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Original Research Article

Effect of Intravenous Ondansetron on Sub-Arachnoid Block Induced Hypotension and Bradycardia in Patients Undergoing Caesarean Section

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Conflict of interest: Nil

Abstract:

Background: Spinal anesthesia is a safe and effective alternative to general anesthesia when the surgical site is located on the lower extremities, perineum (eg, surgery on the genitalia or anus), or lower body wall (eg, inguinal herniorrhaphy).

Objective: To compare post spinal (SAB) haemodynamic changes (hypotension and bradycardia) between two groups.

Methods: This Prospective observational study was conducted in Department of Anaesthesiology and Critical Care in M GM Medical College and LKS Hospital. ASA physical status II, between 18 to 40 years of age, parturient undergoing elective caesarean section at term was enrolled in this study. Study period was August 2022- August 2023.

Results: Intra-Op pulse rate was less in Normal Saline group compared to Ondansetron group which was statistically significant. Intra-op lowest SBP, DBP and MAP were less in Normal Saline group compared to Ondansetron group which were statistically significant. Episodes of bradycardia in intra-op were more in Normal Saline group compared to Ondansetron group though it was not statistically significant. The mean Episodes of hypotension in intra-op was more in Normal Saline group compared to Ondansetron group which was statistically significant.

Conclusions: Use of intravenous ondansetron before sub-arachnoid block in parturients undergoing caesarean section, causes significant reduction of hypotension and variable reduction of bradycardia intra operatively

Keywords: Intravenous Ondansetron, Sub-Arachnoid Block, Hypotension, Bradycardia Caesarean Section.

Introduction

Spinal anesthesia has become the gold standard anesthetic technique for elective caesarean section. It is a simple, fast performed, powerful, and reliable technique. The main problem is hypotension associated with a decrease in cardiac output and uteroplacental flow which may induce fetal morbidity [1]. It is therefore crucial to prevent and/or to treat it quickly and effectively.

The spinal anesthesia for cesarean indeed requires a sensory block until T5, which always leads to an extended sympathetic block and hypotension occurs in 55% to 90% of cases, despite the partial left lateral decubitus (with the objective of limiting the aortocaval compression caused by the gravid uterus).

The main treatment is the vascular filling with crystalloid or starches and use of vasopressors. However, many studies [2,3] showed that it was inefficient, and a recent review found that no intervention reliably prevents hypotension during spinal anesthesia for caesarean section [4].

The physiopathological mechanism involved in the occurrence of hypotension is systemic vascular resistance and central venous pressure from sympathetic block with vasodilation [5,6,7]. Bradycardia can occur from shift in cardiac autonomic balance toward the parasympathetic system, from activation of left ventricular mechanoreceptors from a sudden decrease in left ventricular volume (Bezold-Jarisch reflex) (BJR).

Pharmacological and animal studies [8] 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 [9]. Ondansetron is one of the new classes of 5-HT3 receptor antagonists. Ondansetron, a widely used antiemetic and

serotonin antagonist, has been safely used to blunt the Bezold–Jarisch reflex, resulting in less bradycardia and hypotension in humans undergoing spinal anesthesia [10].

Materials and Methods: This Prospective observational study was conducted in Department of Anaesthesiology and Critical Care in M G M Medical College and LKS Hospital. ASA physical status II, between 18 to 40 years of age, parturient undergoing elective caesarean section at term was enrolled in this study. Study period was August 2022- August 2023.

Sample Size Calculations: we estimated that 23 subjects would be required per group in order to detect a 6 mm of Hg difference in MAP between groups with 80% power and 5% probability of type 1 (Alpha) error. This calculation was based on a 7 mm of Hg difference observed by Owczuk et al. in non-pregnant patients. Data will be summarized by descriptive statistics. Numerical variables normally distributed will be compared between groups by Student's independent samples t test. Categorical variables will be compared between groups by Fisher's exact probability test. Repeated measures ANOVA will be employed for intra group comparison of numerical variables, followed by Dunnet's test (with baseline value as the control value) for post hoc testing. All analyses are 2-tailed. P<0.05 is considered statistically significant.

In this study, we took 60 participants with 30 participants in each group.)

