ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 09 | September - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY OF EFFECT OF INTRAVENOUS ONDANSETRON IN ATTENUATION OF SPINAL INDUCED HYPOTENSION IN CAESAREAN SECTION - A PROSPECTIVE RANDOMISED CONTROLLED DOUBLE BLINDED STUDY

Anesthesiology

Dr. Navin Kumar K* PG student, Dept of anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan – 326001, Affiliated to RUHS. * Corresponding Author

Dr. Asha Sharma Assistant professor, Dept of anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan – 326001, Affiliated to RUHS.

Dr. Manesh Kumar Kumawat Senior resident, Dept of anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan – 326001, Affiliated to RUHS.

Dr. Suresh Pandey Senior professor, Dept of anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan – 326001, Affiliated to RUHS.

Dr. S.P. Chittora Senior professor & HOD, Dept of anaesthesia, Jhalawar Medical College, Jhalawar, Rajasthan – 326001, Affiliated to RUHS.

ABSTRACT

Introduction : Spinal anaesthesia is a preferred choice of anaesthesia for caesarean section. but it is associated with adverse effects, of which most common is hypotension. Hypotension occurs due to sympathetic blockade, aortocaval compression and Bezold Jarisch Reflex (BJR). BJR can be inhibited by 5-HT3 antagonist like ondansetron. This study evaluates the effect of ondansetron on attenuation of spinal induced hypotension.

Aims: To study the effect of intravenous (IV) ondansetron on spinal induced hypotension in elective caesarean section. Also to study the requirement of number of bolus doses of vasopressor, perioperative nausea, vomiting & shivering.

Study design: Prospective, randomized controlled study.

Materials & methods: After ethical committee clearance, 120 parturients were included in the study. Parturients were randomly divided into 2 groups - ondansetron group & normal saline group. Parturients in ondansetron group were given IV ondansetron 4mg(2ml) diluted with 3ml normal saline 5 minutes before giving spinal anaesthesia & those in normal saline(NS) group were given 5ml normal saline. Intraoperatively patients were monitored for hemodynamics, vasopressor requirement & side effects. Hemodynamic variables were compared by student t test whereas vasopressor requirement is compared by chi square test.

Results: The changes in HR, SBP, DBP, MAP were all highly significant ($P<0.001$) when compared within the group with preoperative values, in both ondansetron & NS group. When compared between the group fall in SBP & MAP were more in NS group than in ondansetron group which was statistically highly significant ($P<0.001$) whereas in DBP no significant difference was seen. The requirement of vasopressor was more in NS group than ondansetron group which was statistically highly significant ($P<0.001$).

Conclusion: IV ondansetron given before spinal anaesthesia reduces spinal induced hypotension & requirement of vasopressors.

KEYWORDS

Introduction

Spinal anaesthesia is a anesthesia of choice for caesarean section, particularly in case of elective cases, as it eludes the most common hazards linked with general anaesthesia, such as aspiration of gastric contents, challenging intubation & negative effects of GA on the foetus.[1] However, there are definite adverse effects of spinal anesthesia, the utmost common being hypotension, which reduces uterine blood flow & foetal circulation, and thus reason for foetal hypoxia and acidosis.[2] Hypotension during caesarean section under spinal anaesthesia has been the matter of research in medical field for > 50 years.[3] The occurrence of hypotension diverges in different studies, extending from 7.4 to 74.1%.[4] The choice of effective treatment approach to attain hemodynamic steadiness during spinal anaesthesia for caesarean section remains to be one of the key challenges in obstetric anaesthesiology.

The physio pathological mechanisms involved in the occurrence of hypotension are Sympathetic blockade with parasympathetic overdrive, aortocaval compression, Bezold Jarisch Reflex (BJR). Systemic vascular resistance is reduced because of sympatholysis resulting in vasodilation and pooling blood in lower limbs resulting in reduction of central venous pressure. This is treated by vascular filling with crystalloid or colloids and use of vasopressors. Aortocaval compression can be reduced by left lateral tilt of operating table or by placing a wedge under the right hip so that the right hip is elevted by 15^{0}.[4]

BJR is due to activation of chemosensitive vagal C fibers in cardiopulmonary region by variety of substances including serotonin . The 5-HT_3 receptors mediate this reflex. Previous studies have shown that serotonin is released during hypotension by platelets which stimulate 5-HT_3 receptors resulting in BJR causing profound hypotension & bradycardia.[4]

Pharmacological and animal studies suggest that 5-HT (serotonin) may be an important factor associated with inducing the BJR and this effect can be blocked at the 5-HT3 receptor.

