Acta Anaesth. Bel., 2023, 74 (4): *267-273*

*Original article*

# Effect of ondansetron in maternal hypotension during cesarean delivery: an observational study

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## *Abstract*

**Background: Spinal anesthesia is the most common anesthetic technique for cesarean delivery. Thus, hypotension is associated with a reduction in uteroplacental flow which may induce fetal morbidity. Activation of the Bezold Jarisch reflex (mediated by 5HT3 receptors) can worsen hypotension and decrease cardiac output. We studied the effect of ondansetron administration before spinal anesthesia on the trajectory of blood pressure during cesarean delivery.**

***Methods:*** **We conducted a retrospective chart review of all cesarean deliveries that occurred between April 1st 2020 and April 1st 2021 and included 85 pregnant women (43 with ondansetron and 42 in the control group). Data were obtained from the electronic medical record database of the British Hospital of Buenos Aires. Socio-demographic, obstetric, anesthetic and perioperative characteristics of patients were assessed.**

***Results:*** **There were no significant differences in the trajectories of the change from baseline of mean arterial blood pressure between ondansetron and control group (0.14% (95% CI: 0.06 to 0.21) per minute). This also applied to heart rate (-0.10% per minute (95% CI: -0.19 to 0.01). The need of any infusion (phenylephrine or atropine) comparing ondansetron to the reference group was 1.12 (95% CI: 0.68, 1.85). There were eight events of shivering (16.3%) in the ondansetron exposed group and four events of shivering (8.5%) in the reference group. APGAR values showed no clinical difference between groups.**

***Conclusions:*** **In this single-center cohort study, we did not observe an effect of routine administration of ondansetron before spinal anesthesia in cesarean section on improving arterial blood pressure or heart rate throughout the procedure.**

***Keywords:*** **Cesarean delivery, Hypotension, Ondansetron, Spinal anesthesia.**

## Introduction

Spinal anesthesia is the most common anesthetic technique for caesarean delivery, usually chosen to avoid the risks of the general anesthesia[1]. The adverse effect most frequently associated with spinal anesthesia is hypotension originated by a decrease of peripheric vascular resistance and cardiac preload[2]. Hypotension is associated with a decrease in cardiac output and a reduction in uteroplacental flow which may induce fetal morbidity[3]. In severe cases, can lead to unconsciousness, pulmonary aspiration and placental hypoperfusion with fetal hypoxia, acidosis and neurologic injury[1,4]. Bradycardia can occur secondary to sympathetic nerve blockade, increase activation of baroreceptors or induction in Bezold-Jarisch reflex (BJR)[2], a reflex that activates mechanoreceptors in the ventricular walls leading to vasodilatation, bradycardia, and hypotension[5]. Serotonin may be an important factor in inducing BJR[5] and pharmacological and animal studies[6] suggest that the BJR can be prevented by blockade of 5-HT3 receptor[7].

Previous studies tried to demonstrate that administration of ondansetron, a potent and highly selective 5-HT3 receptor antagonist, minutes before spinal anesthesia could attenuate hypotension and bradycardia. While a few studies showed that ondansetron administration might be beneficial[7–9], most have shown evidence of little or no protection[10–14]. Small sample sizes, differences in the administration of co-interventions (e.g.,

pre-loading/co-loading fluids) and heterogeneity in the definitions of hypotension might be some of the causes for this discrepancy. To this day, clinical guidelines do not include a recommendation in cesarean section to use ondansetron as premedication to avoid the decrease in cardiac output following spinal anesthesia.

Because the incidence of hypotensive events is very high in most observational settings and the definition of hypotension is not consistent in the literature[2,15,16], we explored whether the use of ondansetron modifies the trajectory of mean arterial pressure and heart rate during the entire cesarean section. While the majority of studies measured the arterial pressure in intervals of five minutes, we extracted data from anesthetic medical records every two minutes to better characterize arterial pressure trajectories. Secondarily, we evaluated the use of vasopressors and/or atropine, the APGAR score, and perioperatory shivering associated with the use of ondansetron in comparison to a control group that received treatment as usual.