Sample Design:

- Age- Between 18 to 40 years
- Sex- Parturient mother

Inclusion criteria

ASA physical status II aged between 18 to 40years Parturient undergoing elective caesarean section at Term

Exclusion criteria:

- Hyperemesis gravidarum,
- Contraindication to spinal anesthesia (patient refusal, unstable haemodynamic and coagulation abnormalities)
- Chronic hypertension or preeclampsia
- Morbid obesity, and/or
- Any allergy to the study drugs.

Study Technique: After clearance from the ethical committee of the institute, the study was conducted in the Operation Theatre, M G M Medical College and LKS Hospital. A written informed consent was taken from the patients enrolled in the study after applying inclusion and exclusion criteria.

Parturients with ASA physical status II, aged between 18 to 40 years undergoing elective caesarean section at term was enrolled in this Prospective, randomized, controlled, double-blinded study. Patients were randomized during preanesthetic consultation to one of the 2 groups using a random sequence: Group 'O' had receive intravenously 4mg Ondansetron in 10mL saline, 5 minutes before spinal puncture, and the control group had receive 10mL of saline in the same way with the same timing as group 'C'.

All hemodynamic parameters were recorded every 2 minutes to 20 minutes and then every 5 minutes until skin closure. Hypotension, defined as SBP<90mm of Hg or DBP<60 mm of Hg or MAP < 65mmHg or < 30% reduction in baseline SBP/DBP, was treated by an infusion of crystalloids (100 ml) and Mephenteremine bolus (6mg) or Inj Phenylephrine 50 mcg until restoration of baseline values. Bradycardia, defined as a 30% drop in HR or ≤50 Bpm, was also treated with fluids and IV atropine 0.3mg was given every 30 seconds until resolution. We had taken note of total dose of atropine and Mephenteremine/ Phenylephrine needed.

Statistical Analysis: For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 20.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. p-value ≤ 0.05 was considered for statistically significant.

Results

Association of Age in years vs group was not statistically significant (p>.05).

In Normal Saline, 13(43.3%) patients had Gravida, 13(43.3%) patients had Gravida and 4(13.3%) patients had Gravida.

In Ondansetron, 14(46.7%) patients had Gravida, 12(40.0%) patients had Gravida and 4(13.3%) patients had Gravida

Association of Gravida vs group was not statistically significant. (Chi-square value: .0770; p-value: 0.9622)

Association of Parity vs group was not statistically significant (p=0.3466). Association of Co-morbidity vs group was not statistically significant (Chi-square value: 2.3570,p-value:0.5017). Association of Total dose of mephentermine/phenylephrine (intraop) vs group was statistically significant (p=0.0015)

In Normal Saline, the mean Age (Mean± SD.) of patients was 28.3000± 3.3337. In Ondansetron, the mean Age (Mean± SD) of patients was 27.4667± 3.8393. Difference of mean Age with both Group was not statistically significant (p=0.3731)

In Normal Saline, the mean Gravidae (Mean± SD) of patients was 1.7000± .7022. In Ondansetron, the mean Gravidae (Mean± SD.) of patients was 1.6667± .7112. Difference of mean Gravidae with both Group was not statistically significant (p=0.8557).

In Normal Saline, the mean Weight (Kg) (Mean± SD) of patients was 73.8333± 4.9625. In Ondansetron, the mean Weight (Kg) (Mean± SD) of patients was 72.6000± 5.7271. Difference of mean Weight (Kg) with both Group was not statistically significant (p=0.3764).

Table 1: Distribution of mean Pulse rate/min (before SAB): Group

		Number	Mean	SD	Minimum	Maximum	Median	pvalue
Pulse rate/min (before SAB)	Normal Saline	30	91.3333	7.1983	77.0000	106.0000	92.5000	0.9174
	Ondansetron	30	91.5333	7.6597	77.0000	108.0000	90.0000	

In Normal Saline, the mean Pulse rate/min (before SAB) (mean± s.d.) of patients was 91.3333± 7.1983. In Ondansetron, the mean Pulse rate/min (before SAB) (mean± s.d.) of patients was 91.5333± 7.6597. Difference of mean Pulse rate/min (before SAB) with both Group was not statistically significant (p=0.9174).

