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Comparative Study between Two Doses of Intravenous Ondansetron on Maternal Haemodynamics during Elective Caesarean Delivery under Spinal Anaesthesia

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Abstract

Background: Hypotension is one of the most common intra-operative complications associated with spinal anaesthesia. Its incidence in caesarean section has been estimated to be as high as 50-60%. Despite fluid preloading, lateral uterine displacement and the use of vasopressor agents. It occurs due to sympathetic block which leads to autonomic nervous system disturbances and a decrease in systemic vascular resistance. This can occur because the level of block must be at least at T4 to ensure adequate analgesia severe hypotension following spinal anaesthesia in caesarean section is a dangerous complication. If it is unnoticed or inadequately treated, it can lead to serious maternal or fetal compromise.

Aim of Study: To evaluate the effect of two doses of prophylactic ondansetron on spinal anesthesia-induced hypotension and bradycardia among patients undergoing elective cesarean deliveries.

Patients and Methods: This study was carried out in Ain Shams Hospital Obstetric Theatres from March 2020 to September 2020. Written informed consent was obtained from every parturient included in the study. Ethical approval for this study was provided by the Ethics Committee of Faculty of Medicine, Ain Shams University. FAMSU MS 155/2020 (FWA 000017585) 23/2/2020.

Results: In our study, there is statistically significant difference between the studied groups regarding dose of vasopressor use. About 53.3% and 46.7% of those within ondansteron 4mg group received 10 and 12.5mg respectively. About 51.1% and 48.9% of those within ondansteron 8mg group received 12 and 15mg respectively. In terms of side effects, no patient within either group developed shivering, vomiting or bradycardia. Regarding nausea, there is statistically non-significant difference between the studied groups regarding occurrence of nausea.

Conclusion: Prophylactic bolus of intravenous onandsetron 8mg and to a lesser extent 4mg could decrease the fall in the MBP of parturients following spinal anesthesia as well as ephedrine needed dose that could decrease neonatal acidosis associated with ephedrine use.

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Introduction

HYPOTENSION is one of the most common intra-operative complications associated with spinal anaesthesia. Its incidence in caesarean section has been estimated to be as high as 50-60% **[1]**. Despite fluid preloading, lateral uterine displacement and the use of vasopressor agents **[1]**. It occurs due to sympathetic block which leads to autonomic nervous system disturbances and a decrease in systemic vascular resistance **[3,4]**. This can occur because the level of block must be at least at T4 to ensure adequate analgesia severe hypotension following spinal anaesthesia in caesarean section is a dangerous complication. If it is unnoticed or inadequately treated, it can lead to serious maternal or fetal compromise **[4,5]**.

Several measures were adopted to prevent or at least reduce the incidence of hypotension induced by spinal anaesthesia. In spite of using all the prophylactic measures, none of them can totally avoid maternal hypotension post-spinal anaesthesia. Therefore, there should be an interventional study to prevent or at least reduce the incidence of hypotension following spinal anesthesia in caesarean section **[9]**.

Ondansetron is a highly specific and selective serotonin 5-HT3 receptor antagonist with low affinity for dopamine receptors. Several studies have shown that it can prevent hypotension after spinal anaesthesia in pregnant and non-pregnant women **[10,11]**. A recent meta-analysis concluded that ondansetron may reduce the incidence of hypotension induced by spinal anesthesia **[14,16]**.

The mechanism of action is believed to be inhibition of the Bezold-Jarisch Reflex (BJR).

In this study two doses of Ondansetron will be compared to prevent or at least reduce post-spinal hypotension in caesarean section [12,13].

Patients and Methods

Technical design:

Site of study: This study was carried out in Ain Shams Hospital Obstetric Theatres. Written informed consent was obtained from every parturient included in the study. Ethical approval for this study was provided by the Ethics Committee of Faculty of Medicine, Ain Shams University. FAMSU MS 155/2020 (FWA 000017585) 23/2/2020.

Sample size: A comprehensive sample was taken including pregnant patients during period of six months. A group sample size of at least 45 cases per group in two groups achieved 80% power to detect a moderate to large effect size of 96 and a significance level of 0.05 using two sided two samples independent *t*-test. Therefore, the sample was 90 cases. Patients were randomly assigned into 2 groups; each group was 45 patients.

Inclusion criteria: Full-term. Singleton. Age from 18 to 35 years old. Physical status; American Society of Anesthesiologists (ASA) I and II. Type of operation; elective cesarean section under spinal anesthesia.

Exclusion criteria: Patient refusal. Patients with contraindications to spinal anesthesia (e.g. infection, vertebral column deformity, or coagulopathy). Patients with hypersensitivity to the used drugs. Pre-operative use of ondansetron. Patients with severe cardiac, pulmonary, renal, hepatic, neuromuscular disorders and diabetes mellitus. Patients who take antidepressants in the form of selective serotonin reuptake inhibitors or on migraine therapy. Patients with morbid obesity, pregnancy-induced hypertension. Parturients with high-risk pregnancy.

