Original Research Paper

Volume - 11 | Issue - 01 | January - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anesthesiology

EFFECT OF INTRAVENOUS ONDANSETRON AND GRANISETRON ON POST SPINAL HYPOTENSION IN PARTURIENTS UNDERGOING CESAREAN SECTION UNDER SPINAL ANAESTHESIA.

Dr Aparna Bagle — Professor, Dept of anaesthesia , Dr D Y Patil Medical College, Dr D Y Patil Veedypeeth, Pimpri, Pune, Maharashtra, India. Pincode 411018.

Dr Tripti Nagdev — Senior Resident, Dept of anaesthesia, Dr D Y Patil Medical college, Dr D Y Patil Veedypeeth, Pimpri, Pune Pimpri, Pune, Maharashtra, India. Pincode 411018.

Dr Shivani Shrirang Phansalkar* — Postgraduate third year resident, Anaesthesiology department, Dr. D. Y. Patil Medical College and Hospital and Research Centre, Pimpri, Pune, 411018. *Corresponding Author

ABSTRACT

Background: Spinal anaesthesia related triggering of Bezold-Jarisch reflex is known to result from stimulation of 5-HT3 receptors in vagal nerve endings. The goal of this study was to compare the effect of two serotonin receptor antagonists (Ondansetron and Granisetron) on hemodynamics in parturients undergoing caesarean section under spinal anaesthesia.

Methods: Double blind randomized control trial was done on 60 parturients aged between 20-40 years scheduled for elective caesarean section, divided into two groups containing 30 patients each. After preloading with Ringer Lactate 10ml/kg body weight, baseline heart rate(HR), arterial oxygen saturation (SpO2) , systolic blood pressure (SBP) , diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were recorded.Group O received 4mg ondansetron diluted in 10 ml normal saline and group G received1mg granisetron diluted in 10 ml of normal saline intravenously and drug injected over 1 minute.Subarachnoid block with 2ml 0.5% hyperbaric bupivacaine was given after 5 minutes. HR, SBP, DBP and MAP were recorded every 3 minutes for first 15 minutes and then every 5 minutes till the end of surgery. Time to attain highest sensory and motor block, intraoperative blood loss, regression of block and side effects were noted.

Results: Fall in MAP and vasopressor requirement was significantly less in group G as compared to group O. Two segment sensory level regression was faster in group G than group O. Time to achieve highest sensory block was significantly less in group O as compared to group G. Time to achieve complete motor block, intraoperative blood loss and side effects were comparable in both the groups.

Conclusion: Prophylactic use of iv granisetron was better for prevention of post spinal hypotension in caesarean section patients as compared to iv ondansetron , though faster recovery of sensory block was noticed with granisetron.

KEYWORDS : Ondansetron, Granisetron, Spinal anaesthesia, Cesarean section.

INTRODUCTION

Spinal anaesthesia is a popular technique for caesarean section as it is easy to perform and provides a rapid-onset, dense surgical block. Spinal anaesthesia has low failure rate, low drug requirement and no maternal or fetal risk of local anaesthetic toxicity.[1,2] Spinal anaesthesia is frequently associated with hypotension and bradycardia, which may be deleterious to both parturient and baby.[3,4,5] Hypotension can cause loss of consciousness, aspiration and even cardiac arrest in the mother. Hypotension can also lead to placental hypoperfusion and fetal problems.[6] Various preventive methods are currently used to prevent or minimize hypotension, including left uterine displacement, crystalloids or colloid preloading, and utilizing compression stocking on the lower extremities.[7]

This study concentrates on the effect of two medications (Ondansetron and Granisetron) on maternal hypotension after spinal anaesthesia. Ondansetron and Granisetron are selective 5-hydroxytryptamine 3 (5-HT3) receptor antagonists.[8] These receptors are located peripherally as cardiac chemoreceptors on the cardiac vagal afferent and centrally in the chemoreceptor trigger zone.[9] The decrease in preload caused by spinal anaesthesia may initiate vagally mediated cardiodepressor reflexes, the Bezold Jarisch Reflex, which may be mediated by peripheral serotonin receptors (5-HT3 type).[10]

