Baghdad Journal of Biochemistry and Applied Biological Sciences

2026, VOL. 7, NO. 1, 57–67, e-ISSN: 2706-9915, p-ISSN: 2706-9907

RESEARCH ARTICLE

Crystalloid Co-loading versus Ondansetron Effect on Hemodynamic Stability of Cesarean Section Patients Anesthetized by Subarachnoid Block in Karbala, Iraq

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Article Info.

Keywords:
Ondansetron,
Co-loading,
Subarachnoid Block,
Hypotension,
Bezold–Jarisch Reflex,
Cesarean Section

Received: 06.26.2025
Accepted: 08.19.2025
Published online: 01.09.2026
Published: 01.09.2026

Abstract

Background: Subarachnoid block-induced hypotension and bradycardia remain a frequent and clinically significant complications during cesarean section. Strategies such as fluid co-loading and ondansetron have been employed to mitigate these effects, but their comparative effectiveness remains under investigation.
Objective: To compare the effectiveness of 8 mg IV ondansetron versus 500 mL crystalloid co-loading in reducing subarachnoid block-induced hypotension and bradycardia.
Methods: A prospective randomized comparative study carried out in the Gynecology and Obstetrics Hospital, Imam Al-Hassan Al-Mujtaba Teaching Hospital, Gynecology and Obstetrics Department, Karbala, Iraq from October 2024 to March 2025. A total of 180 women were assessed for eligibility, and only 172 were included and allocated into three groups: the co-loading group (57 women) received 500 mL saline solution 0.9% IV starting rapidly with intrathecal injection of local anesthesia; the ondansetron group (58 women) received 8 mg of ondansetron IV and both intervention groups (co-loading and ondansetron) received preloading ~10-mL/kg saline solution 0.9% IV; and the control group (57 women) received only preloading ~10-mL/kg saline solution 0.9% IV.
Results: Ondansetron reduced the overall hypotension from 73.7% (control) to 55.2% (P = 0.038) and vasopressor dose from 18.7±12.9 mg to 8.5±9.8 mg (P < 0.001). Co-loading did not significantly reduce the overall hypotension (64.9%, P = 0.31). Bradycardia incidence was non-significant among all groups (P = 0.233). Ondansetron also reduced nausea/vomiting (P = 0.007) and shivering (P = 0.019).
Conclusion: Ondansetron demonstrated superior effectiveness in reducing subarachnoid block-induced hypotension, vasopressor use, intraoperative nausea/vomiting, and shivering, compared to crystalloid co-loading.

1. Introduction

Subarachnoid block (SAB), or spinal anesthesia (SA), has been historically the preferred anesthetic method for pregnant women undergoing elective cesarean sections because of its effectiveness, simplicity, maintenance of maternal awareness during delivery, limited maternal morbidity, and the ability to circumvent drugs that could affect the fetus [1]. Hypotension continues to be a common and difficult consequence following SAB, with occurrence rates as high as 80% in pregnant women [2].

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How to cite this article: Kareem AA, Mohammed HN., Crystalloid Co-loading versus Ondansetron Effect on Hemodynamic Stability of Cesarean Section Patients Anesthetized by Subarachnoid Block in Karbala, Iraq. Baghdad Journal of Biochemistry and Applied Biological Sciences, 2026, VOL. 7, NO. 1, 57–67. https://doi.org/10.47419/bjbabs.v7i1.435

Subarachnoid block-induced hypotension (SABIH) and bradycardia primarily result from sympathetic blockade, leading to vasodilation and reduced venous return, which activates the Bezold–Jarisch reflex (BJR) mediated by serotonin (5-HT) receptors [3]. This reflex triggers hypotension and bradycardia through vagal stimulation and can cause significant hemodynamic instability, particularly in vulnerable populations, such as the elderly and during cesarean sections [4,5]. BJR is mediated by stimulation of intracardiac receptors, including mechanoreceptors and chemoreceptors. Mechanoreceptors located in all cardiac chambers are sensitive to decreased venous return, resulting in stimulation of receptors and activation of BJR. Chemoreceptors are sensitive to serotonin released from activated thrombocytes and are an important factor for triggering BJR during hypovolemic conditions. This causes an increased efferent vagal signaling leading to boost hypotension and bradycardia [6].

The favored approach for addressing maternal hypotension has evolved throughout the decades because of advancements in research and data. The literature discusses evidence-based strategies, such as crystalloid preloading (administration of crystalloid fluid prior to SAB) versus co-loading (administration of crystalloid fluid starting rapidly with intrathecal injection of local anesthesia), application of colloid versus crystalloid IV fluids, administration of vasopressors (including ephedrine, phenylephrine, and norepinephrine), utilization of lower extremity sequential compression devices, low-dose spinal anesthesia, patient positioning, and using 5-HT3 receptor antagonists such as ondansetron [1,7].

