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A Randomised Controlled Trial to Evaluate the Effect of Ondansetron to Attenuate Hypotension and Bradycardia during Spinal Anaesthesia in Caesarean Section

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Abstract

Background and Aim*: Spinal anaesthesia has been an easy, rapid and safe anesthesia given to the parturients for cesarean section with advantages such as less maternal mortality, use of fewer drugs, direct maternal and paternal experience of childbirth and decreased blood loss while providing excellent postoperative pain control. Hypotension and bradycardia are the most common side effects of spinal anesthesia. This study was undertaken to assess the efficacy of prophylactic dose of ondansetron in reducing the incidence of hypotension, bradycardia apart from nausea and vomiting in patients receiving spinal anaesthesia for elective caesarean section.*

Material and Methods*: After obtaining approval from institutional ethical committee*

[SVIEC/ON/MEDI/RP/AUG/24/4], 80 parturients of ASA II posted for elective caesarean section under spinal anaesthesia were enrolled and divided into 2 groups. Group (A) (40 patients): Inj. Ondansetron 4mg diluted in 10 ml normal saline given intravenously over 1 min, 5 min before spinal anaesthesia. Group (B) (40 patients): Injection 10 ml of normal saline given intravenously over 1 min, 5 min before spinal anaesthesia. The primary aim was to study the effect of ondansetron in decreasing incidences of bradycardia and hypotension during caesarean section. The secondary aim was to evaluate requirement of amount of ephedrine and atropine following hypotension and bradycardia caused by spinal anaesthesia. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation (SpO2) were recorded.

Results: *Incidence of fall in systolic blood pressure in group A was 22.50 % and in Group B was 52.50% (p value of 0.006). However, there was no significant difference in diastolic blood pressure, mean arterial pressure and heart rate. Mean ephedrine consumption in group A was less than group B which was statistically significant. (p value of 0.007). Incidence of nausea and vomitting in group A was less than group B which was statistically significant with p value of 0.029.*

Conclusion: *Prophylactic administration of ondansetron, a 5HT-3 receptor antagonist produces a significant*

reduction in the incidence of hypotension in caesarean sections. It also reduces the number of patients who requires ephedrine and its overall dose for the treatment of hypotension. Ondansetron significantly reduces the incidence of nausea and vomiting.

Key Words: *Bradycardia, Hypotension Ondansetron, Spinal Anaesthesia*

Introduction

Delivery of safe and effective anaesthesia with minimal side effects and rapid recovery is the prime goal of anaesthesia in a caesarean section.

Subarachnoid block has been an easy, rapid, safe and most common type of anesthesia provided to the parturient for cesarean section and it has several advantages such as less maternal mortality, use of fewer drugs, direct maternal and paternal experience of childbirth and decreased blood loss while providing excellent postoperative pain control [1].

Although it is considered a safe technique, it has many side effects, including hypotension, nausea, vomiting, bradycardia, and other dysrhythmias [1].

The incidence of hypotension and bradycardia has been reported to be 33% and 13%, respectively in non-obstetric patients [2,3]. In obstetric, non-laboring patients, the incidence of hypotension has been estimated to be as high as 50-60%; this is less common after the onset of labour [4].

In spinal anaesthesia, the unopposed parasympathetic action leads to a constricted gut with increased peristaltic activity. Nausea, retching or vomiting may occur in the awake patient, which may be inconvenient to the patient and surgeon, and are often the first symptoms of impending or established hypotension [5].

Hypotension in pregnant women is much worse than in the non-pregnant counterpart as it also compromises the fetal safety. Hypotension may also lead to placental hypo perfusion leading to foetal hypoxia, acidosis and neurologic injury [4]. It is therefore crucial to prevent and treat it quickly and effectively.

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 (BJR) [2].

Maternal symptoms of low blood pressure include nausea, vomiting, dizziness, and decreased consciousness [5].

