*Nat. Volatiles & Essent. Oils, 2021; 8(5): 8129-8137*

NVEO
Natural Volatiles & Essential Oils

# The Effects of Different Doses of Intravenous Ondansetron on Hemodynamic Changes and Motor and Sensory Block Induced by Spinal Anesthesia in Women Undergoing Caesarean Section

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**Abstract**

**Background:** Spinal anesthesia is a common method used in caesarean section (C- section). One of the common complications of spinal anesthesia is hypotension that is controlled through pharmacotherapy and fluid therapy. This study aimed to evaluate the effects of 4 and 8 mg intravenous (IV) ondansetron on hemodynamic changes and motor and sensory block induced by spinal anesthesia in women undergoing elective C-section.

**Materials and Methods:** This clinical trial included a group of healthy pregnant women (n=96) undergoing elective C-section at the Amiralmomenin Hospital, Zabol, Iran, in 2014. The participants (n=96) were randomly assigned into the following three groups: (i) control group (n=32) receiving IV placebo, (ii) low-dose group (n=32) receiving 4 mg IV ondansetron, and (iii) high-dose group (n=32) receiving 8 mg IV ondansetron. The data were analyzed using SPSS software version 22.0. Analysis of variance (ANOVA), Chi-square test and repeated-measures ANOVA were used to compare the significance of the differences among groups.

**Results:** The findings showed that 8 mg IV ondansetron improved hypotension and nausea when being applied 5 minutes before spinal anesthesia as compared to the low dose (P=0.080) and control (P=0.005) groups, suggesting there is a statistically significant difference in this regard among the groups.

**Conclusion:** An 8-mg single IV dose of ondansetron significantly reduces hypotension induced by anesthesia, use of vasoconstrictors as well as nausea and vomiting before subarachnoid block in women undergoing elective C-section.

**Keywords**: Spinal Anesthesia, Ondansetron, Hypotension, C-Section.

## Introduction

Due to different reasons, like breech, repeat caesarean section (C-section), congenital anomalities, cervical cancer, giant condyloma of cervix (GCC) and history of vaginal colporrhaphy, a C-section is often performed (1). Anesthesia as one of the requirements for any surgery, like C-section, is divided into general anesthesia and regional anesthesia, in which the health and safety of the mother and fetus should always be considered. General anesthesia is associated with some complications, like inability of airway management when brain anoxia and aspiration of stomach contents occur. It has been shown that among 30 patients, one patient was hardly managed for control of breathing and intubation when using general anesthesia; therefore, despite its benefits, general anesthesia is only used for patients undergoing a real emergency surgery (2). For regional anesthesia, spinal (intrathecal) and epidural are administered. Due to fast onset of effect, minimum drug dose and simplicity, spinal anesthesia is considered as the most common method with low failure rate (2-9). One of the side effects related to spinal anesthesia is cardiovascular complication, in which sympathetic inhibition reduces vascular resistance and vasodilation that lead to lower blood pressure (BP) and heart rate (HR) through reducing venous return (2, 3, 5, 6). Hypotension is another common complication that occurs in 80% of the cases (1, 2, 6-11) with an increased risk for

maternal and fetal complications including reduced blood supply to the placenta, fetal asphyxia, fetal bradycardia, decreased level of mother' s consciousness, aspiration and even maternal cardiac arrest (3, 10, 11). To prevent hypotension, fluid therapy, pharmacotherapy as well as some physical methods such as position of a patient, genuflection and left uterine displacement are recommended (2, 3, 10). A number of studies have shown that fluid therapy did not prevent hypertension, although a combination of fluid therapy and position of a patient were considered as an effective method. When protective measures fail, pharmacotherapy replaced other methods (2, 7, 9, 10).

