ORIGINAL RESEARCH PAPER

Volume-7 | Issue-11 | November-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

"EFFECT OF INTRAVENOUS ONDANSETRON ON HAEMODYNAMIC PARAMETERS IN TOTAL ABDOMINAL HYSTERECTOMY POST SUBARACHNOID BLOCK" A DOUBLE BLIND RANDOMIZED CONTROL STUDY

Anaesthesiology

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ABSTRACT

BACKGROUND: Subarachnoid block (SAB) is the preferred method of anaesthesia for lower abdominal surgeries, but is associated with hypotension and bradycardia, which may be deleterious to the patients. Studies suggest that in the presence of decreased blood volume, serotonin (5-HT) may be an important factor inducing the Bezold Jarisch reflex (BJR) via 5-hydroxytryptamine 3 (5-HT3) receptors located in intracardiac vagal nerve endings. In this study, we evaluated the effect of ondansetron, as a 5-HT3 receptor antagonist, on the haemodynamic response post SAB in patients undergoing elective total abdominal hysterectomy (TAH).

METHODS: One hundred patients scheduled for elective TAH were allocated into two groups using sealed envelope technique. 5 minutes prior to induction of SAB, Group O (n = 50) received intravenous ondansetron 4 mg; Group N (n = 50) received normal saline. Blood pressure, heart rate and vasopressor requirements were assessed.

RESULTS: There was fall in systolic, diastolic and mean arterial pressure as well as in heart rate, compared with baseline values in both the groups. Except for the baseline, at all other time intervals, statistically significant difference in blood pressure was seen between the ondansetron and normal saline group, with a lower systolic diastolic and mean arterial pressure in normal saline group as compared to ondansetron group (P = <0.0001). No significant difference in heart rate values were observed between the groups (P = >0.05).

Reduction in use of vasopressor, incidence of nausea and vomiting and occurrence of shivering were also significant between the groups.

CONCLUSION: Thus, we conclude in our study that prophylactic i/v use of 4 mg ondansetron reduces the severity of SAB induced hypotension, the need for rescue vasopressor, incidence of nausea and vomiting and occurrence of shivering.

SUMMARY: From the present study it can be summarized that Intravenous Ondansetron 4mg when given 5 minutes prior to subarachnoid block for total abdominal hysterectomy is effective in preventing hypotension with minimal side effects and reduced requirement of rescue vasopressor.

KEYWORDS

INTRODUCTION

The most popular form of anaesthesia for lower abdominal surgeries is subarachnoid block, which is frequently associated with hypotension and bradycardia[1]. Hypotension results primarily from decreased vascular resistance, while bradycardia is secondary to a relative parasympathetic dominance, increased baroreceptor activity, or induction of the Bezold-Jarisch Reflex[2] which is an inhibitory response usually described as a cardioinhibitory reflex.

The incidence of hypotension and bradycardia has been reported to be 33% and 13%, respectively, in non-obstetric patients[2].

Hypotension may cause nausea and vomiting as well as have detrimental effects, such as apnea. It has been demonstrated that ondansetron treatment, preloading with crystalloid infusion reduces hypotension in patients undergoing TAH.

Owczuk et al observed that intravenous ondansetron attenuated SAB induced hypotension[3]. Animal studies suggest that 5-HT may be an important factor associated inducing the BJR in the setting of decreased blood volume[4-7]; this effect can be blocked at the 5-HT3 receptor.

Moreover, 5-HT is a critical thermoregulatory neurotransmitter. In non-anesthetized individuals, ondansetron decreases core temperature attenuation that triggers shivering. Ondansetron and other selective 5-HT3 receptor antagonists, may thus be beneficial for preventing bradycardia and hypotension.

We hypothesized that SAB induced hypotension and bradycardia could be minimized with pre-induction use of i/v Ondansetron, a 5-HT3 receptor antagonist, in the patients undergoing TAH.

MATERIALS AND METHODS

This prospective, randomized, double blind study was conducted at a tertiary care after approval from the hospital Ethics Committee. One hundred female patients in the age group 30-60 years, height between 140 – 170 cms, belonging to American society of Anesthesiologists (ASA) physical status I or II and scheduled for elective total abdominal hysterectomy were included in the present study after taking informed and written consent. Patients with contraindication to spinal anesthesia or major neurological, cardiovascular, metabolic, respiratory, renal disease, or coagulation abnormalities were excluded from the study.

In the operating room, fasting status, consent, PAC were checked, and intravenous access was secured. Baseline values of pulse oximetry (SpO2), noninvasive BP, heart rate and electrocardiogram were recorded and intravenous Ringer lactate 10ml/kg used for preloading. Patients were randomly allocated into two groups (50 in each group) using sealed envelope technique.

Group O – received i/v Ondansetron 4mg (2ml) + 8 ml normal saline over 1min duration; 5mins prior to subarachnoid block.