Hence the purpose of this study is that spinal-induced hypotension and bradycardia could be minimized with the use of intravenous ondansetron, a 5-HT3 receptor antagonist, in obstetric patients undergoing caesarean section.

Materials & methods

This study was conduted after obtaining ethical committee clearance from February 2020 to march 2020 in zanana hospital attached to jhalawar medical college, Jhalawar. 120 parturients with ASA II undergoing elective caesarean section were included in the study after taking informed consent. All the patients underwent a thorough pre anaesthetic evaluation and those who had conditions listed under exclusion criteria were excluded.

Inclusion Criteria:

- Term singleton parturients of >37 weeks
- ASA Grade II
- Elective caesarean section

Exclusion criteria:

- Patient refusal
- ASA Grade >II
- Pregnancy with co-morbidities like mitral stenosis, aortic stenosis,
- raised ICT.
- Allergy to ondansetron
- Allergy to local anaesthetic
- Patients on selective serotonin reuptake inhibitors (SSRIs) like fluoxetine, paroxetine, citalopram, escitalopram
- Raised intracranial pressure

- Hypovolemia
- Infection of skin over spine
- Bleeding diathesis & coaugulopathy

All the 120 patients who were included in the study were instructed for NBM overnight. After identification of patient, pre anaesthetic checkup was verified & patient was taken into OT.

Demographic details like maternal age, gestational age, height, weight were checked & noted. Intravenous line was secured with 18 G cannula in both forearm & preloaded with 500ml ringer lactate. Patients were randomized into two groups with 60 patients in each group. Grouping was done in such way that both patient & monitoring anaesthetist were blinded for the study. Baseline vitals noted were – SBP, DBP, MAP, HR, SpO2. Patients in each group received one of the test drug intravenously 5 minutes before giving Subarachanoid block as mentioned below.

Group A – Ondansetr

on 4mg (2ml) + 3ml normal saline IV.

Group B – Normal saline 5ml IV.

Subarachanoid block was given with 25G quincke's spinal needle using 0.5% hyperbaric bupivacaine 2ml in sitting position & then made to lie down in supine position with left lateral tilt by placing a wedge under a right hip joint so that it is raised by 15^0. Intravenous fluids were started & oxygen started at a rate of 4L/min through facemask. Intraoperative vitals i.e. SBP, DBP, MAP, PR, S_pO2 were noted every 1 minute till 5 minutes, then at a interval of 5 minutes till 15 minutes, then at a interval of 10 minutes till end of the surgery. Hypotension was treated with injection Mephentermine 6mg iv bolus & bradycardia was treated with injection atropine 0.6mg iv. Requirement of mephentermine & atropine were noted. Hemodynamic variables in both groups were compared by one way analysis of variance (ANOVA). Vasopressor requirement, senory level achieved & APGAR scores were compared by chi square test.

Results

Table 1 : comparison of heart rate between the group

Heart rate	Ondansetron group Mean ± SD	Normal saline group Mean ± SD	P value
Baseline	82.34 ± 8.86	81.75 ± 9.75	0.68
0 min	83.9 ± 8.77	83.75 ± 9.56	0.92
1 min	84.6 ± 8.91	87.52 ± 9.73	0.54
2 min	87.32 ± 10.52	90.95 ± 9.46	**0.04**
3 min	90.12 ± 10.74	94.22 ± 11.29	**0.04**
4 min	91.25 ± 12.3	94.88 ± 10.48	0.53
5 min	90.45 ± 11.62	94.35 ± 11.28	0.23
10 min	92.55 ± 9.09	96.67 ± 11.94	0.38
15 min	92.67 ± 9.32	95.82 ± 11.61	0.10
25 min	91.27 ± 9.81	95.90 ± 10.80	0.01
35 min	88.45 ± 9.56	91.98 ± 11.19	0.06
45 min	87.05 ± 9.67	88.68 ± 9.65	0.35

Comparison of heart rate between the groups:
The baseline HR in ondansetron group and normal saline group was 82.34±8.86 beat/min and 81.75±9.75 beat/min respectively and the difference was statistically non-significant (P=0.68). Post spinal HR was also comparable between the groups every 1 minute till 5 minutes, then at an interval of 5 minutes till 15 minutes, then at an interval of 10 minutes till end of the surgery. In comparing with independent sample t test between two groups, HR at 2nd minute & 3rd minute is statistically significant ($p < 0.05$).

