

## **The effect of intravenous administration of ondansetron compared to aminophylline on incidence and severity of post-dural puncture headache (PDPH) in cesarean section surgeries.**

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### **Abstract**

**Background:** Post-dural puncture headache is a common complication of spinal anesthesia mostly in parturient. The aim of this study is to evaluate and compare the effect of ondansetron and aminophylline on PDPH.

**Methods:** In this study we administered (1 mg/kg) of aminophylline in group A, (0.15 mg/kg) of ondansetron in group B and 5 cc of normal saline as placebo in control group. Blood pressure and heart rates were monitored since entrance of the patient to the operating room till the end of stay in recovery room and any significant changes were documented. Afterwards, PDPH and post-operative nausea and vomiting were followed during 24, 48 and 72 h periods since the performance of spinal anesthesia by calling each patient and the severity of headache was noted by numerical rating scale which had been already explained to the patients.

**Results:** Although there was no difference in the incidence of PDPH among three group cases ( $p=0.89$ ), the severity of the headache was significantly lower in the ondansetron group (NRS: 4.82) comparing to aminophylline (NRS: 7.71) and control (NRS: 6.65) groups ( $P<0.001$ ). Moreover, the data showed that significant hypotension occurring during operating time, results in twice as much PDPH afterwards ( $p=0.009$ ).

**Conclusion:** This study shows that although (0.15 mg/kg) ondansetron does not reduce the incidence of PDPH, it significantly reduces the severity of headache also shows that aminophylline has no effect on reduction of incidence nor severity of PDPH.

**Keywords:** Ondansetron, Aminophylline, Post-dural puncture headache, Cesarean.

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### **Introduction**

Local spinal anesthesia is one of the most common procedures in cesarean surgeries [1] with a common headache complication named as post-dural puncture headache (PDPH). PDPH is caused by the leakage of cerebrospinal fluid (CSF) from subarachnoid space, which causes decrease in the volume and pressure of CSF, tension of dura, traction placed on intracranial pain-sensitive structures to elicit pain, a compensatory increase in blood volume, vasodilatation of the epidural venous plexus and increased arterial pressure gradient and consequently a headache [2,3]. PDPH is occurred following the dural puncture [4] accompanied by photophobia, nausea, vomiting, neck stiffness, dizziness [5], tinnitus and hypoacusia [6].

The incidence of PDPH has been reported in previous studies ranging from 2.5% to 70% [3,5]. Common risk factors of PDPH include female gender, particularly females during pregnancy [7], younger age groups (20-40 y), prior history of PDPH or headache, size of needle as well as design and its orientation, the number of punctures [8,9] and dehydration [10].

Shaikh et al. suggested that PDPH is a neuraxial anesthesia complication which can disrupt daily life of patients if lasting more than few days. They also suggested conservative methods if other treatments are not effective [11]. Several drug treatments, such as the use of intravenous ondansetron (5HT3 antagonist) [12] and aminophylline (methylxanthine) [13-15] have been suggested to decrease and prevent PDPH.

Aminophylline, like theophylline and caffeine, can prevent PDPH by adenosine antagonization and vasoconstriction effect [16]. Sadeghi et al. observed PDPH prophylaxis through intravenous administration of a single dose of aminophylline in the patients undergoing spinal anesthesia for cesarean surgery [17].

Despite all of these studies and treatments, it seems that none of these therapies is still ideal [18] and there is still no agreement to control or prevent of PDPH. Therefore, this study is aimed to compare the effect of aminophylline and ondansetron to prevent PDPH incidence in pregnant women as a high risk group for PDPH, and also to find a proper prophylaxis drug using obtained results.

## Materials and Methods

First, the permissions of Ethics in Biological Research (code: IR.SUMS.MED.REC.1395.41) from Shiraz University of Medical Sciences (Faculty of Medicine) as well as from the Iranian Registry of Clinical Trials (code: IRCT2016110519470N50) were obtained. This study was conducted as a double-blind randomized placebo-controlled clinical trial at the Hafez Educational Center of Shiraz University of Medical Sciences in 2016.