Spinal anaesthesia induced bradycardia is multifactorial but is partially due to the Bezold-Jarisch reflex. Receptors for this reflex are mechanoreceptors located in the heart walls, and also include chemoreceptor's sensitive to serotonin (5-HT3 receptors) [6]. Both types of receptors are involved in the induction of hypotension and bradycardia after spinal blockade. Although mechanoreceptors located in all cardiac chambers are normally sensitive to distension, diminished venous return of blood, as observed after spinal block, induces deformation of the cardiac wall, resulting in irritation of mechanoreceptors and activation of the Bezold-Jarisch reflex (BJR). Chemoreceptors are activated by serotonin released from activated thrombocytes [7,8]. Bezold Jarisch Reflex is mediated by serotonin receptors within the wall of the ventricle in response to systemic hypotension. It is a cardio inhibitory reflex producing bradycardia, hypotension, and cardiovascular collapse via nonmyelinated, type C fibers whose terminals lie in the chambers of the heart [9].

Serotonin released during low-volume or ischemic states have been suggested as a possible trigger for the BJR and it acts at 5HT3 receptors. The stimulation of these peripheral 5hydroxytryptamine subtype 3 (5HT3) receptors results in increased parasympathetic activity and decreased sympathetic activity, resulting in bradycardia, vasodilatation, and hypotension [10,11]. Animal studies suggest that serotonin may be an important factor inducing BJR in cases of decreased blood volume and the mechanism of triggering the reflex depends on activation of peripheral 5-HT3 receptors located in intracardiac vagal nerve endings by serotonin [12].

Ondansetron is a selective 5-HT3 receptor antagonist and is currently approved by the Food and Drug Administration (FDA) for treatment of nausea and vomiting caused by chemotherapy, radiation therapy and surgery [13]. A study was conducted in 176 pregnant females which showed that ondansetron does not appear to be associated with an increased risk for major malformations above baseline [14]. The FDA has assigned ondansetron as category B drug in pregnant patients and animal studies have also demonstrated no harm to their offspring [15].

This study was undertaken to assess the efficacy of prophylactic dose of ondansetron in reducing the incidence of hypotension, bradycardia, nausea and vomiting in patients receiving spinal anaesthesia for elective caesarean section.

Material and Methods

This prospective randomised controlled study was conducted at Department of Anaesthesia, Shrimati Bhikhiben Kanjibhai Shah Medical Institute and Research Centre, Piparia, Vadodara, Gujarat, India, after obtaining approval from Institutional Ethical Committee (SVIEC/MEDI/RP/AUG/24/4).

Sample size calculation

Taking Data from the study conducted by Ahmed A. Eldaba, Yasser M. Amr et al [13] on effectiveness of intravenous granisetron in the prevention of hypotension and bradycardia during spinal anesthesia in cesarean delivery where 200 parturients scheduled for elective cesarean section were included in this study. The incidence of hypotension after spinal anesthesia was low in granisetron group (P value < 0.0001).

With 3% incidence rate of hypotension under null hypothesis and 64% incidence rate under alternate hypothesis. Type I error 5% and 0.9 power of the study, the calculated sample size was 37 in each group but we included 40 patients in each group to compensate for drop outs and exclusions. Total 80 patients posted for elective caesarean section were enrolled for study after obtaining informed Consent.

Inclusion Criteria

Pregnant patient's belonging to ASA II and age group 18-45 years with gestational age ≥ 37 weeks.

Exclusion Criteria

Patient who refused to participate, belonging to ASA grade III and IV, having hypersensitivity to ondansetron, hypertensive disorders of pregnancy, history of nausea and/or vomiting during or 24 hours before induction of anesthesia, cardiovascular insufficiency, patients on selective serotonin reuptake inhibitors, having contraindication for spinal anesthesia and those with post partum haemorrhage were excluded from the study.

They were blinded and randomly allocated to two groups via computer generated method, either to

Group A : received Inj. ondansetron 4mg diluted to 10 ml normal saline intravenously over 1 min, 5 min before spinal anaesthesia

Group B : received 10 ml Inj. normal saline intravenously over 1 min, 5 min before spinal anaesthesia

Anaesthesiologist performing the procedure was blinded and provided with a prefilled syringe having either ondansetron or normal saline.

After preoperative history taking and physical examination, detailed procedure was explained to the patient and patients were informed to communicate about the perception of any discomfort, pain or nausea vomiting during surgery.