## Materials and Methods

### *Study design and data extraction*

This study was conducted at British Hospital of Buenos Aires, Argentina, a general Hospital with an obstetric service with approximately 1100 deliveries per year and a cesarean delivery rate of 20%. The number of deliveries dropped around 20-30% in 2021 after the COVID-19 pandemic. We conducted a retrospective chart review of all cesarean deliveries that occurred between April 1st, 2020 and April 1st, 2021 in our institution. The institutional review board provided approval for this study (protocol reference number: PRIISA CODE BA: 6937), and it was developed in accordance to the amended declaration of Helsinki. Included patients belonged to a local health plan. All data were obtained from the electronic medical record database of the British Hospital of Buenos Aires. In the operation room, we used DATEX OMEDA® 9100c that can record patient information every minute or using other pre-determined interval. For each cesarean delivery performed, we extracted data included in the anesthetic record: preoperative history and physical data, description of the surgery, intraoperative physiologic and vital signs, complications, medication, fluid administration, and post-operative recovery room data.

In our institution the standard practice of cesarean delivery anesthesia is based on the following description. Medication is not administered prior to spinal anesthesia except for prophylactic antiemetics (ondansetron 4-6-8mg, metoclopramide 10-20mg). Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and oxygen saturation ($SpO_2$) is measured at 2 minutes intervals using a noninva-sive electrocardiography monitor from DATEX OMEDA. Mean SBP, DBP, MAP, HR, and $SpO_2$ from three measurements before surgery is considered as the baseline SBP, DBP, MAP, HR, and $SpO_2$ levels. In our institution, no parturient received oxygen during cesarean section. Before spinal anesthesia, a standard venous catheter (16-gauge or 18-gauge) is placed into the superficial vein of the forearm, and physiological solution or lactated Ringer's solution is infused at a minimal rate. With patients in the sitting position, spinal anesthesia is performed at the L2-L3, L3-L4 or L4-L5 with a 25G or 27G Whitacre needle. Lumbar spaces are identified by palpation of the iliac crests and the posterior superior iliac spines. Patients received intrathecal dose between 2mL-3ml of a hyperbaric 5mg/mL bupivacaine solution and 15-25 µg of a 50 µg/mL fentanyl solution. Parturient are placed in a supine position immediately after the injections is completed. Co-loading of fluids is administrated. Sensory block is assessed according to loss of temperature sensation. Surgery is started as soon as the T6 dermatome is anesthetized. All hemodynamic parameters are recorded every 2 minutes. Hypotension, defined as a decrease from baseline values below 90 mmHg in systolic blood pressure is treated by an infusion of crystalloids (100 mL) and phenylephrine bolus (25-50mg) until restoration of baseline values. Bradycardia, defined as a heart rate below 50 bpm, is treated with atropine bolus (0.6-1mg). Oxytocin (3-5 IU in 100 ml physiological saline) is given as intravenous drip after delivery.

### *Study population*

We identified all consecutive pregnancies undergoing cesarean deliveries with an indication of spinal anesthesia between April 1st 2020 and April 1st 2021 who (i) were American Society of Anesthesiologists Physical Status (ASA) II, (ii) 18 to 55 years old, (iii) 28 to 42 weeks of gestation, and (iv) Body Mass Index (BMI) between 18 and 38. We excluded all patients who received ondansetron before and after the five to ten minutes window of administration prior spinal anesthesia. Also were excluded parturient who underwent cesarean delivery with general anesthesia or epidural anesthesia in response to an emergency delivery; and patients with a documentation of any of the following: congestive heart failure, valvular heart disease and hypertensive disorders (Eclampsia, Preeclampsia, Chronic Hypertension with alfametyldopa).

### *Covariates*

Demographic and clinical variables were age (years), weight (kg), height (cm), and body mass index (kg/m$^2$). Obstetric data (indication for caesarean delivery, gestational age, twin pregnancy, urgent surgery), anesthetic technique: (a) fluid administration (mL), (b) place of dural puncture (i.e., second, third, fourth, fifth lumbar space), (c) intrathecal dose of bupivacaine (mL), (d) fentanyl (μg), and (e) total intrathecal volume administrated (mL). Finally, we recorded use and dose of metoclopramide (10 or 20 mg), and time of fasting (< six hours, six to eight hours, eight to 10 hours, 10 to 12 hours, > 12 hours).

