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Effect of Prophylactic Intravenous Ondansetron on Hemodynamic Parameters in Elective Cesarean Section under Spinal Anesthesia

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ABSTRACT

Background: Maternal Spinal anesthesia frequently has side effects like hypotension and bradycardia during caesarean delivery. Maternal Spinal anesthesia frequently has side effects like hypotension and bradycardia during caesarean delivery. **Objective:** The current study aimed to evaluate effect of prophylactic intravenous ondansetron on hemodynamic parameters in elective cesarean section (CS) under spinal anesthesia.

Patients and methods: A total of 80 patients with physical condition as defined by the ASA class II and ages ranging from 21 to 45 years old scheduled for surgery at Zagazig University's Department of Anesthesia and Surgical Intensive Care Hospitals; elective CS and Surgery were lasting no longer than 60 minutes. Patients in the control group (group C) got 10 ml of saline. Individuals in the ondansetron group (group O) received intravenously 4 mg of ondansetron diluted in 10 ml of saline five minutes before subarachnoid block. The following variables were measured throughout the course of the trial in both groups: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAO), heart rate, oxygen saturation percentage, and intraoperative need for ephedrine. Moreover, any issues that arise throughout or following operation were recorded. **Results:** The frequency of hypotension in expectant women undergoing spinal anesthesia for elective caesarean delivery was significantly reduced, when prophylactic 4 mg ondansetron was administered. The use of vasopressors Ondansetron significantly decreased the incidence of hypertension. Systolic blood pressure was consistently higher and fewer vasopressor medications were used in the ondansetron group. **Conclusion:** Intravenous premedication with 4mg ondansetron can effectively reduce the drop in SBP, DBP, and MAP in expectant mothers scheduled for CS.

Keywords: Ondansetron, Spinal Anesthesia, Hemodynamic, Clinical trial, Cesarean section, Zagazig University.

INTRODUCTION

A straightforward, dependable, and widely used anesthetic approach is spinal numbness. The drawbacks of spinal anesthesia include trembling, hypotension, and bradycardia [(1)].

In fact, a sensory block up until T5 is required for spinal anesthesia during caesarean sections (CS), which in 55% to 90% of instances always results in a protracted sympathetic block and hypotension [(2)].

Hypotension, which can significantly increase the most common side effect of spinal anesthesia during CS section is the risk of morbidity and mortality for both the mother and the fetus. Due to peripheral blood pooling and diminished systemic vascular resistance brought on by sympathetic nervous system blockage, hypotension develops, which lowers cardiac output [(3)].

Hypotension and bradycardia may be caused by excessive parasympathetic activity, the Bezold-Jarisch reflex (BJR), and enhanced baroreceptor activity. Chemoreceptors and mechanoreceptors, which are serotonin sensitive, set off the Bezold-Jarisch reflex. In hypovolemic people, serotonin is an additive BJR trigger and animal and human researches have demonstrated that 5HT3 antagonists reduce serotonin-induced BJR. Ondansetron has little side effects but antagonistic effects on 5HT3 [(4)].

Despite the ease and safety of spinal anesthesia, uncommon problems such unresponsive hypotension and bradycardia pose significant anesthetic difficulties. Instead than treating hypotension, it is preferable to prevent it. Lower-leg compression, intravenous fluids, and vasopressor drugs are a few methods that have been recommended to lessen the possibility of spinal anesthesia-induced hypotension after cesarean delivery; however, no single strategy has been proven to be entirely efficient [(5)]. Ondansetron is a medicine that is becoming more and more popular during subarachnoid block patients' treatment for hypotension, which is the focus of the majority of studies on the prophylactic management of hypotension. In addition to treating and preventing nausea and vomiting, ondansetron, a 5-hydroxytryptamine subtype 3 (5-HT3) receptor antagonists, may also reduce the hemodynamic changes brought on by spinal anesthesia, according to previous studies [(6)].