In the operation theatre, after securing peripheral 18-gauge intravenous cannula, preloading with 15 ml/kg of Ringer lactate solution was done. Baseline values of pulse oximetry (SpO2), noninvasive BP and Electrocardiogram (ECG) were recorded. The study solution was administered intravenously 5 min before spinal anaesthesia. The spinal anaesthesia was performed with the patient in the sitting position at L2-3 or L3-

4 intervertebral space with 2 ml of 0.5% Bupivacaine (Heavy) after confirmation of free flow of cerebrospinal fluid through a 25 gauge Quincke's spinal needle. Patients were immediately placed in the supine position.

Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure and oxygen saturation (SpO2) were recorded at time of spinal drug administration and at 3-min intervals up to 30 min, followed by 5-min intervals until the end of surgery.

Hypotension was defined [16] as systolic blood pressure <90 mmHg or Mean arterial pressure <60 mmHg and was treated with Injection Ephedrine 6 mg intravenous and further as per requirement. Bradycardia defined as heart rate <50 beats/min was treated with Injection Atropine 0.6 mg intravenous. Rigors and pain were treated with Injection Tramadol 25 mg intravenous and Injection Fentanyl 50 mcg intravenous respectively after delivery of baby.

Statistical Method

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.

Statistical tests were applied as follows-

1. Quantitative variables were compared using Independent/unpaired t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups.

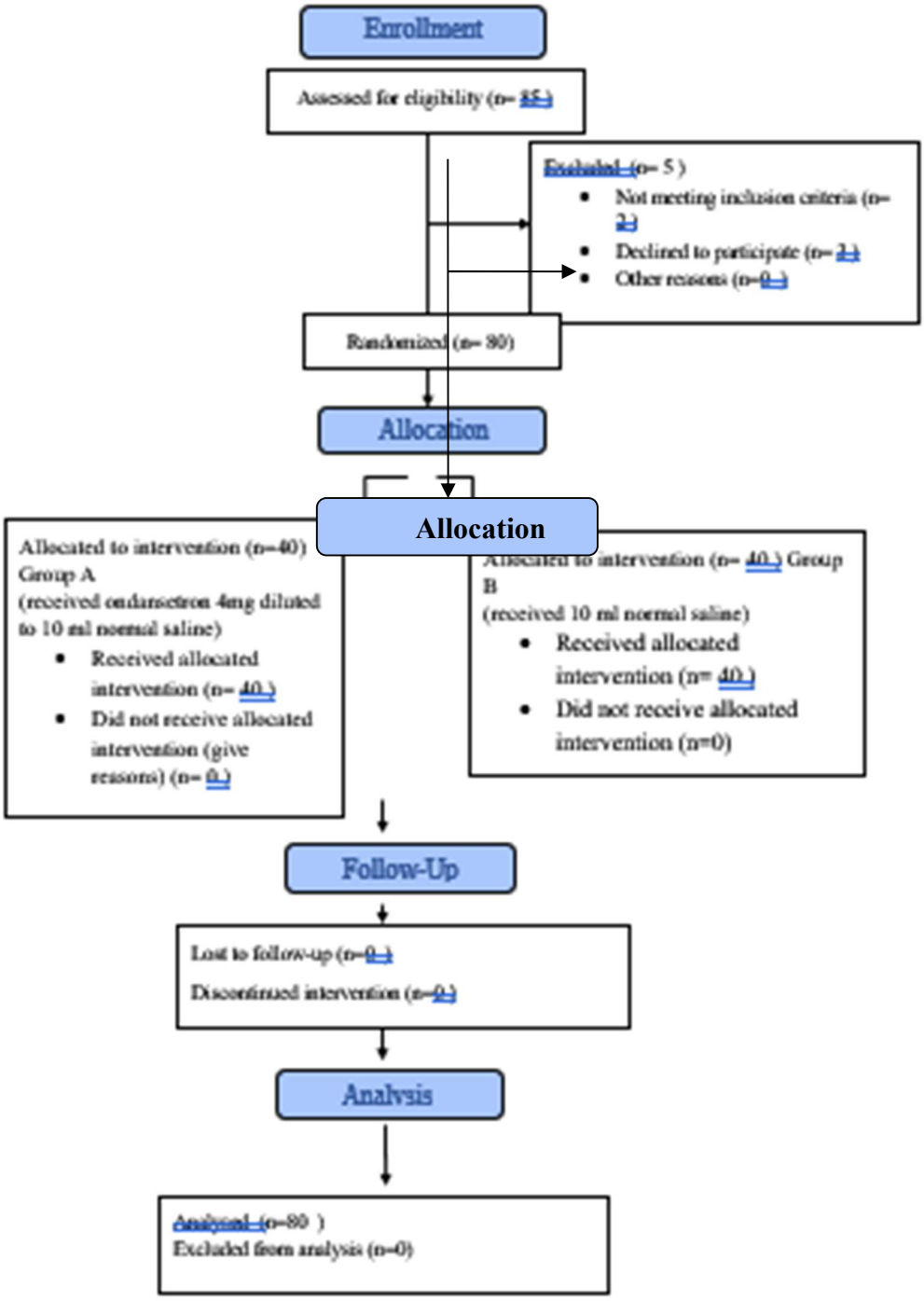
2. Qualitative variables were correlated using Chi-Square test/Fisher's exact test.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet (Microsoft® Corp., Redmond, WA) and analysis was done using Statistical Package for Social Sciences (SPSS) version 22.0 2 (IBM SPSS, Armonk, NY).

