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THE EFFECT OF ONDANSETRON ADMINISTRATION 20 MINUTES PRIOR TO SPINAL ANAESTHESIA ON HAEMODYNAMIC STATUS IN PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: COMPARISON BETWEEN TWO DIFFERENT DOSES

Dr Ketki Jandial* Medical Officer Super Specialty Hospital, Jammu, J&K. *Corresponding Author

Dr Shagufta Tabassum Resident, Department of Anesthesiology and Critical Care, GMC Jammu, J&K.

ABSTRACT

Background: Risks involved in general anaesthesia has made spinal anaesthesia the standard anaesthetic technique for caesarean section. Spinal anaesthesia has its own side effects that may affect the mother and the unborn child's well-being. Ondansetron is a 5-HT receptors antagonist, basically used as an antiemetic drug and is thought to counteract bradycardia and hypotension induced by spinal block. The primary aim of the study was to assess systolic blood pressure (SBP), diastolic blood pressure (DBP), and the mean arterial pressure (MAP) among different ondansetron doses and a control group in different time intervals.

Methods: A prospective, double-blinded, placebo- controlled, randomized clinical trial was conducted during a period of 6 months on a total of 90 patients, scheduled to undergo elective caesarean delivery under spinal anesthesia, in SMGS Hospital, Jammu. All patients with ASA I and II parturient, who were included in the study.

Results: Number of patients with hypotension, was not significantly different between the study groups. Total number of hypotensive episodes showed significant difference and was lower in Group 2. (p=0.044) Patients of group 1 had increased frequency of administration of mephtermine in response to fall in blood pressure. In Ondansetron group, there was a dose dependant decrease in ephedrine requirement.

Conclusion: Administering ondansetron (6 mg) 20 minutes before spinal block can raise the hope of increasing the efficacy of Spinal anesthesia. It may not cause reduction in the incidence of hypotension in caesarean section under spinal block, but can significantly decrease the consumption of adrenergic agonists.

KEYWORDS : Caesarean section, hypotension, ondansetron

INTRODUCTION

Risks of aspiration pneumonitis, difficult airways and foetal exposure to hypnotic drugs, are to be dealt with in obstetric population undergoing general anaesthesia. Therefore, spinal anaesthesia has become the standard anaesthetic technique for caesarean section as it helps in avoiding all such risks accompanying general anaesthesia. However, spinal anaesthesia has its own complications and side effects that may affect the mother and the unbornchild's well- being, like hypotension with or without bradycardia.[1-3] Spinal induced hypotension can affect as much as 90% of obstetric patients.[4]

Possible pathophysiological mechanism for hypotension during spinal anesthesia is the rapid onset of sympatholytic, which may be due to increased sensitivity of nerve fibers to local anesthetics during pregnancy or relative dominance of para-sympathetic system or due to Bezold Jarish reflex (BJR).[5] Bezold-Jarisch reflex, 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.[6] After verifying that serotonin can induce BJR reflex in animals, and can cause bradycardia or hypotension, researchers have started to evaluate the effect of serotonin antagonists to decrease the effect in human beings. [7] Ondansetron is one such 5-HT receptors antagonist, which is basically used as an antiemetic drug and is thought to counteract bradycardia and hypotension induced by spinal block. Ondansetron used 5 minutes before performing spinal block has been seen to prevent hypotension and bradycardia with moderate reduction in hypotension during caesarean section.[8] Ondansetron, used intra operatively has many secondary advantages like: decreasing nausea, vomiting, shivering, etc. It has its peak plasma concentration within 30 minutes of intravenous administration.[9-10] Ondansetron shows promising effect on spinal anesthesia induced hypotension in some studies, while not so promising in others. [11] In the present trial, it was proposed to give ondansetron 20 minutes before performing spinal block and assess the efficacy of prophylactic ondansetron in counteracting hypotension during spinal block in caesarean section. The primary aim was to assess systolic blood pressure (SBP), diastolic blood pressure (DBP), and the mean arterial pressure (MAP) among different ondansetron doses and a control group in different time intervals.

METHODS

A prospective, double-blinded, placebo- controlled, randomized clinical trial was conducted during a period of 6 months on a total of 90 patients, in SMGS Hospital, Jammu.

Inclusion Criteria:

All patients with ASA I and II parturient, who were scheduled to undergo elective caesarean delivery under spinal anesthesia, were included in the study.

Exclusion Criteria:

Patients with ASA physical status classification III, IV or V, emergent caeserean sections, multiple parities (twins/triplets), patients who presented with a cardiac history (coronary artery disease, myocardial infarction, congestive heart failure), anemia, diabetes and placenta previa, were excluded from the study. Any patient receiving intra-operative antiemetic therapy was also excluded from the study.

