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Original Research Article

Ondasetron and its effects on haemodynamics during LSCS under regional anaesthesia- A Randomized double blind controlled trial

Sahil Garg[1], Hersimran Kaur[2]*, Madhav Choudhary[2], Ashita Rukmini[2], Neha Jha[2], Pankaj Kumar[2]

[1]*Dept. of Anaesthesia and Intensive Care, PGIMER, Satellite Centre, Sangrur, Punjab, India*
[2]*Dept. of Anaesthesiology & Critical Care, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Haryana, India*

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ABSTRACT

Introduction: Subarachnoid block (SAB) is also known as the method of choice of anaesthesia for lower segment caesarean section. The most common complications associated with it include hypotension and bradycardia. Ondansetron, now days is emerging as an effective alternative for the prevention of spinal induced hypotension in elective LSCS patients.

Aims & Materials and Methods: Our aim was to analyse & study the effect of Ondansetron 6mg I.V. on hemodynamics in lower segment caesarean section (LSCS) under regional anaesthesia. Study was conducted on a total of 60 parturients divided into 2 groups (Group I & Group II) scheduled for elective lower segment cesarean sections under Subarachnoid block.

Results: Comparison of mean heart rate between the Group I and Group II was found to be statistically not significant ($p>0.05$) at all the time intervals. The difference was found to be statistically significant ($p=0.001$), showing significantly higher intraoperative fluid requirement in Group II in comparison to Group I.

Conclusion: We observed that ondansetron 6mg I.V. given as a premedication 15 minutes before the administration of SAB resulted in a lesser incidence of hypotension following SAB.

1. Introduction

Subarachnoid block (SAB) is known as the ideal method of choice of anaesthesia for lower segment caesarean section.[1,2] It has rapid onset of sensory and motor blockade, decreased systemic analgesic requirement, provision of excellent muscle relaxation during surgery and substantial pain relief in the post operative period.

The most common complications associated with it include hypotension and bradycardia with a reported incidence of 33 % and 13% respectively for non-obstetric population and up to 50-60% in obstetric population.[3] This may be a major contributory factor for maternal morbidity and mortality related to regional anaesthesia.

The Bezold Jarisch Reflex (BJR) is also known to contribute to hypotension and bradycardia induced by SAB. It was introduced by Von Bezold in 1867. It is mediated by serotonin receptors (5-HT3 subtype) present on the vagus nerve and within the walls of cardiac ventricles.

Till date, vasopressors have remained the mainstay of management of SAB induced hemodynamic instability along with fluid preloading or co-loading. Ephedrine and phenylephrine are the most common drugs used to treat SAB induced hypotension. Though both vasopressors reliably raise maternal blood pressure, drug-associated discomfort especially due to tachycardia, bradycardia and intraoperative nausea, and vomiting cannot be

* *Corresponding author*.
E-mail address: hersimran89mbbs@gmail.com (H. Kaur).

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overlooked.[4–8]

The present data available regarding the utility of ondansetron for blunting of hemodynamic changes during SAB for elective caesarean section has been contradictory. If the efficacy of ondansetron is proved, it may be used successfully as a prophylactic agent to prevent SAB induced hypotension and bradycardia without the side effects of vasoactive drugs which are quite severe as compared to diarrhoea, headache, constipation, weakness, fever, tiredness and dizziness which are commonly associated with the use of ondansetron.[9–12]

2. Aims and Objectives

To study intravenous ondansetron and its effects on hemodynamics in lower segment caesarean section (LSCS) under regional anaesthesia.

