes prior to spinal anaesthesia and another group receiving the placebo i.e normal saline. Patients with hyper emesis gravidarum, contraindication to spinal anesthesia (patient refusal, unstable hemodynamic, coagulation abnormalities), chronic hypertension or preeclampsia, morbid obesity, twin pregnancy, placenta praevia, placenta acreta ,severe dehydration, weight below 45 kg and above 65kg, short stature, extreme tall stature, DM, any known cardiac disease, acute infection or presence of significant fever, Spinal cord abnormalities, spinal surgery, or preexisting neurological dysfunction Baseline HR <65, Failed spinal anesthesia/inadequate sensory block for surgery, patient not within ASA 1 and 2, hypo and hyperthyroidism were exclusion criteria.

Baseline values of non invasive blood pressure, ECG, pulse-oximetry were recorded in the operating room, every patient was co-loaded with 500ml crystalloid(RL) and fluid Infusion was restricted to total 1500ml crystalloid(RL-NS-RL) plus correction of blood beyond expected level(If Any).

With the patient in left lateral position, spinal anesthesia was performed at the L3-L4 with a 24 G Whitaker needle and 5 mins after the administration of ondansetron/placebo solution, patients will receive 2.2ml of a hyperbaric 5mg/ml inj Bupivacaine solution with 60 microgram of inj buprenorphine.

All hemodynamic parameters was recorded every 3 minutes till 39 minutes.Simultaneously requirement of vasopressors were also recorded.

Hypotension, defined as decrease from mean arterial pressure(MAP) <85 mm Hg, and it was treated by inj Mephentermin bolus (6mg),mephentermin was used up to 30mg when required .If hypotension was not controlled then inj Phenylephrine 100 microgram bolus was to be given until restoration of baseline values. In presence of bradycardia and hypotension inj atropine were to be used to restore the baseline blood pressure. Bradycardia, defined as heart rate below 45 beat/min and IT will be treated with inj Atropine 0.6mg iv.

In the cases where normal saline as placebo was amd in those cases if vomiting occurred then inj metoclopremide was to be used.

STATISTICALANALYSIS:

Numerical variables normally distributed were compared between groups by t test. Categorical variables were compared between groups by Chi square test. All analyses were 2-tailed. $P < 0.05$ was considered statistically significant.

RESULTS:

100 patients were recruited , 50 in each group. Group A receiving

Normal saline and Group B receiving 4 mg Ondansetron.

No significant difference were observed in patients demographics between the two groups . The mean age (years) in group A is 27± 3.64 and in group B is 26.48± 4.27.The mean weight (kg) in group group A 58.62± 5.062 and in group B is 56.50 ± 5.48 . Mean height (cm) of group A is 155.6 ± 4.708 and in group B is 155.28± 5.357.

Decrease in heart rate were observed in group A and group B and the difference was found to be statistically significant at every 3 minutes interval except at 12 mins. (Table 1)

Table 1: Table showing the changing pattern of heart rate in two groups.

Time interval	Group A (n=50)	Group B (n= 50)	P value
3 mins	82.6 (11.620)	97.80 (10.9)	0.00
6 mins	77.84 (7.22)	87.30 (9.74)	0.00
9 mins	78.68 (9.44)	89 (10.05)	0.00
12 mins	83.46 (10.80)	84.82 (10.75)	0.530
15 mins	69.48 (11.12)	86.94(12.86)	0.00
18 mins	69.40 (12.60)	87.42 (12.57)	0.00
21 mins	79.30 (13.55)	91.28 (12.05)	0.00
24 mins	80.16 (9.36)	95.96 (10.06)	0.00
27 mins	83.98(9.07)	94.68(12.99)	0.00
30 mins	80.42(10.94)	90.12(11.27)	0.00
33 mins	74.08 (8.08)	86.36 (10.82)	0.00
36 mins	75.10 (8.33)	84.60 (10.49)	0.00
39 mins	79.90 (8.59)	84.38 (10.24)	0.00

Data represents mean (SD).

Table2: Table showing comparison of mean arterial pressure between two groups at 3 minutes time interval.