### *Exposure*

Our primary exposure of interest was ondansetron use, defined as intravenous administration five or 10 minutes before spinal anesthesia, as premedication of nausea and vomiting. Dose of ondansetron received (four, six or eight mg) was also recorded.

### *Outcomes*

The primary outcome was first event of hypotension (defined as a systolic blood pressure below 90 mmHg)[1,7] and first event of bradycardia (defined as a heart rate below 50 bpm)[1,7]. As secondary outcomes we explored the (i) use of phenylephrine or atropine, (ii) presence of other adverse effects (shivering, discomfort) and (iii) APGAR scores (at one and five minutes).

### *Follow-up*

Each patient was followed from the moment the patient was connected to the monitors on the operating room and the anesthesiologist started recording the vital signs on the anesthetic record before the spinal anesthesia was performed, until the end of the surgery. We extracted information every two minutes for analysis.

### *Statistical analysis*

To compare baseline characteristics of those receiving ondansetron and those not receiving ondansetron, quantitative variables are presented as mean and standard deviation or, in case of noticeably skewed data, as the median and interquartile range.

A broad range of potential confounders and proxies for confounders were considered, including treatment indication (nausea and vomiting during pregnancy, hyperemesis gravidarum), co-loading fluid administration, fasting, age, BMI, intrathecal dose of anesthetic, spinal block height, concomitant medication use, maternal conditions (gestational diabetes, hypothyroidism). We selected the included covariates because they are potential risk factors for the outcomes or potential proxies for such risk factors.

We used a linear mixed-effects model with a random intercept to model the change in mean arterial pressure and heart rate during follow-up as a function of treatment and also adjusted for the potential confounders.

All analyses were conducted using R statistical software version 3.4.4

## Results

A total of 99 patients were assessed for eligibility criteria. Of those, 85 were included in the present analysis (Fig. 1). We exploited natural variations in the prescribing pattern of ondansetron during cesarean section. 43 patients received at least one dose of ondansetron. Ondansetron-exposed and not exposed individuals were very similar regarding all measured characteristics, except for a higher baseline heart rate in the ondansetron-exposed individuals (Table I).

There were 17 hypotensive events in the ondansetron-exposed individuals (39.5% of the sample) and 15 events in the reference group (35.7% of the sample). There were two bradycardic

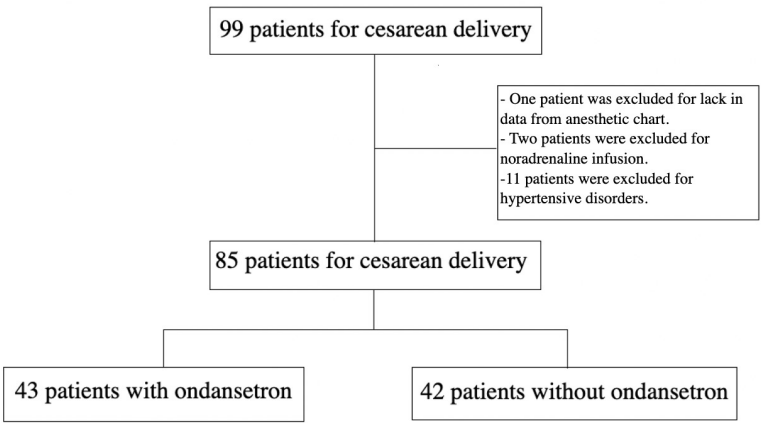


*Fig. 1* — Study participants.