The inclusion criteria were: the pregnant women who were candidate for elective cesarean surgery under spinal anesthesia; whose anesthesia risk were classified as American Society of Anesthesiologists (ASA) Classes I and II (completely healthy or with a controlled disease). Exclusion criteria included: pregnant women with prior history of any cardiovascular disease (including rhythm or rate disorder, etc.); migraine and pressure headaches; chronic or gestational hypertension; pre-eclampsia; seizure; liver or kidney failure; psychiatric problems; history of allergy to ondansetron, aminophylline or theophylline; history of drug addiction; more than one attempt of penetration for administering spinal anesthesia; failure of the spinal anesthesia and leading to general anesthesia.

Before the operation, the aim of the study was explained and a written informed consent was obtained from the patients. An anesthetist, who did not participate in data collection, randomly assigned 300 eligible women into 3 groups *via* randomization using [www.randomized.org](http://www.randomized.org) website. Patients were randomly assigned to group A (receiving 1 mg/kg intravenous aminophylline), or B (receiving 0.15 mg/kg IV ondansetron) or C (control group receiving 5 cc normal saline as placebo). Aminophylline, ondansetron and normal saline syringes with a total volume of 5 cc (for each group) were prepared and labeled by an anesthetist who did not mediate in the study. As pregnancy category of aminophylline is "C", so we should better not inject the aminophylline before delivery of baby in group A of our study. Ondansetron in contrast, should be injected before spinal anesthesia regarding previous studies. So to ensure double blinding of our clinical trial we designed two injections for each group: 1) the studying drug in a 5 cc syringe and in 5 cc volume. 2) A 5 cc normal saline injection in a 5 cc syringe. One of which is injected before administration of

spinal anesthesia and the other one after delivery of the baby, usage of oxytocin which is routinely used for contracting the uterus, and after assurance of the stability of the patient's vitals.

For group A, the first injection is 5 cc N/S in syringe A' before doing spinal anesthesia and the second injection, after child birth, is 1 mg/kg aminophylline in syringe A.

For group B, the injection before spinal anesthesia in syringe B is 0.15 mg/kg ondansetron and the injection after child birth in syringe B' is 5 cc N/S.

And for group C, both injections consist of 5 cc N/S in syringes C and C'.

The patients and the researcher who collected the data did not know the contents of the syringes. Usual monitoring including electrocardiogram, pulse oximetry and blood pressure cuff were connected to the patient since they entered the operating room. Then the patients were hydrated with 500 cc of crystalloid fluid using intravenous line that was established in their non-dominant hand. For about 5 min before spinal anesthesia, the first injection was performed on the groups under study. After this injection, the patients with stable condition were placed in a sitting position and then spinal anesthesia was performed in intervertebral space L3-L4 with a 25 G spinal needle (Quincke). Anesthesia was performed using 10 mg of bupivacaine (0.5%) (Mylen Co. Ltd) plus 10 mcg of fentanyl (Abu-Reyhan Co. Ltd) which was injected when the proper site for leakage of CSF fluid from the needle was confirmed. Afterwards, the patients were placed in a supine position; the operating table was tilted to the left (15°) to prevent the supine hypotension. Acceptable level of anesthesia was T4. Cases with higher levels of anesthesia or cases eventually need general anesthesia would exclude the study. For the cases developing hypotension (>20% of basal blood pressure) after spinal anesthesia, 5 mg ephedrine was used. Also 10 mg of metoclopramide would be used in case of anti-emetic need.

As mentioned, after the baby is born and the umbilical cord is clamped, oxytocin drug is routinely prescribed for patients undergoing cesarean. So after checking the blood pressure and the heart rate and if the patient was had stable hemodynamics, our second injection was administered as already explained. BP and HR were monitored every 15 min until the surgery ended as well as in the recovery room. Any changes (more than 20% of the basal level for each patient) were recorded in this study. Before the patients left the recovery room, the numerical rating scale (NRS) (from 0: no headache to 10: The most severe headache tolerable for patient) was described and they were told that they would be called within 24, 48, and 72 h to be asked about the presence or absence of headache and N/V as well as the severity of the headache if present. The researcher calling the patients did not have any information about the study groups.