Group N – received 10ml Normal saline over 1min duration; 5mins prior to subarachnoid block.

SAB was performed after 5 mins of administering the study solution to both the groups with the patient in the sitting position through L3-4 intervertebral space, using 0.5% hyperbaric bupivacaine 3 ml + 25 µgm fentanyl under all aseptic precautions, after confirmation of cerebrospinal fluid through a 25-gauge Quincke spinal needle. Patients were immediately placed in the supine position, intravenous fluids started and supplemental oxygen was delivered through a Venturi facemask at a rate of 4 l/min.

Monitoring of haemodynamic parameters was done at 1 min interval for 1st 10min and then every 5mins for rest of the duration of surgery. Any occurrence of hypotension (decrease in MAP more than 15-20% from the baseline) was treated with i/v Ephedrine 6 mg Any occurrence of bradycardia (decrease in heart rate by 20% from baseline) was treated with i/v Atropine 0.6 mg. Nausea and vomiting were treated with i/v Metoclopramide 10mg and i/v Promethazine 12.5 mg. Shivering was treated with i/v Tramadol 25 mg.

STATISTICAL ANALYSIS

For sample size calculation, we estimated that 37 patients will be required considering a mean difference of 10 mm Hg systolic blood pressure with a standard deviation of 15 mm Hg between the two groups at an alpha of 0.05 with a power of 80%. Hence, we propose to take more than 37 patients in our present study. This calculation was

based on a 7 mmHg difference observed by Owczuk et al[5] in non pregnant patients. Data was summarized by descriptive statistics.

Numerical variables normally distributed were compared between groups by unpaired Student's Two-Samples T test. Categorical variables were compared between groups by Student T test with two sample proportion. Paired T Test was employed for intra-group comparison of numerical variables. P < 0.05 was considered statistically significant.

RESULTS

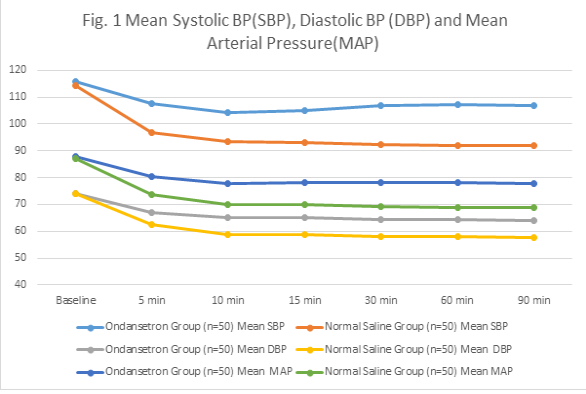
One Hundred patients were included in the study, with 50 persons in each group. Demographic data of the study population were recorded. There were no significant differences in patient age, body weight, height, or ASA classification between the groups.

Except for the baseline, at all other time intervals, statistically significant difference was seen between the ondansetron and normal saline group, with a lower mean systolic and diastolic blood pressure and mean arterial pressure in normal saline group as compared to ondansetron group. (Table 1)(Fig.1). There was a statistically significant change in mean arterial pressure from baseline at all the time intervals in each group (P < 0.05).

TABLE No. 1 Comparison of mean arterial pressure between ondansetron and normal saline group at different time intervals

(N=100)

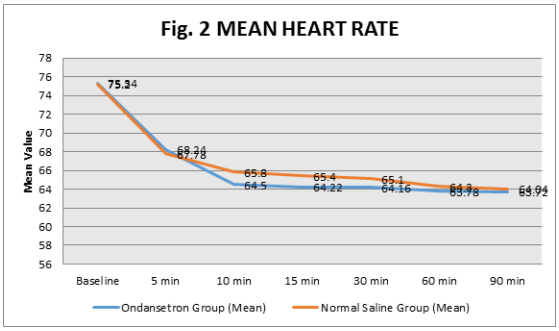
	Ondansetron Group (n=50) (Mean ± SD)	Normal Saline Group (n=50) (Mean ± SD)	't' value	P value
Baseline	87.74 ± 9.48	87.1 ± 10.1	0.35	0.730, NS
5 min	80.30 ± 9.63	73.68 ± 8.77	3.59	<0.0001, Sig.
10 min	77.94 ± 8.30	70.10 ± 7.22	5.04	<0.0001, Sig.
15 min	78.06 ± 8.33	69.78 ± 6.66	5.49	<0.0001, Sig.
30 min	78.18 ± 7.44	69.28 ± 6.03	6.57	<0.0001, Sig.
60 min	78.24 ± 7.87	68.84 ± 5.48	6.93	<0.0001, Sig.
90 min	77.96 ± 7.52	68.92 ± 5.28	6.95	<0.0001, Sig.