2.1. Primary outcome

1. HR & BP in the two groups from start of SAB till the delivery of baby.

2.2. Secondary outcome

1. Total amount of I.V. fluid given
2. Amount of vasopressors used
3. Amount of Atropine used
4. APGAR score at 1 minute and 5 minutes

3. Materials and Methods

A Randomised double blind prospective study was conducted in Bombay hospital, Indore (2019-2020) on a total of 60 parturients belonging to American Society of Anesthesiologists' (ASA) grade II scheduled for elective lower segment cesarean sections under Subarachnoid block after approval from ethical committee. Informed consent was taken from all the patients before the procedure. Parturients were allocated randomly into two groups: Group I: Parturients received 6 mg (3ml) ondansetron diluted to 10 ml of 0.9 % normal saline 10 minutes before administration of SAB. Group II: Parturients received 10 ml of 0.9% normal saline 10 minutes before administration of SAB.

Parturients undergoing elective lower segment caesarean section under SAB and ASA grade II patients were included in the study. Patients with history of pregnancy induced hypertension, uncontrolled diabetes mellitus, cardiac disease, Known allergy to ondansetron were excluded from the study.

Pre anaesthetic check up was conducted prior to surgery comprising of detailed history, general physical and systemic examination of all patients. Routine investigations included complete haemogram, coagulation, renal function tests, ECG, blood grouping & cross matching.

After shifting the patient to OT, routine multipara monitor was attached to record ECG, NIBP, SPO2. The parturient was allocated into one of the two groups by random envelope generated allocations. The syringe was filled with the study drug by an anaesthesiologist who was not a part of the study. Group I, the ondansetron group, received 6 mg ondansetron diluted to 10 ml of 0.9 % normal saline. Group II, the placebo group received 10 ml of 0.9% normal saline.

4. Observations and Results

Demographic variables i.e. age, weight, BMI between two groups were comparable (P>0.05)(Table 1). All the baseline hemodynamic parameters viz. heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate and oxygen saturation were found to be statistically not significant (p>0.05)(Table 2). The comparison of mean heart rate between the Group I and Group II was found to be statistically not significant (p>0.05) at all the time intervals (Figure 2). The comparison of mean systolic blood pressure between the two groups at Basal, Drug Delivery, 5 minutes and 10 minutes was statistically not significant (p>0.05), while the mean systolic blood pressure at SAB, Incision time, 2 minutes, 4 minutes, 6 minutes, 8 minutes, 10 minutes and 12 minutes was significantly higher in Group I in comparison to Group II (p<0.05). Again at 14 minutes, 16 minutes, 18 minutes, 20 minutes post incision, the mean systolic blood pressure was also not statistically significant (p>0.05)(Figure 3). The mean diastolic blood pressure at basal, drug delivery, 5 minutes and 10 minutes was statistically not significant (p>0.05), while the mean diastolic blood pressure at SAB, incision time, 2 minutes post incision, 4 minutes, 6 minutes, 8 minutes, 10 minutes and 12 minutes post incision was significantly higher in Group I in comparison to Group P (p<0.05). Again the mean diastolic blood pressure at 14 minutes post incision, 16 minutes, 18 minutes, 20 minutes post incision was statistically not significant (p>0.05)(Figure 4). The mean MAP at Basal, drug delivery, 5 minutes and 10 minutes between Group I and Group II was found to be statistically not significant (p>0.05), while it was significantly higher at SAB, Incision time, 2 minutes post incision, 4 minutes, 6 minutes, 8 minutes, 10 minutes and 12 minutes post incision in Group I in comparison to Group II (p<0.05). Again the mean MAP at 14 minutes, 16 minutes, 18 minutes, 20 minutes and post incision between Group I and Group II was found to be statistically not significant (p>0.05)(Figure 5). The mean respiratory rate at Basal, drug delivery, 5 minutes, 10 minutes, SAB, incision time, 2 minutes post incision, 4 minutes, 6 minutes, 8 minutes, 10 minutes, 12 minutes, 14 minutes, 16 minutes, 18 minutes, 20 minutes post incision between the Group I and Group II was found to be statistically not significant (p>0.05)(Figure 6).