Operational design:

Type of study: Randomized, prospective, double blinded clinical trial.

Methods:

Parturients had to be fasting for 6hr. before the operation. In the preparation room, consent was taken, history was taken from all patients with documentation of the age, American Society of Anesthesiologists' score and gestational age. Then, pre-operative preparations were done to all patients in the form of recording the laboratory investigations as complete blood picture, coagulation profile, liver, and renal functions and after that an intravenous access will be obtained. Then, the patient was transferred to the operating room and baseline vital signs were recorded 30 minutes before conduction of anaesthesia including non-invasive measurement of systolic, mean, diastolic arterial pressures, heart rate, ECG, oxygen saturation and urine output. A peripheral 18-G intravenous (i.v.) cannula was inserted into the dorsum of the nondominant hand and a preload of 5ml/kg of warm normal saline 0.9% was administered. An infusion of 5ml/kg of saline solution was administrated approximately 15-30 minutes before anaesthesia. Patients were randomly assigned into 1 of 2 groups, using computer generated sequence and opaque envelopes, according to the prophylactic intravenous drug dose used:

- *Group 1 (45 patients):* Patients received 4mg ondansetron IV in 5ml. normal saline 5 minutes before spinal anesthesia.
- *Group 2 (45 patients):* Patients received 8mg ondansetron IV in 5ml. normal saline 5 minutes before spinal anesthesia.

The patient was placed in the sitting position, sterilization of the back and local anaesthetic infiltration was done. After that, spinal anaesthesia was performed at the level L3-L4 or L2-L3 with a 25G Whitacre needle using a hyperbaric bupivacaine solution 5mg/ml. In a dose of 0.06mg/cm patient's height with 15ug fentanyl solution [14].

The patient was placed in a supine position immediately after regional blockade with a left lateral tilt. The sensory and motor block was assessed bilaterally by cold discrimination using a frozen sachet of normal saline or ice cube and by modified bromage scale (0: No motor block, 1: Inability to raise extended legs, 2: Inability to flex knees, 3: Inability to flex ankle joints) respectively to ensure adequate anaesthetic block.

Sensory block was examined by loss of sensation to pin prick at midclavicular line every 2min until fixation of the sensory level in two consecutive times. The surgeon could start surgery when the sensory block level was established at T6. Time to reach the highest sensory level from the injection time of bupivacaine into the subarachnoid space was recorded.

All hemodynamic parameters (as blood pressure using non-invasive measurement, heart rate and oxygen saturation) were immediately recorded after resuming the supine position then every 5

minutes in the first 30 minutes and then every 10 minutes until skin closure. Oxygenation was facilitated by using nasal cannula at flow of 3-4L/min. Other complications of hypotension as dizziness, nausea, vomiting, post anaesthetic shivering as well as side effects of the used drugs were monitored and recorded. In case of failed spinal anesthesia, patient was informed, and general anesthesia was delivered. MBP, HR, and oxygen saturation (SpO_2) were recorded.

Side effects of ondanestron were headache, fatigue, constipation, diarrhea, dizziness, rash, hiccup, and flushing. Hypotension is defined as a decrease of mean arterial pressure 20% below the baseline. In case of hypotension, 1 0mg of ephedrine with 100ml. Normal saline was administrated intravenously and was repeated until restoration of baseline values **[8]**.

Outcomes:

The primary investigated outcome was the incidence of post-spinal hypotension in caesarean section. Secondary outcomes included nausea, vomiting, bradycardia, total dose of vasopressors used and shivering.

Vomiting was treated by 10mg i.v. bolus dose of metclopromide. Bradycardia was defined as HR below 60 beat/min. and it was treated by a 0.5mg i.v. bolus dose of atropine, followed by incremental doses of 0.1mg as required.

Statistical analysis:

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 20. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies and to compare the proportion of categorical data, chi-square test and fisher exact tests were used when appropriate. Kolmogorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify assumptions for use in parametric tests.

To compare quantitative parameters among two groups, independent sample *t*-test (for normally distributed data) and Mann Whitney test (for not normally distributed data) were used. To compare change over time in means in each group, repeated measure ANOVA test (for normally distributed data) was used.

The level of statistical significance was set at 5% ($p<0.05$). Highly significant difference was present if $p\leq0.001$.

Results

Table (1): Distribution of the studied groups according to baseline characteristics, and ASA.

Parameters	Groups		Test	
	Ondansteron 4mg group (n=45)	Ondansteron 4mg group (n=45)	t/χ^2	*p*
Age (year):				
Mean ± SD	31.84±5.608	30.29±5.723	1.302	0.169
Range	25-49	18-40		
Weight (kg):				
Mean ± SD	72.71±9.82	76.18±6.82	–1.945	0.055
Range	60-97	55-90		
Height (cm):				
Mean ± SD	167.91±8.439	170.6±4.277	–1.907	0.061
Range	156-180	159-180		
BMI (kg/m ^{2}):				
Mean ± SD	25.743±2.507	26.163±2.035	–0.872	0.385
Range	20.047-33.594	19.031-29.388		
Gestational age (week):				
Mean ± SD	38.56±0.659	38.38±0.912	1.06	0.292
Range	38-40	37-40		
ASA:				
I	44 (97.8)	39 (86.7)	Fisher	0.11
II	1 (2.2)	6 (13.3)		

t_2: Independent sample *t*-test.
χ^2: Chi square test.
$p>0.05$ is statistically non-significant.