Despite the availability of various evidence-based therapies, determining the best treatment approach for maintaining hemodynamic stability during SAB for cesarean section remains a major issue in obstetric anesthesiology [8]. Recently, crystalloid co-loading has been shown to effectively reduce the incidence of SAB during cesarean sections, unlike crystalloid preloading, which was found ineffective [9].

Other trials examined the potential use of ondansetron to treat SABIH. Researchers have suggested that serotonin may trigger the BJR by stimulating 5-HT3 receptors. This might explain the hypotension and bradycardia that often happen during SAB [2,10]. Ondansetron has been safely used to attenuate the BJR, resulting in less bradycardia and hypotension in patients receiving SAB [11].

Multiple randomised controlled trials (RCTs) in the last few years have explored the effectiveness of ondansetron in preventing SABIH and bradycardia, with many of these studies finding statistically significant differences in the incidence of hypotension among patients who had received ondansetron prior to SAB and those who did not receive [2,3,12–14]. Preliminary studies suggest that intravenous ondansetron administered prior to SAB may reduce the incidence and severity of hypotension, but its efficacy relative to traditional crystalloid co-loading remains underexplored in cesarean section patients [14]. This study addresses that gap and explores potential changes in clinical practice by evaluating whether ondansetron can replace or augment fluid-based prophylaxis.

2. Materials and Methods

This is an RCT carried out in Anesthesia and Obstetrics Departments of both Gynecology and Obstetrics Hospital and Imam Al-Hassan Al-Mujtaba Teaching Hospital, Karbala, Iraq from October 2024 to March 2025. Ethical approval was obtained from the Research Committee of Training and Human Development Center, Karbala Health Directorate (Decision No.: 2025218).

A total of 180 eligible parturients were assigned unique identification numbers from 1 to 180. Randomization was carried out using Microsoft Excel by applying the RAND() function to each participant, generating a random decimal number between 0 and 1. The list was then sorted in ascending order based on these random numbers. Participants were allocated sequentially to three groups in a 1:1:1 ratio: the first 60 participants were assigned to the co-loading group, the next 60 to the ondansetron group, and the final 60 to the control group. All participants were informed about the purpose of the study and asked to provide written informed consent prior to inclusion. Selection of eligible women prior to inclusion in the study was based on the evaluation of those with single pregnancies indicating elective cesarean section and presenting at the Gynecology and Obstetrics Hospital and Imam Al-Hassan Al-Mujtaba Teaching Hospital.

2.1. Inclusion and exclusion criteria

Inclusion criteria included patients aged 18–45 years undergoing cesarean delivery under SAB, and ASA physical status I and II. The exclusion criteria included hypersen-sitivity to ondansetron, preeclampsia, placental disorders, cardiovascular insufficiency, patients receiving a selective serotonin reuptake inhibitor or migraine medication, and contraindications of SAB.

Demographic and characteristic data included age, weight, and before surgical procedure, the investiga-tor-reported systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and mean arterial pres-sure (MAP) were recorded at the baseline prior to SAB, and then 1, 5, 10, 20, 30, 40, and 60 min after SAB till end of the surgery. Intravenous access was established with two 18-gauge cannula. As mentioned above, pregnant women were randomly allocated to three groups with equal number of patients. The first group (Group C) included 60 patients who received 500 mL 0.9% saline solution IV starting rapidly with intrathecal injection of local anesthesia for 10–15 min and preloaded with ~10 mL/kg 0.9% saline solution IV within 15–20 min of spinal block. In this group, three cases were rejected due to protocol deviation (as shown in Figure 1). The second group (Group O) included 60 patients who received 8 mg of intravenous ondansetron

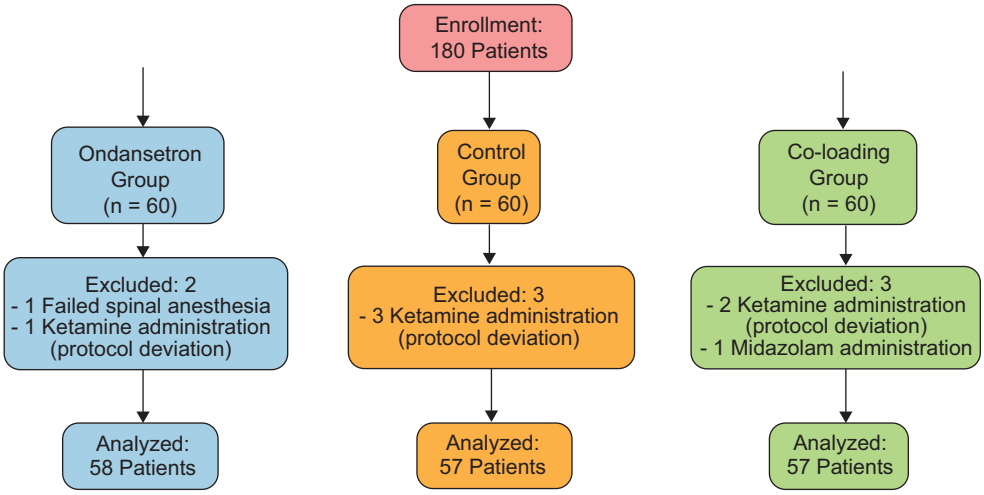

Figure (1): The CONSORT flow diagram for the present study shows subject allocation.