Ephedrine (an alpha-agonist) has been known as a selected drug for prophylaxis against hypotension after spinal anesthesia, but its rate of nausea and vomiting has been reported about 66% (1, 2, 6-8, 10, 11). It has been shown that phenylephrine also improved nausea and vomiting

for 17% (2, 6, 8, 10, 11). Mechanism of low blood pressure works through 5-hydroxytryptamine (5-HT) receptor that is a peripheral co-receptor (12, 13), indicating that 5-TH plays a major key in hypertension. During anesthesia with bupivacaine, stimulation of periaqueductal with an unknown mechanism increases 5-Th in the spinal dorsal horn and subarachnoid space (13). Increased sympathetic activity and reduced venous return lead to a ventricular volume reduction, sudden activity of the parasympathetic nervous system, and vasovagal response (named Bezold-Jarisch reflex) that finally result in a drop in BP and HR. Due to inhibition of 5-th receptor by serotonin antagonist, 5-Th reduces the volume of this reflux (13, 14).

Ondansetron (antiemetic drug) is considered as an effective method to prevent nausea and vomiting induced by spinal anesthesia and also inhibits 5-TH receptors (15, 16). Furthermore, add of 4 mg ondansetron to anesthetic drugs such as lidocaine improves the quality of anesthesia in patient through reducing the time to achieve complete motor and sensory block (17). Therefore, this study aimed to evaluate the effects of 4 and 8 mg intravenous (IV) ondansetron on hemodynamic changes and motor and sensory block induced by spinal anesthesia in women undergoing elective C-section.

## Materials and Methods

This clinical trial included a group of healthy pregnant women (n=96) undergoing C-section at the Amiralmomenin Hospital, Zabol, Iran, in 2014. For sampling, the access method was applied. Exclusion criteria were as follows: (i) contraindications to local anesthetic nerve blocks [including hemodynamic impairment, coagulation disorders, a history of hypersensitivity to ondansetron or local anesthetic agents, cardiovascular disease (CVD), and treated with selective serotonin reuptake inhibitors (SSRIs) or migraine drugs] and (ii) severe pain indicating failure of numbness. After obtaining the approval of the Ethics Committee of Zabol University of Medical Sciences and the permission of the Amiralmomenin Hospital, we described the purpose and method of the research to the eligible patients before they signed an informed consent form. The ethical code was Zbmu.1.rec.1393.3.

We determined a required sample size of 32 individuals for each group with a 95% confidence level and 80% power using the following formula when $\delta_1$=1.8, $\delta_2$=2.0, $\mu_1$=9.5, $\mu_2$=10.9 and $n\sqrt{k-1}$ (k= number of groups):

$$n = \frac{\left(z_{1-\alpha/2} + z_{\beta}\right)^2 (\delta_1^2 + \delta_2^2)}{(\mu_1 - \mu_2)^2}$$

Then, ninety-six pregnant women (15-45 years old) were randomly divided into the following groups: (i) control group (n=32) receiving 10 ml IV normal saline, (ii) low-dose group (n=32) receiving 4 mg IV

ondansetron diluted in 10 ml normal saline, and (iii) high-dose group (n=32) receiving 8 mg IV ondansetron diluted in 10 ml normal saline, in minutes 1 and 5 before starting the block.

In order to assess the effects of IV ondansetron in the prevention of maternal hypotension after spinal anesthesia, all participant underwent spinal anesthesia for elective SC with 2 ml bupivacaine 0.5% after receiving 20 ml/kg of lactated Ringer's solution during 30 minutes. Spinal anesthesia was performed at $L_{3-4}$ and $L_{4-5}$ levels before the patient was placed in the supine position. Systolic BP (SBP), diastolic BP (DBP) and arterial BP (ABP), HR and arterial oxygen saturation (SaO2) were measured at the admission time, pre-operative time, pre-spinal anesthesia, and every 2 minutes post-spinal anesthesia from minute 10 to 20, every 5 minutes post-spinal anesthesia from minute 20 to 35, and every 2 minutes post-operative time for 8 minutes. The time required to create sensory block in each of the levels and time to return of complete sensation were determined. The time required to reach each stage of the motor block was also recorded using a Bromage scale, in which 0 indicating ability to move the hips, knees, ankles and toes; 1 indicating unable to move hip, able to move knee, ankle, and toes; 2 indicating unable to move hip and knee, able to move ankle and toes; 3 indicating inability to move the hip, knee and ankle, the ability to move fingers; and 4 indicating inabilities to move hips, knees, ankles and toes.

