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To study the effect of Ondansetron on hypotension induced in ASA 1 and 2 patients scheduled for caesarean section under sub arachnoid block

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ABSTRACT: For conducting caesarean sectionssub arachnoid blocks are shown to be an easy, safe, and most commonly followed anaesthetics technique. Nonetheless its connotation with some side effects like perioperative hypotension, bradycardia nausea and vomiting can't be ignored. The majority of these side effects are induced by sympathetic blockade, hypovolemia and Bezold-Jarisch reflex through intra-cardiac serotonin (5HT3) receptors and vagus nerve. Various studies have already established the use of 5HT3 antagonists like Ondansetron in preventing the serotonin induced BJR and thus peri-operative hypotension.In the present study, it was hypothesized that blocking type 3 serotonin receptors with intravenous (i.v.) ondansetron reduces the incidence of hypotension induced by spinal anaesthesia

Material and methods: After obtaining approval of institutional ethical committee, and written informed consent we conducted a study in 100 pregnant patients aged between 18-45 years with ASA 1 and 2status planned for an electivecaesarean section at term. This is a prospective, randomized, controlled, double blinded study. Group I (n=50) received 4milligram ondansetronin 10 ml saline intravenously 5 mins before spinal puncture. Group II (n=50) received10 ml saline in the same way and at the same timing. Patients in both the group I and II received 1000 ml of Ringers lactate solution over 30 minutes in the pre-operative room prior to induction of spinal anaesthesia which was induced using2.2 ml of 0.5% Bupivacaine heavy injected inintrathecal space in both the groups by same anaesthesiologist.Standard ASA monitoring including, ECG, Pulse oximetry and NIBP wasrecorded in both the groups. Measurements of BP and heart rate (HR) was taken every 5 minutes for 60 minutes. Mean Arterial Pressure (MAP) drop more than 20 % was considered as incidence of hypotension and 3 mg of mephentermine was given intravenously. HR drop >20 % was regarded as bradycardia and atropine 0.6 mg iv was given intravenously

ResultsBoth groups are comparable in demographic. Statistically significant difference was noted in the Systolic Blood Pressures in both the groups at 0, 10, 20, 30, 40, 50 mins and 1 hour post sub arachnoid block. Requirement of vasopressor was significantly low in Group I 9 patients (18%) with a p=0.005 as compared to group II 32 (64%) patients

Conclusion: It was safely concluded that administering intravenous ondansetron prior to spinal puncture significantly depress the incidence of hypotension and requirement of vasopressors.

KEYWORDS: Ondansetron, hypotension, subarachnoid-block caesarean section

I. INTRODUCTION

For conducting caesarean sectionssub arachnoid blocks are shown to be an easy, safe, and most commonly followed anaestheticstechnique worldwide. Nonetheless its association with potential lethal side effects like perioperative hypotension, bradycardia can't be overlooked[1]. Hypotension after the onset of Sub Arachnoid Block is thought to be caused either by decrease in

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systemic vascular resistance (SVR) or cardiac output (CO) or both which finally manifests as fall in Mean Arterial Pressure [2]. Spinal-induced bradycardia is however multifactorial and the most common pathway postulated is over activity of parasympatheticnervous system,Bezold-Jarisch reflex(BJR), decreased SA nodal stretch reflex and Atrial Brain-bridge reflex[3]. Association of BJR by chemoreceptors and mechanoreceptors which are serotonin sensitive has already been establishedin literature [4].Various studies have already established the use of 5HT3 antagonists like Ondansetron in preventing the serotonin induced BJR and thus peri-operative bradycardia andhypotension. [5]Although sub-arachnoid block is a simple and safe procedure, rare complications such as unresponsive hypotension and bradycardia are real anaesthetic challenges and sometimes difficult to treat [6]. Hence It is preferred to prevent hypotension rather than treating it.

In the present study, it was hypothesized that blocking type 3 serotonin receptors with intravenous (i.v.) ondansetron reduces the incidence of hypotension induced by spinal anaesthesia. The purpose of this prospective, randomized, double-blind study was to compare the efficacy of i.v. ondansetron with a placebo in reducing the incidence of hypotension caused by spinal anaesthesia as primary outcome

II. MATERIAL AND METHODS

This prospective randomized controlled double-blind study was carried out at the Department of Anaesthesiology and Critical Care, of a service hospital of Armed forcesin the ASA 1 and II patients aged between 18-45 years planned for elective caesarean at term from December 2017 to December 2018. A total of 100 subjects were included in the study.

Study design: Prospective double blind randomized study

Study location: Tertiary care center of Armed Forces

Study duration: December 2017 to December 2018

Sample size: 100 patients

Subjects and selection method: After taking informed consent hundred patients aged 18 to 45 years and in ASA physical status ASA I and II, scheduled for elective caesarean section at term were included in the study. The patients who volunteered in the study were randomly assigned to one of the two groups of 50 patients each in a double blinded manner to receive ondansetron or placebo.