**Table I.** — Socio-demographic and perioperative base line characteristics of patients undergoing cesarean section under spinal anesthesia.

| | Control (n=42) | Ondansetron (n=43) |
|---|---|---|
| Age, years (standard deviation) | 33.95 (4.94) | 34.70 (5.72) |
| BMI | 29.91 (7.07) | 30.56 (5.80) |
| Gestational Age | 39.08 (1.13) | 38.27 (2.16) |
| Medical Record | | |
| Seizures | 0 (0.0) | 2 (18.2) |
| IV Fertilization | 0 (0.0) | 1 (9.1) |
| Antiphospholipid Syndrome | 0 (0.0) | 1 (9.1) |
| Hypothyroidism | 4 (50.0) | 5 (45.5) |
| Panic Attack | 0 (0.0) | 1 (9.1) |
| Asthma | 1 (12.5) | 0 (0.0) |
| Gestational Diabetes/Diabetes | 2 (25.0) | 1 (9.1) |
| Cerebrovascular Accident | 1 (12.5) | 0 (0.0) |
| Urgent/Emergent cesarean section | 17 (40.5) | 9 (20.9) |
| Surgical determination | | |
| **Failure to progress during labor** | **10 (25.0)** | **6 (14.3)** |
| **Previous Cesarean section** | **16 (40.0)** | **19 (45.2)** |
| **Pelvic presentation delivery** | **5 (10.0)** | **6 (14.3)** |
| **Patient decision** | **5 (10.0)** | **2 (2.4)** |
| **Others*** | **6 (15)** | **10 (23.8)** |
| **Bolus Phenylephrine (mean, SD)** | **2.2 (2.6)** | **3.1 (4.2)** |
| **Bolus Atropine (mean, SD)** | **0.1 (0.2)** | **0.2 (0.4)** |
| SBP (mmHg) | 133.07 (13.00) | 133.07 (13.39) |
| DBP (mmHg) | 74.88 (9.41) | 75.84 (12.91) |
| MBP (mmHg) | 98.07 (10.08) | 98.95 (11.63) |
| HR (beat/min) | 86.71 (16.92) | 89.74 (12.01) |
| Spo2 | 98.15 (0.91) | 98.10 (0.82) |
| Bupivacaine Dose Spinal Anesthesia | 10.55 (0.94) | 10.79 (1.17) |
| Fasting | | |
| < 6hs | 3 (7.1) | 3 (7.0) |
| 6 to 8 hs | 12 (28.6) | 6 (14.0) |
| 8 to 10 hs | 15 (35.7) | 27 (62.8) |
| 10 to 12 hs | 5 (11.9) | 4 (9.3) |
| > 12hs | 7 (16.7) | 3 (7.0) |

SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; Spo2: oxygen saturation. Others*: Oligohydramnios, Seizures, Fetal Bradycardia, Myomectomy, Twin pregnancy, Fetal growth restriction, Vasa Previa, Uncontrolled Pain, Fetal Macrosomia.

events in the ondansetron-exposed patients (4.1%) and four events in the reference group (8.5%) by the end of the follow-up period.

### *Analysis of trajectories*

The trajectories of the change from baseline of mean arterial blood pressure and heart rate during follow-up are shown in Fig. 2. After adjusting for all measured variables, in the linear mixed-effects model treatment with ondansetron was associated with an overall change in mean arterial blood pressure of 0.14% (95% CI: 0.06 to 0.21) per minute and an overall change in heart rate of -0.10% per minute (95% CI: -0.19 to 0.01).

### *Secondary outcomes*

There were eight patients that received an atropine bolus (16.3%) and 34 patients that were given phenylephrine (69%) in the ondansetron-exposed patients, while three patients received an atropine bolus (6.4%) and 31 patients were given phenylephrine (66.0%) in the reference group by the end of follow-up. The adjusted risk ratio for the administration of any bolus comparing ondansetron to the reference group was 1.12 (95% CI: 0.68, 1.85). There were eight events of shivering (16.3%) in the ondansetron exposed group and four events of shivering (8.5%) in the reference group. Finally, the median APGAR score in the ondansetron-treated patients was 10 (SD: 0.4) and 10 (SD: 0.3) in the reference group.

## Discussion

In our study, we found that premedication with ondansetron did not meaningfully alter the incidence of hypotension, as compared to standard-of-care.