P value < 0.05 was considered significant. Figure *1* represents consort diagram of the study.

Figure 1: CONSORT FLOW DIAGRAM



Results

Out of total 85 patients, 3 patients declined to participate in the study and 2 patients were excluded for having cardiac disease and hypertension respectively. Therefore, 80 patients participated in the study and were able to finish the study without any drop- outs.

All parameters like demographic profile, duration of surgery, gestational age and baseline hemodyanamic parameters were compared.

Table 1 shows age distribution, weight, height, BMI, gestational age and duration of surgery of patients in both the groups. There was no statistical significance in the two groups.

	Group A	**Group B**	**p value**
	Mean + SD	Mean + SD	
Age (years)	31 ± 4.54	31.48 ± 3.62	0.606
Weight (kg)	71.08 ± 5.43	70 ± 5.26	0.371
Height (mtrs)	1.59 ± 0.04	1.57 ± 0.05	0.055
BMI (kg/m^2)	28.24 ± 2.08	28.5 ±2.07	0.575
Gestational age (weeks)	37.75 ± 0.78	37.75 ±0.67	0.833
Duration of surgery (minutes)	54 ± 5.45	52 ± 4.39	0.119

Table 1: Comparison of demographic profile, gestational age and duration of surgery between group A and B

Table 2 shows that the incidence of hypotension observed in group A was 22.50 % and in Group B was 52.50%. Overall incidence was 37.50%. The difference in incidence of hypotension is statistically significant with p value of 0.006.

	Hypotension				
	Group A		Group B		p value
	Frequency	%	Frequency	%	
Present	9	22.50%	21	52.50%	0.006
Absent	31	77.50%	19	47.50%	
Total	40	100%	40	100%	

Table 2: Comparison of Incidence of hypotension in group A and B

Table 3 shows systolic blood pressure variation between the two groups from Baseline value up to 60 min. Although there was drop in systolic blood pressure in both the groups but drop was more in group B than group A. It was statistically significant at 21, 27 and 60 minutes with p value < 0.05.

TIME	**Systolic Blood Pressure**			
	Group A	Group B	Statistical Analysis	
	Mean±SD	Mean±SD	p value	Results