The current study aimed to evaluate effect of prophylactic intravenous ondansetron on hemodynamic parameters in elective CS under spinal anesthesia.

PATIENTS AND METHODS

A total of 80 patients with physical condition as defined by the ASA class II and ages ranging from 21 to 45 years old and body mass index (BMI Kg/m2) >35, scheduled for surgery at Zagazig University's Department of Anesthesia and Surgical Intensive Care Hospitals were included in the current randomized, double-blinded, controlled clinical trial. Elective CS and Surgery were lasting no longer than 60 minutes.

A total of 40 patients in the control group (group C) got 10 ml of saline. Meanwhile, 40 individuals in the

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ondansetron group (group O) received intravenously 4 mg of ondansetron diluted in 10 ml of saline 5 minutes before subarachnoid block.

Prior to surgery, every patient was seen and informed in detail the anesthetic procedure. General medical examination and examinations were done for tumors, infection, or spinal column deformity at the site of the intrathecal injection to rule out the presence of any contraindications.

A complete blood count (CBC) (PT, PTT, bleeding time, and INR), liver function tests, a coagulation profile, and renal function tests were performed (serum creatinine and BUN), random blood sugar, and ECG when indicated. All patients before the procedure (6 hours for light meals, 8 hours for fatty meals, and 2 hours for clear liquids). The selected patients were randomly split into two groups using basic random sampling. The optimum bowl selection approach was used. Eighty paper cards were used to create a frame. A serial number was obtained from the frame and written on each of these papers. Every aspect of the papers was the same, they were all folded the same way, placed in the right bowl, and completely mixed before being chosen.

No premedication were given for all patients. On arrival to the operating room, monitoring Oxygen saturation, heart rate, and mean arterial blood pressure (MABP) (SPO2), (baseline data) were recorded.

Patients received IV fluids prior to spinal anesthesia using an 18-gauge intravenous cannula positioned on the dorsum of the non-dominant hand. 8–10 ml/kg warmed lactated ringer solution to 37˚C within 30 minutes and then 5ml/kg/hr. In all groups, solutions (ondansetron/normal saline) were infused immediately before administering spinal anesthesia. All the drugs was made by one group of anesthesiologists and administered by a different group, and neither the patient nor the doctor knew the kind of medication delivered. The answers were developed by an anesthetist not affiliated with the study (double-blinded).

The patients were blocked in the sitting position, and all aseptic measures were performed to avoid infection, subcutaneous local anesthesia at site of needle insertion, a 25 after verifying that the needle was positioned correctly, following a gradual injection of 3 ml of 0.5% hyperbaric bupivacaine, the patients were immediately placed in the supine position with a 15° left tilt.

The following variables were measured throughout the course of the trial in both groups: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), heart rate (HR), oxygen saturation % and intraoperative need for ephedrine. Any issues that occurred before, during, or after surgery were also noted.

Data were recorded during the first 15 minutes at intervals of 3 minutes, followed by 5 minutes thereafter of surgery and in first 6 hours post-operative with 2 hours interval. In cases that MAP decreases more than 20% from baseline of the patient, intravenous fluids and 10 mg IV ephedrine were administered. When HR decreases more than 20% from baseline of the patient, 0.5 mg IV atropine was administrated. Fall of SpO2 below 92% was evaluated as hypoxia and 4 l/min 100% oxygen was administered via a face mask.

Ethical Consideration:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University. After explaining the study to all patients including study's design, procedure, drugs, and possible adverse effects, the informed consents were obtained. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

All data were collected, tabulated and statistically analyzed using (SPSS version 20.0) for windows (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Percent of categorical variables were compared using Chi-square test or fisher exact test when appropriate. Mann Whitnney u test was used to compare median of variables of two groups. All tests were two sided. p-value < 0.05 was considered statistically significant (S), and p-value ≥ 0.05 was considered statistically insignificant.

RESULTS

Table 1 showed that there was no significant differences between the two groups regard the demographic data.