A written informed consent was obtained from all participants. Ethical clearance was duly obtained from institutional ethical committee before the start of the study. Preoperative assessment was done by an anaesthetist the day before surgery. Demographic data such as age, weight, height, body mass index were also recorded.

Patients, anaesthesia assistant and anesthetist were blinded for the administration of ondansetron and saline. 5 ml syringes of same color were used for both ondansetron and saline were used. Patients were randomly allocated into two groups with the help of a computer-formulated randomization technique, using consecutively numbered opaque sealed envelopes, which were opened on the day of surgery only.

All patients fasted for 8 hours and were not given premedication other than ranitidine 50 mg intravenously 2 hours pre-operatively. Then, in the operating theatre, baseline values of non-invasive systolic blood pressure (SBP) and diastolic blood pressure (DBP), and mean arterial pressure (MAP) were obtained. SBP, DBP, and HR were measured and MAP was calculated using aforementioned formula, at 1-minute intervals for ten minutes, 2-minute intervals for another 10 minutes, then at 5-minute intervals till 40 minutes after spinal block by the responsible anaesthesiologist. Heart rate (HR) and pulse oximetry (SpO_2) were recorded, and two intravenous gauge 18 cannulae were secured in each patient.

The participants were randomised into two groups of 45 each: ***Group 1(Control Group) received 2ml saline and Group 2 (Cases Group) received 4 mg IV (2 ml) ondansetron, prepared in 5cc syringes, 20 minutes before the spinal block.*** At the due moment, all patients were preloaded with 500 ml of lactated Ringer's solution. Then, they were put in a sitting position and under aseptic technique; a subarachnoid block was done by injecting 2 mL of 0.5% (10 mg) hyperbaric

bupivacaine through a 25 gauge Quinke's spinal needle at the level of L3-L4 or L4-L5. Each patient was then immediately put in the supine position with left uterine displacement. Sensory block levels were assessed every minute after subarachnoid block using perception to cold, and motor block levels using modified Bromage scale.[12] After delivery of the foetus, all patients received 10 international units of oxytocin direct IV and then 30 international units in 250 ml compatible IV fluids over four hours. Intra-operative nausea and vomiting were treated with elevation of blood pressure.

Hypotension was defined as drop in SBP ≥20% of the baseline value or SBP less than 100 mmHg. The hypotension was treated by increasing rate of crystalloids infusion and intravenous (IV) mephtermine in increments of 3mg. Bradycardia was defined as ≥30% drop from baseline heart rate or when the HR dropped below 50 beats per minute; the patient was treated with IV atropine 0.5 mg.

MS Excel 2010 software was used in our analysis. Demographic data which include age, weight, height, SBP, DBP, MAP, HR and SpO_2were analysed using One-way analysis of variance (ANOVA). Chi- square test was used to compare between the three groups regarding episodes of hypotension requiring treatment with mephtermine. All underlying assumptions were met, unless otherwise indicated. *P* value less than 0.05 was considered statistically significant.

RESULTS

90 pregnant patients participated in the study over the study period. There were 45 patients in Group 1 (control group) and 45 patients in Group 2 (Ondansetron Group). The study groups were statistically comparable with regard to demographic variables and baseline parameters, as shown in Table 1.

Table 1: Demographic and Baseline data parameters

Data Parameters	Group 1 (n = 45)	Group 2 (n = 45)	*p-value*
Age (years)	30.66 ± 4.46	31.12 ± 4.97	0.553
Height (M)	1.62 ± 0.48	1.61 ± 0.47	0.419
Weight (Kg)	70.46 ± 10.69	70.37 ± 12.52	0.709
BMI	25.82 ± 1.92	26.04 ± 1.94	0.633
Fluids given (ml)	2246 ± 563	2169 ± 605	0.428
Duration of surgery (minutes)	71.5 ± 15.5	70.5 ± 12.5	0.493
Weight of newborn (Kg)	3.36 ± 0.18	3.41 ± 0.19	0.565
SBP (mmHg)	126.31 ± 10.22	125.74 ± 10.49	0.203
DBP (mmHg)	74.02 ± 9.40	74.52 ± 9.69	0.368
MAP (mmHg)	91.16 ± 10.56	90.77 ± 10.05	0.186
Heart Rate(beat/minute)	93.8 ± 7.4	94.1 ± 7.9	0.190
O2 saturation, SpO2 (%)	97.5 ± 1.1	97.5 ± 0.9	0.389

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure

There was no statistically significant difference in the readings of SBP, DBP, and MAP among the two groups in different time intervals after spinal block. (Table 2)

Table 2: Comparison in mean rates of SBP, DBP and MAP, at defined / measured time points