BASELINE	124.8 ± 11.29	122.05 ± 10.25	0.258	NS
3 MIN	121.28 ± 10.49	119.8 ± 10.34	0.528	NS
6 MIN	115.78 ± 11.45	113.9 ± 15.8	0.545	NS
9 MIN	109.1 ± 15.94	105.55 ± 18.6	0.362	NS
12 MIN	110.22 ± 16.51	104.58 ± 17.43	0.141	NS
15 MIN	112.35 ± 15.15	107.62 ± 17.47	0.200	NS
18 MIN	111.78 ± 13.96	108 ± 15.16	0.250	NS
21 MIN	115.78 ± 11.91	109.8 ± 13.01	0.035	SS
24 MIN	116.32 ± 10.63	110.95 ± 13.84	0.055	NS
27 MIN	115.1 ± 11.01	109.18 ± 12.72	0.029	SS
30 MIN	113.58 ± 10.59	109.48 ± 11.27	0.098	NS
35 MIN	113.2 ± 9.71	110.38 ± 10.14	0.207	NS
40 MIN	113.12 ± 10.07	112.42 ± 10.61	0.763	NS
45 MIN	115.38 ± 8.73	115.1 ± 10.16	0.894	NS
50 MIN	116.8 ± 9.51	118.24 ± 9.98	0.544	NS
55 MIN	117.09 ± 8	121.81 ± 6.82	0.064	NS
60 MIN	113.31 ± 6.1	120.33 ± 7.09	0.040	SS

Table 3: Comparison of Systolic Blood Pressure (SYSTOLIC BLOOD PRESSURE) variations between groups A and B

Table 4 shows Diastolic Blood Pressure variation between the two groups from baseline value up to 60 min. Although there was more drop in diastolic blood pressure in group B but it was not statistically significant (p value >0.05).

TIME	**Diastolic Blood Pressure**			
	Group A	Group B	Statistical Analysis	
	Mean±SD	Mean±SD	p value	Results
BASELINE	77.35 ± 10.09	76.3 ± 9.02	0.625	NS
3 MIN	74.32 ± 10.1	73.72 ± 9.24	0.782	NS
6 MIN	70.75 ± 10.42	69.12 ± 11.14	0.502	NS
9 MIN	65.7 ± 14.22	62.15 ± 13.74	0.260	NS
12 MIN	66.58 ± 15.57	62.42 ± 12.84	0.197	NS
15 MIN	67.12 ± 12.95	64.8 ± 12.06	0.409	NS

18 MIN	66.5 ± 13.64	65.4 ± 11.92	0.702	NS
21 MIN	69.6 ± 11.8	65.7 ± 9.57	0.109	NS
24 MIN	69.7 ± 11.03	65.38 ± 11.99	0.097	NS
27 MIN	67.12 ± 12.74	65.32 ± 10.44	0.492	NS
30 MIN	68.92 ± 10.7	66.05 ± 10.03	0.219	NS
35 MIN	67.72 ± 11.17	66.18 ± 9.51	0.506	NS
40 MIN	68.2 ± 11.72	68.32 ± 10.03	0.959	NS
45 MIN	69.41 ± 10.02	68.5 ± 9.77	0.684	NS
50 MIN	69.77 ± 10.8	70.48 ± 9.4	0.773	NS
55 MIN	70.96 ± 10.04	71.75 ± 9.36	0.806	NS
60 MIN	68.77 ± 10.03	73.83 ± 3.92	0.254	NS

Table 4: Diastolic Blood Pressure variations between groups A and B

Table 5 showing mean arterial pressure variation between the two groups from baseline value up to 60 min after subarachnoid block. Although there was drop in mean arterial pressure in both the groups and comparatively drop was more in group B but the difference was not statistically significant (p value >0.05).

TIME	**Mean Arterial Pressure**			
	Group A	Group B	Statistical Analysis	
	Mean±SD	Mean±SD	p value	Results
BASELINE	93.32 ± 9.56	91.32 ± 9.06	0.338	NS
3 MIN	89.5 ± 9.77	88.86 ± 8.67	0.757	NS
6 MIN	85.6 ± 10.49	83.96 ± 11.99	0.516	NS
9 MIN	83.96 ± 11.99	76.58 ± 14.48	0.448	NS
12 MIN	81.45 ± 14.21	76.65 ± 12.77	0.116	NS
15 MIN	81.75 ± 13.29	78.72 ± 12.86	0.304	NS
18 MIN	81.72 ± 13.69	79.87 ± 12.57	0.529	NS
21 MIN	84.8 ± 11.1	80.22 ± 9.52	0.051	NS
24 MIN	84.32 ± 10.77	80.4 ± 11.91	0.126	NS
27 MIN	82.39 ± 12.03	79.53 ± 10.04	0.251	NS
30 MIN	83.58 ± 11.34	80.78 ± 10.08	0.247	NS
35 MIN	83.28 ± 9.9	80.74 ± 8.96	0.234	NS
40 MIN	82.78 ± 11.39	82.64 ± 9.27	0.954	NS