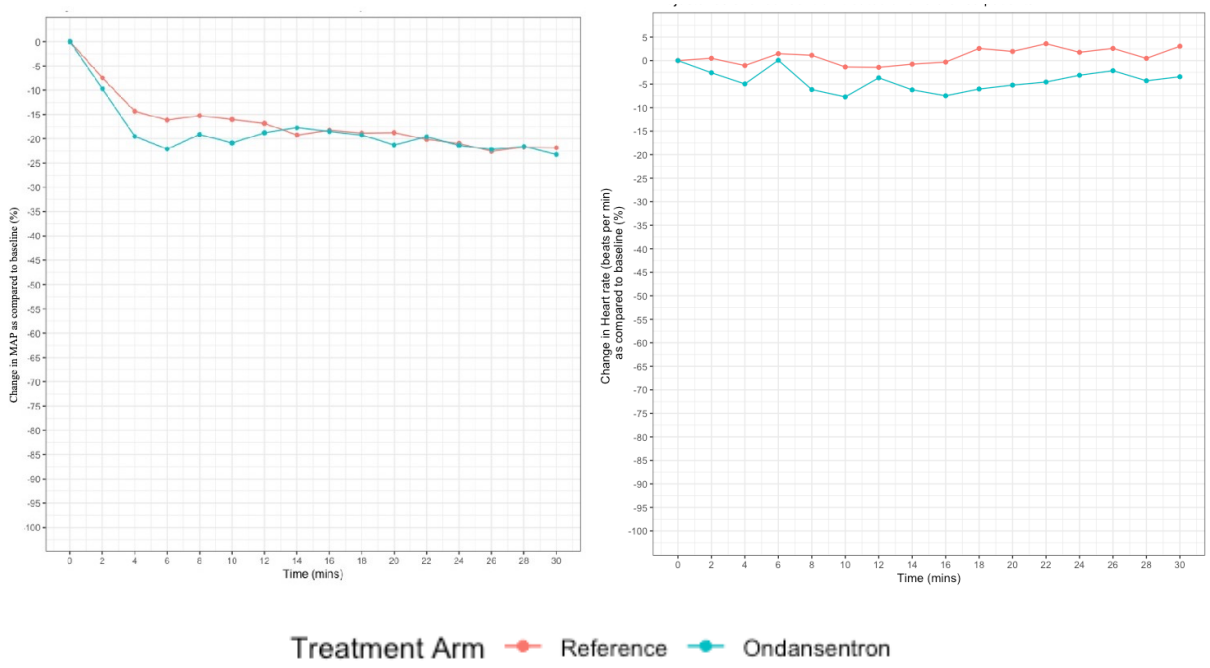


*Fig. 2* — Unadjusted trajectories of mean blood arterial pressure during cesarean section.

The longitudinal trajectory of the mean arterial pressure throughout the cesarean section was similar in both groups. Similarly, we found little evidence that ondansetron prevented bradycardia: the analysis of the heart rate trajectory showed virtually identical curves in both groups. Similarly, we found no differences in the risk of requiring atropine or phenylephrine administration between both groups.

This study sheds light on the available evidence on this topic to this date. Prior studies have explored the use of ondansetron on the risk of incident hypotension and bradycardia and reported that this medication does not provide clinical benefit[10–13]. Meta-analysis performed by Chengmao Zhou et al.[14] with 21 randomized controlled trials found no statistically difference in hypotensive events between groups. However, these studies suffered from a non-uniform definition of hypotension. Here, we complemented these prior studies by evaluating whether this medication significantly altered the entire trajectory of arterial pressure and heart rate during cesarean section, a more relevant outcome for patients and clinicians. Our analysis using linear mixed effects model found very little evidence to support a difference in the trajectories of arterial blood pressure or heart rate between groups.

Our results contrast those published by Owczuk et al.[7], Sahoo et al.[8] Heesen et al.[9] and Aksoy et al.[17].This discrepancy can be explained by many factors: Owczuk et al. administered spinal anesthesia at a dose higher than usual: 4 ml of bupivacaine 0,5% intrathecal which can lead to a more profound hypotension. Sahoo et al. reported hypotensive events only from minutes 14 to 35. The meta-analysis by Heesen et al.[9] of 10 randomized controlled trials reported high heterogeneity, a high risk of publication bias, heterogeneity in spinal anesthesia and fluid management techniques, as well as variations in hypotension and bradycardia definitions.