Table (2): Comparison between the studied groups regarding heart rate findings over time.

Heart rate	Ondansteron 4mg group (n=45) Mean ± SD	Ondansteron 8mg group (n=45) Mean ± SD	*t*	*p*
• 30min. before induction	87.13±3.527	85.64±4.558	1.733	0.087
• On induction	90.31±4.522	87.47±3.917	3.189	0.002*
• At 5 minutes	88.93±3.928	83.2±5.268	5.853	<0.001**
• At 10 minutes	88.27±3.085	80.96±4.311	6.23	<0.001**
• At 15 minutes	87.36±2.414	82.84±4.194	–3.451	0.002*
• At 20 minutes	87.33±2.403	82.93±3.033	6.21	<0.001**
• At 25 minutes	84.29±3.259	78.29±9.605	3.968	<0.001**
• At 30 minutes	84.96±4.467	80.56±9.715	2.76	0.008*
• At 40 minutes	86.16±3.778	86.67±10.002	–0.321	0.75
• At 50 minutes	87.78±3.45	82.27±10.616	3.312	0.002*
• At 60 minutes	87.73±2.606	86.78±6.557	0.908	0.367
• P (F)	<0.001**	<0.001**		

t : Independent sample *t*-test.
F : Repeated measure ANOVA test.
* : $p<0.05$ is statistically significant.
** : $p\leq0.001$ is statistically highly significant.

Table (3): Comparison between the studied groups regarding heart rate findings over time.

Maximum change in heart rate	Ondansteron 4mg group (n=45) Mean ± SD	Ondansteron 8mg group (n=45) Mean ± SD	Z	*p*
Median (range)	3 (–6, 11)	11 (1, 21)	–2.74	0.006*

*: $p<0.05$ is statistically highly significant. Z: Mann Whitney test.

Table (4): Comparison between the studied groups regarding mean arterial blood pressure findings over time.

MAP	Ondansteron 4mg group (n=45) Mean ± SD	Ondansteron 8mg group (n=45) Mean ± SD	*t*	*p*
• 30min. before induction	81.02±8.706	79.56±8.92	0.789	0.432
• On induction	79.69±5.896	81.49±8.468	–1.17	0.245
• At 5 minutes	76.47±5.845	77.6±8.405	–0.743	0.46
• At 10 minutes	75.56±4.874	76.27±8.3	6.23	0.622
• At 15 minutes	71.82±5.674	75.04±6.303	–0.496	0.002*
• At 20 minutes	69.04±5.604	71.27±6.583	–2.549	0.013*
• At 25 minutes	68.04±4.327	68.13±5.591	–1.742	0.088
• At 30 minutes	69.27±5.565	73.6±5.921	–3.577	0.001 **
• At 40 minutes	73.8±4.251	75.6±5.246	–1.788	0.077
• At 50 minutes	74.09±5.67	80.51±6.025	–5.169	<0.001 * *
• At 60 minutes	77.62±5.271	83.04±6.954	–4.168	<0.001 * *
•*p*	<0.001 **	<0.001**		

t : Independent sample *t*-test.
F : Repeated measure ANOVA test.
* : $p<0.05$ is statistically significant.
** : $p\leq0.001$ is statistically highly significant.

Table (5): Comparison between the studied groups regarding maximum change in mean arterial blood pressure findings.

Maximum change in blood pressure	Ondansteron 4mg group (n=45) Mean ± SD	Ondansteron 8mg group (n=45) Mean ± SD	Z	*p*
Median (range)	10 (0, 19)	13 (1, 24)	–2.034	0.042*

*: $p<0.05$ is statistically highly significant.
Z: Mann Whitney test.

Table (6): Comparison between the studied groups regarding dose of vasopressor use.

Vasopressor use	Ondansteron 4mg group (n=45) %	Ondansteron 8mg group (n=45) %	χ^2/t	*p*
10mg	24 (53.3)	0 (0)	19.108	<0.001 * *
12mg	0 (0)	23 (51.1)		
12.5mg	21 (46.7)	0 (0)		
15mg	0 (0)	22 (48.9)		
Mean ± SD	11.222±1.264	13.467±1.517	–7.626	<0.001**
Range	10-12	12-15		

χ^2 : Chi square for trend test.
**: $p\leq0.001$ is statistically highly significant.

Table (7): Comparison between the studied groups regarding occurrence of shivering.