within 5 min of SAB and were preloaded with ~10 mL/kg 0.9% saline solution IV within 15–20 minutes of spinal block. In this group, two cases were rejected due to protocol deviation. The third group (Group P), the con-trol group, included 60 patients receiving only crystalloid preloading with ~10 mL/kg 0.9% saline solution IV before 15–20 min of spinal block. This group served as the baseline for comparing the effectiveness of interventions. In this group, three cases were rejected due to protocol deviation. The SAB was performed to a patient in a sitting posi-tion, and the subarachnoid space was punctured following sterilization at the L3–L4 or L4–L5 level with 25 -gauge spinal needles. After identification of the subarachnoid space, 2.5 mL of 0.5% bupivacaine heavy was injected after confirming the clear free flow of cerebrospinal fluid (CSF). Immediately after finishing the subarachnoid injec-tion, patients were turned into a left lateral tilted supine position using a 10–15° wedge. Levels of sensory block were measured with the absence of pinprick feeling. Each pregnant woman received 5 L/min of oxygen via a simple face mask to prevent expected hypoxia. Incidence of hypo-tension is defined if systolic blood pressure decreased by >20% from baseline or mean arterial pressure <60 mm Hg, and bradycardia is defined if a heart rate <50 bpm was recorded.

Administration of vasopressor and doses needed: Adverse effects, such as shivering, intraoperative nausea, and vomiting, were assessed and recorded. All patients who developed hypotension were administered 6-mg ephedrine IV and repeated as needed. The total vasopressor dose for each patient was calculated, while those who developed bradycardia received 0.6 mg of atropine IV.

2.2. Statistical analysis

Based on preliminary data and assumptions derived from previous literature indicating a 75% incidence of hypotension in the control group, a sample size of 53 patients per group was calculated to detect a 25% absolute reduction in incidence with 80% power and a significance level, $\alpha = 0.05$. To enhance statistical robustness and account for potential dropouts, we enrolled 60 patients in each group (N = 180). Prior to analysis, after exclusion of cases, the final number of cases was 57 in the control group (Group P), 57 in the co-loading group (Group C), and 58 in the ondansetron group (Group O). The analysis was conducted based on this final distribution.

Data were analyzed using SPSS version 26. Descriptive statistics were expressed as mean ± SD for continuous variables and percentages for categorical variables. A two independent samples *t*-test was used to compare mean values across the three groups for continuous variables. Categorical variables were analyzed using the Chi-squared test. The level of significance was set at $P > 0.05$, and $P < 0.05$ was considered nonsignificant.

3. Results

The demographic data across the three groups: control (group P), co-loading (group C), and ondansetron (group O) showed no significant differences in mean age or weight.

There was no statistically significant difference between all three groups regarding the administration of the fluid preloading strategy as observed in Table 2.

3.1. Primary outcomes

The overall incidence of hypotension based on predefined SBP drop criteria was as follows: ondansetron group (55.2% vs control 73.7%; $P = 0.038$); co-loading)64.9% vs control 73.7%; $P = 0.31$). The results revealed a non-statistically significant difference between groups P and C, and a statistically significant difference between groups P and O as observed in Table 3.

The overall incidence of hypotension, based on pre-defined MAP drop criteria was as follows: ondansetron

Table (1): Demographic characteristics of the studied groups.

Characteristics		**Groups**			***P* value**	
		P	**C**	**O**	**P & C**	**P & O**
Age	Mean	28.59	28.63	28.55	0.978	0.973
	SD	6.860	6.422	7.535		
Weight	Mean	75.79	77.35	77.17	0.460	0.513
	SD	11.592	10.89	11.007		

$P > 0.05$: nonsignificant, $^{*}P < 0.05$: significant.

Table (2): Comparison of fluid preloading according to the studied groups.

Variable		**Groups**			***P* value**	
		P	**C**	**O**	**P & C**	**P & O**
Preload fluid	Mean	766.67	776.66	782.59	0.629	0.443
	SD	111.94	108.72	109.86		

Note. $P > 0.05$: nonsignificant, $^{*}P < 0.05$: significant.

Table (3): Incidence of hypotension (based on SBP drop) according to the studied groups.