Timing	Component	Group 1	Group 2	*p-value*
0 to 10 Minutes	SBP	108.3 ± 14.4	106.2 ± 13.3	0.822
	DBP	56.6 ± 9.8	54.2 ± 8.2	0.557
	MAP	74.5 ± 10.3	74.5 ± 8.6	0.976
10 to 20 Minutes	SBP	107.5 ± 11.3	108.8 ± 12.6	0.965
	DBP	54.4 ± 8.4	55.2 ± 8.8	0.682
	MAP	73.1 ± 11.3	74.9 ± 9.0	0.308
30 to 40 Minutes	SBP	106.7 ± 11.4	110.2 ± 12.7	0.447
	DBP	52.2 ± 7.7	56.9 ± 9.7	0.789
	MAP	71.5 ± 11.8	76.0 ± 9.5	0.317

Data expressed as mean ± SD. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean blood pressure

As for heart rate readings significant difference was exhibited between the two groups (P <0.05). (Table 3)

Table 3: Comparison in Heart Rate (HR)

Timing (minutes)	Group 1 (n = 45)	Group 2 (n = 45)	*p-value*
0 to 10 Minutes	101.9 ± 16.2	95.4 ± 14.4	0.039*
10 to 20 Minutes	99.4 ± 15.3	93.9 ± 14.6	0.105
30 to 40 Minutes	98.5 ± 11.4	91.1 ± 10.6	0.026*

Data expressed as mean ± SD. * p<0.05 = significant

Number of patients with hypotension, was not significantly different between the study groups. However, the total number of hypotensive episodes showed significant difference and was lower in Group 2. (Table 4). Moreover, patients of group 1 had increased frequency of administration of mephtermine in response to fall in blood pressure.

Table 4: Different doses of ephedrine and overall hypotensive episodes

Dose of Ephedrine (mg)	Group 1 (n = 45)	Group 2 (n = 45)	P-value
Average dose of Ephedrine given	15 mg	12 mg	P < 0.001
Atropine given	1	0	–
Adrenaline infusion given	1	0	--
Number of patients with hypotension	34	32	0.117
Overall number of hypotensive episodes	87	68	0.044*

DISCUSSION:

Prevention of hypotension, after spinal block, during caesarean section, relies on IV fluids infusion and vasopressors administration such as phenylephrine, ephedrine, mephentermine.[13] Studies have shown that ondansetron, given 5 minutes before initiation of spinal block, is beneficial in reducing incidence of hypotension which accompanies spinal block in caesarean section. [14] In studies done on general surgical patients,[15] ondansetron administered 5 minutes before spinal block attenuated hypotension of the spinal block more than the control. In yet another study by Marashi et al.[16] 4 mg ondansetron given 5 minutes before spinal block for caesarean section attenuated mean blood pressure and diastolic blood pressure hypotension.

It is known that ondansetron reaches its peak plasma concentration within 30 minutes of IV administration,[9] therefore, in the current study, ondansetron was injected 20 minutes prior to spinal block and in a collective dosage of 4 mg, to observe its effect in counteracting hypotension. We found that ondansetron given 20 minutes before spinal block, and compared with saline did not reduce the incidence of hypotension in caesarean section; however we found a dose dependant decrease in ephedrine requirement.

There was no significant difference in the incidence of bradycardia between the two groups, which is consistent with the findings of Ortiz-Gomez et al.[17] who found bradycardia in only patient in ondansetron group, while Karacaer et al [18] had found 11 patients in the ondansetron group and similarly 6 patients in control group had bradycardia. On the whole, our study significantly showed an effect on heart-rate on the patients administered with ondansetron, given 20 minutes prior to surgery, as compared to the controls.

At the same time, in our study, there was a high incidence of hypotension, the amount of IV crystalloids and the dose of mephtermine given were relatively high, if compared to other studies. Savant et al. [9] has concluded that 4 mg is the optimum dose of ondansetron for the prevention of hypotension after spinal block in caesarean section, however, they did not use fentanyl in spinal block, the protocol of oxytocin administration was giving 10 IU of oxytocin in 250 mL of normal saline as intravenous infusion, and they compared the changes in blood pressure, but not comparing the true values of blood pressures and heart rates.

There is no difference in blood loss or uteri-tonic drug consumption between the two groups that might affect blood pressure during caesarian section Ortiz-Gomez et al has also reported these factors, controlling the dose of oxytocin after clamping of umbilicus and continued infusion of 21 u/h.[17]

Ondansetron did reduce hypotension in obstetric patients undergoing caesarean section but the preventive effect may not have been superior to vasoconstrictors.[19] Hence the major limitation of the study is that it did not produce sufficient data to analyse the comparative effect of vasoconstrictors in absence or in presence of ondansetron.