Our study has several strengths. First, we adjusted a wide range of potential confounders including demographical, clinical, obstetrical, and surgical variables that are usually not recorded in most observational studies. Adjusting for all those potential covariates allowed us to make conclusions with more comparable groups. Secondly, by measuring blood pressure every two minutes and measuring all potential co-interventions we were able to compare our results with the rest of published literature. We detected an overall incidence of hypotension after spinal anesthesia of 38% (32 patients of the 85 total sample). These results were in contrast with other studies[2,16,18] reporting incidence as high as 70-80%. The wide difference in these results can be attributed to the lack of a unified definition of hypotension in cesarean section. Some authors defined hypotension as a systolic arterial pressure <100mmHg[13,14], change ≥ 20%[13,19] or ≥25% 10 from baseline; or change of MAP from baseline ≥25%4 or ≥20%[20], or diastolic blood pressure < 60 mmHg[21]. Other source of discrepancy that we were able to assess was the presence of co-loading of fluids during cesarean section to treat a decrease in preload, or the time of fasting. The different doses of bupivacaine intrathecal can also explain the difference in overall hypotension and bradycardia rates. We assume that our finding of 38% of hypotensive events (lower than studies reported above) is because of the administration of

intravenous coloading fluid and lower intrathecal doses of bupivacaine 0,5% (10-12mg) than usually described in other studies. These actions can decrease hypotensive events22. Finally, our statistical model provides a more clinically relevant result for the association between ondansetron and arterial blood pressure and heart rate by comparing the entire trajectory of these variables during cesarean section, rather than comparing the proportion of patients who experienced the definition of hypotension or not (which varies widely from study to study).

However, this study has some limitations. First, we use fentanyl in our spinal anesthesia to improve anesthetic management. Intrathecal opioids may affect the mechanism of ondansetron in the central nervous system, but we administered a lower dose than recommended (< 25mcg). Second, we did not monitor invasive arterial blood pressure that shows a precisely variation in arterial pressure. Consequently, we decided to measure every two minutes after spinal anesthesia to record changes in blood pressure that could be missed using usual care (every five minutes). Third, when the anesthesiologist notices that blood pressure is dropping rapidly from baseline, usually does not wait until the definition of hypotension is met to start a phenylephrine infusion and that decision can underestimate the overall risk of hypotension, if this practice is not consistent in different settings. Fourth, this is an observational study and there is not a placebo control or blinding in the anesthesiologist. Finally, our sample size was probably modest for a study focused on adverse effects. Because of the retrospective design the timing and dose of ondansetron administration were not standardized which may have an influence on hemodynamic stability.

In conclusion, our study suggests that the routine administration of ondansetron given five minutes before spinal anesthesia in cesarean section in parturient has no impact on improving arterial blood pressure or heart rate throughout the cesarean section. More studies with larger sample size are required to clarify this issue.

*Discosure:* The authors declare that they received no funding from any external organization for the submitted work and have no conflicts of interest to declare. The data generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request