Table 2: Distribution of mean Systolic BP before SAB (mm of Hg): Group

		Number	Mean	SD	Minimum	Maximum	Median	Pvalue
Systolic BP before SAB (mm of Hg)	Normal Saline	30	116.6000	6.5527	107.0000	130.0000	115.0000	0.4270
	Ondansetron	30	118.0667	7.6109	104.0000	134.0000	117.0000	

In Normal Saline, the mean Systolic BP before SAB (mm of Hg) (Mean± SD) of patients was 116.6000± 6.5527.

In Ondansetron, the mean Systolic BP before SAB (mm of Hg) (Mean± SD) of patients was 118.0667± 7.6109. Difference of mean Systolic BP before SAB (mm of Hg) with both Group was not statistically significant (p=0.4270). In Normal Saline, the mean Diastolic BP before SAB (mm of Hg) (Mean± SD) of patients was 70.6000± 6.1229. In Ondansetron, the mean Diastolic BP before SAB (mm of Hg) (Mean± SD) of patients was 72.9667± 6.8304. Difference of mean Diastolic BP before SAB (mm of Hg) with both Group was not statistically significant (p=0.1630). In Normal Saline, the mean MAP before SAB (mm of Hg) (Mean± SD) of patients was 85.8000± 5.7018.

In Ondansetron, the mean MAP before SAB (mm of Hg) (Mean± SD) of patients was 88.0333± 6.9107. Difference of mean MAP before SAB (mm of Hg) with both Group was not statistically significant (p=0.1774).

Table 3: Distribution of mean Intra Op lowest pulse rate/min: Group

		Number	Mean	SD	Minimum	Maximum	Median	pvalue
Intra Op lowest pulse rate/min	Normal Saline	30	75.0000	9.1388	54.0000	89.0000	76.5000	0.0050
	Ondansetron	30	81.0000	6.6020	70.0000	96.0000	80.0000	

In Normal Saline, the mean Intra Op lowest pulse rate/min (Mean± SD.) of patients was 75.0000± 9.1388. In Ondansetron, the mean Intra Op lowest pulse rate/min (Mean± SD) of patients was 81.0000± 6.6020. Difference of mean Intra Op lowest pulse rate/min with both Group was statistically significant (p=0.0050).

Table 4: Distribution of mean Intra Op lowest SBP (mm of Hg): Group

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Intra op lowest SBP (mm of Hg)	Normal Saline	30	87.1333	6.2683	80.0000	106.0000	86.0000	<0.0001
	Ondansetron	30	98.5000	10.3948	84.0000	124.0000	98.5000	

In Normal Saline, the mean Intra op lowest SBP (mm of Hg) (Mean± SD.) of patients was 87.1333± 6.2683. In Ondansetron, the mean Intra op lowest SBP (mm of Hg) (Mean± SD.) of patients was 98.5000± 10.3948. Difference of mean Intra op lowest SBP (mm of Hg) with both Group was statistically significant (p<0.0001).

Table 5: Distribution of mean Intra op lowest DBP (mm of Hg): Group

		Number	Mean	SD	Minimum	Maximum	Median	pvalue
Intra Op lowest DBP(mm of Hg)	Normal Saline	30	54.3333	5.1950	50.0000	68.0000	52.0000	0.0002
	Ondansetron	30	60.0333	6.0371	51.0000	70.0000	61.5000	

In Normal Saline, the mean Intra op lowest DBP (mm of Hg) (mean± s.d.) of patients was 54.3333± 5.1950.

In Ondansetron, the mean Intra op lowest DBP (mm of Hg) (Mean± SD.) of patients was 60.0333± 6.0371. Difference of mean Intra op lowest DBP (mm of Hg) with both Group was statistically significant (p=0.0002).In Normal Saline, the mean Intra op lowest MAP (mm of Hg) (Mean± SD) of patients was 65.4000± 5.7930. In Ondansetron, the mean Intra op lowest MAP (mm of Hg) (Mean± SD.) of patients was 72.8667± 7.2242. Difference of mean Intra op lowest MAP (mm of Hg) with both Group was statistically significant (p<0.0001). In Normal Saline, the mean Episodes of Bradycardia (intra op) (Mean± SD.) of patients was .0333± .1826.

In Ondansetron, the mean Episodes of Bradycardia (intra op) (Mean± SD.) of patients was .0000± .0000. Difference of mean Episodes of Bradycardia (intra op) with both Group was not statistically significant (p=0.3215).