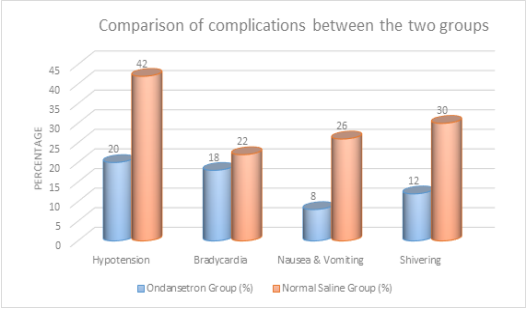
There was no statistically significant difference in mean heart rate between the two groups at any of the time intervals (P>0.05). Thus, mean heart rate was comparable between the two groups at all the time intervals. (Table No.2)(Fig.2)

TABLE No. 2 Comparison of heart rate between ondansetron and normal saline group at different time intervals

	Ondansetron Group (n=50) (Mean ± SD)	Normal Saline Group (n=50) (Mean ± SD)	't' value	P value
Baseline	75.34 ± 7.84	75.20 ± 8.10	0.09	0.930, NS
5 min	68.24 ± 8.27	67.78 ± 8.49	0.27	0.784, NS
10 min	64.50 ± 7.21	65.80 ± 13.5	0.60	0.549, NS
15 min	64.22 ± 7.36	65.4 ± 12.3	0.58	0.563, NS
30 min	64.16 ± 6.77	65.1 ± 12.3	0.48	0.631, NS
60 min	63.78 ± 6.07	64.3 ± 10.6	0.28	0.782, NS
90 min	63.72 ± 5.50	64.04 ± 9.49	0.21	0.837, NS



In the Ondansetron group, vasopressor was required in 20% patients, anticholinergic was needed in 18% patients, 8% patients required antiemetic and shivering was noted in 12% patients. While in the normal saline group, vasopressor was required in 42% patients, anticholinergic in 22% patients, antiemetic was required in 26% patients and shivering was seen in 30% patients.



DISCUSSION

This study revealed that decreases in SBP and MAP were reduced with the use of i/v Ondansetron 4 mg given 5 min before SAB in patients undergoing elective TAH. The use of ephedrine, incidence of nausea & vomiting, and occurrence of shivering were also significantly reduced with Ondansetron. Although differences in heart rate were comparable between the groups, the frequency of bradycardia was too small to achieve statistical significance.

Sympathetic blockade from SAB decreases systemic vascular resistance and induces peripheral pooling of blood leading to hypotension. In response to hypovolemia, stimulation of cardiac sensory receptors in the left ventricle induces the BJR and results in reflex bradycardia, vasodilation and hypotension[8-10]. Chemoreceptors are activated in response to decreased blood volume by serotonin[9] which is released from activated thrombocytes [11,12]. Activation of 5-HT3 receptors, which are G protein coupled, ligand-gated fast-ion channels, results in increased efferent vagal nerve activity[9], frequently producing bradycardia[13]. However, bradycardia occurs less frequently than hypotension following spinal anaesthesia[3] ranging from 2.1–13% vs. 36.8–52%, respectively[2].

We believe our results indicate that ondansetron prevented the serotonin-induced BJR, suppressed venodilatation, augmented venous return to the heart and resulted in lesser reductions in SBP and MAP. Blockade of the 5-HT3 receptor antagonizes the BJR induced by serotonin[14,15].

Owczuk et al.[3] in a mixed group of patients aged 20–70 years, found that i/v Ondansetron 8 mg decreased the incidence of bradycardia and hypotension after SAB. Martinek[4] concluded that i/v Ondansetron 4 mg with atropine 0.6 mg could revert asystole during SAB.

Moreover, Sahoo et al.[1] demonstrated that ondansetron preloading can effectively prevent maternal hypotension and nausea after SAB during caesarean delivery[16]. Although 4 mg of ondansetron preloading has been commonly used to reduce maternal hypotension and nausea[1,16]. Studies by Sahoo et al.[1] and Wang.Q et al[16] have demonstrated that 4 mg of ondansetron can effectively prevent maternal hypotension during caesarean delivery but like us, both studies only used one given dose.

In line with our results, Marashi et al.[17] found that two different doses of i/v Ondansetron, 6 and 12 mg, significantly attenuated SAB induced hypotension and bradycardia compared with the control saline group.

It was found that the studied drug also reduced shivering in comparison with the placebo group, similar to the findings of Shakya *et al.*[18], who suggested that the prophylactic administration of low dose ketamine (0.25 mg/kg) and ondansetron (4 mg) produces significant antishivering effect in comparison with placebo in patients undergoing SAB.

CONCLUSION

Thus, we conclude in our study that prophylactic i/v use of 4 mg Ondansetron reduces the severity of SAB induced hypotension, the need for rescue vasopressor, incidence of nausea and vomiting and occurrence of shivering.

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