Table (1): Demographic data distribution among studied groups

Variable			O Group (N=40)	C Group (N=40)	t/X^2	P value
Age (years)			23.95±3.9	24.85±3.88	-1.033	0.305
BMI (kg/m^2)			30.45±2.72	30.35±2.23	0.179	0.858
Parity	PG	N	18	13	1.31	0.25
		%	45.0%	32.5%		
	Multi	N	22	27		
		%	55.0%	67.5%		

t= t test. X^2 = Chi square. P= P value. N= Number. BMI= Body Mass Index. P >0.05= non-significant difference. P< 0.05= significant difference. O Group= Ondansteron group. C Group= Control group.

There was no statistically significant difference in SBP between the two groups at all studied times except at 5,10,30,45and 60 min were it was significantly lower among the C group compared to O group (**Figure** 1).

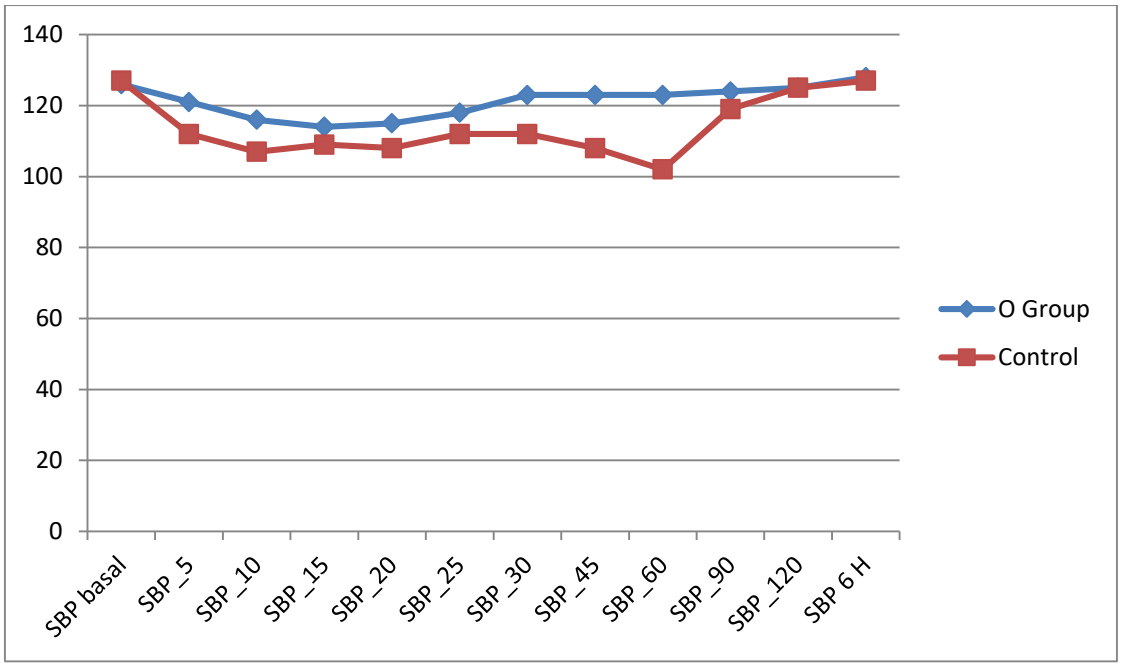

Figure (1): Systolic blood pressure (SBP) (mmHg) distribution among studied groups at different times. O Group= Ondansteron group, C Group= Control group.

Regarding DBP there was statistically significant difference between the two groups at all studied times except at basal time, 15, 120 minutes and 6 hours, there was no statistically significant difference between the two groups (**Figure** 2).