Table 6: Distribution of mean Episodes of hypotension (intra op): Group

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Episodes of hypotension (intraop)	Normal Saline	30	1.8000	1.3746	0.0000	4.0000	2.0000	<0.0001
	Ondansetron	30	.3333	.5467	0.0000	2.0000	0.0000	

Difference of mean Episodes of hypotension (intra op) with both Group was statistically significant (p<0.0001).

Table 7: Distribution of mean Post op pulse rate/min: Group

		Number	Mean	SD	Minimum	Maximum	Median	pvalue
Post op pulse rate/min	Normal Saline	30	85.1667	7.5798	68.0000	105.0000	86.0000	0.9314
	Ondansetron	30	85.0000	7.3485	70.0000	102.0000	84.0000	

Difference of mean Post op pulse rate/min with both Group was not statistically significant (p=0.9314).

Table 8: Distribution of mean Post op SBP (mm of Hg): Group

		Number	Mean	SD	Minimum	Maximum	Median	pvalue
Post op SBP (mm of Hg)	Normal Saline	30	101.5333	4.9392	94.0000	116.0000	100.0000	0.0009
	Ondansetron	30	107.3333	7.6579	95.0000	128.0000	105.0000	

Difference of mean Post op SBP (mm of Hg) with both Group was statistically significant (p=0.0009). In Normal Saline, the mean Post op DBP (mm of Hg) (mean± s.d.) of patients was 62.5667± 2.9558. In Ondansetron, the mean Post op DBP (mm of Hg) (mean± s.d.) of patients was 66.5667± 4.3997. Difference of mean Post op DBP (mm of Hg) with both Group was statistically significant (p<0.0001). In Normal Saline, the mean Post op MAP (mm of Hg) (mean± s.d.) of patients was 75.6667± 3.3356. In Ondansetron, the mean Post op MAP (mm of Hg) (mean± s.d.) of patients was 80.1000± 5.3198. Difference of mean Post op MAP (mm of Hg) with both Group was statistically significant (p=0.0003).

Discussion

Sahoo T et al [11] found that, Ondansetron 4 mg, given intravenously 5 min before subarachnoid block reduced hypotension and vasopressor use in parturients undergoing elective caesarean section. Tatikonda CM et al [12] showed that, prophylactic use of ondansetron before spinal anesthesia significantly reduces the requirement of ephedrine and shivering. Shabana AA et al [13] found that , in parturient women undergoing elective cesarean section, intravenous 4 mg ondansetron significantly decreased the hypotension, HR fluctuation, and vasopressor doses used. Attri A et al [14] found that, intravenous ondansetron premedication can successfully attenuate SAB-induced fall in SBP,

DBP, and MAP in parturients undergoing elective caesarean sections.

Raghu K et al [15] found that, prophylactic administration of ondansetron is effective in reducing the incidence of spinal anesthesia-induced hypotension. Shabana AA et al [16] found that, in parturient women undergoing elective cesarean section, intravenous 4 mg ondansetron significantly decreased the hypotension, HR fluctuation, and vasopressor doses used. Baig R et al [17] found that, Ondansetron is effective in preventing spinal induced hypotension.

Tubog TD et al [18] found that, intravenous ondansetron may mitigate the risks of SIH (spinal induced hypotension) and bradycardia following spinal anesthesia. Amanda Thornton DN et al [19] showed that the administration of ondansetron 4 mg 5 minutes before SA as an adjunct to traditional treatment has shown to attenuate hypotension and excessive VU.

Al Zahraa AA et al [20] found that, in parturient women undergoing elective cesarean section, intravenous 4-mg ondansetron significantly decreased the hypotension, bradycardia, and vasopressor doses used.

Abbas N et al [21] found that, administration of 04 mg of intravenous ondansetron, 05 minutes prior to subarachnoid block, is effective in decreasing frequency of hypotension. Ipe S et al [22] found that, there was significant reduction in systolic, diastolic and mean BP in saline group compared to ondansetron group. But the heart rate in both the groups was comparable. Prophylactic ondansetron decreases incidences of hypotension after spinal anaesthesia in caesarean section.

Conclusion

Prophylactic use of intravenous ondansetron before sub-arachnoid block in parturients undergoing caesarean section, causes significant reduction of hypotension and variable reduction of bradycardia intra operatively and also there was significant reduction in total dose of vasopressor (mephentermine/Phenylephrine) or atropine needed

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