Exclusion criteria:

1. Patientrefusal
2. Hypersensitivity to ondansetron
3. ASA physical status III orhigher
4. Contraindication for sub arachnoid block
   - History of allergy to local anaesthetics
   - Bleeding disorders
   - Mental disease
   - Infection at the site of injection
   - Unstable hemodynamics
   - Active infection/sepsis
   - Cardiac disease
5. Hypertensive disorders of pregnancy
6. Patients receiving SSRI or migraine medication.

III. PROCEDURE METHODOLOGY

After obtaining approval of the institutional ethical committee, written informed consent was taken from the patients included in the study.Patients scheduled for elective caesarean section were randomly allocated to any of the two groups Group I (n=50) received ondansetron 4mg in 10 ml normal saline 05 mins before spinal puncture and Group II (n=50) received normal saline in the same way and at the same time. The observer was totally blind about the groups or medications received by the patients. Group sizes of 50 were determined by power analysis based on standard deviation data.

Preoperative orders:

- Nil orally 8 to 10 hours prior tosurgery.
- Written informedconsent.

In the pre anaesthesia room patients of both the groups received 1000 ml of Ringers Lactate solution over a period of 30 minutes. On patient arrival in the operation theater, standard ASA monitors were attached and baseline vital parameters including pulse oximetry, noninvasive BP and ECG were recorded.

Subarachnoid block was administered by a senior anaesthesiologist in both the groups with the patient in the sitting position at the level of L3-L4 using 2.2 ml of 0.5 % hyperbaric bupivacaine after confirmation of cerebrospinal fluid free flow through 26-G spinal needle. The patients were placed in supine position with 15^0tabletilts, and sensory block was assessed to the loss of temperature sensation every 2 minutes for a period of 10 minutes. Patients whose sensory level loss was noted below level of T6 were excluded from the study.

Hemodynamic parameters including baseline heart rate, systolic BP, diastolic BP and MAP were recorded before administering the sub-

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arachnoid block and just after administering the block. These parameters were also sequentially recorded at an interval of 5 minute during intra operative period and at the first hour after surgery. Hypotension was defined as decrease of >20 % of mean arterial blood pressure and was treated with 3 mg bolus of mephentermine intravenously. Bradycardia was defined as a drop of >20 % of base line of heart rate or up to 45 beats per minute and was treated with 0.6 mg of Inj. Atropine intravenously. Total dosage of mephentermine needed was recorded.

IV. STATISTICAL ANALYSIS

Data were statistically described in terms of range, mean ± SD, median, frequencies, and percentages when appropriate. Comparison of quantitative variables between the study groups was done using the Student t-test for independent samples. For comparing categorical data, the chi square -test was performed. Fisher's exact P test was used when the expected frequency was less than 5. A P value less than 0.05 was considered statistically significant.

HAEMODYNAMICS OF STUDIED GROUP BEFORE SUB-ARACHNOID BLOCK			
HAEMODYNAMIC CHARACTERISTICS	GROUP A (N=50) (Mean ± SD)	GROUP B (N=50) (Mean ± SD)	P value
Heart Rate (beats/min)	92.18 ± 19.64	90.52 ± 12.84	0.2098
SBP (mmHg)	118.52 ± 18.26	122.1 ± 16.86	0.1718
DBP (mm Hg)	74.78 ± 9.27	80.16 ± 8.13	0.9083
Mean BP (mm Hg)	88.48 ± 12.03	92.20 ± 8.31	0.6708
SYSTOLIC BP OF STUDIED GROUP AFTER SUB-ARACHNOID BLOCK			
SBP (mm Hg)	GROUP A (N=50) (Mean ± SD)	GROUP B (N=50) (Mean ± SD)	P value
Just after	110.2 ± 15.83	91.46 ± 15.49	<0.001
10 mins	103.08 ± 13.03	96.44 ± 13.48	0.01
20 mins	108.62 ± 11.05	96.20 ± 12.04	0.001
30 mins	109.56 ± 12.02	97.50 ± 11.74	0.001
40 mins	107.56 ± 9.57	97.91 ± 9.54	0.003
50 mins	113.30 ± 9.76	99.76 ± 10.01	0.005
1 hr	113.16 ± 9.30	112.70 ± 12.12	<0.001
MEAN ARTERIAL PRESSURE STUDIED GROUP AFTER SUB-ARACHNOID BLOCK			
MAP (mm Hg)	GROUP A (N=50) (mean ± SD)	GROUP B (N=50) (mean ± SD)	P value
Just after	78.74 ± 12.89	66 ± 9.61	0.006
10 mins	72.94 ± 12.29	66.86 ± 8.09	1.51

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20 mins	73.04 ± 8.45	68.50 ± 7.34	0.51
30 mins	**73.90 ± 7.82**	**65.26 ± 7.48**	**0.07**
40 mins	**71.64 ± 7.96**	**69.08 ± 6.09**	**0.37**
50 mins	75.26 ± 9.21	72.48 ± 6.86	0.09
1 hr	83.90 ±7.57	81.86 ±5.44	0.91
VASOPRESSOR AND ITS DOSE IN STUDY GROUPS			
	GROUP A (N=50)	GROUP B (N=50)	P value
VASOPRESSOR (N%))			
YES	9 (18 %)	32 (64%)	0.005
NO	41 (82 %)	18(36 %)	