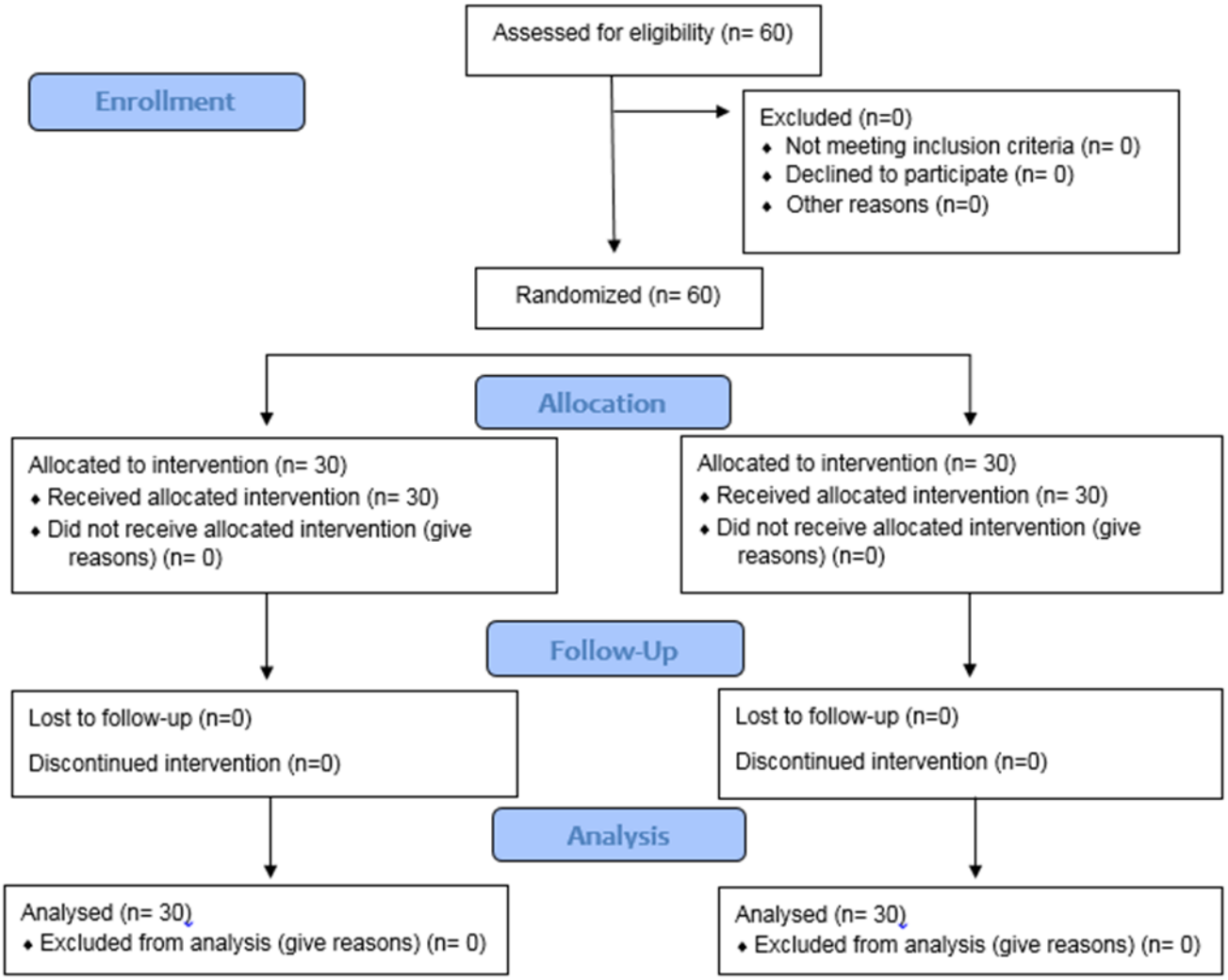

Figure 1: Consort flow diagram showing distribution of patients.