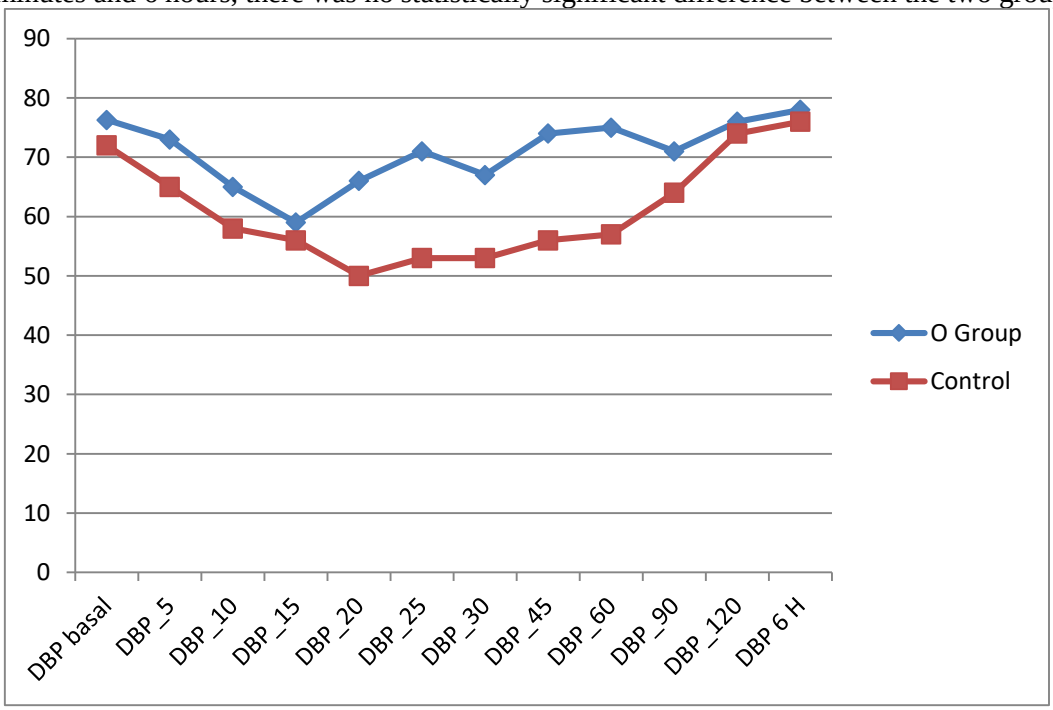

Figure (2): Diastolic blood pressure (mmHg) distribution among studied groups at different times. DBP=Diastolic blood pressure. O Group= Ondansteron group. C Group= Control group.

There was statistically significant difference between the 2 groups as regarding the MAP where it was lower among C group at time 10 and the interval from 20 to 60 minutes, and there was no statistically significant difference between the 2 studied groups in the remaining studied times (**Figure** 3).