Table 2 : comparison of SBP between the groups

SBP	Ondansetron group Mean ± SD	Normal saline group Mean ± SD	P value
Baseline	122.65 ± 7.29	122.35 ± 7.87	0.829
0 min	120.82 ± 7.79	118.98 ± 7.76	0.197
1 min	116.93 ± 8.37	115.02 ± 7.57	0.192
2 min	113.75 ± 9.46	111.23 ± 8.38	0.125
3 min	111.45 ± 10.90	108.45 ± 8.65	0.09
4 min	111.92 ± 11.8	108.3 ± 8.72	0.05
5 min	112.07 ± 10.51	107.67 ± 9.73	0.02
10 min	115.25 ± 10.29	107.65 ± 10.89	< 0.001
15 min	118.87 ± 9.30	109.22 ± 9.90	< 0.001
25 min	119.65 ± 8.41	110.62 ± 9.34	< 0.001
35 min	120.75 ± 7.50	115.42 ± 8.61	< 0.001
45 min	122.47 ± 6.45	120.88 ± 6.60	0.187

Comparison of SBP between the groups:
The baseline SBP in ondansetron group and normal saline group was 122.65±7.29 mmHg and 122.35±7.87 mmHg respectively and the difference was statistically non-significant (P=0.829). In comparing with independent sample t test between two groups 5, 10, 15, 25 & 35 minutes are statistically highly significant ($p < 0.001$).

Table 3 : Comparison of DBP between the groups

DBP	Ondansetron group Mean ± SD	Normal saline group Mean ± SD	P value
Baseline	76.77 ± 6.75	76.50 ± 6.45	0.825
0 min	75.02 ± 7.34	74.42 ± 6.23	0.631
1 min	71.35 ± 6.91	70.72 ± 6.25	0.600
2 min	68.20 ± 6.95	67.67 ± 6.05	0.655
3 min	65.03 ± 7.84	65.65 ± 5.19	0.613
4 min	65.48 ± 8.78	65.97 ± 5.98	0.725
5 min	66.72 ± 7.92	66.03 ± 7.08	0.619
10 min	66.87 ± 6.67	64.92 ± 7.54	0.136
15 min	68.50 ± 6.10	67.27 ± 7.62	0.330
25 min	71.30 ± 6.70	70.15 ± 7.79	0.388
35 min	73.70 ± 7.44	73.28 ± 7.51	0.761
45 min	75.10 ± 7.46	75.78 ± 6.94	0.605

Comparison of DBP between the groups:
The baseline DBP in ondansetron group and normal saline group was 76.77±6.75mmHg and 76.5±6.45 mmHg respectively and the difference was statistically non-significant (P=0.825). In comparing with independent sample t test between two groups, all are statistically not significant ($p > 0.05$).

Table 4 : Comparison of MAP between the groups

MAP	Ondansetron group Mean ± SD	Normal saline group Mean ± SD	P value
Baseline	91.78 ± 6.25	91.93 ± 7.98	0.082
0 min	89.17 ± 7.33	86.67 ± 8.12	0.079
1 min	85.12 ± 8.83	84.43 ± 8.09	0.660
2 min	80.85 ± 9.95	82.02 ± 8.58	0.493
3 min	77.47 ± 11.7	79.80 ± 8.74	0.219
4 min	78.48 ± 11.5	78.10 ± 8.73	0.838
5 min	78.98 ± 9.94	75.97 ± 8.94	**0.03**
10 min	79.70 ± 9.24	75.47 ± 9.50	**0.01**
15 min	81.53 ± 7.80	76.57 ± 9.76	**0.003**
25 min	83.88 ± 6.77	77.95 ± 9.33	**<0.001**
35 min	86.48 ± 7.34	80.07 ± 9.44	**<0.001**
45 min	88.43 ± 7.17	83.77 ± 8.27	**0.001**

Comparison of MAP between the groups
The baseline MAP in ondansetron group and normal saline group was 91.78 ±6.25 and 91.93 ± 7.98 respectively and the difference was statistically insignificant (P>0.05). In comparing with independent sample t test between two groups, 5, 10, 15, 25, 35 and 45 minutes were statistically highly significant ($p < 0.001$).