Stimulation of cardiac chemoreceptors in the heart by decreased venous return increases the parasympathetic activity, decreases the sympathetic activity resulting in vasodilatation and bradycardia.[11] Hypotension results primarily from decreased vascular resistance, whereas bradycardia is secondary to a relative parasympathetic dominance, increased baroreceptor activity or induction of the Bezold–Jarisch reflex (BJR).[12]

Hence primary objective of study was aimed to compare the efficacy of two serotonin receptor antagonists ondansetron and granisetron for preventing post spinal hypotension after spinal anaesthesia in parturients undergoing cesarean section. The secondary objective was to determine effect on sensory and motor blockade after intrathecal hyperbaric bupivacaine and any adverse effects in perioperative period.

MATERIAL AND METHODS

After approval from the institutional ethics committee this study was conducted in sixty pregnant women, ASA I-II physical status, aged from 20-40years scheduled for elective caesarean section were enrolled in the study. Patients with contraindication for neuraxial block like coagulation defects, history of hypersensitivity to ondansetron/ granisetron or local anaesthetics,cardiovascular insufficiency, disturbed hemodynamics, on selective serotonin reuptake inhibitors or patient refusal were excluded from the study. All patients were kept nil by mouth for 6 hours preoperatively. Informed written consent was taken from all the patients. In the operation theatre, all the monitors were attached. A 20G IV cannula was inserted into the dorsum of the non dominant hand and all patients were preloaded with Ringer's lactate solution 10ml/kg body weight. Baseline heart rate (HR), systolic blood pressure (SBP) , diastolic blood pressure (DBP) , mean arterial pressure (MAP) , oxygen saturation (SpO2) and ECG were recorded.

Patients were randomly allocated by lottery method into two equal groups containing 30 patients each. Group O received 4mg ondansetron diluted in normal saline upto 10ml. Group G received 1mg granisetron diluted in normal saline upto 10ml, given slowly intravenously over 5mins before spinal anaesthesia.

Spinal anaesthesia was given in the sitting position at the level L3-L4 with a 26-gauge Quincke needle. After free flow of cerebrospinal fluid, 2ml 0.5% hyperbaric bupivacaine was injected intrathecally. Then patient placed in supine position with wedge under right buttock. A resident anaesthesiologist blinded to the study drug, measured and recorded the hemodynamic parameters, sensory and motor blockade. HR, SBP, DBP and MAP recorded every 3 minutes for first 15 minutes and then every 5 minutes till surgery ends. Time to attain highest sensory and motor block, intraoperative blood loss were recorded. Two segment regression of sensory block, presence of nausea, vomiting and shivering was noted .Decrease in MAP more than 20% of pre operative value, was considered as hypotension and treated with vasopressor. The height of sensory level was assessed as the highest dermatome every minute using an alcohol swab in midclavicular line till the fixation of level at two consecutive times. Then postoperatively patient was evaluated every 15 minutes till the two segment regression of

sensory level. The time to upper sensory block was defined as the time between intrathecal injection and achievement of the highest level of sensory blockade. Two-segment regression was defined as the time between achievement of the highest level of sensory blockade and its regression to a level two segments down. Also, motor block was assessed every 2 minutes by the modified bromage scale till the complete motor block then postoperatively every 15 minutes till complete motor recovery .

Any complication such as bradycardia was treated with i.v. 0.6mg atropine , nausea and vomiting were treated with i.v. 10mg metoclopramide , and shivering was treated with i.v. 50 mg tramadol. Ifdesired sensory blockade failed to achieve by 10 minutes, it was considered as failed spinal and the patient was excluded from the study. Modified Bromage scale. [13]

0 Able to move hip, knee, ankle and toes
1 Unable to move hip , able to move knee , ankle and toes.
2 Unable to move hip and knee, able to move ankle and toes
3 Unable to move hip, knee and ankle , able to move toes
4 Unable to move hip , knee , ankle and toes .