Shivering	Ondansteron 4mg group n=45 (%)	Ondansteron 8mg group N=45 (%)	χ^2	*p*
No	45 (100)	45 (100)	0	>0.999

χ^2 : Chi square test.

Table (8): Comparison between the studied groups regarding nausea, vomiting and bradycardia.

Parameters	Ondansteron 4mg group N=45 (%)	Ondansteron 8mg group N=45 (%)	χ^2	*p*
Vomiting:				
No	45 (100)	45 (100)	0	>0.999
Nausea:				
No	41 (91.1)	35 (77.8)	Fisher	0.142
Yes	4 (8.9)	10 (22.2)		
Bradycardia:				
No	45 (100)	45 (100)	0	>0.999

χ^2 : Chi square test. $p>0.05$ is non-significant.

Discussion

Cesarean delivery is usually performed with spinal anesthesia to avoid the risks of general anesthesia. The advantages of spinal anesthesia such as rapidity, reliability, safety, ease of performance, and avoidance of the hazards of general anesthesia make it the goldstandard anesthetic technique for elective cesarean delivery **[15]**.

Its use has a major limitation, which is development of hypotension and bradycardia, with a subsequent decrease in uteroplacental blood flow, which leads to fetal acidosis and increase in fetal morbidity and mortality **[15]**.

Several techniques were tried to decrease the incidence and severity of maternal hypotension that usually follows spinal anesthesia include preloading with fluids, and left lateral tilt to prevent the gravid uterus from compression on the inferior vena cava, with a subsequent decrease in the venous return **[6]**.

Spinal anesthesia induces sympathetic block that leads to vasodilatation, pooling of venous blood, decrease of venous return, and low ventricular volume state, which leads to activation of chemoreceptors and mechanoreceptors in the cardiac wall with abrupt withdrawal of sympathetic supply, and unopposed vagal tone to the heart, which leads to bradycardia and hypotension; this reflex is called the Bezold-Jarisch Reflex (BJR) and it is triggered by serotonin (5-HT3) released from thrombocytes under low ventricular volume conditions that stimulate cardiac chemoreceptors and increase the vagal tone. Serotonin (5-HT3) antagonists are suggested to be used in the prevention of hypotension and bradycardia caused by BJR in response to spinal anesthesia **[16]**.

Onandsetron is a 5-HT3 antagonist that has been used to prevent nausea and vomiting caused by chemotherapy, radiotherapy, and surgery and

there are clinical trials for its use in the prevention of BJR after spinal anesthesia in obstetric patients [17].

Serotonin (5-HT3) receptors are present in the spinal cord and it was found that the 5-HT3 level increased in the cerebrospinal fluid after spinal anesthesia with bupivacaine; thus, there was a query about the effects of the 5-HT3 antagonist onandsetron on the specifications of spinal anesthesia [18].

Ephedrine is a noncatecholamine sympathomimetic that has a and 0 adrenergic activity, and it is the classical vasopressor of choice for the treatment of postspinal hypotension in cesarean delivery, but it can induce maternal cardiovascular adverse effects such as supraventricular tachycardia, tachyphylaxis, and fetal acidosis [19].

The aim of this study was to evaluate the effect of two doses of prophylactic ondansetron on spinal anesthesia-induced hypotension and bradycardia among patients undergoing elective cesarean deliveries. Ninety pregnant patients were randomly divided into two groups:

- *Group 1:* 45 Patients received 4mg ondansetron in 5ml normal saline (IV).
- *Group 2:* 45 Patients received 8mg ondansetron in 5ml normal saline (IV).

In our study, there were statistically non-significant differences between the studied groups regarding age, weight, height, gestational age, BMI or ASA. Larger percentage within each group had ASA I (97.8% and 86.7% within Ondansteron 4 and 8mg groups respectively).

Mohamed and Mansour [20] compared between two doses of ondansetron (2mg, 4mg) and ephedrine in prevention of maternal hypotension and bradycardia induced by spinal anesthesia. One hundred and twenty parturients were eligible for this study. The following groups were established: Group A received 2mg of ondansetron, group B received 4mg of onandsetron, group C received 10mg of ephedrine, and group D received normal saline only. There was no significant difference between the four groups in parturients' demographic data and duration of surgery. There was a decrease in the HR values in the four groups in comparison with the baseline values that became significant in the ephedrine and control groups at 5, 10, and 15min. HR values were the highest in the onandsetron 4mg group and the lowest in the ephedrine group, with a significant difference between the two groups of onandsetron (2 and 4mg) and ephedrine, and the control groups at 5, 10, and 15 minutes.

In terms of the changes in the heart rate, there is statistically non-significant difference between the studied groups regarding heart rate 30 minutes before induction, 40 or 60 minutes after induction. On the other hand, there is statistically significant difference between them regarding heart rate at induction, at 5, 10, 15, 20, 25, 30, and 50 minutes after induction. Both groups showed significant change in heart rate over time. Also, there is statistically significant difference between both groups regarding maximum change in heart rate. Owczuk et al., [21] studied 72 parturients scheduled for cesarean delivery with spinal anesthesia by 4ml of 0.5% bupivacaine and the parturients were treated with 8mg of onandsetron as a prophylaxis for postspinal hypotension and they found that 8mg onandsetron had no influence on the decrease in HR after spinal anesthesia, which could be explained by the high dose of intrathecal bupivacaine (20mg) used in the study.