CONCLUSION:

It can be concluded that, administering ondansetron (6 mg) 20 minutes before spinal block can raise the hope of increasing the efficacy of Spinal anesthesia. It may not cause reduction in the incidence of hypotension in caesarean section under spinal block, but can significantly decrease the consumption of mephtermine or other adrenergic agonists.

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REFERENCES

1. Liu SS, McDonald SB. Current issues in spinal anesthesia. Anesthesiology 2001;94:888-906.
2. Mercier FJ, Auge M, Hoffmann C, Fischer C, Le Gouez A. Maternal hypotension during spinal anesthesia for caesarean delivery. Minerva Anestesiol 2013;79:62-73.
3. Puthenveettil N, Sivachalam SN, Rajan S, Paul J, Kumar L. Comparison of norepinephrine and phenylephrine boluses for the treatment of hypotension during spinal anaesthesia for caesarean section - A randomised controlled trial. Indian J Anaesth 2019;63:995-1000.
4. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and risk factors for side effects of spinal anesthesia. Anesthesiology 1992;76:906-16.
5. Sivvski A. Spinal anaesthesia for cesarean section with reduced dose of intrathecal bupivacaine plus fentanyl. Prilozi 2006;27(2):225-36.
6. Mark AL. The Bezold-Jarisch reflex revisited: Clinical implications of inhibitory reflexes originating in the heart. J Am Coll Cardiol 1983;1:90-102.
7. Skillman CA, Plessinger MA, Woods JR, Clark KE. Effect of graded reductions in uteroplacental blood flow on the fetal lamb. Am J Physiol Heart Circ Physiol 1985;249(6):H1098-105.
8. Heesen M, Klimek M, Hoeks SE, Rossaint R. Prevention of spinal anesthesia-induced hypotension during cesarean delivery by 5-hydroxytryptamine-3 receptor antagonists: A systematic review and meta-analysis and meta-regression. Anesth analg 2016;123:977-88.
9. Savant K, Khandeparker RV, Berwal V, Khandeparker PV, Jain H. Comparison of ondansetron and granisetron for antiemetic prophylaxis in maxillofacial surgery patients receiving general anesthesia: A prospective, randomised, and double blind study. J Korean Assoc Oral Maxillofac Surg 2016;42:84-9.
10. Bhattacharya D, Banerjee A. Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological laparoscopy. Indian J Anaesth 2003;47:249-82.
11. Ferre F, Martin C, Bosch I, Kurrek M, Laireh O, Minville V. Control of spinal anesthesia-induced hypotension in adults. Local Reg Anesth. 2020; 13:39.
12. Rashad MM, Farmawy MS. Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section. Egypt J Anaesth 2013;29:369-74.
13. Kinsella S, Carvalho B, Dyer R, Fernando R, McDonnell N, Mercier F, *et al*. International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. Anaesthesia 2018;73:71-92.
14. Trabelsi W, Romdhani C, Elaskri H, Sammoud W, Bensalah M, Labbene I, *et al*. Effect of ondansetron on the occurrence of hypotension and on neonatal parameters during spinal anesthesia for elective caesarean section: A prospective, randomized, controlled, double-blind study. Anesthesiol Res Pract 2015;2015:158061.
15. Owczuk R, Wenski W, Polak-Krzeminska A, Twardowski P, Arszulowicz R, Dylczyk-Sommer A, *et al*. Ondansetron given intravenously attenuates arterial blood pressure drop due to spinal anesthesia: A double-blind, placebo-controlled study. Reg Anesth Pain Med 2008;33:332-9.
16. Marashi SM, Soltani-Omid S, Mohammadi SS, Aghajani Y, Movafegh A. Comparing two different doses of intravenous ondansetron with placebo on attenuation of spinal-induced hypotension and shivering. Anesth Pain Med 2014;4:e12055.
17. Ortiz F J, Palacio A F, Morillas RF, Fornet RI, Lorenzo JA, Bermejo AM. The effect of intravenous ondansetron on maternal haemodynamics during cesarean delivery under spinal anaesthesia: a double blind randomized placebo controlled trial. Int J Obstet Anesth. 2014; 23(2): 138-43.
18. Karacer F, Biricik E, Onal L, et al. Does prophylactic ondansetron reduce norepinephrine consumption in patients undergoing cesarean section with spinal anesthesia? J Anesth 2018;32(1): 90-7.
19. Wang Q, Zhuo L, Shen MK, Yu YY, Yu JJ, Wang M. Ondansetron preloading with crystalloid infusion reduces maternal hypotension during cesarean delivery. Am J Perinatol 2014;31:913-22.