SBP		**Groups**			***P* value**	
		P	**C**	**O**	**P & C**	**P & O**
Overall	No	15	20	26	0.310	0.038*
		26.3%	35.1%	44.8%		
	Yes	42	37	32		
		73.7%	64.9%	55.2%		

Note. $P > 0.05$: nonsignificant, $^{*}P < 0.05$: significant.

group (13.8% vs control 49.1%; $P = 0.008$); co-loading (22.8% vs control 49.1%; $P = 0.148$). The results revealed a non-statistically significant difference between groups P and C, and a statistically significant difference between groups P and O as observed in Table 4.

Regarding hemodynamic variables, SBP at baseline, 1, 20, 30, and 40 min after SAB showed a statistically significant difference between groups P and C, but after 5, 10, and 60 min, it showed a statistically nonsignificant difference. In contrast, SBP at baseline, 1, and 60 min after SAB showed no statistically significant difference between groups P and O. However, after 5–40 min, there was a statistically significant difference, as observed in Figure 2.

Regarding MAP at baseline, 1, 5, and 60 min after SAB, there was non-statistically significant difference between groups P and C, but after 10–40 min, it showed a statistically significant difference. In contrast, there was a statistically significant difference between groups P and O for all readings after SAB, except after 1 and 60 min, which showed a nonsignificant difference, as observed in Figure 3.

About DBP at baseline, 1, 5, and 60 min after SAB, there was non-statistically significant difference between groups P and C, but after 10–40 minutes, it showed a statistically significant difference. In contrast, there was a statistically significant difference between groups P and O for all readings after SAB, except baseline, 1, 20, and 60 min, which showed a nonsignificant difference, as observed in Figure 4.

The overall incidence of bradycardia showed a non-statistically significant difference between all three groups ($P = 0.463$; $P = 0.233$) as observed in Table 5.

Table (4): Incidence of hypotension (based on MAP drop) according to the studied groups.

MAP		**Groups**			***P* value**	
		P	**C**	**O**	**P & C**	**P & O**
Overall	No	37	44	50	0.148	0.008**
		50.9%	77.2%	86.2%		
	Yes	20	13	8		
		49.1%	22.8%	13.8%		

Note. $P > 0.05$: nonsignificant; $^{*}P < 0.05$: significant; $^{**}P \leq 0.01$: highly significant.

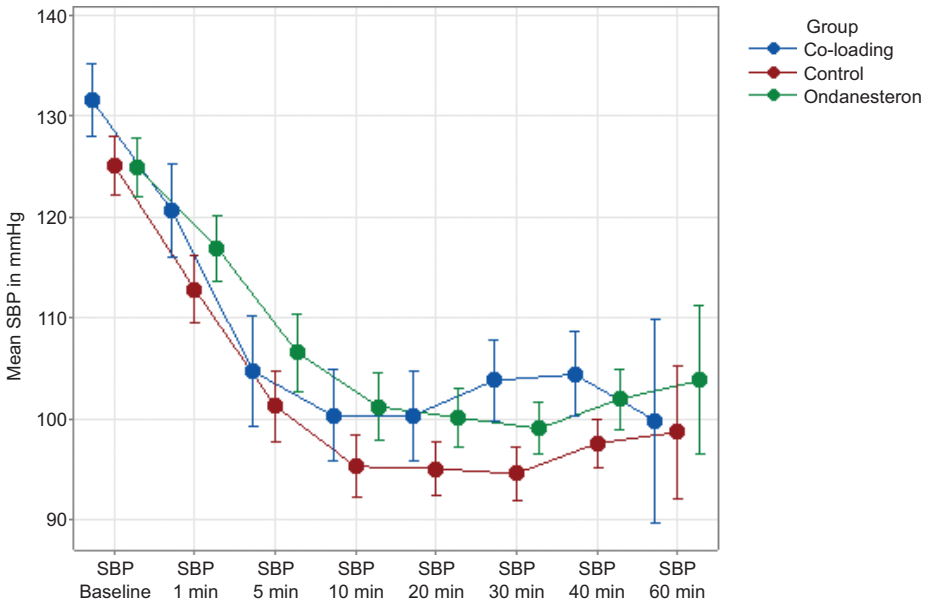

Figure (2): Interval plot of mean SBP (mm Hg) over 60-min post-subarachnoid block.