In terms of the changes in the mean arterial blood pressure, there is statistically non-significant difference between the studied groups regarding mean arterial blood pressure 30 minutes before induction and 5, 10, 25 and 40 minutes after induction. On the other hand, there is statistically significant difference between them regarding mean arterial blood pressure at induction, at 15, 20, 30, 50 and 60 minutes after induction. Both groups showed significant change in mean arterial blood pressure over time. Also, there is statistically significant difference between both groups regarding maximum change in blood pressure. It affect MBP and systolic but not diastolic Owczuk et al., [21] found that 8mg onandsetron could attenuate the decrease of systolic and MBP only, but it had no influence on the decrease in diastolic blood pressure after spinal anesthesia.

Sahoo et al., [10], in their study on 52 parturients scheduled for elective cesarean delivery under spinal anesthesia and parturients who were treated with 4mg onandsetron, observed a significant reduction in MAP at 5 minutes, 6 minutes in the control group and significant reduction in MAP between 14 and 35 minutes only in the control group compared to pre-operative values. The incidence of decreases in SBP and MAP were reduced with the use of intravenous ondansetron 4mg given 5 minutes before SA in parturients undergoing elective caesarean section.

In our study, there is statistically significant difference between the studied groups regarding dose of vasopressor use. About 53% and 47% of those within ondansteron 4mg group received 10 and 12.5mg respectively. About 51% and 49% of those within ondansteron 8mg group received 12 and 15mg respectively.

Sahoo et al., **[10]** found that onandsetron decreased the requirement of vasopressor use.

Rashad and Farmawy **[22]** concluded that in parturient females undergoing elective cesarean section, intravenous 4mg ondansetron before subarachnoid block significantly decreased the doses of vasopressor used.

Ortiz-Gómez et al., **[11]**, in their post-operative randomized placebo-controlled trial on 128 pregnant women scheduled for elective cesarean delivery with spinal anesthesia, found that prophylactic 2, 4, 8mg of onandsetron played no role in reducing vasopressor consumption; this difference may be related to the dose of intrathecal bupivacaine that was individualized in each parturient to be 9.7 ± 0.4mg in the placebo group and 9.6 ±0.3mg in the onandsetron group.

Wang et al., **[12]** studied 66 parturients scheduled for elective cesarean section under spinal anesthesia and found that prophylactic administration of 4mg onandsetron 5min. before spinal anesthesia with crystalloid preloading decreased vasopressor requirements.

Khalifa **[23]** compared a traditional vasopressor 'ephedrine' with 'ondansetron' in preventing hypotension of spinal anesthesia during cesarean section. They concluded that prophylactic i.v. use of 4mg ondansetron, and 10mg ephedrine reduces the need for rescue vasopressor. Gao et al., **[24]**, in a meta-analysis study conducted on 863 patients, found that prophylactic onandestron reduced vasopressor consumption in obstetric patients.

In terms of shivering, no patient within either group developed shivering. Shakya et al., **[25]** suggested that the prophylactic administration of low-dose ketamine (0.25mg/kg) and ondansetron (4mg) produces significant antishivering effect in comparison with placebo in patients undergoing spinal anesthesia.

Gao et al., **[24]** found that prophylactic onandestron reduced shivering. Mohamed and Mansour **[20]** found that incidence of shivering was higher in the control group (50%) in comparison with the other groups; where it was 20% in the onandsetron 2mg group, and 13.3% in the onandsetron 4mg group.

In our study, no patient within either group developed vomiting or bradycardia. Marashi et al., **[26]** compared prophylactic i.v. onandsetron 6 and 12mg and placebo in the attenuation of bradycardia,and they concluded that pretreatment with either 6 or 12mg i.v. onandsetron could reduce hemodynamic changes following spinal anesthesia without significant differences between the two doses of onandsetron.

Trabelsi et al., **[27]** studied 80 parturients scheduled for cesarean delivery under spinal anesthesia with 10mg bupivacaine plus 2.5 µg sufentanil after preloading with 10ml/kg saline; half of them received 4mg onandsetron 5min before spinal anesthesia and it was found that onandsetron could protect the parturients against bradycardia. They suggested that onandsetron has a dual action: On the heart, improving contractility. Gao et al., **[24]** found that prophylactic onandestron reduced vomiting. Mohamed and Mansour **[20]** found thatnone of the parturients developed bradycardia in the onandsetron group.

Regarding nausea,there is statistically non-significant difference between the studied groups regarding occurrence of nausea (non-significantly higher among Ondansteron 8mg group 22.2% versus 8.9% in Ondansteron 4mg group).

