

Comparison of injection ondansetron with granisetron on maternal haemodynamics and regression of sensory and motor blockade in elective caesarean section: A randomised non inferiority exploratory trial

Debanjali Ray¹, Mrinal Saha², Asoke Chakraborty^{3*}, Mohan Chandra Mandal⁴

¹Assistant Professor, ²Junior Resident, ³Professor, ⁴Associate Professor, Dept. of Anaesthesiology, ^{1,2}North Bengal Medical College & Hospital, West Bengal, ³KPC Medical College & Hospital, Kolkata, West Bengal, ⁴NRS Medical College & Hospital, Kolkata, West Bengal, India

Article Info

Received: 7th June, 2019

Accepted: 11th July, 2019

Published Online: 22nd August, 2019

Keywords: Ondansetron, Granisetron, Haemodynamics, Sensory and motor blockade.

Abstract

Introduction: Spinal anesthesia has many advantages for cesarean section in parturients, but hypotension is considered the most frequent complication and can be managed by different interventions. Hypotension may be induced by sympathetic blockade and Bezold-Jarisch reflex (mediated by peripheral serotonin receptor, 5-HT₃ type). Besides, early regression of sensory and motor blockade are also necessary to prevent various complication. It has been found that level of serotonin is increased in cerebrospinal fluid after spinal anaesthesia. So use of 5HT₃ antagonist can have effect on both.

Objectives: To compare between two serotonin receptor antagonists on the hemodynamics, sensory, and motor blockade induced by intrathecal bupivacaine in parturients undergoing cesarean section.

Materials and Methods: Forty four patients undergoing elective cesarean section under spinal anesthesia by intrathecal bupivacaine were randomly divided into two groups (22 pregnant females of ASA I–II physical status in each group). Group O received intravenous 8 mg ondansetron diluted in 8 ml normal saline and injected 5 min before spinal anesthesia, group G given intravenous 1 mg granisetron in 8 ml normal saline by the same route. Mean arterial blood pressure, heart rate, vasopressor use, sensory and motor blockade were assessed.

Results: use of vasopressors was significantly low in group O ($p < 0.05$), and there was significant faster sensory as well as motor recovery in group G than groups O ($P < 0.05$).

Conclusion: In parturient females undergoing elective cesarean section, intravenous 8 mg ondansetron significantly reduces the demand of vasopressors and granisetron 1 mg provides faster recovery from sensory and motor blockade.

Introduction

For last few decades use of general anaesthesia in caesarean section has decreased and spinal anaesthesia is the popular mode of anaesthesia for both elective and emergency procedures. Although it is safer but not without complications. Common complications following spinal anaesthesia includes hypotension, bradycardia, nausea, vomiting and shivering. In obstetric population incidence of hypotension and bradycardia is higher compared to non-obstetric population, estimated to be 50-60% incidence of hypotension.¹ Several mechanism is attributed to the cause of hypotension and bradycardia, one of which is role of Bezold-Zarisch reflex as cardiodepressor operated by peripheral mediated serotonin receptor (5-HT₃ type).² Ondansetron, a serotonin receptor antagonist has been shown to reduce spinal anaesthesia induced hypotension³ and granisetron induce faster sensory recovery.⁴ There is paucity of literature on comparative role of ondansetron and

granisetron to counter spinal anaesthesia induced haemodynamic effects and sensory regression time and further extensive studies can only produce robust evidence. Our study aims to compare role of ondansetron and granisetron in parturient mother.

Aim of the Study

1. To observe and compare the incidences of hypotension and bradycardia between the groups.
2. To observe and compare the time of regression of sensory and motor blockade after 0.5% hyperbaric bupivacaine induced spinal anaesthesia between the groups.
3. To observe any adverse events.

Materials and Methods

After obtaining Institutional Ethics Committee's approval, the study was conducted from January to May 2017 and 50

*Corresponding Author: Asoke Chakraborty, Professor, Dept. of Anaesthesiology, KPC Medical College & Hospital, Kolkata, West Bengal, India

Email: asokchakraborty65@gmail.com

<http://doi.org/10.18231/ijca.2019.063>

non-laboring women were included in the study. The inclusion criteria were older than 18 years, American Society of Anesthesiologists (ASA) physical status I or II, weighing more than 50 kg and less than 90 kg, height 145–165 cm, having uncomplicated singleton pregnancy beyond 36 weeks, scheduled to have elective caesarean section under spinal anaesthesia. Based on a previous study, the mean difference and the pooled standard deviation were calculated and the sample size was determined (25 in each group), with power of study being 80% and confidence interval being 99%.^{18/5} The exclusion criteria were foetal malpresentation, pregnancy-induced hypertension (PIH), hypertension, cardiac disease, renal disease, foetal anomaly, diabetes mellitus and patients on chronic medication. Written informed consent was obtained in their own language from every patient. Haemodynamic variables were noted and patients were advised for over night fasting. Standard monitoring done, baseline maternal haemodynamic variables were recorded.