The comparison of mean oxygen saturation at basal, drug delivery, 5 minutes, 10 minutes, SAB, incision time, 2 minutes post incision, 4 minutes, 6 minutes, 8 minutes, 10 minutes, 12 minutes, 14 minutes, 16 minutes, 18 minutes, 20 minutes post incision between Group I and Group II was found to be statistically not significant (p>0.05)(Figure 7). The mean intraoperative fluid requirement in the Group I was 1690.33 ± 140.04 ml, while in the Group II was 2196.67 ± 135.15 ml.

The difference was found to be statistically significant (p=0.001), showing a significantly higher intraoperative fluid requirement in Group II in comparison to Group I($). The mean intraoperative blood loss in Group I was 889.00 ± 94.29 ml and in Group II was 924.00 ± 67.75 ml. The difference was found to be statistically not significant (p=0.104)(Table 4). The mean Apgar score in Group I was 8.43 ± 0.50 and in Group II was 7.57 ± 0.63. The difference was found to be statistically significant (p=0.001), showing a significantly lower Apgar score at 1 minute in Group II in comparison to Group I(Table 5). The mean phenylephrine dose in Group I was 20.00 ± 0.00 μg and in Group II it was 25.00 ± 9.05 μg. The difference was found to be statistically not significant (p=0.201)(Table 6). The mean atropine dose in Group I was 0.00 ± 0.00 mg and in Group II it was 0.02 ± 0.00 mg. The difference could not be calculated as in Group I, none of the patients had not received any dose of atropine (Table 7).

Table 1: Comparison of demographic data between two groups.

Demographic data	Group I	Group II	P Value
Age	30.07 ± 6.17	30.60 ± 8.08	0.775
Weight	53.90 ± 7.93	54.10 ± 8.10	0.923
BMI (kg/m^2)	22.17 ± 2.47	23.08 ± 4.37	0.325

Table 2: Comparison of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate and oxygen saturation at baseline.

Parameter	Group O [Mean±SD]	Group P [Mean±SD]	P value
Heart Rate	103.23 ± 10.11	99.00 ± 7.27	0.068
Systolic Blood Pressure	122.53 ± 9.02	119.90 ± 8.30	0.244
Diastolic Blood Pressure	73.53 ± 8.05	76.83 ± 9.23	0.145
Mean Arterial Pressure	89.87 ± 7.86	91.19 ± 8.11	0.527
Respiratory Rate	21.27 ± 2.73	22.67 ± 3.57	0.093
Oxygen Saturation	98.40 ± 1.45	98.53 ± 2.08	0.774

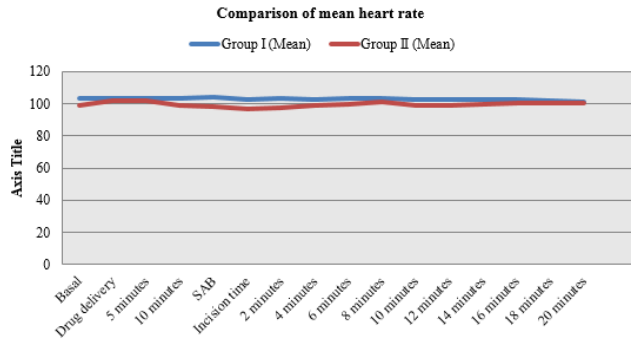

Figure 2: Line diagram showing comparison of mean heart rate between Group I and Group II at different time intervals.

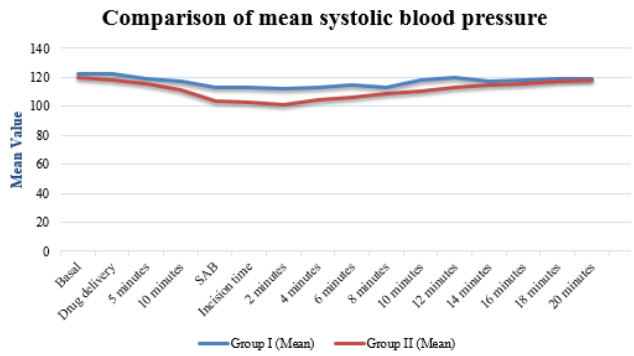

Figure 3: Line diagram showing comparison of mean systolic blood pressure between Group I and Group II at different time intervals.

