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Effect of Intravenous Ondansetron for Prevention of Spinal Anaesthesia Induced Hypotension during Caesarean Section

Kriti Devkota,[1] Kiran Adhikari,[2] Bijay Pradhan,[3]

[1]Lecturer, Department of Anaesthesia, College of Medical Sciences, Bharatpur, Chitwan, Nepal [2]Lecturer, Department of Anaesthesia, Chitwan Medical College, Bharatpur, Chitwan, Nepal [3]Resident, Department of Anaesthesia College of Medical Sciences, Bharatpur, Chitwan, Nepal

ABSTRACT

Introduction

Hypotension is one of the most common complications associated with spinal anaesthesia. Maternal hypotension during caesarean section is more dangerous as it can compromise fetal outcome. Serotonin (5-HT3) has been found to induce Bezold Jarisch Reflex (BJR) causing bradycardia and hypotension in background of decreased blood volume. Ondansetron, a serotonin antagonist may play important role in prevention of spinal induced hypotension. The aim of this study is to determine the effect of intravenous ondansetron to prevent spinal induced hypotension during caesarean section.

Methods

A prospective randomised double blind study was done among singleton parturients scheduled for elective caesarean delivery under spinal anaesthesia from 2nd July 2020 to 31st October 2021 in College of Medical Sciences Teaching Hospital. One hundred and thirty patients were randomised by lottery method into two groups (group S and group O) each with 65 patients to receive either 4 mg of intravenous (IV) ondansetron diluted in 10 ml of normal saline or 10 ml of normal saline alone. Various haemodynamic parameters like systolic and diastolic blood pressure (SBP/DBP), mean arterial pressure (MAP), heart rate (HR), oxygen saturation (Spo_2) and vasopressor requirement were compared between the two groups using SPSS 20. Student's t test and chi-square test were used for comparison of parametric and non-parametric data.

Results

Incidence of hypotension was 28 (43.07%) in saline group and 11 (16.92%) in ondansetron group. There were statistically significant differences in SBP, DBP and MAP at three, six, nine twelve, fifteen and eighteen minutes. Incidence of shivering was 15 (23.07%) in ondansetron while 28 (43.07%) in saline group which was statistically significant. No other benefit of ondansetron was observed in present study.

Conclusions

Prophylactic administration of IV ondansetron could significantly reduce the incidence of spinal induced hypotension during caesarean section.

Keywords: Caesarean section; Hypotension; Ondansetron; Spinal anaesthesia

Correspondence: Dr. Kriti Devkota, Lecturer, Department of Anaesthesia, College of Medical Sciences Teaching Hospital. Email: dr.kriti.devkota@gmail.com. Phone: +977-9851215676.

INTRODUCTION

Neuraxial block is considered as standard care of anaesthesia for caesarean section as it reduces anaesthesia related maternal morbidity and mortality.[1] Spinal anaesthesia is safer, quicker and reliable anesthetic option but has its own adverse effects. Bradycardia and hypotension are most commonly encountered side effects with incidence of 13 % and 33 % respectively in non-obstetric population.[2]In parturients the incidence reaches upto 83 % which can compromise fetal outcome resulting in fetal hypoxia, acidosis and low APGAR scores.[2] Various techniques like physical methods (leg wrap), vasopressors (ephedrine, phenylephrine) and use of fluids (crystalloids or colloids) have been used for its prevention.[3]

Spinal induced hypotension (SIH) is caused due to sympathetic blockade resulting in decreased systemic vascular resistance whereas bradycardia occur secondary to parasympathetic dominance, increased baroreceptor activity or activation of Bezold Jarisch reflex (BJR). BJR is a triad of bradycardia, hypotension and peripheral vasodilation which arises from stimulation of mechanoreceptors and chemoreceptors located in the left ventricle. [4-6] Serotonin (5HT) has been found to trigger this reflex in various animal studies in hypovolemic settings.[7-10]

Aim of this study was to compare the effect of ondansetron, a 5-HT3 antagonist with placebo for attenuation of spinal induced hypotension.

METHODS

This was a prospective randomised double blind study conducted in the Department of Anaesthesia of College of Medical Sciences, Teaching Hospital (COMS-TH), Chitwan, Nepal. After approval from institutional review committee (Ref. 2020-065), all ASA II singleton parturients undergoing elective caesarean section under spinal anaesthesia from July 2nd 2020 to October 31st 2021 were taken up for study.