STATISTICALANALYSIS

Data was recorded in preformed data collection sheet. All data were entered in Microsoft office Excel worksheet 2007. For the analysis of the data, Statistical Package for the Social Science (SPSS) was used. Data was expressed as mean ± SD for variables, numbers and percentage for categorical variables. Independent t test was used for quantitative comparison between two groups.
P value less than 0.05 was considered significant.

RESULTS

There was no significant difference between the two groups with respect to demographic data (age , weight , height , ASA physical status and duration of surgery).

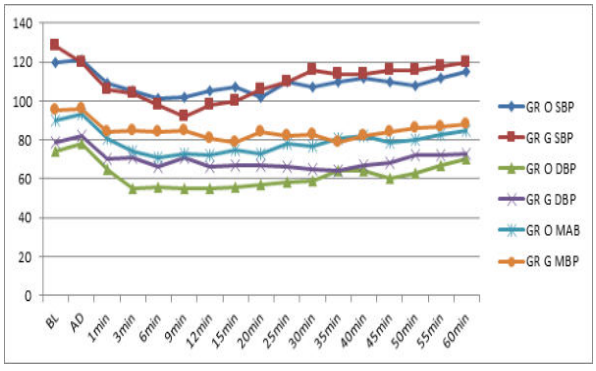
There was no significant difference among the two groups as regard to basal HR, SBP, DBP and MAP. After induction of spinal anaesthesia, fall in SBP was more in group G as compared to group O at 1, 3, 6, 12 and 15 minutes. (Graph 1). Those in group O had significantly lower MAP between 3to 60 minutes. The fall in diastolic blood pressure in group O was greater than group G from 3 minutes till end of surgery. (Graph 1). There was no significant difference in heart rate among both the groups.

The number of hypotensive episodes were more in group O than group G. (figure 2).

All were managed with fluid bolus and ephedrine IV 6 mg bolus. On comparing the need for ephedrine as a rescue vasopressor, significant difference was seen among the groups, with more number of parturients who needed vasopressor being in group O. (figure 3).

Both the groups were comparable in respect to highest sensory level achieved, time of fixation of sensory level and complete motor block.

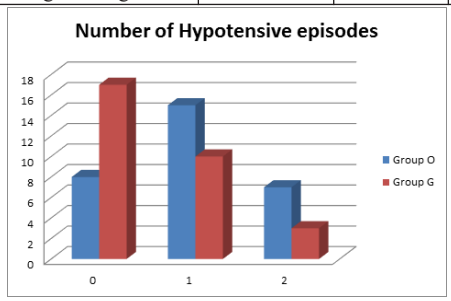
However, significantly faster two segment regression was observed in group G (95±12.04 minutes) as compared to group O (110.83±18.44 minutes). Oxygen saturation did not change significantly in both groups. No patient in both groups suffered from nausea, vomiting, shivering or pain. There was no incidence of bradycardia in both the groups.



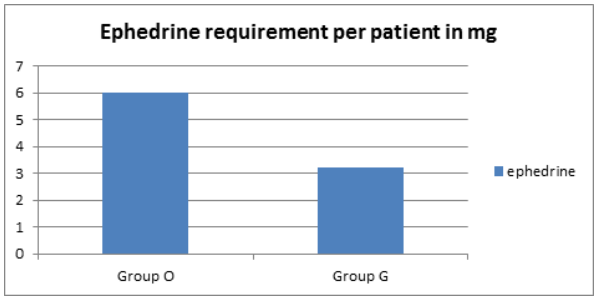
Graph 1Intraoperative blood pressure changes in both the groups