The hemodynamic changes, nausea, vomiting, shivering, or any other post-anesthesia symptoms were then reordered. Furthermore, the upper sensory level (at the midclavicular line) was found in order to determine the time required to reach peak levels of sensory block, regression time to T10 and T12 levels as well as regression time to S1 level. Furthermore, the patients in cases of complications were treated as follows: (i) a BP of less than 20% than normal BP (a cases of hypotension) with 6 mg IV ephedrine, (ii) a HR of less than 50 beats per minute (BPM) with 0.5 mg IV epinephrine, (iii) shivering with 25 mg IV pethidine, (iv) nausea and vomiting with 10 mg IV metoclopramide, and (v) pain with 50 µg IV fentanyl.

## Statistical analyses

The Statistical Package for the Social Sciences (SPSS; SPSS Inc., USA) version 22.0 was used to analyze the study data. The significance of the differences among the groups were analyzed using analysis of variance (ANOVA), Chi-square test and repeated-measures ANOVA. The categorical variables are presented as number of cases (N) and percentage (%) and the continuous variables as mean ± standard deviation (SD). Statistically significant effects were accepted for $P<0.05$.

## Results

The participants (n=96) were assigned into three groups (n=32/each group). The mean age and body mass index (BMI) are shown in Table 1, indicating there is no significant differences regarding mean age and BMI among the groups ($P> 0.05$). Figs. 1, 2 and 3 illustrate that after spinal anesthesia, SBP, DBP and ABP dropped in all three groups. It is noted that this drop was less in the high-dose group as compared to the control group. Fig. 4 shows that mean HR dropped in all three groups, indicating there is no significant difference in this regard among groups. Furthermore, after spinal anesthesia, SaO2 level decreased in all three groups, indicating there is no significant difference in this regard between both treatment and control groups (Fig. 5). The frequencies of shivering and pain in the control group were more than both treatment groups, but there is no statistically significant difference in this regard among the groups. The frequencies of nausea, bradycardia and hypotension were significantly higher in the control group than both treatment groups (Table 2). As shown in the Table 3, high-dose group received a minimum drug dose and shorter duration of first dose.

**Table 1:** Comparison of the mean age and BMI among the three groups

| Variables \ Group | Control n=32 | Low-dose group n=32 | High-dose group n=32 | P value |
|---|---|---|---|---|
| Age (year) | 29.8(6.8) | 27.4(6.1) | 29 (6.7) | 0.3 |
| BMI | 29.9(1.7) | 30(1.8) | 29.8(1.9) | 0.9 |

Data are presented as mean (SD), SD; Standard deviation, BMI; Body mass index.

**Table 2**: Comparison of the frequencies of shivering, nausea, bradycardia, hypotension and pain among the three groups

| Variables \ Group | | Control n=32 | Low-dose group n=32 | High-dose group n=32 | P-value |
|---|---|---|---|---|---|
| Shivering | Yes | 5(16.7) | 3(10) | 0 | 0.09 |
| | No | 25(83.3) | 27(90) | 30(100) | |
| Nausea | yes | 12(40) | 2(6.7) | 0 | <0.001 |
| | No | 18(60) | 28(93.3) | 30(100) | |
| Pain | Yes | 2(6.7) | 1(3.3) | 1(3.3) | 0.8 |
| | No | 28(93.3) | 29(96.7) | 29(96.7) | |
| Bradycardia | Yes | 6(20) | 1(3.3) | 0(0) | 0.01 |
| | No | 24(80) | 29(96.7) | 30(100) | |
| Hypotension | Yes | 15(50) | 3(10) | 0(0) | <0.001 |
| | No | 15(50) | 27(90) | 30(100) | |

Data are presented as N (%)