	Group A (n=50)	Group B (n= 50)	p value
3 mins	87.70 (9.93)	94.22 (8.26)	0.001
6 mins	79.94 (9.90)	84.92 (7.15)	0.005
9 mins	78.60 (8.19)	81.10 (7.32)	0.111
12 mins	71.28 (7.19)	79.12 (7.44)	0.00
15 mins	77.89(7.38)	83.26 (8.38)	0.001
18 mins	74.76 (6.93)	77.94 (5.97)	0.016
21 mins	69.74 (7.59)	79.52 (7.55)	0.00
24 mins	72.82 (7.85)	71.94 (8.38)	0.589
27 mins	75.50 (8.66)	75.88 (8.26)	0.823
30 mins	74.50 (8.70)	78.56 (6.28)	0.009
33 mins	80.84 (7.31)	73.04 (7.95)	0.00
36 mins	77.26 (7.51)	74.82 (5.84)	0.073
39 mins	78.62 (6.86)	75.04 (6.17)	0.007

Data represents mean (SD)

Decrease in mean arterial pressure from the base line was observed in both the groups A and B. Group A has comparatively lower mean arterial pressure compared to Group B except in 24 mins, 33 mins, 36 mins, 39 mins. Statistically significant difference was observed at 3 mins, 6 mins, 12 mins, 15 mins, 18 mins, 21 mins, 30 mins, 33 mins, 39 mins.

Table 3: Table showing use of vasopressors in the two groups.

		Drugs (vasopressor) (mg)					Total	P value
		0	6	12	18	24		
Group A	No. of patients	18	20	7	4	1	50	0.025
	% within group	36%	40%	14%	8%	2%	100%	
	% within those receiving drugs	40%	52.6%	70%	66.7%	100 %	50%	
Group B	No. of patients	27	18	3	2	0	50	
	% within group	54%	36%	6%	4%	0%	100%	
	% within those receiving drugs	60%	47.4%	30%	33%	0%	50%	
Total	No. of patients	45	38	10	6	1	100	
	% within group	45%	38%	10%	6%	1%	100%	
	% within those receiving drugs	100%	100%	100%	100%	100 %	100%	

Table 3, shows that 36% of group A patients requires no vasopressors compared to group B which is 54% . Vasopressor requirement in group A patients are as following, 6mg (40%), 12mg (14%). 18mg (8%), 24 mg (2%) . Vasopressor requirement in group B patients are as following, 6mg (36%), 12mg (6%), 18 mg (4%), 24 mg (0%).

The table depicts that the group receiving ondansetron requires less vasopressors compared to its placebo control group, and the difference between the two group is found to be statistically significant.

DISCUSSION:

This study revealed that decrease in MAP was reduced with the use of i.v. ondansetron 4 mg given 5 min before spinal anaesthesia in parturients undergoing elective caesarean section. Although significant differences in heart rate were observed between the groups in almost all occasions except at 12 mins.

Sympathetic blockade from spinal anaesthesia decreases systemic vascular resistance and induces peripheral pooling of blood leading to hypotension.

Mechanoreceptors in the heart wall that trigger the BJR, participate in systemic responses to hyper- and hypo-volaemia.[7,8] In response to hypovolaemia, stimulation of cardiac sensory receptors in the left ventricle induces the BJR and results in reflex bradycardia, vasodilation and hypotension.[9] Chemoreceptors are activated in response to decreased blood volume by serotonin, which is released from activated thrombocytes. [10] Activation of 5-HT3 receptors, which are G protein coupled, ligand-gated fast-ion channels, results in increased efferent vagal nerve activity,13 frequently producing bradycardia.[11]

Thus, spinal anaesthesia causes vasodilatation, hypotension, and bradycardia by sympathetic blockade, the BJR and stimulation of 5-HT3 receptors in vagal nerve endings.[4] Blockade of the 5-HT3 receptor antagonizes the BJR induced by serotonin.[3] White et al. observed that i.v. administration of the 5-HT3 antagonist granisetron 50 microgm/kg was efficacious in suppressing bradycardia and hypotension associated with the BJR in a rabbit model.[12] Martinek concluded that i.v. ondansetron 4 mg with atropine 0.6 mg could revert asystole during spinal anaesthesia.[4] Finally, Owczuk et al. in a mixed group of patients aged 20– 70 years, found that ondansetron 8 mg decreased the incidence of bradycardia and hypotension after spinal anaesthesia.[2] Sahoo et. Al concluded that Ondansetron 4 mg, given intravenously 5 min before subarachnoid block reduced hypotension and vasopressor use in parturients undergoing elective caesarean section.[13]

Limitation of our study is that we could not evaluate the effect of different doses of ondansetron in preventing hypotension in patients receiving spinal anesthesia. We could not evaluate the effect of ondansetron in nausea and vomiting and its effect in systolic blood pressure.

We conclude that i.v. ondansetron 4 mg given before spinal anaesthesia can attenuate decreases in mean arterial pressure following spinal anaesthesia in parturients undergoing elective caesarean section.

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