Table no 1 Characteristics of spinal anaesthesia

Variable	Group O	Group G	P value
Highest sensory level(T)	6.27+/-1.12	6.06+/-0.99	0.445
Time to Highest sensory level(min)	5.33+/- 1.71	5.53+/-1.45	0.08
Time to complete motor block	6.24+/-2.67	6.58+/-2.89	0.65
Time to 2 segment regression	110.83+/-18.44	95+/-12.04	<0.001



Graph 2 Number of Hypotensive episodes



Graph 3 Ephedrine Requirement/patient

DISCUSSION

Studies have revealed the effectiveness of different strategies for the prevention of spinal anaesthesia induced hypotension such as pre or co-loading of IV fluid, use of vasopressors and compression devices. [14, 15, 16] However, a Cochrane review concluded that none of these techniques alone was sufficient in eliminating hypotension. [7] This double blind randomized controlled study was designed to test the effectiveness of pretreatment with intravenous anti emetics, Granisetron and Ondansetron as regard their effects on blood pressure changes, sensory , and motor block of spinal anaesthesia given to parturients as both medications have the same mechanism of action.

Animal Studies clarified that serotonin has antinociceptive effect at the spinal cord level by inhibiting the excitatory transmitters and increasing the inhibitory transmitters. [17, 18] Serotonin antagonists also decrease the nociceptive threshold as proved by Giordano and Dyche. [19]

Spinal anaesthesia for caesarean section may cause hypotension, which can jeopardize the fetus and the mother . [20] Hypotension occurs frequently during spinal anesthesia. Physiologic research indicated that hypotension results from peripheral pooling of blood that decrease venous return to the heart and decrease cardiac output from a decrease in systemic vascular resistance or from a combination of both. [21]

Our results disagree with those of Fassoulaki et al, who reported that systemic ondansetron, caused a faster regression of the sensory block after spinal. [22] Our results were similar to study by White Cm et al , that grainsteron was effective in preventing paradoxical bradycardia and preventing a fall in the systolic blood pressure(SBP) due to bleeding. [23]

In a study by Mowafi et al They found that IV granisetron facilitated a faster recovery of the sensory block but not motor block after bupivacaine subarachnoid anesthesia which correlated with our study. [24]

In contrast to ondansetron, which acts on mixed receptors, Granisetron strongly and selectively binds to the 5-HT3 receptors with minimal or no affinity for other 5-HT receptors, dopaminergic, adrenergic, histaminic or opioid receptors. [25]

In our study, the fall in SBP, DBP was less in group G. The number of hypotensive episodes were also less in group G as compared to group O and the requirement of ephedrine also was less in group G. Faster recovery of sensory bloackade was found in the granisetron group.

Regarding the **limitations** of the study, oscillatory method was used for noninvasive blood pressure measurements but invasive blood pressure monitoring would give more precise assessment of haemodynamic changes. Different dose granisetron were not compared. Non invasive cardiac output monitor would have been better parameter to monitor hemodynamic changes but we could not do it, due to unavailability at our institute.

CONCLUSION

IV granisetron as a pre medication better attenuates hypotension in parturients undergoing LSCS.