Wang et al., **[12]** concluded that 4mg of ondansetron preloading was the optimal dose to prevent nausea, and other adverse effects during cesarean delivery.

Gao et al., **[24]** found that prophylactic onandestron reduced nausea.

Khalifa **[23]** concluded that prophylactic i.v. use of 4mg ondansetron, and 10mg ephedrine reduces the incidence of nausea. Mohamed and Mansour **[20]** found that none of the parturients complained of nausea in the onandsetron 2 and 4mg groups.

Pazoki et al., **[28]** evaluated the efficiency of two doses (8mg and 4mg) of ondansetron in preventing PONV in 195 patients referred for cesarean section (C/S) under spinal anesthesia, and then the subjects were assigned to three equally sized groups using block randomization. Participants in the first, second, and control groups received 8mg, 4mg of ondansetron, and normal saline, respectively, 5 minutes before surgery. A final volume of 5cc was prepared by adding normal saline. The PONV incidence was significantly higher in the placebo

group than in the other two groups at 24 hours. The hemodynamic variables were same in three groups. They concluded that the PONV was lower in 8mg ondansetron than 4mg ondansetron. The decreasing effect of MBP and MHR was same in all groups.

Our study estimated the dose of ephedrine from previous researches that studied the effect of different doses of ephedrine on the prevention of hypotension that developed after spinal anesthesia. Loughrey et al., **[29]** compared two doses of prophylactic ephedrine (6 and 12mg) and placebo in 68 parturients scheduled for cesarean delivery under spinal anesthesia and found that the higher dose (12mg) of ephedrine was associated with less incidence of hypotension.

Magalhães et al., **[30]** compared prophylactic i.v. 10mg ephedrine and 80 µg phenylepherine and found that 10mg of ephedrine would be efficient prophylaxis for postspinal hypotension in parturients with slight neonatal acidosis, but without serious clinical effects on the neonatal condition as shown by the Apgar score, and suggested that the lower pH values in the ephedrine group were linked to the increased fetal metabolism by the β-adrenergic activity of ephedrine.

Gunda et al., **[31]** studied 100 parturients scheduled for cesarean section under spinal anesthesia and found that a prophylactic i.v. bolus dose of 5mg ephedrine was efficient in the prevention of postspinal hypotension and the neonatal outcome was satisfactory as shown by the Apgar score at 1 and 5min.

In terms of the effect of onandsetron on the characteristics of spinal anesthesia, this study found that i.v.onandsetron had no effect on the onset, duration, and the level of sensory, and motor block of spinal anesthesia, although it was assumed that onandsetron, which is a 5-HT3 antagonist, would affect the onset, duration, and intensity of spinal anesthesia as the serotonin (5-HT3) level in cerebrospinal fluid increased after spinal anesthesia. This is in agreement with the study of Samra et al., **[32]**, who evaluated the effects of systemic 4mg onandsetron on the characteristics of spinal anesthesia in urinary bladder tumors, and concluded that it had no effects on the intensity or the duration of motor or sensory block; this difference could be attributed to the action of onandsetron on other receptors such as adrenergic, histaminic, dopaminergic, and opioid receptors.

This study had a major limitation: Cardiac output and systemic vascular resistance should have been measured to evaluate the effects of onandsetron on cardiac contractility, but these measurements require invasive hemodynamic monitoring such as a Swan-Ganz catheter or tansesophageal echo, which was difficult in conscious female patients.

Conclusion:

Prophylactic bolus of intravenous onandsetron 8mg and to a lesser extent 4mg could decrease the fall in the MBP of parturients following spinal anesthesia as well as ephedrine needed dose that could decrease neonatal acidosis associated with ephedrine use.

References

1- NORRIS M.C.: Spinal Anesthesia for caesarean section. Handbook of obstretic anesthesia, 309-12, 2000.

2- RUSSEL I.F.: Levels of Anaesthesia and intraoperative pain at caesarean section under regional block. Int. J. Obst. Anesth., 4 (2): 71-7, 1995.

3- CARPENTER R.L., CAPLAN R.A., BROWN D.L., STEPHENSON C. and WU R.: Incidence and risk factors for side effects of spinal anesthesia. Anesth., 76 (6): 906-16, 1992.

4- TARKKILA P.J. and KAUKINEN S.: Complications during spinal anesthesia: A prospective study. Reg. Anesth., 16 (2): 101-6, 1991.

5- HANSS R., BEIN B., WESELOH H., BAUER M., CAVUS E., STEINFATH M., et al.: Heart rate variability predicts severe hypotension after spinal anesthesia. Anesth., 104: 537-45, 2006.

6- CYNA A.M., ANDREW M., EMMETT R.S., MIDDLETON P. and SIMMONS S.W.: Techniques for preventing hypotension during spinal anesthesia for caesarean section. Cockrane Database Syst. Rev., 4: CD002251, 2006.

7- MONK T.G., SAINI V., WELDON B.C. and SIGL J.C.] Anesthetic management and one-year mortality after non cardiac surgery. Anesth. Analg., 100: 4-10, 2005.