## References

1. Birnbach DJ, Browne IM. Anesthesia for Obstetrics. 2010.
2. Liu SS, McDonald SB. Current Issues in Spinal Anesthesia. Anesthesiology 2001;94(5):888–906.
3. Stewart A, Fernando R, McDonald S, et al. The Dose-Dependent Effects of Phenylephrine for Elective Cesarean Delivery Under Spinal Anesthesia. Anesth Analg 2010;111:1230–7.
4. Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. in: Cyna AM, editor. Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2006.
5. Aviado DM, Aviado DG. The Bezold-Jarisch reflex. A historical perspective of cardiopulmonary reflexes. Ann N Y Acad Sci 2001;940:48–58.
6. Yamano M, Kamato T, Nishida A, et al. Serotonin (5-HT)3-Receptor Antagonism of 4,5,6,7-Tetrahydrobenzimidazole Derivatives against 5-HT-Induced Bradycardia in Anesthetized Rats. Jpn J Pharmacol 1994;65(3):241–8.
7. Owczuk R, Wenski W, Polak-Krzeminska A, et al. Ondansetron Given Intravenously Attenuates Arterial Blood Pressure Drop Due to Spinal Anesthesia. Reg Anesth Pain Med 2008;33:332–9.
8. Sahoo T, SenDasgupta C, Goswami A, Hazra A. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: A double-blind randomised, placebo-controlled study. Int J Obstet Anesth 2012;21(1):24–8.
9. Heesen M, Klimek M, Hoeks SE, Rossaint R. Prevention of Spinal Anesthesia-Induced Hypotension During Cesarean Delivery by 5-Hydroxytryptamine-3 Receptor Antagonists: A Systematic Review and Meta-analysis and Meta-regression. Anesth Analg 2016;123(4).
10. Ortiz-Gómez JR, Palacio-Abizanda FJ, Morillas-Ramirez F, et al. The effect of intravenous ondansetron on maternal haemodynamics during elective caesarean delivery under spinal anaesthesia: a double-blind, randomised, placebo-controlled trial. Int J Obstet Anesth 2014;23(2):138–43.
11. Karacaer F, Biricik E, Ünal İ, Büyükkurt S, Ünlügenç H. Does prophylactic ondansetron reduce norepinephrine consumption in patients undergoing cesarean section with spinal anesthesia? J Anesth 2018;32(1):90–7.
12. Samarah WK, Alghanem SM, Bsisu IK, et al. The effect of ondansetron administration 20 minutes prior to spinal anaesthesia on haemodynamic status in patients undergoing elective caesarean section: A comparison between two different doses. Indian J Anaesth 2020;64(11):954–9.
13. Neumann C, Velten M, Heik-Guth C, et al. 5-HT3 blockade does not attenuate postspinal blood pressure change in cesarean section: A case-control study. Medicine 2020;99(36):e21864–e21864.
14. Zhou C, Zhu Y, Bao Z, Wang X, Liu Q. Efficacy of ondansetron for spinal anesthesia during cesarean section: a meta-analysis of randomized trials. J Int Med Res 2018;46(2):654–62.
15. Practice Guidelines for Obstetric Anesthesia: An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology*. Anesthesiology 2016;124(2):270–300.
16. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R. Incidence and Risk Factors for Side Effects of Spinal Anesthesia. Anesthesiology 1992;76(6):906–16.
17. Aksoy M, Dostbil A, Aksoy AN, Ince I, Bedir Z, Ozmen O. Granisetron or ondansentron to prevent hypotension after spinal anesthesia for elective cesarean delivery: A randomized placebo-controlled trial. J Clin Anesth. 2021;75:110469.
18. Mercier FJ, Augè M, Hoffmann C, Fischer C, le Gouez A. Maternal hypotension during spinal anesthesia for caesarean delivery. Minerva Anestesiol 2013;79(1):62–73.

19. Mohamed S, Befkadu A, Mohammed A, et al. Effectiveness of prophylactic ondansetron in preventing spinal anesthesia induced hypotension and bradycardia in pregnant mother undergoing elective cesarean delivery: A double blinded randomized control trial, 2021. International Journal of Surgery Open 2021;35:100401.
20. Friedly C, Simmons S. Prophylactic ondansetron for prevention of maternal hypotension following spinal anesthesia in women undergoing cesarean section: a systematic review protocol. JBI Evid Synth 2015;13(9).
21. el Khouly NI, Meligy AM. Randomized controlled trial comparing ondansetron and placebo for the reduction of spinal anesthesia-induced hypotension during elective cesarean delivery in Egypt. International Journal of Gynecology & Obstetrics 2016;135(2):205–9.
22. Article R, Hunie M, Wubishet T, et al. A multifaceted review journal in the field of pharmacy The Effect of Preloading and Co-Loading in the Prevention of Hypotension among Mothers Who Underwent Cesarean Delivery under Spinal Anesthesia: A Prospective Cohort Study n.d.

doi.org/10.56126/74.4.27