The presence of PDPH as a throbbing headache which often felt in the frontal or occipital lobe, aggravates with standing and relieves with laying, accompanied with photophobia,

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dizziness, tinnitus, hearing loss, nausea and vomiting were recorded in data collection forms. The severity of headache was recorded *via* NRS scale. Rest with lying position, consumption of analgesic drugs (acetaminophen and NSAIDs), coffee and fluids containing caffeine were recommended for patients to improve their headaches. In this study, the effect of aminophylline and ondansetron on the incidence and severity of PDPH in cesarean surgery was evaluated as an initial outcome and also their effects on the incidence of nausea and vomiting as well as on blood pressure and heart rate in the patients were studied as secondary outcome.

The collected data was analysed using SPSS 24 software.

The sample size of this study (N=91 in each group) was calculated based on the frequency and incidence of PDPH according to Fatahi et al. [12] and Naghibi et al. [19] with 5% type I error and 8% power. We designated 100 patients per group and a total of 300 patients were examined in this study. After data analysis, Kolmogorov Smirnov test was used to evaluate the test normality. To compare variables between groups, Q-square, one-way ANOVA, Logistic Regression, Fisher and Post Hoc tests were used as needed.

### Results

In this study, the effects of aminophylline and ondansetron were evaluated in A-C groups of 100 patients aged between 17 to 45 y ( $30 \pm 4.92$  y, on average) and compared with each other and with the control group. There was no significant difference between the mean age of patients in different groups ( $p=0.78$ ). Also, the weights of patients in three groups were ranged from 59 to 125 kg with the mean of  $80 \pm 11.24$  kg. The results showed that there was no significant difference between the weight in groups A-C ( $p=0.07$ ).

The most common reported disease among the patients with ASA class II was hypothyroidism with the frequency of 13%, followed by gestational diabetes with a frequency of 3% among the total population. 83% of all patients did not use any medication and 12% of them took levothyroxine. However, in this study, there was no significant relation between the history of disease ( $p=0.2$ ) or medication use ( $p=0.12$ ) in different groups.

The changes in blood pressure, heart rate, and the need for drugs to control blood pressure in the operating room have been described in Table 1.

The changes of blood pressure in different groups were significantly different ( $P<0.001$ ) and the fewest occurrence of hypotension was observed in group B (receiving ondansetron). The patients in group A (receiving aminophylline) showed the highest degree of hypotension. The decline in heart rate was significantly different among the groups ( $p<0.02$ ). The most commonly used drug in the surgery room due to hypotension was ephedrine. The administration of ephedrine was significantly different between the groups ( $p<0.001$ ) and it was maximum in group A (Aminophylline group) and was minimum in group B (ondansetron group). During the

recovery, there was no significant change in blood pressure and heart rate.

The results showed that the incidence of PDPH after 24, 48 and 72 h in three groups of A (Aminophylline), B (ondansetron) and control were not significantly different ( $p=0.59$ ,  $p=0.84$  and  $p=0.92$ , respectively) (Table 2). In fact, the drugs used in this study did not cause to decrease the incidence of headache. Total incidence of headache was not significantly different between the groups ( $P=0.89$ ) (Table 2).

The means of PDPH severity based on NRS scale after 24, 48, and 72 h in each group has been presented in Figure 1. The results showed that PDPH severity was not significantly different in different times ( $p=0.26$ ) in each group. Therefore, by omitting the effect of time, the means of total PDPH severity (Figure 2) were different between the three groups ( $p<0.001$ ), which showed that the study groups had a significant effect on PDPH severity (Table 3).

PDPH severity among aminophylline (A) and ondansetron (B) groups was significantly different ( $p<0.001$ ) as well as among ondansetron (B) and control groups ( $p=0.01$ ) (Table 4). PDPH severity was significantly lower in group B (receiving ondansetron) than both other groups (Figure 2).

The relation between blood pressure changes in the operating room and the incidence of PDPH was evaluated by a chi-square test and it showed that 72.3% of total patients who developed PDPH, have already had hypotension in the operating room. Also, 33.1% of all patients who had hypotension in the operating room showed PDPH. 20% of the total population ( $n=300$ ) had both PDPH and hypotension in the operating room ( $p=0.009$ ). The results showed that the risk of PDPH in patients who experienced hypotension in the operating room (a hypotension greater than 20% relative to basal pressure) was about 2.07 times higher than of those who did not have changes in blood pressure. There was no significant correlation between decline of heart rate in the operating room and the incidence of PDPH ( $p=0.59$ ). The incidence of PONV was also studied in the three groups and at all three times which occurred in less than 1% of the total population, and therefore was not statistically significant.