8- KINSELLA S.M., CARVALHO B., DYER R.A., FERNANDO R., McDONELL N., MERCIER F.J., et al.: International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. Anaesthesia, 73: 71-92, 2018.

9- MITRA J.K., ROY J., BHATTACHARYYA P., YUNUS M. and LYNGDOH N.M.: Changing trends in the management of hypotension following spinal anesthesia in cesarean section. J. Postgrad. Med., 59: 121-6, 2013.

10- SAHOO T., SENDASGUPTA C., GOSWAMI A. and HAZRA A.: Reduction in spinal- induced hypotension with ondansetron in parturient undergoing caesarean section: A double-blind randomized, placebo-controlled study. Int. J. Obstet. Anesth., 21: 24-8, 2012.

11- ORTIZ-GÓMEZ J.R., PALACIO-ABIZANDA F.J., MORILLAS-RAMIREZ F., FORNET-RUIZ I., LORENZO-JIMENEZ A. and BERMEJO-ALBARES M.L.: The effect of intravenous ondansetron on maternal haemodynamics during elective caesarean delivery under spinal anesthesia:

A double-blind, randomized, placebo-controlled trial. Int. J. Obstet. Anesth., 23: 138-43, 2014.

12- WANG M., ZHUO L., WANG Q., SHEN M.K., YU Y.Y., YU J.J., et al.: Efficacy of prophylactic intravenous ondansetron on the prevention of hypotension during Cesarean delivery: A dose-dependent study. Int. J. Clin. Exp. Med., 7: 5210-6, 2014.

13- WANG Q., ZHUO L., SHEN M.K., YU Y.Y., YU J.J. and WANG M.: Ondansetron preloading with crystalloid infusion reduces maternal hypotension during cesarean delivery. Am. J. Perinatol., 31: 913-22, 2014.

14- YUN S.H., SONG S.W. and PARK J.C.: Beneficial effects of the addition of intrathecal fentanyl to bupivacaine for spinal anesthesia in cesarean section. Anesth. Pain Med., 12: 233-9, 2017.

15- MEBAZAA M.S., OUERGHI S., BEN MEFTAH R., BEN CHEIKH M., MESTIRI T. and BEN AMMAR M.S.: Reduction of bupivacaine dose in spinal anaesthesia for caesarean section may improve maternal satisfaction by reducing incidence of low blood pressure episodes. Middle East J. Anaesthesiol., 20: 673-8, 2010.

16- NALLAM S.R. and DARA S.: Effect of intravenous ondansetron on reducing the incidence of hypotension and bradycardia events during shoulder arthroscopy in sitting position under interscalene brachial plexus block: A prospective randomized trial. Indian J. Anaesth., 59: 353-8, 2015.

17- CHRISTOFAKI M. and PAPAIOANNOU A.: Ondansetron: A review of pharmacokinetics and clinical experience in post-operative nausea and vomiting. Expert. Opin. Drug Metab. Toxicol., 10: 437-44, 2014.

18- FASSOULAKI A., MELEMENI A., ZOTOU M. and SARANTOPOULOS C.: Systemic ondansetron antagonizes the sensory block produced by intrathecallidocaine. Anesth. Analg., 100: 1817-21, 2005.

19- KANSAL A., MOHTA M., SETHI A.K., TYAGI A. and KUMAR P.: Randomized trial of intravenous infusion of ephedrine or mephentermine for management of hypotension during spinal anaesthesia for caesarean section. Anaesthesia, 60: 28-34, 2005.

20- MOHAMED A.Z.E. and MANSOUR H.S.: Assessment of the effect of two doses of prophylactic ondansetron on maternal hemodynamics, neonatal outcome and spinal blockade specifications, in parturients scheduled for cesarean delivery. Intensive Care, 5: 187-94, 2018.

21- OWCZUK R., WENSKI W., POLAK-KRZEMINSKA A., TWARDOWSKI P., ARSZU-OWICZ R., DYLCZYK-SOMMER A., et al.: Ondansetron given intravenously attenuates arterial blood pressure drop due to spinal anesthesia: A double-blind, placebo-controlled study. Reg. Anesth. Pain Med., 33: 332-9, 2008.

22- RASHAD M.M. and FARMAWY M.S.: Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section. Egypt J. Anaesth., 29: 369-74, 2013.

23- KHALIFA O.S.M.: A comparative study of prophylactic intravenous granisetron, ondansetron, and ephedrine in attenuating hypotension and its effect on motor and sensory block in elective cesarean section under spinal anesthesia. Ain-Shams Journal of Anesthesiology, 8: 166-72, 2015.

24- GAO L., ZHENG G., HAN J., WANG Y. and ZHENG J.: Effects of prophylactic ondansetron on spinal anesthesia-induced hypotension: A meta-analysis. Int. J. Obstet. Anesth., 24: 335-43, 2015.