Patients were randomly allocated into two groups by block randomization method, by using computer generated random numbers. Intravenous preloading was done with 15 ml/kg lactated Ringer's solution over 15 min in all patients. Group G received injection granisetron 1 mg diluted in 8 ml normal saline and group O received injection ondansetron 8 mg diluted in 8 ml of normal saline 5 min before spinal anaesthesia. A second anaesthesiologist who was not aware of the study protocol and random allocation administered injections to the patients. Spinal Anaesthesia was administered at L3-L4 or L4-L5 interspace with 26-G Quincke type needle in sitting or left lateral position. A dose of 12.5 mg hyperbaric 0.5% bupivacaine was injected over 10-15 seconds.

A third anaesthesiologist, blinded to the study, was keeping the records of haemodynamic changes, highest level of sensory block, regression of sensory and motor block as well as the incidence of any adverse effects.

After spinal injection, data [systolic blood pressure (SBP), diastolic blood pressures (DBP), heart rate (HR)] were taken every 3 minute for 15 minutes and every 5 minutes thereafter until the surgery ends. Hypotension was defined as decrease in MAP (mean arterial pressure) more than 20% from baseline. Bradycardia was defined as heart beat less than 50 beats / min.

Upper level of sensory block was observed after 5 minutes of spinal injection and every 5 minutes thereafter till upper level of sensory block reached T5 and surgery was started. Level of motor block was assessed every 2 minutes by Modified Bromage Score (MBS; 0 = able to lift legs; 1 = ability to flex knees but not the hip; 2 = unable to flex knees, but no problems with ankle movement; and 3 = no movement possible in any lower extremity joint). Regression of sensory block was defined as two segments regression below the highest level of sensory block. It was evaluated every 20 minutes after highest level of sensory block achieved till it regressed to S1. Regression of motor block was defined as achieving full motor power (Modified Bromage Score: 0) and was assessed at 20 min interval after

completion of surgery till complete recovery. Any adverse events like post operative nausea vomiting (PONV), shivering were noted.

Statistical Analysis

Data were plotted on Microsoft excel sheet. Numerical variables were compared between groups by Student's independent samples t test. Categorical variables were compared between groups by Fisher's exact probability test. Repeated measures ANOVA were employed for intra-group comparison of numerical variables. All analyses were 2-tailed. $P < 0.05$ was considered statistically significant.

Result

Fifty patients were recruited for the study. There was a failure of spinal anesthesia procedure in one patient, four patients did not cooperate in immediate post operative period, so response could not be noted and one patient developed post partum hemorrhage and thus were excluded from analysis.

Calculation was done having 22 patients ($n=22$) in each group. No significant differences were observed in demographic parameters between the two groups (Table 1). Regarding MAP those two groups were also comparable (Table 2). But in group G requirement of vasopressor were more than group O (Graph 1). In group O only 9 patients required single dose of injection mephentermine 5mg, whereas in group G 17 patients required injection mephentermine (5mg) and in multiple doses. This difference was statistically significant. Regarding changes in the heart rate no statistical significant difference was found between the groups (Table 3). There was not a single incidence of bradycardia. Onset of sensory block was comparable between the groups ($p = 0.024$). The regression up to S1 level was much faster in group G than group O (136.36 ± 17.87 versus 162.27 ± 15.09 , $p = < 0.0001$). The difference of regression of motor block was also statistically significant between G and (150 ± 20.70 versus 174.54 ± 21.97 , p value < 0.0001) group O. (Table 4).