Table 3: Comparison of mean intraoperative fluid requirement.

Group	Number	Intraoperative Fluid Requirement(ml) [Mean ± SD]	P value
Group I	30	1690.33 ± 140.04	0.001*
Group II	30	2196.67 ± 135.15	

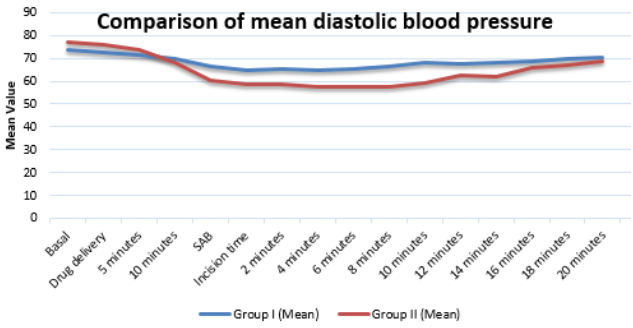

Figure 4: Line diagram showing comparison of mean diastolic blood pressure between Group I and Group II at different time intervals.

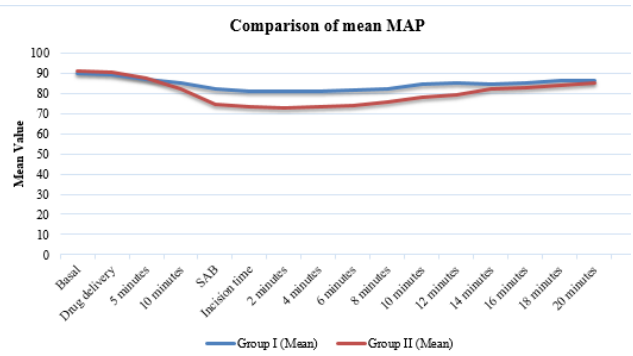

Figure 5: Line diagram showing comparison of mean MAP between Group O and Group P at different time intervals.

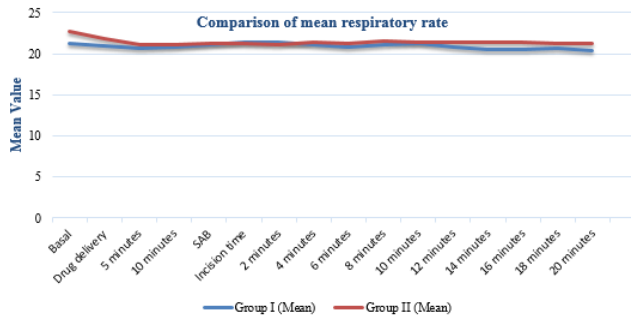

Figure 6: Line diagram showing comparison of mean respiratory rate between Group O and Group P at different time intervals.

Table 4: Comparison of mean intraoperative blood loss.

Group	Number	Intraoperative Blood Loss(ml) [Mean ± SD]	P value
Group I	30	889.00 ± 94.29	0.104
Group II	30	924.00 ± 67.75	

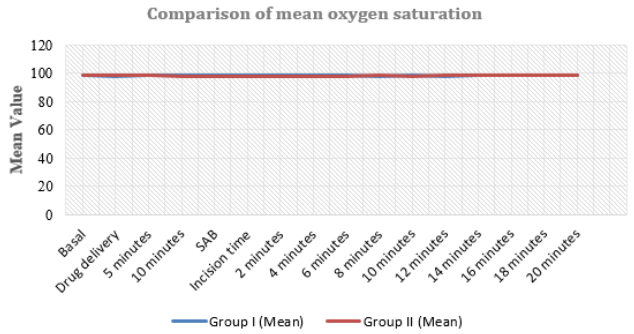

Figure 7: Line diagram showing comparison of mean oxygen saturation between Group O and Group P at different time intervals.