25- SHAKYA S., CHATURVEDI A. and SAH B.P.: Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anesthesia. Anaesthesiology Clinical Pharmacology, 26: 465-9, 2010.

26- MARASHI S.M., SOLTANI-OMI D.S., SOLTANI MOHAMMADI S., AGHAJANI Y. and MOVAFEGH A.: Comparing two different doses of intravenous ondansetronwith placebo on attenuation of spinal-induced hypotension and shivering. Anesth. Pain Med., 4: e 12-55, 2014.

27- TRABELSI W., ROMDHANI C., ELASKRI H., SAMMOUD W., BENSALAH M., LABBENE I., et al.: Effect of ondansetron on the occurrence of hypotension and on neonatal parameters during spinal anesthesia for elective caesarean section: A prospective, randomized, controlled, double-blind study. Anesthesiol. Res. Pract., 158061, 2015.

28- PAZOKI S., MODIR H., KAMALI A., ZAMANI A. and SHAHIDANI M.: Ondansetron 8mg and 4mg with normal saline against post-operative headache and nausea / vomiting after spinal anesthesia: A randomized double-blind trial. Med. Gas. Res., 8 (2): 48-53, 2018.

29- LOUGHREY J.P., WALSH F. and GARDINER J.: Prophylactic intravenous bolus ephedrine for elective Caesarean section under spinal anaesthesia. Eur. J. Anaesthesiol., 19: 63-8, 2002.

30- MAGALHÃES E., GOVÊIA C.S., De ARAÚJO LADEIRA L.C., NASCIMENTO B.G. and KLUTHCOUSKI S.M. Ephedrine versus phenylephrine: Prevention ofhypotension during spinal block for cesarean section and effects on thefetus. Rev. Bras. Anestesiol., 59: 11-20, 2009.

31- GUNDA C.P., MALINOWSKI J., TEGGINMATH A., SURYANARAYANA V.G. and CHANDRA S.B.: Vasopressor choice for hypotension in elective cesarean section: Ephedrine or phenylephrine? Arch. Med. Sci., 6: 257-63, 2010.

32- SAMRA T., BALA I., CHOPRA K. and PODDER S.: Effect of intravenous ondansetron on sensory and motor block after spinal anaesthesia with hyperbaric bupivacaine. Anaesth Intensive Care, 39: 65-8, 2011.

دراسة مقارنة بين جرعتين من الآوندانسيترون على الدوره الدموية فى الآمهات الخاضعين للولادة القيصرية الإختيارية تحت تآثير التخدير النصفى

يعد إنخفاض ضغط الدم آحد آكثر المضاعفات آثناء العملية شيوعا المرتبطة بالتخدير النصفى.

كان الهدف من هذه الدراسة هو تقييم تآثير جرعتين من عقار آوندانسيترون الوقائى على إنخفاض ضغط الدم الناجم عن التخدير النصفى وبطء القلب بين المرضى الذين يخضعون لعمليات قيصرية إختيارية. تم تقسيم تسعين مريضة حامل بشكل عشوائى إلى مجموعتين:

- المجموعة الآولى: ٤٥ مريضاً تلقوا ٤ ملغ آوندانسيترون فى ٥ مل من محلول ملح وريدياً.
- المجموعة الثانية: ٤٥ مريضاً تلقوا ٨ ملغ آوندانسيترون فى ٥ مل من محلول ملح وريدياً.

فى دراستنا، توجد فروق ذات دالالة إحصائية بين المجموعات المدروسة فيما يتعلق بالعمر والوزن والطول وعمر الحمل ومؤشر كتلة الجسم ASA.

من حيث التغيرات فى معدل ضربات القلب. آظهرت كلتا المجموعتين تغيراً كبيراً فى معدل ضربات القلب بمرور الوقت. آيضاً، هناك فرق معتد به إحصائياً بين المجموعتين فيما يتعلق بآقصى تغير فى معدل ضربات القلب. من حيث التغيرات فى متوسط ضغط الدم الشريانى، آظهرت كلتا المجموعتين تغيراً كبيراً فى متوسط ضغط الدم الشريانى بمرور الوقت. كما توجد فروق ذات دلالة إحصائية بين المجموعتين فيما يتعلق بآقصى تغير فى ضغط الدم.

فى دراستنا، يوجد فرق ذو دلالة إحصائية بين المجموعات المدروسة فيما يتعلق بجرعة الآدوية القابضة من حيث الآثار الجانبية، لم يصاب آى مريض داخل آى من المجموعتين بالرعشة آو القئ آو بطء القلب. فيما يتعلق بالغثيان، توجد فروق غير ذات دلالة إحصائية بين المجموعات المدروسة فيما يتعلق بحدوث الغثيان إستخدام الآوندانسيترون بجرعة ٨ مجم وإلى حد ما ٤ مجم يقلل إنخفاض ضغط الدم الناتج عن التخدير النصفى ويقلل كذلك الجرعة المطلوبة من الآدوية القابضة للآوعية الدموية.