45 MIN	84.94 ± 9.03	83.82 ± 8.75	0.579	NS
50 MIN	85.79 ± 8.81	86.26 ± 8.95	0.827	NS
55 MIN	87.32 ± 8.82	88.35 ± 7.92	0.712	NS
60 MIN	84.23 ± 6.91	87.83 ± 4.96	0.269	NS

Table 5: Comparison of Mean Arterial Pressure variations between groups A and B

Table 6 show the incidence of bradycardia in both the groups. There were no events of bradycardia in both groups.

TIME	Bradycardia				
	Group A		Group B		p value
	Frequency	%	Frequency	%	
Present	0	0%	0	0%	-
Absent	40	100%	40	100%	
Total	40	100%	40	100%	

Table 6: Comparison of Incidence of bradycardia in group A and Bmparison of Incidence of bradycardia in group A and B

Table 7 are showing heart rate variation between the two groups. There is no statistically significant difference between the two groups in relation to heart rate.

TIME	Heart Rate			
	Group A	Group B	Statistical Analysis	
	Mean±SD	Mean±SD	p value	Results
BASELINE	88.58 ± 12	86.92 ± 11.69	0.535	NS
3 MIN	91.62 ± 12.2	90.35 ± 12.89	0.651	NS
6 MIN	91.48 ± 13.48	90.05 ± 15.44	0.661	NS
9 MIN	90.95 ± 13.79	89.88 ± 15.02	0.740	NS
12 MIN	91.12 ± 15.4	91.02 ± 13.62	0.976	NS
15 MIN	91.42 ± 14.45	91.95 ± 15.41	0.876	NS
18 MIN	88.68 ± 11.53	91.95 ± 15.23	0.281	NS
21 MIN	88.58 ± 11.69	89.78 ± 12.98	0.665	NS
24 MIN	88.28 ± 10.79	90.02 ± 11.44	0.484	NS
27 MIN	88.35 ± 12.37	87.48 ± 9.19	0.721	NS
30 MIN	87.75 ± 11.8	85.7 ± 9.06	0.386	NS

35 MIN	86.2 ± 10.98	85.38 ± 10.1	0.727	NS
40 MIN	85.62 ± 10.32	86.35 ± 8.7	0.735	NS
45 MIN	84.69 ± 10.11	84.38 ± 9.17	0.884	NS
50 MIN	81.37 ± 10.59	82.7 ± 9.42	0.588	NS
55 MIN	81.59 ± 9.96	83.88 ± 9.33	0.478	NS
60 MIN	81.15 ± 8.22	82.17 ± 7.76	0.803	NS

Table 7: Heart Rate (Beats/min) variations between groups A and B

Table 8 shows that ephedrine consumption in group A was 2.4 ± 5.05 mg while in group B was 5.85 ± 6.72 mg. The difference in ephedrine consumption is statistically significant in both the groups (p value of 0.007)

Ephedrine Consumption (mg)		
Group A	Group B	p value
Mean ± SD	Mean ± SD	
2.4 ± 5.05	5.85 ± 6.72	0.007

Table 8: Ephedrine consumption (in mg) in group A and B

Table 9 shows that the incidence of nausea and vomiting in group A was 2.50% and group B was 20% and overall incidence was 11.25%. It is statistically significant with p value of 0.02

PARAMETER	**Nausea and Vomiting**				
	Group A		Group B		p value
	Frequency	%	Frequency	%	
Present	1	2.50%	8	20%	0.029
Absent	39	97.50%	32	80%	
Total	40	100%	40	100%	

Table 9: Incidence of nausea and vomiting in groups A and B

Table 10 showed that there is no requirement of atropine in either of the group.