Table 5: Comparison of mean apgar scores.

Group		Number	[Mean ± SD]	P value
Apgar at 1 minute	Group I	30	8.43 ± 0.50	0.001*
	Group II	30	7.57 ± 0.63	
Apgar at 5 minute	Group I	30	8.47 ± 0.68	0.384
	Group II	30	8.33 ± 0.48	

Table 6: Comparison of mean phenlephrine dose between Group I and Group II.

Group	Number	Phenylephrine (μg) [Mean ± SD]	P value
Group I	6	20.00 ± 0.00	0.201, NS
Group II	12	25.00 ± 9.05	

Table 7: Comparison of mean atropine dose between Group I and Group II.

Group	Number	Atropine (mg) [Mean ± SD]	P value
Group I	0	0.00 ± 0.00	-
Group II	1	0.02 ± 0.00	

5. Discussion

SAB for cesarean sections produces vasodilation, hypotension and bradycardia by sympathetic blockade, the BJR and via stimulation of 5-HT_3 receptors in vagal nerve endings. In the present study, it was postulated that ondansetron which is a 5-HT3 receptor antagonist can prevent SAB induced bradycardia and hypotension by preventing serotonin induced BJR.[13–16] Blockade of 5-HT 3 receptors in the vagal nerve endings antagonises the BJR induced by serotonin released from activated thrombocytes. It also suppresses venodilation and increases the venous return to the heart hence causing lesser reduction in SBP, MAP, DBP and HR.[17] On the other hand, higher doses might be associated with lactic acidosis in the fetus. In our study, ondansetron was given 15 minutes before the initiation of SAB as compared to 5 minutes in other studies as the peak effect of intravenous ondansetron is achieved at 10 minutes. A study by Terkawi, et al. concluded that they could not achieve attenuation of fall in SBP, DBP, MAP or HR with ondansetron as it was given 5 minutes before the administration of SAB and thus peak effect of the drug was not achieved.[18] However, none of these studies reported a statistically significant effect of ondansetron on DBP which was observed in our study.

Difference in mean APGAR score at 1 minute between the 2 groups was statistically significant (p=0.013). Our findings were consistent with the results of Trabelsi, et al. who observed higher APGAR scores in the ondansetron group until 5^{th} minute after birth when compared to a placebo. They also observed lower lactate levels in newborns whose mothers belonged to the ondansetron group and the pH of blood from the umbilical artery was also closer to the physiological ranges.[19] This has been a major limitation in our study as we did not perform a blood gas analysis of cord blood due to institutional protocols and cost containment. Contrary to our results, Wang M, et al. observed insignificant differences in the APGAR scores at 1 and 5 minutes among the 5 groups receiving different doses of ondansetron or a placebo.[20]

6. Conclusion

We observed that intravenous ondansetron 6 mg given as a premedication 15 minutes before the administration of SAB resulted in a lesser incidence of hypotension following SAB. The neonatal outcomes were also better with the use of ondansetron as evidenced by better APGAR scores at 1 minute in the ondansetron group.

7. Limitations of the study

1. We couldn't comment upon its effect on HR due to an infrequent occurrence of bradycardia in our study population.
2. We also did not study the effect of ondansetron for prevention of perioperative shivering

8. Declaration of Patient Consent

Written informed consent were taken from all patients before collection of data.

9. Conflict of Interest

None.

10. Source of Funding

None.

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Author biography

Sahil Garg, Assistant Professor

Hersimran Kaur, Assistant Professor

Madhav Choudhary, Junior Resident

Ashita Rukmini, Junior Resident

Neha Jha, Junior Resident

Pankaj Kumar, Junior Resident

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