Table 1: Various haemodynamic parameters of both study groups

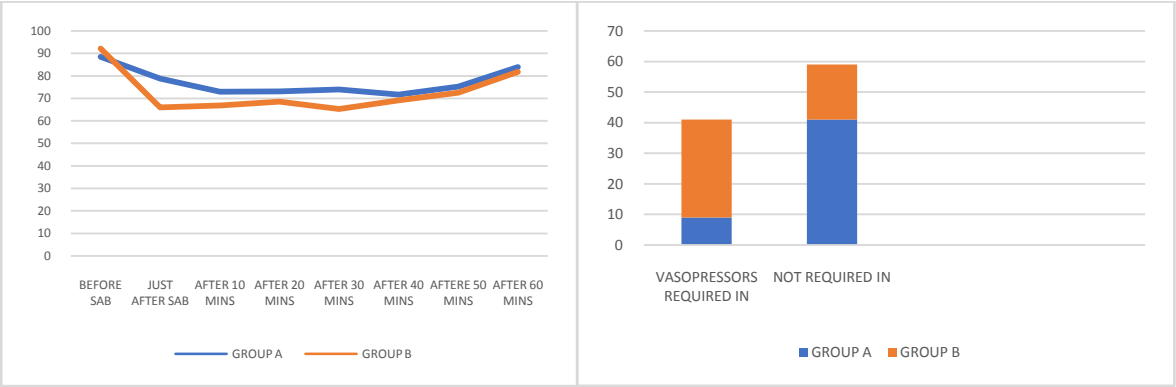

Fig 1. Trends in Mean Arterial BP in both Groups
Fig 2. Trends In requirement of vasopressors in both groups

V. RESULT

The mean age in both the study groups was 26.5 years. Before administering sub arachnoid block no statistically significant difference was noted between the two groups in regards to mean heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP regards), and mean blood pressure (MBP). However, post administration of block difference between mean systolic BP was found to be statistically significant in both the groups. Similarly difference in mean arterial BP in both groups was also found to be significant just after spinal anaesthesia and at intervals of 30 and 40 minutes. It was also seen that there was statistically significant difference in the requirement of vasopressors in both the groups(Table 1, Fig. 2). The need for vasopressor was significantly lower in group I than in group II (18% vs. 64 %) respectively.

VI. DISCUSSION

Unless contraindicated sub arachnoid block is regarded as, reliable, safeand most commonly followed technique of regional anaesthesia for caesarean section worldwide. However, its association with life-threatening risks viz. hypotension and severe Brady-arrhythmias need to be taken into account [1]. It is abundantly established in various clinical publications that the requirement of block height of up to the level of T4 is required for lower segment caesarean section [7]. This level of blockade causes decreased sympathetic outflow leading to a decrease in systemic vascular resistance, venous return and in turn a decrease in preload which finally through various mechanisms manifests asarterial hypotension [8]. Decrease in preload stimulates serotonin sensitive chemoreceptors and mechanoreceptors in the ventricular wall, which stimulate Bezold-Jarisch reflex. [9]. Various other mechanisms including but not restricted to decreased SA nodal stretch reflex, Atrial Bainbridge reflex lead to Bradycardia and when compounded with a decrease pre-load this leads to a sudden haemodynamic collapse [10]. Hence, measures to prevent or treat the hemodynamic changes caused by spinal anaesthesia are required.Various methods of preventing cardiovascular consequences of subarachnoid block including preloading and coloading with i.v.

infusion, administration of sympathomimetic, administration of atropine, and patient positioning facilitating venous return have already been published in literature[11].But all these methods have their own set of complications viz.use of volume preload and vasopressors is associated with complications including but not restricted to volume overload and increase in cardiac workload respectively which may cause peri-operative haemodynamic collapse in labile patients [12]. Hence a study was conducted to see the effect of ondansetron to attenuate the post spinal hypotension caused after spinal anaesthesia by blocking the 5 HT receptors.

A meta-analysis conducted by Gao et al. included 10 randomized controlled trials with 863 patients who underwent surgical procedures under spinal anaesthesia. This database review suggested that prophylactic administration of i.v. ondansetron reduces the incidence of spinal anaesthesia-induced hypotension and vasopressor consumption in both obstetric and non-obstetricpatients. [13]

In a study conducted by Terkawi et al. in 86 parturient for caesarean section who were pre-medicated with i.v. ondansetron 8 mg, showed no significant difference in SBP, DBP, MAP, and HR between the ondansetron and placebo groups.[14].

VII. CONCLUSION

In accordance with the earlier studies the present study also shows that the fall in mean systolic blood pressure, mean arterial blood pressure and use of vasopressors was significantly reduced when ondansetron was administered before spinal anaesthesia. Hence it is safely concluded that 5 HT3 antagonist i.e. ondansetron can be used in preventing the haemodynamic instability in patients post sub arachnoid block.

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