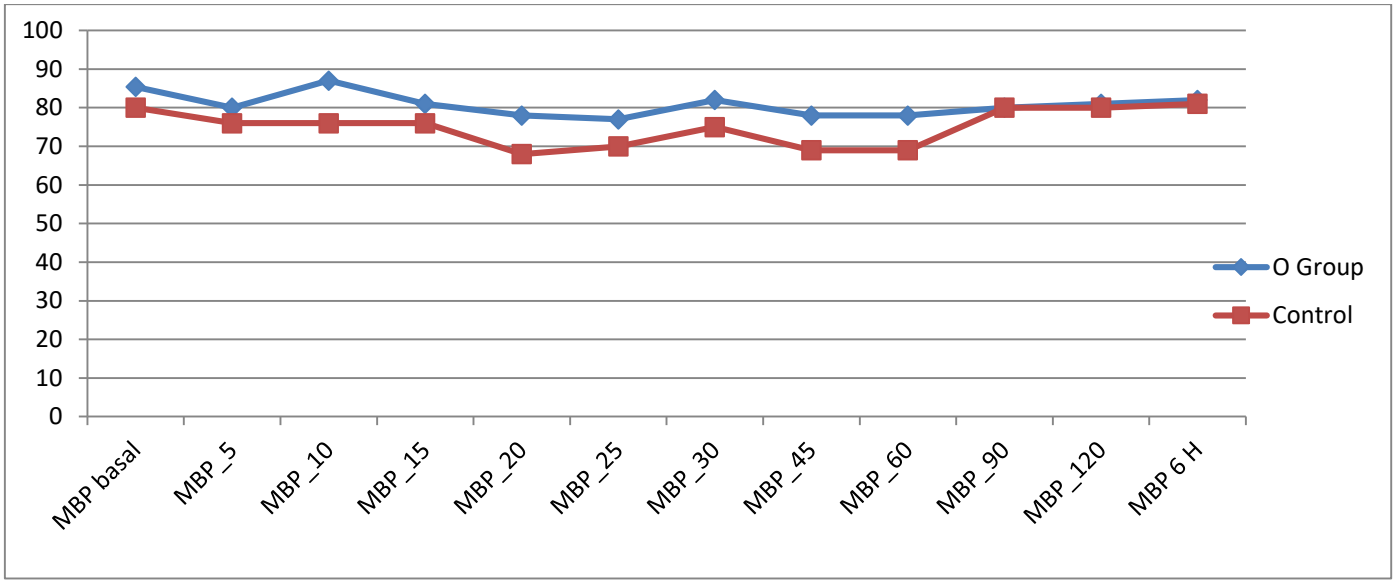

Figure (3): Mean blood pressure (mmHg) distribution among studied groups at different times. MBP= Mean blood pressure. O Group= Ondansteron group. C Group= Control group.

Regarding the heart rate there was no difference between the two studied groups except at time 30 and 45 minutes there was statistically significant difference with low values toward the group C (**Table 2**).

Table (2): Heart rate (beats/minute) distribution among studied groups.

Variable	O Group (N=40)	C Group (N=40)	t-test	P value
HR basal	92.72±6.78	92.52±5.31	0.304	0.739
HR_5	94.67±6.78	92.52±5.31	0.14	0.884
HR_10	98.02±8.21	98.27±8.87	0.131	0.896
HR_15	93.12±8.21	96.52±11.11	1.449	0.151
HR_20	87.97±11.37	89.51±12.41	0.573	0.568
HR_25	89.92±3.7	90.50±9.24	0.365	0.716
HR_30	86.87±6.01	80.52±8.47	3.004	0.008*
HR_45	88.67±4.08	82.57±8.63	3.243	0.002*
HR_60	88.12±3.33	89.72±9.18	1.034	0.306
HR_90	87.42±4.02	87.87±5.86	0.411	0.690
HR_120	85.80±7.68	86.82±5.86	0.588	0.487
HR 6H	88.65±8.45	87.05±4.23	0.743	0.369

HR= Heart Rate. P= P value, P>0.05= Non-significant difference, P<0.05= Significant difference, O Group= Ondansteron group, C Group= Control group.

According to the SpO2 values there was no significant difference between the two studied groups (**Table 3**).

Table (3): Oxygen saturation (SPO2) (%) distribution among studied groups.

Variable	O Group (N=40)	C Group (N=40)	t-test	P value
SPO2_basal	97.5±1.8	97.4±1.64	0.001	0.999
SPO2_5	97.58±1.8	97.5±1.53	0.069	0.933
SPO2_10	97.88±1.86	97.83±0.7	0.195	0.823
SPO2_15	97.83±1.71	96.83±1.76	1.600	0.282
SPO2_20	97.25±1.62	96.91±1.3	0.257	0.774
SPO2_25	97.75±1.72	97.83±1.8	0.464	0.631
SPO2_30	97.58±1.88	96.83±1.43	2.046	0.137
SPO2_45	97.5±1.74	97.25±1.6	0.355	0.702
SPO2_60	97.83±1.57	97.29±1.23	1.172	0.316
SPO2_90	98.5±1.47	97.9±0.78	1.039	0.359
SPO2_120	98.85±0.98	98.7±0.78	1.214	0.315
SPO2 6H	99.02±0.95	98.9±0.88	1.226	0.307

SPO2= Peripheral oxygen saturation. O Group= Ondansteron group. C Group= Control group. P> 0.05= Non-significant difference. P<0.05= significant difference.