Patients with known contraindication to spinal anaesthesia, allergic to the study drug, patients with comorbidities like pregnancy induced hypertension, gestational diabetes mellitus, coronary artery disease or heart disease, patients taking drugs like selective serotonin receptor inhibitors (SSRIs) and patients converted into general anaesthesia were excluded from our study.

The sample size was calculated based on study conducted by Sahoo et al[11] using formula:

$$n = \frac{(z\alpha + Z\beta)^2 \times (g1^2 + \sigma 2^2)}{(m^1 - m^2)^2}$$

$$n = \frac{(1.96 + 0.85)^2 \times (11.7^2 + 10.5^2)}{(88 - 82.2)^2}$$

n = 58

So, minimum of 58 samples in each group was required. We included 65 parturients in each group of our study.

Pre anesthetic evaluation was done a day before surgery and informed written consent was taken. They were asked for preoperative fasting period of eight hours and brought to pre anesthetic room the other day. An 18G cannula was inserted and Inj.ranitidine 150 mg and Inj. metoclopramide 10 mg were given intravenously. Ringer's Lactate (RL) 20ml/kg was started to be given for 20 minutes. Folded paper with O or S written was kept in a box and parturients were asked to pick one from the box. It was handed over to an anaesthesia assistant who unfolded the paper and checked the group. The anaesthesia assistant not involved in the study noted the group O and group S according to the chosen paper and maintained in a register. He then prepared Inj. ondansetron 4 mg diluted in 10 ml of NS for Group O while 10 ml of normal saline was prepared for group S.

Patient was then taken to the operating room and baseline heart rate (HR), noninvasive blood pressure (NIBP) and oxygen saturation (Spo2) were recorded. Maintenance fluid (RL) was then started at the rate of 100 ml/hr. Anesthesiologist blinded to the prepared drug solution slowly administered 10 ml solution over 10 seconds. After 5 minutes, spinal anaesthesia was performed in L3-L4 or L4 –L5 interspace with 25 G Quincke's spinal needle using 2.2 ml of 0.5% heavy bupivacaine in sitting position. Patient was then immediately placed in supine position with 15 degree tilt to the left.

HR, SBP, DBP, MAP and oxygen saturation was recorded in individual proforma at the time of spinal anaesthesia and then every three minute interval upto 30 minutes. Level of sensory block was measured at five minute intervals for loss of cold sensation using alcohol swabs till 15 minutes. Surgery was allowed to start once upper sensory level reached T6. Motor block was also assessed at same time interval using the modified Bromage scale.[12,13]

Inj Oxytocin 3 unit bolus over 15 seconds was given to all patients after delivery of the baby. Any additional use of oxytocin was noted. Inj mephentermine 6 mg IV bolus was used to treat hypotension (SBP <90 mm Hg or DBP <60 mm Hg or MAP <60 mm of Hg) and Inj atropine 0.6mg for bradycardia (HR <50 bpm). Values before use of these drugs were recorded for calculation. Amount of blood loss and occurrence of pain and rigor were also recorded. After completion of surgery, patients were shifted to recovery room and observed for 30 minutes after which they were transferred to post-operative unit.

The recorded data from patient's proforma and register of anesthesia assistant was transferred in MS excel which was later prepared and was analyzed using SPSS 20. Student's t test for parametric data and chi-square test for non-parametric data were performed for comparison.

RESULTS

One hundred and thirty patients were included in this study, 65 in each group, all of whom completed the study. There was no statistically significant difference among the demographic variables in both groups shown in Table 1. There was no significant difference in SBP, DBP, MAP, Spo_2 and HR in baseline recording between the groups (Table 1)

Table 1. Demographic and baseline recording values of two groups

	Group O	Group S	p-value
	Mean ± S.D	Mean ± S.D	
Age (in years)	26.86 ± 4.16	27.88 ± 4.09	0.163
Height (in cms)	153.29 ± 3.14	152.65 ± 3.12	0.241
Weight (in Kg)	67.03 ± 6.54	66.92 ± 5.29	0.918
Body mass index(BMI)	28.52 ± 2.53	28.69 ± 2.40	0.697
Baseline SBP (mm Hg)	118.22 ± 8.75	117.37 ± 7.17	0.547
Baseline DBP (mm Hg)	71.89 ± 8.33	69.80 ± 7.68	0.139
Baseline MAP (mm Hg)	82.82 ± 7.95	80.86 ± 7.32	0.147
Baseline HR (mm Hg)	89.62 ± 11.29	88.45 ± 9.40	0.522
Baseline Spo_2 (%)	98.66 ± 0.97	98.57 ± 0.81	0.558