Table 5 : Vasopressor requirement in both the groups

Mephentermine	Ondansetron group Number of patients (%)	Normal saline group Number of patients (%)	P value
0 bolus	32 (53.3 %)	11 (18.3 %)	< 0.001
1 bolus	22 (36.7 %)	16 (26.67 %)	
3 bolus	6 (10 %)	20 (33.3 %)	
4 bolus	0 (0 %)	13 (21.7 %)	
Total	60 (100%)	60 (100%)	

Hypotension is treated with injection Mephentermine 6mg IV bolus. In comparing the total number of bolus given, in ondansetron group - 1 bolus given to 36.7 % of patients and no bolus needed in 53.3% of patients. In normal saline group no bolus needed only 18.3% of

patients, 3 and 4 bolus given to 33.3 % and 21.7 % of patients respectively. Comparing these differences by using chi-square test, it is statistically highly significant (<0.001).

DISCUSSION

The main objective of the study, is to study the effect of attenuation of spinal induced hypotension in elective caesarean section by using ondansetron & comparing with normal saline(placebo) and to prevent bradycardia during elective caesarean section under spinal anaesthesia. In this study 120 patients aged between 18-35 years scheduled for elective caesarean section were divided equally in two groups. Patients in one group receives Ondansetron 4mg (2ml) + 3ml normal saline and another group receives normal saline 5ml, 5minutes IV before giving Subarachanoid block.

In our study the baseline HR in ondansetron group and normal saline group was 82.34±8.86 beat/min and 81.75±9.75 beat/min respectively and the difference was statistically non-significant. Post spinal HR was also comparable between the groups every 1 minute till 5 minutes, then at an interval of 5 minutes till 15 minutes, then at an interval of 10 minutes till end of the surgery. Heart rate was decreased in ondansetron group in comparison to normal saline group at all observed minutes but comparing with independent sample t test between two groups, at 2nd minute & 3rd minute it is statistically significant (P < 0.05). The decrease in HR in ondansetron group could be, because of higher levels of blood pressure (compared to normal saline group). Similar results were seen in a study done by **Sahoo et al(2012)**[5] which revealed decreases in HR were more common in ondansetron group, but the observed differences were statistically significant only twice at 24 min and at 45 min. A study done by **Trabelsi W et al (2015)**[6] revealed HRs were similar in both groups and bradycardia was observed in 6 patients in ondansetron group (15%), whereas it was more frequent in the Normal saline group (15 cases, 37.5%) with a significant statistical difference.

In our study when heart rate is compared within the group, there was significant variation (P<0.0001) in heart rates. In first 15 minutes it was increasing & then it decreased.

In our study the baseline SBP in ondansetron group and normal saline group was 122.65±7.29 mmHg and 122.35±7.87 mmHg respectively. In ondansetron group SBP was higher in all observation minutes comparing with normal saline group. In comparing with independent sample t test between two groups, 5, 10, 15 & 25 minutes are statistically significant (P<0.05).

A study done by **Owczuk R et al (2008)**[7] shows results, SBP values were significantly higher in the ondansetron group at the 10, 15, and 20 minute time points of the study.

In our study though the SBP was higher in ondansetron group compared to normal saline group in all the observation times, when these SBP values were compared within the group highly significant (P<0.001) variation in SBP was seen. SBP values had decreasing trend upto 3minutes in ondansetron group but in normal saline this trend was upto 10 minutes. In a study conducted by **Potdar MP et al (2017)**[8], also showed that similar significant fall (P<0.001) in SBP in both ondansetron & control groups when these groups were compared within the group.

In our study the baseline DBP in ondansetron group and normal saline group was 76.77±6.75mmHg and 76.5±6.45 mmHg respectively. In ondansetron group DBP was higher in some observation minutes and lower in some observation minutes comparing with normal saline group. In comparing with independent sample t test between two groups, all are statistically not significant (P>0.05).

When DBP values are compared within the groups, highly significant variation in DBP was observed and duration of decreasing trend of DBP was for 3 minutes in both the groups. In a study conducted by **Potdar MP et al (2017)**[8], also showed that similar significant fall (P<0.001) in DBP in both ondansetron & control groups when these groups were compared within the group.

In this present study the baseline MAP in ondansetron group and normal saline group was 91.78 ±6.25 and 91.93 ± 7.98 respectively. In comparing with independent sample t test between two groups 5, 10, 15, 25, 35 & 45 minutes are high MAP in ondansetron group when compared to normal saline and it is statistically significant (P<0.05). Similar results were seen in a study done by **Ortiz-Go´mez JR et.al (2014)**[9] which showed significant differences at 15 min in SBP in ondansetron group when compared to placebo group.