**Table 3:** Comparison of different types of drug used among the three groups

| Variables \ Group | | Control n=32 | Low-dose group n=32 | High-dose group n=32 | P value (Comparison between High-dose and Low-dose groups) | P value (Comparison between High-dose and Control groups) | P value (Comparison between Low-dose and Control groups) |
|---|---|---|---|---|---|---|---|
| Pethidine | Number of used drug dose | 2.9(1.7) | 2.2(1.3) | 1.5(1.2) | 0.18 | 0.001 | 0.26 |
| | Duration of first dose (min.) | 92(32.9) | 12.9(43.4) | 121.4(42.8) | 0.03 | 0.04 | 0.001 |
| Ephedrine | Number of used drug dose | 0.7(0.9) | 0.1(0.3) | 0 | <0.001 | <0.001 | <0.001 |
| | Duratio n of first dose (min.) | 3.9(1.4) | 5.3(1.1) | 0 | 0.1 | - | - |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Atropine | Number of used drug dose | 0.2(0.4) | 0.03(0.2) | 0 | 0.15 | 0.004 | 0.001 |
| | Duratio n of first dose (min.) | 4.9(2.6) | 4(0) | 0 | 0.8 | - | - |

Data are presented as mean (SD), SD; Standard deviation, min.; Minute

**Figure 1.** Comparison of mean SBP level at the different time intervals among the three groups.

SBP; Systolic blood pressure, CI; Confidence interval

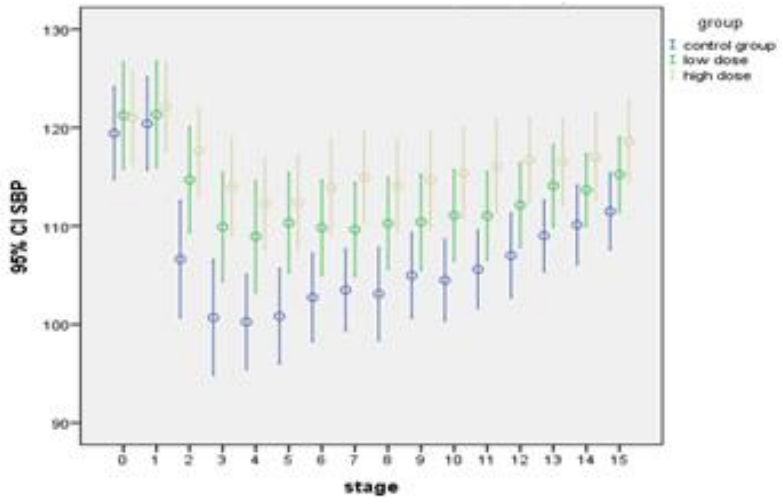



**Figure 2.** Comparison of mean DBP level at the different time intervals among the groups.

DBP; Diastolic blood pressure, CI; Confidence interval

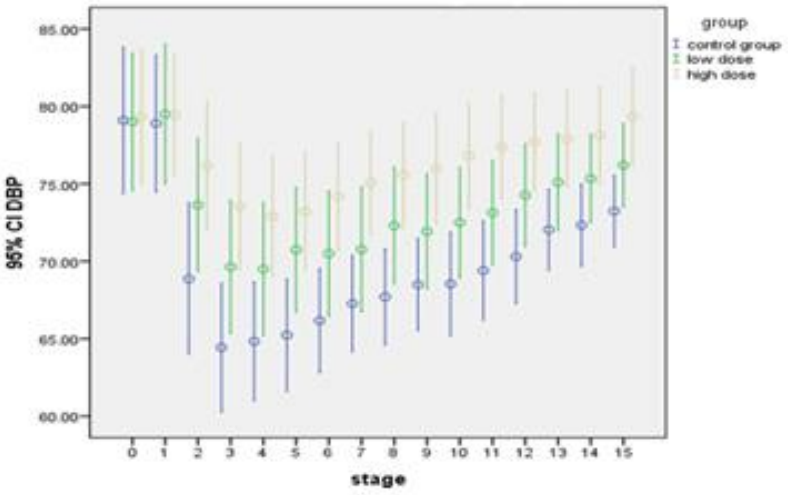


**Figure 3.** Comparison of mean ABP level at the different time intervals among the groups

ABP; Arterial blood pressure, CI; Confidence interval

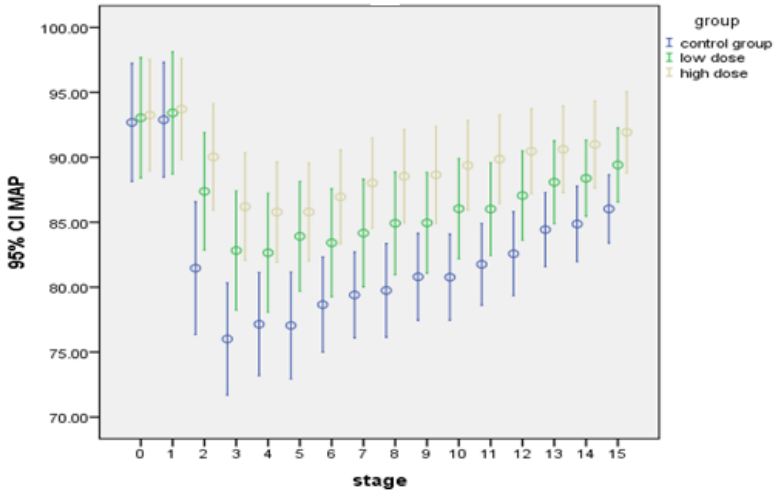



**Figure 4.** Comparison of mean HR at the different time intervals among the groups. HR; Heart rate, CI; Confidence interval

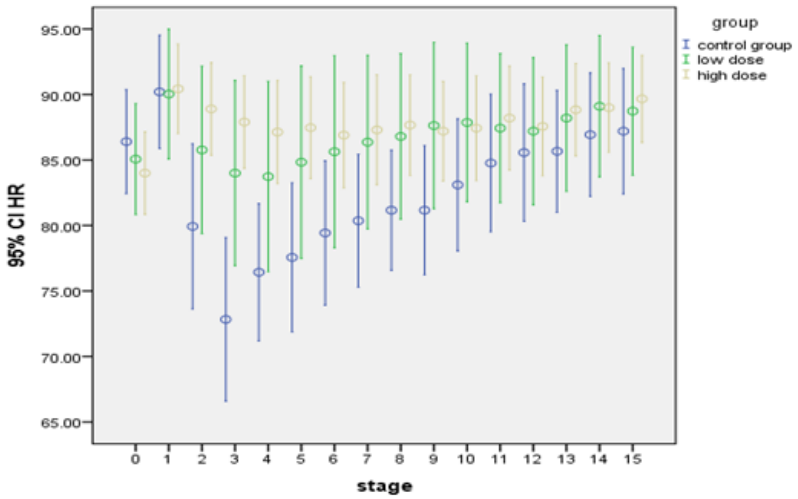
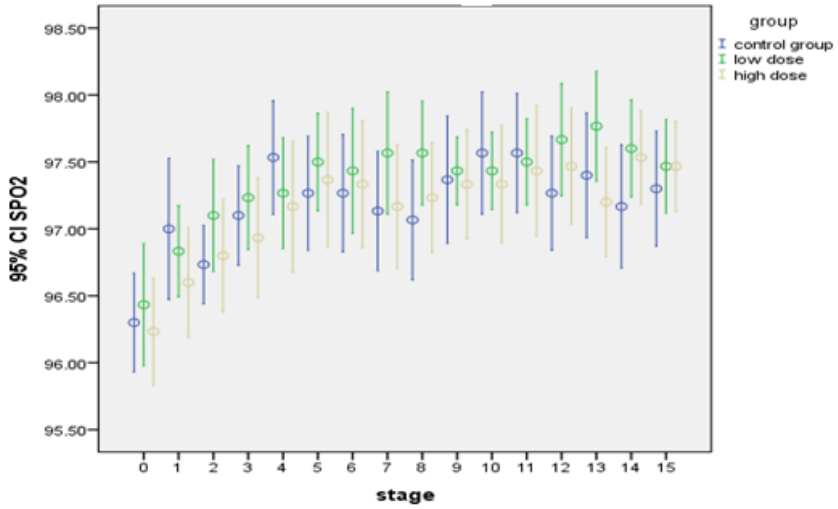