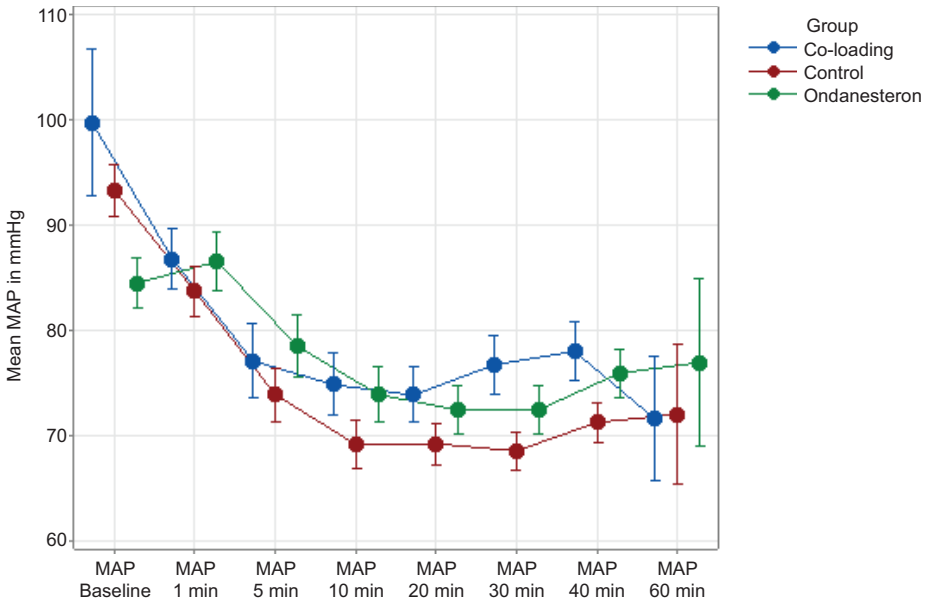

Figure (3): Interval plot of mean MAP (mm Hg) over 60 min of post-subarachnoid block.

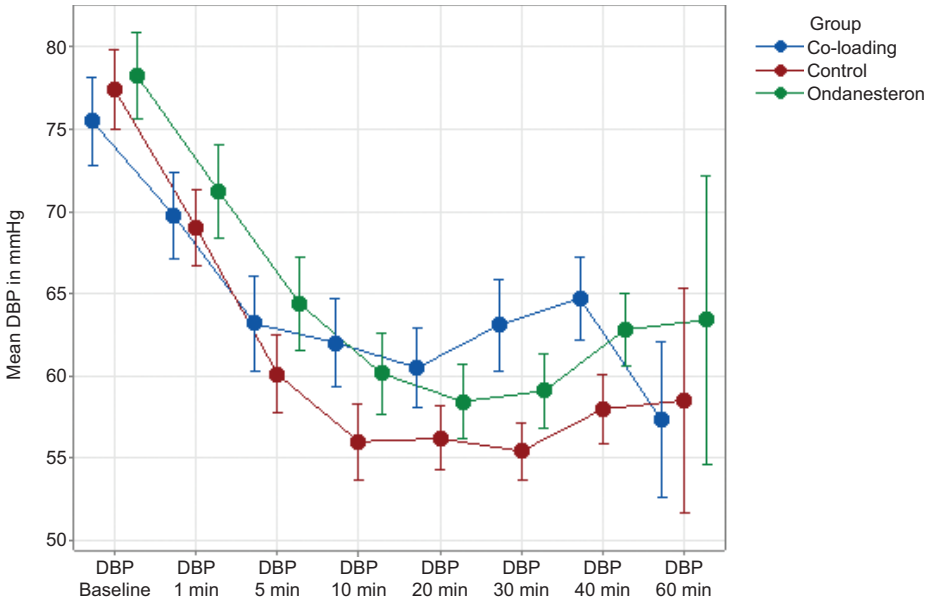

Figure (4): Interval plot of mean DBP (mm Hg) over 60 min post-subarachnoid block.

Table (5): Incidence of bradycardia according to the studied groups.

Bradycardia		**Groups**			***P* value**	
		P	**C**	**O**	**P & C**	**P & O**
Overall	No	52	54	56	0.463	0.233
		91.2%	94.7%	96.6%		
	Yes	5	3	2		
		8.8%	5.3%	3.4%		

Note. $P > 0.05$: nonsignificant, $^{*}P < 0.05$: significant.

Regarding HR at baseline, 1, and 40 min after SAB, there was a statistically significant difference between groups P and C, but after 5, 10, 20, 30, and 60 min, there was no statistically significant difference. In contrast, there was a statistically significant difference between groups P and O at baseline, 10, 30, and 40 min, but after 1, 5, 20, and 60 min, there was a nonsignificant difference, as observed in Figure 5.

Vasopressor requirements showed no significant differences between groups P and C (P = 0.141). Meanwhile, groups P and O showed a high statistically significant difference (P = 0.007). Regarding vasopressor dose, ondansetron showed a very high statistically significant difference (8.5 ± 9.8 mg vs control 18.7 ± 12.9 mg; $P < 0.001$). In contrast, co-loading showed no significant differences (16.06 ± 13.75 vs control 18.7 ± 12.9 mg; $P < 0.285$) as observed in Table 6.