PARAMETER	**Atropine Consumption**				
	Group A		Group B		p value
	Frequency	%	Frequency	%	
Yes	0	0%	0	0%	-
No	40	100%	40	100%	
Total	40	100%	40	100%	

Table 10: Comparison of Atropine consumption in group A and B

Discussion

The most preferred anaesthesia for caesarean section is spinal anaesthesia and it is a safe and effective anaesthetic technique considering its simplicity, rapidity of action, dense neural block, analgesia and minimal foetal exposure to drugs [16]. It is frequently associated with hypotension and bradycardia. Hypotension results primarily from decrease in systemic vascular resistance and central venous pressure from sympathetic block [17,18]. Sudden bradycardia can occur from shift in cardiac autonomic balance toward the parasympathetic system from activation of left ventricular mechanoreceptors or chemoreceptor's responsible for Bezold- Jarisch reflex (BJR) or from an increase in baroreflex activity [18]. Aiming at reducing the incidence of hypotension during spinal anesthesia for caesarean section, different methods can be used with variable degrees of efficacy and no single method has been found to completely prevent hypotension. These methods include preloading with intravenous fluids including crystalloids or colloids, administration of vasoactive drugs including ephedrine or phenylephrine , left uterine displacement, and/or leg compression [19].

Animal studies have demonstrated that 5 HT3 receptor blockade decreases the intensity of hypotension related to Bezold-Jarisch reflex triggered by various factors [20,21].

Spinal anaesthesia- related triggering of Bezold-Jarisch reflex, demonstrated by hypotension, bradycardia and vasodilatation, is known to result from stimulation of 5-HT3 receptors in vagal nerve endings [7,8]. Hence the idea of using ondansetron, a 5 HT3 receptor antagonist to block this reflex was under consideration.

The aim of this study was to compare the effect of ondansetron to reduce the incidence of hypotension and bradycardia in parturients undergoing caesarean section under spinal anaesthesia.

This prospective, double blind, randomized, comparative study was conducted on 80 patients, belonging to ASA grade II, undergoing elective caesarean delivery at term under spinal anaesthesia.

Group (A) (40 patient): Injection. Ondansetron 4mg diluted in 10 ml normal saline.

Group (B) (40 patients): Injection 10 ml of normal saline.

Patients in both groups were comparable in terms of demographic profile, body mass index, gestational age, duration of surgery and baseline hemodynamic parameters.

After study drug administration and spinal anaesthesia, incidence of hypotension in group A was found to be 22.50 % (N= 40) and in group B was 52.50% (N= 40) which was statistically significant with p value of 0.006.

The difference in drop of systolic blood pressure between two groups was statistically significant at 21, 27 and 60 minutes. The drop in diastolic blood pressure and mean arterial pressure was comparable between two groups and was not statistically significant at any point of time throughout the surgery.

Yamano et al [12], in their study, observed that the effect of spinal anesthesia on systolic blood pressure, mean arterial pressure, and HR were reduced with the use of intravenous ondansetron 8 mg given 5 min before spinal anesthesia in pregnant women subjected to elective caesarean section in accordance to our study.

Ahmed A. Eldaba, Yasser M. Amr et al [14] conducted a study to determine the effectiveness of intravenous granisetron in the prevention of hypotension and bradycardia during spinal anesthesia in cesarean delivery and found that the incidence of hypotension after spinal anesthesia was low in granisetron group. The total doses of ephedrine and atropine consumption also low in this group.

Sahoo, T et al [15], did a similar study on 52 parturients scheduled for elective caesarean section. Group O (n=26) received intravenous ondansetron 4mg; Group S (n=26) received normal saline before induction of spinal anaesthesia. Similar to our findings, they observed that mean arterial pressure were significantly lower in Group O than Group S from 14min until 35min. Patients in Group O required significantly less vasopressor (P=0.009) and had significantly lower incidences of nausea and vomiting (P=0.049).

White et al [21] studied 5- HT3 antagonist granisetron in the doses of 50 μg/kg intravenously and they found

that it could suppress bradycardia and hypotension associated with the BJR in a rabbit model.

Owczuk et al [22] studied the effect of ondansetron in a mixed group of patients aged 20-70 years and they found that ondansetron 8 mg attenuates the fall of systolic and mean blood pressure, but does not have an influence on diastolic blood pressure and heart rate in spinal anesthesia.