**Figure 5**. Comparison of mean SaO2 level at the different time intervals among the groups.

SaO2; Arterial oxygen saturation, CI; Confidence interval



## Discussion

In current study, the effects of different doses of IV ondansetron on hemodynamic changes and sensory and motor block were demonstrated in a group of healthy pregnant women undergoing elective C-section. Our findings showed that SBP, DBP, ABP and HR in high-dose group dropped significantly as compared to the low-dose and control groups. Furthermore, there was no significantly different in terms of the effects of ondansetron on motor and sensory block induced by spinal anesthesia among three groups. The frequencies of shivering, nausea, pain, bradycardia and hypotension in high-dose group were less than the control group. Manal et al. have evaluated the effects of ondansetron and granisetron on hemodynamic changes and motor and sensory block induced by spinal anesthesia in women undergoing elective C-section. Their findings have indicated that 4 mg ondansetron significantly controlled hypotension induced by anesthesia, whereas1 mg granisertron diluted with saline showed no significant difference (3). Similarly, in a study by Sahoo et al., they have demonstrated that 4 mg IV ondansetron significantly decreased the risk of hypotension induced by anesthesia(18) . In another study by Owczuk et al. conducted on 71 women undergoing spinal anesthesia, they have compared the effects of 8 mg IV ondansetron on HR, SBP, DBP and ABP between treatment (n=36) and control (n=36) groups. The mean values of SBP and ABP were less in the treatment group during a 20-minute measurement period, whereas there was no significant difference regarding the mean values of HR and DBP between treatment and control groups (19). In a clinical study by Malekianzadeh et al., they have randomly assigned102 healthy pregnant women undergoing elective C-section into the treatment group receiving 4 mg IV ondansetron and the control group receiving 2 ml IV saline. Their results have indicated that the mean values of SBP, DBP and ABP showed no statistically significant difference between two groups before and after intervention, suggesting ondansetron did not prevent hypotension induced by anesthesia (20). In a study by Peixoto et al., they have evaluated the effects of ondansetron and droperidol for the prevention of nausea and vomiting on women receiving IV intrathecal morphine for C-section, and their results have showed that the degree of nausea and vomiting decreased in the ondansetron group as compared to the droperidol and placebo groups (21). In a clinical study by Zahedi et al., 150 pregnant women undergoing elective C-section were assigned into the three groups (n=50/each group). The control group received IV normal saline, first treatment group received 4 mg IV ondansetron, and second treatment group received 10 mg IV metoclopramide, immediately after clamping the umbilical cord. Their findings have indicated that the degree of nausea and vomiting significantly decreased in both treatment groups as compared to the control group. Furthermore, hypertension in the group treated with ondansetron was less than the group treated with metoclopramide (24.5% vs. 31.3%) and control group (24.5% vs. 26%) (22). The incidence of nausea and vomiting after spinal anesthesia for C-section is directly related to hypotension (23). Furthermore, another study has showed hypotension increases the risk of nausea and vomiting by 50% (24). Therefore, the results of the mentioned-studies are similar to the current findings. We had to compare the different parameters in different intervals, so the results might be difficult to interpret.

## Conclusion

The current study demonstrated that an 8-mg single IV dose of ondansetron significantly reduced hemodynamic changes and motor and sensory block induced by spinal anesthesia in women undergoing elective C-section, while it showed less post-anesthesia complications, like nausea. Further studies in different settings are required to prove the effectiveness of this new treatment for practical use.

**Acknowledgments**

This article is a part of general doctoral theses of Malieheh Rakhshanifar (Registration No.: P/56) at Zabol University of Medical Sciences. The authors would like to thank Zabol University of Medical Sciences for their financial support. There is no conflict of interest in this article.

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