In our study when MAP was compared within the groups, highly significant variation in MAP was noted & the decreasing trend was only upto 3minutes whereas, in normal saline group it was upto 10minutes. In a study conducted by **Potdar MP et al (2017)**[8], also showed that similar significant fall (P<0.001) in MAP in both ondansetron & control groups when these groups were compared within the group.

But a study done by **Tatikonda CM et.al (2019)**[10] results are contrast which showed that there was no significant difference in SBP, DBP and MAP between ondansetron and normal saline at any point of 3 min interval in span of 30 min.

Maternal hypotension is one of the most common adverse effect during spinal anesthesia since sympathetic nerve blockade reduces blood arriving to the heart. Ondansetron, a highly active and precise 5-HT3 receptor antagonist, prevents the binding of 5-HT from stimulated platelets to 5 HT3 receptors, then lessens the Bezold Jarisch reflex (BJR) which is prompted by 5-HT, and thereby prevents severe hypotension & bradycardia.

In this present study, hypotension is treated with injection Mephentermine 6mg IV bolus. In comparing the total number of bolus given, ondansetron group - 1 bolus given to 36.7 % of patients and no vasopressor needed in 53.3% of patients. In normal saline group vasopressor is not given only in 18.3% of patients, 3 and 4 boluses given to 33.3 % and 21.7% of patients respectively. Comparing these differences by using chi-square test, it was statistically highly significant (<0.001). Similar results were observed in the study conducted by **Potdar MP et al (2017)**[8], which showed that vasopressor, ephedrine requirement was significantly higher in control group than in the study group. In control group 23% of patients required ephedrine IV bolus, where as in groups where ondansetron 4mg & 8mg IV was given, 1.6% & 5% of patients required ephedrine respectively.

SUMMARY & CONCLUSION

Summary

All patients were divided into 2 groups, study group in whom IV ondansetron 4mg was given before spinal anaesthesia was compared with control group in whom normal saline was given. All patients were given spinal anaesthesia & monitored intraoperatively.

Following inferences were taken

- The mean SBP & MAP showed significant difference between ondansetron group & control group, whereas in DBP no significant difference was obssrved.
- The SBP, DBP & MAP was compared within the groups there was highly significant variation in both ondansetron group & control group.

Conclusion

It can be concluded from this study that, if ondansetron 4mg IV is given before spinal anaesthesia it will be effective in prevention of spinal induced hypotension during caesarean section under spinal anaesthesia.

REFERENCES

1. Morgan P. Spinal Anaesthesia in obstetrics. Can J Anaesth 1995;42(12):1145-63
2. Corke BC, Datta S, Ostheimer GW, Weiss JB, Alper MH. Spinal anaesthesia for Caesarean section. The influence of hypotension on neonatal outcome. Anaesthesia 1982;37(6):658–62.
3. Kennedy RL, Friedman DL, Katchka DM, Selmants S, Smith RN. Hypotension during obstetrical anesthesia. Anesthesiology 1959;20(2):153–5.
4. Klöhr S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anaesthesia for caesarean section: literature search and application to parturients. Acta Anaesthesiol Scand 2010;54(8):909–21.
5. Sahoo T, SenDasgupta 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(1):24–8.
6. 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;2015:158061:1-7
7. Owczuk R, Wenski W, Polak-Krzeminska A, Twardowski P, Arszułowicz 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(4):332–9.

8. Potdar MP, Kamat LL, Jha TR, Talnikar AS, Mahevi ZM, Save MP. Effect of ondansetron in
attenuation of post-spinal hypotension in caesarean section: A comparison of two different doses with placebo. J Obstet Anaesth Crit Care 2017;7(2):69.
9. Ortiz-Gómez JR, Palacio-Abizanda FJ, Morillas-Ramirez F, Fornet-Ruiz I, Lorenzo-Jiménez A, Bermejo-Albares ML. The effect of intravenous ondansetron on maternal haemodynamics
during elective caesarean delivery under spinal anaesthesia: a double-blind, randomised, placebo-controlled trial. Int J Obstet Anesth 2014;23(2):138–43.
10. Tatikonda CM, Rajappa GC, Rath P, Abbas M, Madhapura VS, Gopal NV. Effect of Intravenous Ondansetron on Spinal Anesthesia-Induced Hypotension and Bradycardia: A Randomized Controlled Double-Blinded Study. Anesth Essays Res 2019;13(2):340-6.