3.2. Secondary outcomes

Concerning intraoperative nausea and vomiting (IONV), no significant difference was observed between groups P and C (P = 0.189). However, a highly significant difference was noted between groups P and O (P = 0.007) as observed in Table 7.

There was no significant difference in the incidence of shivering between groups P and C (P = 0.349), while a significant difference was observed between groups P and O (P = 0.019), as observed in Table 8.

4. Discussion

Subarachnoid block is also known as the method of choice for anesthesia in case of caesarean section [15]. Nearly 70–80% of pregnant women develop SABIH without pharmacological prophylaxis. This hypotension is commonly accompanied by reflex tachycardia, nausea, and vomiting, and on rare occasions, bradycardia is observed [16]. The main reasons attributed to SABIH are sympathetic blockade with a parasympathetic overdrive and BJR [6].

Preloading with crystalloid solutions is a common practice aimed at preventing SABIH. Studies indicate that while crystalloid preloading can reduce the incidence of hypotension, its effectiveness is often overshadowed by alternative methods such as co-loading, which administers fluids concurrently with anesthetic to better maintain intravascular volume during the vasodilatory phase of

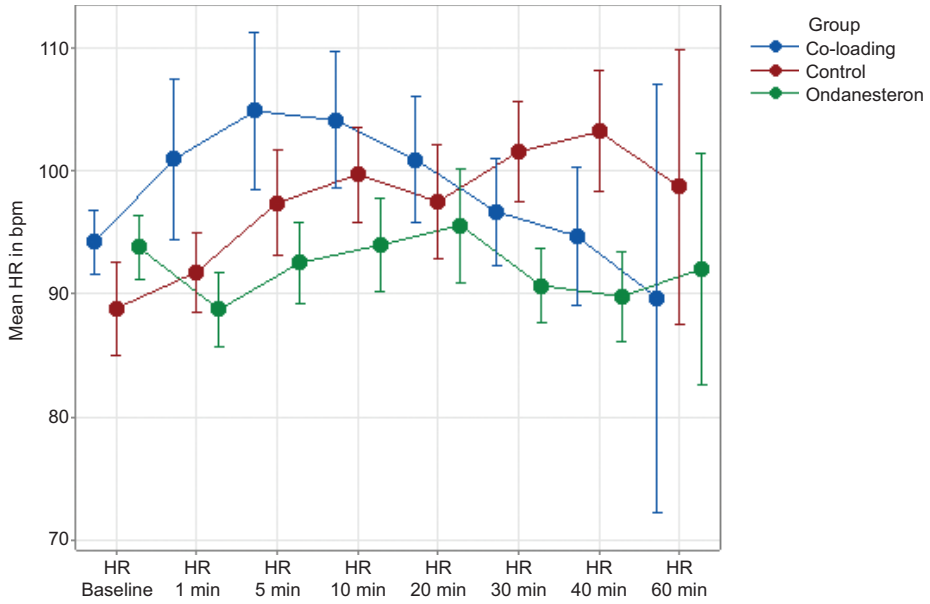

Figure (5): Interval plot of mean HR (bpm) over 60 min post-subarachnoid block.

Table (6): Comparison of vasopressor requirements and dose according to the studied groups.

Parameters		Groups			*P* value	
		P	C	O	P & C	P & O
Vasopressor requirements	No	12	19	26	0.141	0.007**
		21.1%	33.3%	44.8%		
	Yes	45	38	32		
		78.9%	67.7%	55.2%		
Vasopressor dose in mg	Mean	18.74	16.06	8.48	0.285	<0.001***
	SD	12.93	13.75	9.80		

Note. **$P \leq 0.01$: highly significant. ***$P \leq 0.001$: very highly significant.

Table (7): Incidence of nausea and vomiting according to the studied groups.

Nausea & vomiting	Groups			*P* value	
	P	C	O	P & C	P & O
No	23	30	38	0.189	0.007**
	40.4%	52.6%	65.5%		
Yes	34	27	20		
	59.6%	47.4%	34.5%		

Note. $P > 0.05$: nonsignificant; *$P < 0.05$ = significant; **$P \leq 0.01$: highly significant.

sympathetic blockade. Overall, while crystalloid preloading is beneficial, co-loading may offer superior outcomes in preventing hypotension during SAB [17–19].

Ondansetron, a 5HT-3 receptor antagonist, may mitigate SABIH during cesarean delivery. The administration of ondansetron prior to SAB targets the mechanisms causing hypotension, such as sympathectomy and the BJR, which can lead to bradycardia and further drop in blood pressure. By blocking these receptors, ondansetron potentially reduces the incidence and severity of hypotension and reduces the need for vasopressor administration, thereby improving maternal and fetal outcomes during elective cesarean sections [20,21]. Current strategies to maintain hemodynamic stability and reduce hypotension after subarachnoid for cesarean section remain mixed, so this study was planned to assess the efficiency of crystalloid co-loading versus ondansetron on the incidence of SABIH and bradycardia during elective cesarean sections.