Graph 1: comparison of requirement of vasopressor between the groups

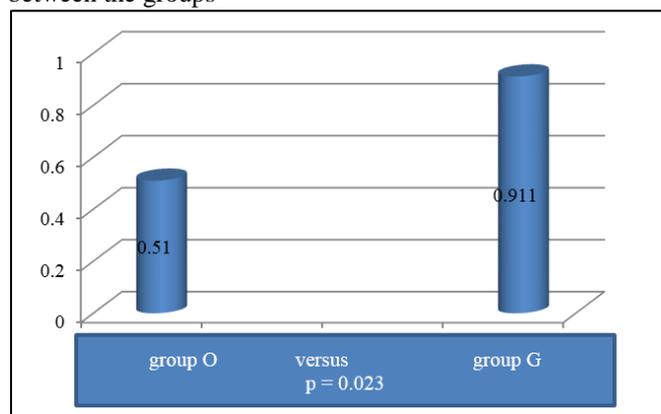


Table 1: Demographic parameters

Variable (Mean \pm SD)	Group 0	Group G	P value
Age (years)	25 \pm 3.436	24 \pm 3.548	0.849
Weight (kg)	52.5 \pm 5.369	55 \pm 5.042	0.776
Height (cm)	5.127 \pm 0.142	5.10 \pm 0.206	0.092
Duration of surgery	37.454 \pm 6.566	40.40 \pm 5.151	

Table 2: Comparison of MAP (Mean Arterial Pressure) between the groups

	MAP (mm of Hg) Basal	MAP (mm of Hg) 3min	MAP (mm of Hg) 6min	MAP (mm of Hg) 9min	MAP (mm of Hg) 12min	MAP (mm of Hg) 15min	MAP (mm of Hg) 20min	MAP (mm of Hg) 25min	MAP (mm of Hg) 30min
Group O	79.04 \pm 18.85	81.71 \pm 8.72	77.57 \pm 5.53	76.08 \pm 17.39	79 \pm 6.03	75.39 \pm 15.05	79.15 \pm 6.64	78.08 \pm 14.21	79.21 \pm 12.94
Group G	82.56 \pm 20.85	78.95 \pm 19.5	77.83 \pm 10.04	81.75 \pm 10.82	77 \pm 8.66	75.50 \pm 8.66	77.56 \pm 16.80	79.22 \pm 6.32	83.82 \pm 7.87
p value	0.5601	0.5484	0.9158	0.2012	0.3792	0.9768	0.6818	0.7327	0.1608

Table 3: Comparison of Heart Rate (beats/min) between the groups

	Heart Rate Basal	Heart Rate 3min	Heart Rate 6min	Heart Rate 9min	Heart Rate 12min	Heart Rate 15min	Heart Rate 20min	Heart Rate 25min	Heart Rate 30min
Group O	96.69 \pm 25.19	98 \pm 29.00	100 \pm 26.40	102.95 \pm 24.84	100.65 \pm 23.39	102.13 \pm 22.61	99.47 \pm 20.41	97.95 \pm 19.10	96.13 \pm 17.70
Group G	89.73 \pm 22.00	90.26 \pm 21.36	88.69 \pm 20.98	95.82 \pm 23.25	98.69 \pm 22.95	98.26 \pm 21.75	94.34 \pm 18.91	93.30 \pm 17.18	98.78 \pm 15.63
p value	0.334	0.319	0.123	0.331	0.780	0.600	0.392	0.400	0.643

Table 4: Comparison of sensory and motor block between the groups

	Onset of highest level of sensory block (in min)	Regression of sensory block up to S ₁ (in min)	Regression of motor block (in min)
Group O	10.45 \pm 2.63	162.27 \pm 15.09	174.54 \pm 21.97
Group G	12.27 \pm 2.55	136.36 \pm 17.87	150 \pm 20.70
P value	0.024	<0.0001	<0.0001

Discussion

Hypotension in spinal anaesthesia is due to sympathetic block, as the level of block must be upto T4 level, as well as due to the effect of gravid uterus on the venous return.^{5,6} Another mechanism for bradycardia and hypotension is hypovolaemia induced Bezold-Jarisch reflex (BJR). The Bezold-Jarisch Reflex is usually described as a cardioinhibitory reflex triggered by stimulation of intracardiac receptors and its consequences include bradycardia, vasodilatation, and hypotension. Earlier studies including animal studies have described Bezold-Jarisch reflex to be triggered by stimulation of 5-HT₃ receptors in vagal nerve endings, which have clinical implications^{2,7} and opened scope for further clinical studies. But there had been few studies showing reduction of spinal anaesthesia related adverse cardiovascular effects through blockade of 5-HT₃ receptors. Comparing 8mg of ondansetron with 1 mg of granisetron in our study gave a variable response on MAP. Hypotension occurred in few patients in both the groups, although that was not statistically significant. But the most interesting finding in our study was significant decrease in