Regarding the incidence of intraoperative hypotension there was significant difference between the two study groups with lower values in group O, while there was no significant difference among the two studied groups regarding the intraoperative bradycardia. Incidence of postoperative nausea, was significantly lower in group O compared to group C. The incidence of postoperative vomiting was significantly lower in group O compared to group C. Regarding shivering there was significant difference between the two study groups with lower value in group O compared to group C (**Table 4**).

Table (4): Complication distribution among the studied groups.

Variable			Group		Total	$X^{2/}$ Fisher Exact	P value
			O Group (N=40)	C Group (N=40)			
Intraoperative hypotension	**No**	**N**	32	16	48	13.33	0.00**
		%	80%	40.0%	60%		
	Yes	**N**	8	24	32		
		%	20%	60.0%	40%		
Intraoperative bradycardia	**No**	**N**	40	36	76	2.36	0.121
		%	100%	90.0%	95%		
	Yes	**N**	0	4	4		
		%	0.0%	10.0%	5%		
Postoperative nausea	**No**	**N**	38	19	57	22.02	0.00**
		%	95%	47.5%	71.2%		
	Yes	**N**	2	21	23		
		%	5%	52.5%	28.8%		
postoperative vomiting	**No**	**N**	40	23	63	21.58	0.00**
		%	100%	57.5%	78.8%		
	Yes	**N**	0	17	17		
		%	0.0%	42.5%	21.2%		
Shivering	**No**	**N**	32	17	49	11.85	0.001**
		%	80%	42.5%	61.2%		
	Yes	**N**	8	23	31		
		%	20%	57.5%	38.8%		

N= Number. P>0.05= Non-significant difference. P<0.05= Significant difference. P<0.05= Significant difference. O Group= Ondansteron group, C Group= Control group.

In both groups, transient hypotension was observed in some patients and treated by 10 mg ephedrine IV. There was a statistically significant difference between the two groups as regards the needs for vasopressor. The need for vasopressor was significantly lower in group O than in group C (**Table 5**).

Table (5): Needs for ephedrine among the studied groups.

Variable			Group		Total	X^2	P value
			O Group (N=40)	C Group (N=40)			
Ephidrine	**No**	**N**	33	25	58	4.01	0.045*
		%	82.5%	62.5%	72.5%		
	Yes	**N**	7	15	22		
		%	17.5%	37.5%	27.5%		

N= Number, P>0.05= Non-significant difference, P<0.05= Significant difference, O Group= Ondansteron group, C Group= Control group.

DISCUSSION

According to our study, the demographic information, including the mean age, did not significantly differ (24 years), BMI, and parity in both groups, between the groups O (n=40) and group C (n=40). These outcomes are consistent with **Trabelsi *et al.*** [2] who contrasted placebo with ondansetron 5 mg (n=40), **Owczuk *et al.*** [6] who compared ondansetron 8mg (n=35) with placebo (n=36), and **Sahoo et al.** [7] who compared ondansetron 4 mg (n=24) with placebo (n=24).

The current study focused on SBP, which revealed that SBP assessed at 5, 10, 30, 45, and 60 minutes was considerably lower among the C group compared to O group. This conclusion is consistent with the outcomes produced by **Sahoo *et al.*** [7]**.** They claimed that the fall in systolic blood pressure was mitigated by 4 mg of ondansetron administered 5 minutes before spinal block for caesarean section. According to other researchers, ondansetron caused SBP in patients undergoing caesarean sections under spinal anesthesia to elevate more than it did in the control group of patients [2].