Table (8): Incidence of shivering according to the studied groups.

Shivering	Group			*P* value	
	P	C	O	P & C	P & O
No	26	31	39	0.349	0.019*
	45.6%	54.4%	67.2%		
Yes	31	26	19		
	54.4%	45.6%	32.8%		

Note. $P > 0.05$: nonsignificant; $^*P < 0.05$: significant.

In the present study, we used our predefined SBP and MAP criteria, which were consistent with most previous studies regarding the definition of hypotension [6,13]. Hypotension occurred most often in the control group (group P). The overall incidence of SBP = 73.7%, MAP = 49.1% was in the control group; SBP = 64.9%, MAP = 22.8% in the co-loading group; and SBP = 55.2%, MAP = 13.8% in the ondansetron group. The incidence of hypotension was lower in the ondansetron group, compared to the co-loading group. These findings strongly support the results of the previous studies that indicated the protective role of ondansetron in reducing the incidence of SABIH [22–24]. Conversely, some studies disagree with these results, finding no statistically significant differences in blood pressure or heart rate between the ondansetron and control groups [25,26]. However, the current study discovered that ondansetron results in a lower incidence of hypotension than in other groups, which supports the evidence that 5-HT_3 blockade blunts the BJR, thereby improving hemodynamic stability in obstetric patients [6,14,24].

Consistent with the incidence of hypotension results, vasopressor requirements differed by group. In the control group, 78.9% of patients required vasopressor support, compared to 67.7% with co-loading and only 55.2% with ondansetron. Likewise, the mean vasopressor dose was much lower in the ondansetron group (8.5 mg) than the co-loading (16.06 mg) and control (18.7 mg) groups. This confirmed that ondansetron substantially reduced vasopressor requirement, reflecting the reduced hypotension. This finding was consistent with the results reported that ondansetron administration was associated with decreased vasopressor requirement and dose during cesarean section [27,28].

Regarding hemodynamic variables, all groups showed the expected SBP decline after SAB, but the patterns differed. Over the first 40 min after induction, the co-loading group maintained higher SBP at 1 min (120.6 ± 17.4 mmHg; $P = 0.008$ vs control) and at later intervals (e.g., at 30 min, co-loading SBP was 103.8 ± 15.0 mmHg vs. control 94.6 ± 9.9 mmHg; $P < 0.001$). At 5–40 min post-block, the ondansetron group consistently maintained higher SBP than the control ($P < 0.05$). Trends in MAP reflected the SBP results. After spinal anesthesia, MAP dropped in all groups. Importantly, MAP in the control vs co-loading group was significantly different only at 10–40 min (co-loading higher, $P < 0.05$); there was no difference between 1 and 60 min. In contrast, control vs ondansetron showed significant MAP differences at most time points after the block (all except 1 and 60 min, $P < 0.05$). Regarding DBP immediate post-block, it was similar across all groups ($P > 0.05$). However, differences emerged after 5 min. At 10–40 min, the co-loading group had significantly higher DBP than the control group (e.g., 10 min: 62.0 vs 56.0 mmHg, $P = 0.001$). The ondansetron group also showed higher DBP than the control group at 5–40 min (all $P < 0.05$).

In practical terms, both interventions attenuated SAIBH over time. Still, at 20–40 min, the SBP, DBP, and MAP values were higher in the co-loading group, compared to the ondansetron group. This stability is potentially attributed to the fact that more patients in the co-loading group experienced hypotension during these time points and consequently received higher doses of ephedrine, which may have led to the transient increase in blood pressure parameters. Ephedrine is a sympathomimetic that rapidly increases blood pressure through α- and β-adrenergic stimulation. When given intravenously, its pressor effect occurs within seconds to minutes and is relatively short-lived [29], but a bolus can temporarily overshoot BP. Thus, each ephedrine dose given to group C patients would elevate SBP, DBP, and MAP at the time of measurement, artificially inflating the observed values.