use of vasopressors in patients who were given IV ondansetron prior to the initiation of spinal anaesthesia (p =0.0237). It corroborates with the finding of Radoslaw et al who found that 8 mg intravenous ondansetron attenuates the SBP and MAP drop in spinal anaesthesia.⁸ This property of ondansetron also matches with the study of Sahoo and associates although they used lesser dose.³ Both of these studies were placebo controlled study. Another study by Manal M. Rashad and his colleague revealed that IV ondansetron actually reduces the use of vaopressor in Caesarean Section.⁹ They used 4mg of injection ondansetron with 1mg of granisetron instead of 8 mg of ondansetron as in our study. Samra et al. used 4mg of injection ondansetron and 1mg of injection granisetron in their study and found that IV ondansetron did not affect sensory or motor block of intrathecal bupivacaine.¹⁰ It goes against the results of Fassoulaki et al. who found that systemic ondansetron enhance the sensory block regression after intrathecal lidocaine.¹¹ In our study we found that the onset of sensory block has no significant difference between the groups. But granisetron group had statistically significant regression of

sensory block than ondansetron group. The achievement of S1 sensation was much faster in patients receiving granisetron 1 mg. This result is similar to the finding of Manal M. Rashad et al.

Recovery of motor blockade was also faster in granisetron group than ondansetron group. It differs from the study of Manal M. Rashad who did not find any significant difference on motor block comparing 4mg of ondansetron with 1mg of granisetron.⁹

Ondansetron and granisetron although are from the same category and have the same mechanism of action, ondansetron acts on mixed receptors (5-HT, adrenergic, histaminic, dopaminergic, opioid receptors) but granisetron is selective 5HT3 receptor antagonist. So the studies comparing 4mg of ondansetron and 1 mg of granisetron showed the granisetron to be more superior in regression of sensory blockade. In our study we used 8 mg of injection ondansetron. In earlier studies 8mg dose of ondansetron has not been compared with granisetron. So this is a kind of exploratory study and further research is required to establish this.

Limitation of the study is small sample size, limited to only parturient female patients.

Conclusion

In parturient females undergoing elective cesarean section under spinal anaesthesia, intravenous 8 mg ondansetron significantly reduces the demand of vasopressors and granisetron 1 mg provides faster recovery from sensory and motor blockade.

Conflict of Interest: None declared.

Source of Funding: None.

References

1. Norris MC. Spinal anesthesia for cesarean delivery. In: Norris MC, editor. Handbook of Obstetric Anesthesia. 5th ed. Philadelphia: Lippincott Williams and Wilkins; 2000. pp. 309–12.
2. Campagna JA, Carter C. Clinical relevance of the Bezold–Jarisch Reflex. *Anesthesiol* 2003;98:1250–60.
3. Sahoo T, Sen Dasgupta C, Goswami A, Hazra A. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: A double-blind randomised, placebo-controlled study. *Int J Obstet Anesth* 2012;21:24–8.

4. Mowafi HA, Arab SA, Ismail SA, Al-Ghamdi A. The effects of intravenous granisetron on the sensory and motor blockade produced by intrathecal bupivacaine. *Anesth Analg* 2008;106(4):1322–5.
5. Russell IF. Levels of anaesthesia and intraoperative pain at caesarean section under regional block. *Int J Obstet Anesth* 1995;4:71.
6. Rocke DA, Rout CC. Volume preloading, spinal hypotension and caesarean section. *Br J Anaesth* 1995;75(3):257–9.
7. Sévoz C, Nosjean A, Callera JC, Machado B, Hamon M, Laguzzi R. Stimulation of 5-HT₃ receptors in the NTS inhibits the cardiac Bezold-Jarisch reflex response. *Am J Physiol* 1996;271(1):H80–87.
8. Radoslaw O, Wojciech W, Agnieszka P, Pawel T, Renata A, Anna D, et al. Ondansetron given intravenously attenuates arterial bloodpressure drop due to spinal anesthesia. *Reg Anesth Pain Med* 2008;33:332–9.
9. Manal M. Rashad, Manal S. Farmawy. Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section. *Egyptian J Anaesth* 2013;29:369–74.
10. Samra T, Bala I, Chopra K. Effect of intravenous ondansetron on sensory and motor block after spinal anaesthesia with hyperbaric bupivacaine. *Anaesth Intens Care* 2011;39:65–8.
11. Fassoulaki A, Melemani A, Zotou M, Sarantopoulos C. Systemic ondansetron antagonizes the sensory block produced by intrathecal lidocaine. *Anesth Analg* 2005;100:1817–21.

How to cite this article: Ray D, Saha M, Chakraborty A, Mandal MC. Comparison of injection ondansetron with granisetron on maternal haemodynamics and regression of sensory and motor blockade in elective caesarean section: A randomised non inferiority exploratory trial. *Indian J Clin Anaesth* 2019;6(3):328–31.