According to the results of the current investigation, DBP measured at 5, 10, 20, 25, 30, 45, 60 and 90 minutes were considerably lower there was no statistically significant difference between the two groups in the C group compared to the O group terms of the two studied groups in the remaining studied times. These findings are consistent with those made by **Sahoo *et al.*** [7] and **Abbas *et al.*** [8] who claimed that if 4 mg of ondansetron were administered The decrease in diastolic blood pressure 5 minutes prior to spinal anesthesia for a caesarean delivery would be lessened. Furthermore, I concur with **Trabelsi *et al.*** [2] who used 5 mg ondansetron in their study.

Regarding blood pressure average MAP, as there was a statistically significant difference between the two groups for MAP after 10 minutes and between 20 and 60 minutes in group C patients, and in the remaining period, there was no statistically significant difference between the two research groups.

These findings are consistent with those made by **Sahoo *et al.*** [7] who had 4 mg of ondansetron, given 5 minutes prior to spinal anesthesia for a caesarean section delivery, **Trabelsi *et al.*** [2] In comparison to the control group, they found that patients who took ondansetron (5 mg) had higher SBP, DBP, and MAP.

Also, **Samarah *et al.*** [9] researchers tested a novel strategy by giving intravenous ondansetron 20 minutes before to spinal anesthesia, and they found no discernible change in blood pressure readings across the trial groups (P>0.05). This discrepancy with the current study may be due to the difference in the type of surgery and population in the first study and the timing difference in the second as mentioned before.

Except for periods of 30 and 45 minutes, when group C's HR was significantly lower than group B's, the current study indicated that there was no significant difference in HR between the 2 groups O's. In line with our findings **Owczuk *et al.*** [6] discovered that infusing 8 5 minutes before spinal anesthesia, provide mg of ondansetron intravenously prevent SBP drop without influencing heart rate. **Abbas *et al.*** [8] found that group II placebo recipients' heart rates were considerably lower than those of group I ondansetron 4 mg recipients.

Regarding SpO2 values the 2 groups did not significantly differ from one another that were examined; this conclusion is consistent with those of **Rashad *et al.*** [10] and **Sahoo *et al.*** [7] They reported that their research group's baseline post-anesthesia SpO2 levels were unchanged.

Contrary to our findings **Jarineshin *et al.*** [11] reported showing the O group's mean SpO2 was much lower than the N group’s only throughout the recovery phase and after block completion.

Regarding intra-operative complications, our investigation revealed that there was no statistically significant difference in the incidence of intraoperative bradycardia between the two study groups, however there was a significant difference in the incidence of intraoperative hypotension, with lower values in group O. These outcomes are consistent with **Shabana *et al.*** [12] researchers employed 100 pregnant women planned for an they conducted a trial on elective caesarean deliveries under spinal anesthesia and found that intravenous ondansetron at a dose of 4 mg greatly reduced hypotension, HR variation, and the amount of vasopressor required.

The current results are consistent with **Kinsella *et al.*** [13] and revealed that vasopressors such phenylephrine, ephedrine, and mephentermine are the mainstays of treatment and prevention for hypotension following spinal block during caesarean delivery.

Furthermore, **Samarah *et al.*** [9] discovered that ondansetron prevented hypotension in caesarean-surgery patients who were pregnant, but the impact was not superior to that of vasoconstrictors.

According to the current study, group O experienced much less postoperative nausea and vomiting than group C. these findings concur with the outcomes listed by **Ray *et al.*** [14] The Preventing incidence of nausea and vomiting during caesarean delivery is more successful with intravenous ondansetron 4 mg, according to research done on 63 pregnant women who underwent cesarean section under spinal anesthesia.

Between the two study groups, there was a considerable difference in shivering, with group O scoring lower than group C. These outcomes align with those attained by **Tatikonda *et al.*** [1] who claimed that its using dramatically lessens shivering.

CONCLUSION

Intravenous premedication with 4mg ondansetron can effectively reduce the fall in SBP, DBP, and MAP

in expectant mothers scheduled for elective caesarean sections. Additionally, it can lessen the likelihood of nausea, vomiting, and shivering with better patient and surgeon satisfaction.

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- **Conflicts of interest:** There are no conflicts of interest, according to the authors.

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