Published evidence underscores this phenomenon. For example, a randomized, controlled, double-blind study found that parturients receiving prophylactic ondansetron had far fewer hypotensive episodes than controls, consuming on average only 5.1 ± 7.8 mg of ephedrine vs 12.9 ± 9.2 mg in the control group [30]. Consistent with that trial, we observed markedly higher ephedrine consumption in group C than in group P. A recent meta-analysis also reported that ondansetron prophylaxis significantly reduces the need for rescue ephedrine (risk ratio ~0.61) and that treated patients have higher MAP and SBP in the first 20 min after spinal anesthesia [31]. In contrast, our raw hemodynamic curves showed Group C with higher pressures only at 20–40 min, suggesting that those points reflected ephedrine corrections. Thus, when corrected for vasopressor usage, the comparison flips: ondansetron appears more effective at preserving baseline hemodynamics, whereas the apparent advantage of co-loading vanishes. The reduced effectiveness of co-loading in preventing hypotension may relate to the rapid redistribution

of fluids in the maternal circulation, which does not adequately counteract the immediate vasodilation caused by spinal anesthesia. In contrast, ondansetron's success may be attributed to its action on 5-HT3 receptors, blunting the BJR, which is implicated in reflexive hypotension and bradycardia [33]. In the current trial, therefore, the ondansetron group's lower recorded BP likely reflected a more physiological state, with vasopressor sparing. The co-loading group with transiently higher BP readings did not indicate superior physiology but instead the rescue effect of drugs. In summary, underlying hemodynamic stability was better preserved by ondansetron, while co-loading required pharmacologic correction to reach the same pressures.

The overall incidence of bradycardia showed no statistically significant difference between the control (8.8%), co-loading (5.3%), and ondansetron (3.4%) groups (all $P > 0.05$). This agreed with a study demonstrating that ondansetron prophylaxis did not significantly affect heart rate or bradycardia incidence [32]. However, a time-stratified analysis revealed clinically relevant patterns: co-loading caused an early increase in heart rate during the first 10 min, which returned to baseline, consistent with the findings of the study conducted by Mohammad et al. that co-loading with crystalloid led to an early increase in heart rate lasting for about 10 min before returning to baseline sooner than in the pre-loading group [18]. Although a higher heart rate was observed in the pre-loading group, the difference was not statistically significant [18]. Conversely, ondansetron showed delayed stabilization with significant differences, compared to the control at 10, 30, and 40 min ($P < 0.05$), aligning with pharmacodynamic studies that indicated peak vagolytic effects at 30–60 min [30]. The current study determined that neither co-loading nor ondansetron significantly reduced the overall incidence of bradycardia. However, observable time-dependent effects included transient early heart rate instability from co-loading, while ondansetron-maintained stability in the later phase.

Ondansetron's well-known antiemetic effect was evident. IONV occurred in 59.6% of control, 47.4% of co-loading, and only 34.5% of ondansetron patients. The difference between control and ondansetron was highly significant ($P = 0.007$), while co-loading was not significantly different from the control ($P = 0.189$). This finding was expected due to ondansetron's mode of action and matched previous numerous trials demonstrating that ondansetron drastically reduces the incidence of nausea and vomiting after SAB [34,35].

Shivering is common after spinal anesthesia and adds to patient's discomfort. In the present trial, the ondansetron group had significantly less shivering than the control group (32.8% vs 54.4%, ($P = 0.019$); however, co-loading (45.6%) did not differ significantly from the control group ($P = 0.349$). This was consistent with the emerging evidence that 5-HT_3 antagonists reduce post-spinal shivering [3,33,36]. The present study's results were inconsistent with the previous results reporting that the incidence of shivering was lower in the ondansetron group, compared to the placebo group (15% vs 25%) with a non-statistically significant difference ($P = 0.2$) [37]. However, the present results were consistent with meta-analysis that indicated higher efficacy for preoperative ondansetron administration in preventing post-anesthesia shivering and decreasing the need for pethidine [38]. Similarly, a recent RCT in cesarean patients showed grade ≥1 shivering in only 2.5% of ondansetron patients versus 22.3% of controls ($P = 0.007$) [25,26]. Our data through in a broader surgical population proposed the same trend. Although the mechanism was not clear, it may involve central serotonin pathways. Importantly, no adverse events or complications of ondansetron were observed [39].

4.1. Limitations

The current study had several limitations, including a moderate sample of 180 patients from two centers and a focus on elective surgery patients. Larger multicenter trials would better generalize the results. The administration of ephedrine for hypotension was calculated without considering the time of administration, potentially causing fluctuations in hemodynamic variables at certain intervals, compared to other groups. The study also lost postoperative follow-up and did not investigate the potential adverse effects of ondansetron. Future research should explore optimal dosing and timing of ondansetron.

5. Conclusions

This study demonstrated that 8-mg ondansetron IV significantly reduced the incidence of hypotension, vasopressor requirements, IONV, and shivering during spinal anesthesia, compared to co-loading strategies. Crystalloid co-loading offered some benefits in mitigating drop in blood pressure.

Acknowledgments

The authors thanked the/Department of Anesthesia, College of Health Sciences, University of Duhok as well as the hospitals of the Karbala Health Directorate for contributing to the completion of this project.

Conflict of Interest

The authors declared no conflict of interest with previous studies.

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