The incidence of hypotension in the saline group was 43.07% compared to 16.92% in ondansetron group. There was statistically significant differences, at three, six and nine minutes, tweleve, fifteen and eighteen minutes in SBP (Figure 1) , DBP (Figure 2) and MAP (Figure 3) . There were no episodes of bradycardia or significant differences in HR recorded over 30 minutes at three minutes interval in both groups.

A total of 11 (16.92%) patients in ondansetron group and 28 (43.07%) patients in saline group required Inj.mephentermine for correction of hypotension. The use of vasopressor was significantly higher in saline group (p= 0.002). (Table 2) Of the 28 patient requiring vasopressor in saline group, eight required once, 15 required twice and five were given three times. In ondansetron group, six patients required once while five patients required vasopressor for two times.

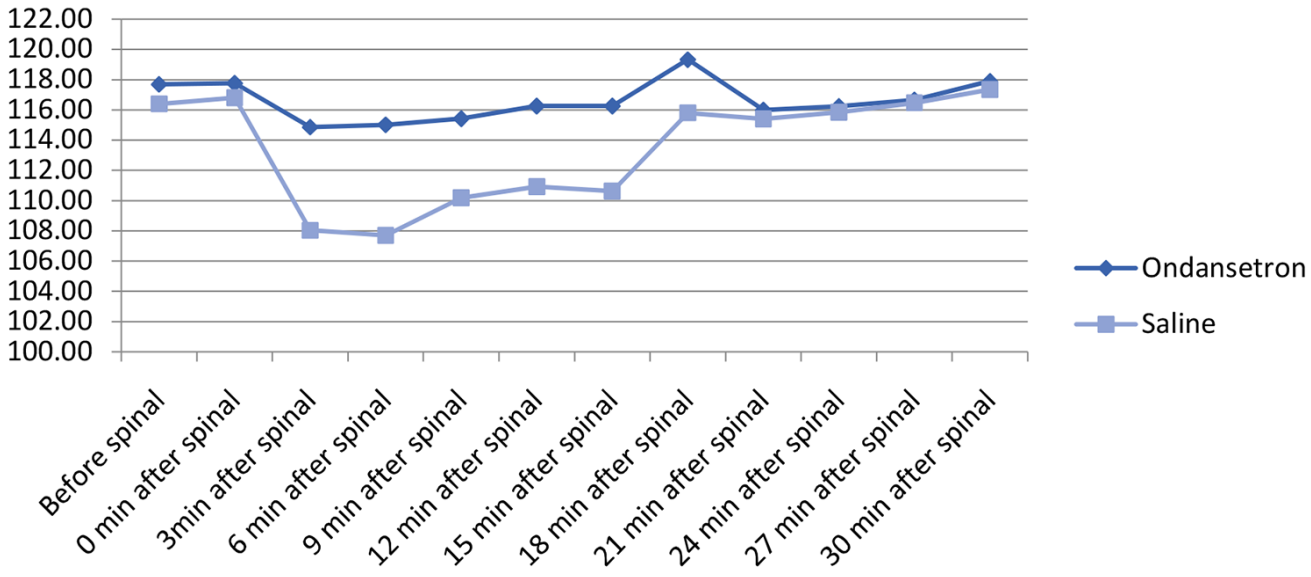

Figure 1. Line diagram showing the mean SBP

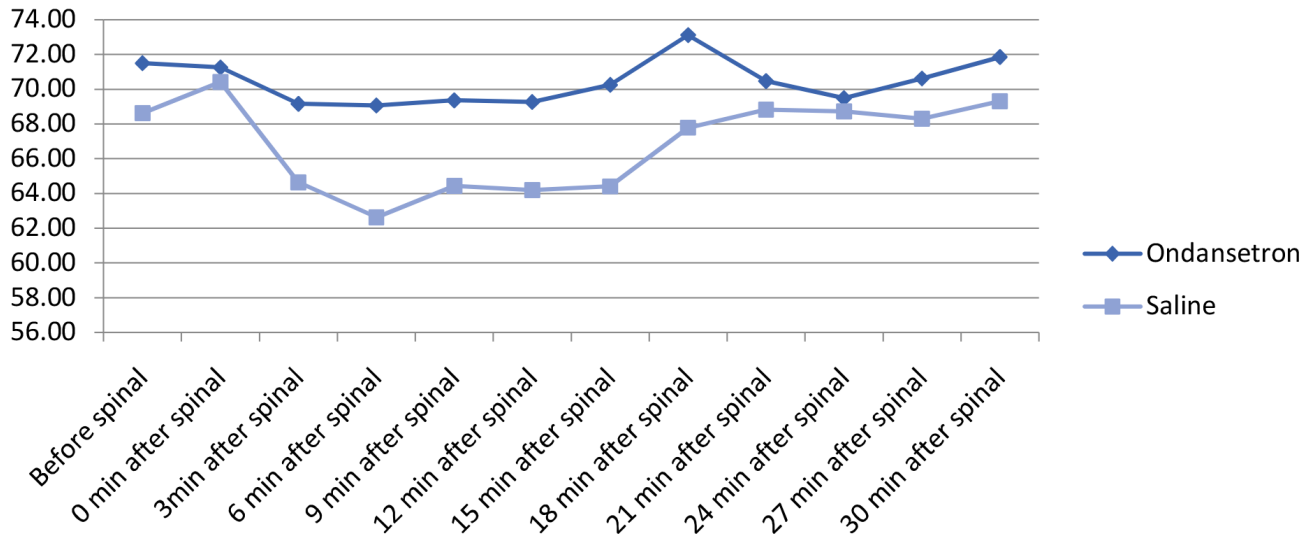

Figure 2. Line diagram showing mean DBP

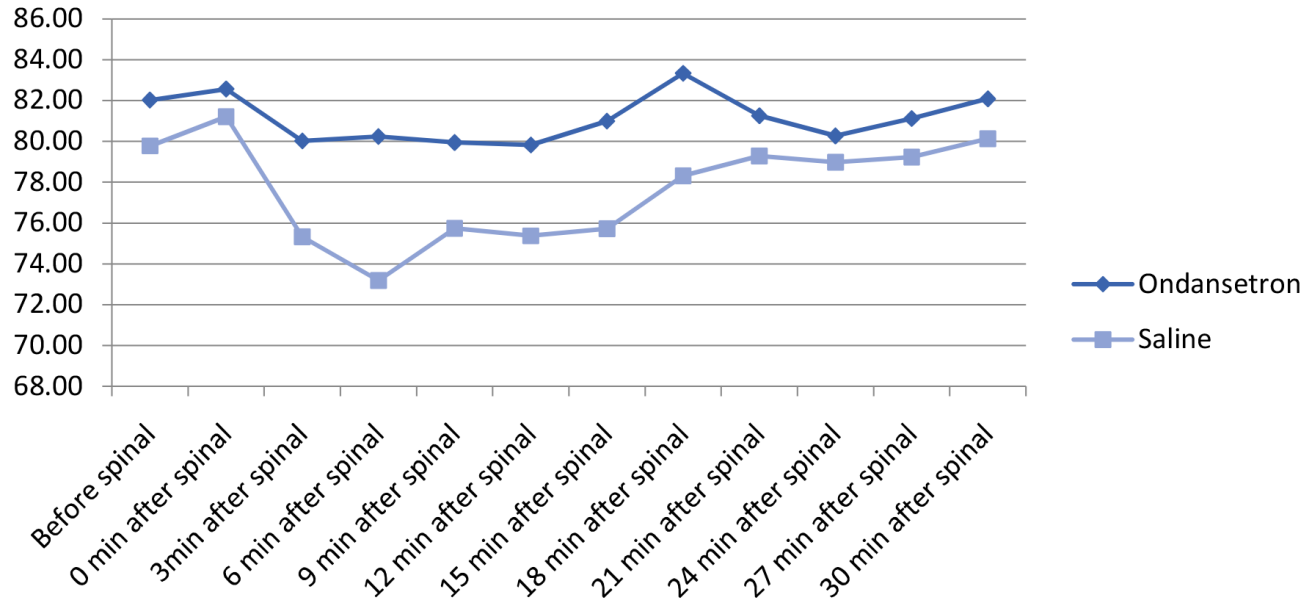

Figure 1. Line diagram showing the mean SBP

Table 2. Use of vasopressor

Group	vasopressor			
	Used	not used		p value
Ondansetron	11	54	65	0.002*
Saline	28	37	65	
	39	91	130	

28 (43.07%) patients in saline group and 15 (23.07%) patients in ondansetron group had shivering which was statistically significant (p=0.025). There were five patients in the saline group who complained of nausea while only two patients in ondansetron group had this complaint. However, this difference was not statistically significant. No patients in both groups had episode of vomiting.