REFERENCES

1. GlostenB. Anaesthesia for obstetrics .In : Miller RD ,editor. Anaesthesia .Philadelphia :Churchill Livingstone:2000.
2. LoubertC. Fluid and vasopressor management for Cesarean delivery under spinal anaesthesia : continuing professional development. Can J Anaesth 2012;59:604-619.
3. SahooT, 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;21:24-28.
4. Ben David B, Miller G, Gavriel R, Gurevitch A. Low–dose bupivacaine-fentanyl spinal anesthesia for caesarean delivery.Reg Anesth Pain Med 2000;25:235-9.
5. Choi DH, Ahn HJ,Kim MH .Bupivacaine-sparing effect of fentanyl in spinal anaesthesia for Caesarean delivery .Reg Anesth Pain Med 2000;25:240-5.
6. Mebaza MS, Ouerghi S, Meftah RB. Reduction of bupivacaine dose in spinal anaesthesia for caesarean section may improve maternal satisfaction by reducing incidence of low blood pressure episodes. MEJ Anesth 2010;20(5):673-8.
7. Cyna AM, Andrew M, Emmett RS, Middle town P, Simmons SW. Techniques for preventing Hypotension during spinal anesthesia for caesarean section. Cochrane Data base Syst Rev 2006;18:4.
8. Van Winjngaar den I, Tulp MT, Soudijn W. The concept of selectivity in 5-HT receptor research. Eur J Pharmacol 1990; 188:301-312.
9. Martik RM. Witnessed asystole during spinal anaesthesia treated with atropine and ondansetron: a case report. Can J Anesth 2004; 51(3):226-30.
10. Campagna JA, Carter C. Clinical relevance of the Bezold–Jarisch Reflex. Anesthesiology 2003; 98: 1250-60.
11. Kinsella SM, Tuckey JP. Perioperative bradycardia and asystole: relationship to vasovagal syncope and the Bezold-Jarisch reflex. Brit J Anesth 2001; 86(6):869-68.
12. Liu SS, McDonald SB. Current issues in spinal anesthesia. Anesthesiology 2001; 94: 888–906.
13. Martin-salvajG, Van Gessel E, Forster A, Schweizer A, Iselinchaves I, Gamulin Z. Influence of duration of lateral decubitus on the spread of hyperbaric tetracaine during spinal anaesthesia : a prospective time – response study. Anesth Analg1994;79: 1107-12.
14. Buggy D, Higgins P, Moran C,O Brien D,O Donovan F, McCarroll M. Prevention of spinal anesthesia – induced hypotension in the elderly : comparison between pre anesthetic administration of crystalloids , colloids, and no prehydration. Anesth Analg 1997;84:106-10.
15. Hemmingsen C, Poulsen JA, Ribso A. Prophylactic ephedrine during spinal anaesthesia: double blind study in patients in ASA group I-III. Br J Anaesth 1989:63:340-2.
16. Adsumelli RSN , Steinberg ES, Saunders TA ,Poppers PJ. Sequential compression device with thigh –high sleeves supports mean arterial pressure during Caesarean section under spinal anaesthesia. Br J Anaesth 2003:91:695-8.
17. Xu W,Qiu XC,Han JS. Serotonin receptor subtypes in spinal antinociception in therat . J Pharmacol ExpTher1994;269: 1182-9.
18. Yoshimura M, Furue H. Mechanisms for the antinociceptive actions of the descending noradrenergic and serotonergic systems in the spinal cord. J Pharmacol Sci 2006;101: 107-117 .
19. Giordano J,Dyche J. Differential analgesic action of serotonin 5-HT3receptor antagonists in three patients. Neuropharmacology1989;28:431-4.
20. Klohr S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anaesthesia for caesarean section : literature search and application to parturient. Acta Anaesthesiol Scand 2010; 54: 909-921.
21. Critchley LA, Conway F. Hypotension during subarachnoid anaesthesia: Haemodynamic effects of colloid and metaraminol. Br J Anaesth 1996;76:734-6.
22. Fassoulaki A, Melemeni A, Zotou M, Sarantopoulos C. Systemic ondansetron antagonizes the sensory block produced by intrathecal lidocaine. Anesth Analg.2005;100(6):1817-21.
23. White CM, Chow MS, Fan C, Kluger J, Bazunga M. Efficacy of intravenous Granisetron in suppressing the bradycardia and hypotension associated with a rabbit model of the Bezold-Jarisch reflex. J Clin Pharmacol 1998; 38:172-7.
24. Mowafi HA, Arab SA, Ismail SA, Al-Ghamdi A. The effects of intravenous Granisetron on the sensory and motor blockade produced by intrathecal bupivacaine. AnesthAnalg.2008;106(4):1322-5.
25. Blower P. A pharmacologic profile of oral Granisetron (Kytril tablets). Semin Oncol.1995; 22 (4Suppl10): 3-5.