Rashad et al [23] concluded that in parturient females undergoing elective cesarean section, intravenous 4 mg ondansetron before subarachnoid block significantly decreased both the incidence of hypotension, doses of vasopressor and also decreases the incidence of nausea and vomiting.

In our study, there was no incidence of significant bradycardia (requiring treatment) in either group and there was no statistical significant difference in drop in heart rate in either of the groups. Hence ondansetron does not significantly reduce the incidence of bradycardia.

Potdar, Kamat et al [24] found that after giving ondansetron in caesarean section in parturients the change in the heart rate (HR) was not statistically significant. The fall of systolic blood pressure, diastolic blood pressure and mean arterial pressure was significantly less in ondansetron group at all time intervals intraoperatively than placebo group after administration of Spinal anaesthesia (p value <0.001) when compared to pre-operative values

In our study, there was statistically significant differences in ephedrine consumption between two groups (p= 0.007). The mean consumption of ephedrine was 2.4 ± 5.05 mg in group A and 5.85 ± 6.72 mg in group B, suggesting that prophylactic ondansetron administration significantly reduced the required dose of ephedrine. This indirectly implies that the degree of hypotension was more in patients not treated with ondansetron.

Trabelsi et al [25] found that average consumption of ephedrine intraoperatively was 5.10 ± 7.78 mg in group O (ondansetron group) while it was 12.90 ± 9.24mg in group S(normal saline group) with a significant difference ($P < 0.001$).

As mentioned above, in Ahmed A. Eldaba [14] study they found that ephedrine consumption in granisetron group (4.07 ± 3.87 mg) was significantly low (p value <0.0001) than control group (10.7 ± 8.9 mg).

According to a study done by Ashagrie et al [26], the incidence of intra-operative nausea and vomiting was 18.5% which is a significant intraoperative morbidity. Nausea and vomiting under spinal anaesthesia is usually following a drop in blood pressure and probably as consequence of cerebral hypoxia, vagal hyperactivity, visceral pain, intravenous opioid supplementation, uterotonic agents [26]. In our study, the incidence of nausea and vomiting in group A was 2.50% while in group B was 20 %. The difference is statistically significant with p value of 0.029.

Ayman A. Shabana et al [27] studied ondansetron use as an antiemetic and serotonin antagonist and to blunt the Bezold-Jarisch reflex, and found less bradycardia, hypotension, less requirement for vasopressor and had significantly lower incidence of nausea and vomiting in ceasarean section under spinal anesthesia.

Shivanand et al [28] also concluded that prophylactic ondansetron 4mg intravenously is more efficacious in preventing post operative nausea and vomiting in LSCS under spinal anaesthesia.

In contrast to this study, Chengmao Zhou, Yu Zhu et al [29] conducted a meta-analysis of 21 randomised controlled trial and showed that the ondansetron group had a lower incidence of nausea, vomiting and bradycardia than the placebo group but there were no significant differences in the incidences of pruritus, hypotension, or shivering during cesarean section under spinal anesthesia.

Limitations of the study

There were few limitations to this study, definition of hypotension was different in different studies which were taken for comparison. The definition of hypotension affects the incidence of hypotension. Fixed dose of Bupivacaine was used in this study irrespective of height and weight of the parturient.

Furthermore, study was conducted on healthy parturients with term pregnancy undergoing elective caesarean section. Therefore, it cannot be extrapolated to emergency delivery with compromised maternal and fetal status.

Apart from above, this was a double blinded study, so observer biased could not be ruled out.

Effectiveness of ondansetron should also be assesed for non-obstetric population in further studies.

Conclusion

Ondansetron, a 5HT-3 receptor antagonist can be safely used in pregnant patients with minimal adverse effects on mother and fetus. Its prophylactic administration not only reduces incidence of nausea and vomiting but also produces a significant reduction in the incidence of hypotension in obstetric population undergoing caesarean section under spinal anesthesia. It lowers the incidence of hypotension and dose of ephedrine required for the treatment of hypotension.

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There are no conflicts of interest.
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