DISCUSSION

Hypotension during spinal anaesthesia is a frequently occurring event with incidence upto 33 % in non-obstetric population which reaches even higher upto 83 % in parturients.[2,4,5] It is hazardous for the fetus due to compromise in uteroplacental circulation. So, a number of techniques have been employed for its mitigation.[3]

In the background of hypovolemia, cardiac receptors in the left ventricle get stimulated and induce BJR resulting in vasodilation, hypotension and reflex bradycardia. This response is also believed to be encited by chemoreceptors sensitive to serotonin. Ondansetron, a 5-HT3 antagonist has been found to be effective in attenuation of spinal induced hypotension in various studies done in both obstetric and non-obstetric population.[11,14-16] We have used intravenous ondansetron 4 mg 5 minutes before spinal anaesthesia for elective caesarean section in our study as a measure to prevent hypotension and found it to be effective.

The incidence of hypotension in ondansetron group in present study was 16.92 % while in saline group was 43.07 %. Our study showed significantly lower incidence (p= 0.002) of hypotension in ondansetron group than that in saline group. Studies done by Khouly et al.[17]

and Sahoo et al.[11] also demonstrated similar results. Both of these studies were done in parturients using similar dose of opioid free heavy bupivacaine comparable to our study (2 ml of 0.5 % heavy bupivacaine).

The use of vasopressor was also significantly higher in saline group in our study. This was relatable to study done by Trabelsi et al. in 80 parturients posted for elective caesarean section ($p < 0.001$).[18]

Wang et al.[19] had done a dose dependent study using 4 different doses (2, 4, 6 and 8 mg) of ondansetron for cesarean deliveries and concluded dose of 4 mg of ondansetron to be optimal for hemodynamic benefit. We also did the present study using 4 mg of ondansetron and showed similar results.

Gomez et al.[20] had also done similar study using 2 mg , 4 mg and 8 mg of ondansetron but did not demonstrate reduction in episodes of hypotension in ondansteron group compared with saline group. They had used a height based dose of bupivacaine (mg = height in cm *0.06) along with fentanyl 20 micrograms whereas we had used fixed dose of 11 mg bupivacaine for all patients. Personalising individual doses might have resulted in lower incidence of hypotension in their study. They had also used a lower dose of only 1 unit of oxytocin after delivery while we had used bolus of 3 units of oxytocin. This might be a reason for more stable hemodynamics in their study.

No episodes of bradycardia were noted in both the groups of our study. Similar results were produced in study done by Terkawi et al.[21] but unlike ours, they did not show advantage of ondansetron even in reduction of episodes of hypotension. They had used a larger dose of 15 mg of bupivacaine along with 20 mcg of fentanyl and 100 mcg of preservative free morphine for spinal anaesthesia in their study compared to opioid free 11 mg of bupivacaine used in our study.

Our study also demonstrated beneficial effects of ondansetron for prevention of shivering with incidence of 43.07% in saline group and 23.07% in ondansteron group. Studies done by Tatikonda et al.[16] and Marashi et al.[14] also demonstrated similar benefit. Both of these studies were done in ceseraen section using 15 mg of bupivacaine which was higher than the dose used in our study (11 mg). However, they had also demonstrated a significant reduction in use of vasopressors in ondansteron group of their study.

Limitations and recommendation: A small sample size and use of a fixed dose of bupivacaine for all the parturients may be the limitations of our study. We had also used noninvasive blood pressure monitoring in our study which might not be able to reflect exact blood pressure measurement of the patient.

Further studies with larger sample size and use of invasive blood pressure monitoring would help to accurately identify the role of ondansetron in attenuation of spinal induced hypotension in caesarean section.

CONCLUSIONS

Ondansetron administered at a dose of 4 mg intravenously before spinal anaesthesia was effective in reducing the incidence of hypotension as well as shivering in pregnant women undergoing caesarean section.

Conflict of interest: Nil

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