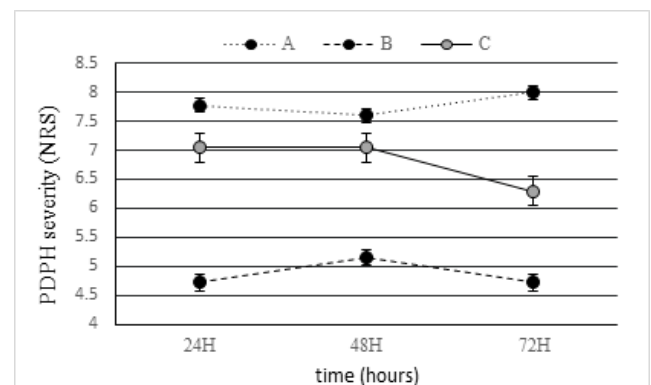
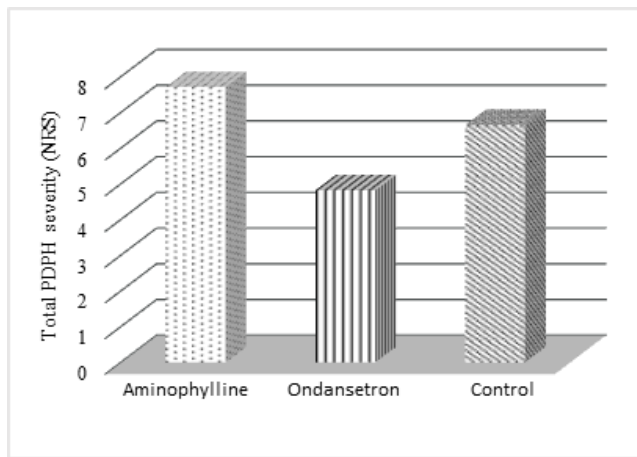


Figure 1. PDPH severity in each group (A: Aminophylline, B: ondansetron, C: Control) over time based on NRS scale.



**Figure 2.** Total PDPH severity in study groups based on NRS scale.

**Table 1.** The percentage of patients who had decline in blood pressure (hypotension) and heart rate as well as requiring administration of ephedrine in the operating room.

Group	Decline in blood pressure (%)	Decline in heart rate (%)	Ephedrine administration (%)
Aminophylline (n=100)	78	4	67
Ondansetron (n=100)	41	9	37
Control (n=100)	62	1	58
Total (n=300)	60	5	54
p-value	p<0.001	p<0.02	p<0.001

**Table 2.** The incidence of PDPH during 24, 48 and 72 h and total incidence of PDPH in three groups.

Group	PDPH (24 h) (%)	PDPH (48 h) (%)	PDPH (72 h) (%)	Total PDPH (%)
Aminophylline (n=100)	24	23	22	26
Ondansetron (n=100)	22	20	22	29
Control (n=100)	17	23	24	28
Total (n=300)	20.3	22	22.7	-
p-value	0.59	0.84	0.92	0.89

**Table 3.** Total PDPH severity in study groups based on NRS scale.

Group	Total PDPH severity (NRS)	SD	p-value
Aminophylline (n=100)	7.71	2.37	p<0.001
Ondansetron (n=100)	4.82	2.77	
Control (n=100)	6.65	2.79	
Total (n=300)			

**Table 4.** Paired comparison between groups.

Groups	Difference	SE	p-value
Aminophylline-ondansetron	2.89	0.71	p<0.001
Ondansetron-control	-1.83	0.7	0.01
Control-aminophylline	1.06	0.72	0.14

## Discussion

The results showed that administration of intravenous ondansetron (0.15 mg/kg) prior to spinal anesthesia significantly decreased PDPH severity in pregnant women undergoing elective cesarean than those receiving aminophylline. Fattahi et al. achieved similar results on the effect of ondansetron (0.15 mg/kg) with a significant decrease in PDPH of patients undergoing cesarean section surgery. Similarly, following the PDPH severity over a 3 d period showed that patients receiving ondansetron had a milder headache. In our study, the effect of ondansetron was compared with normal saline (control) and aminophylline, and it showed that it significantly decreased headache severity comparing to aminophylline and normal saline.

In this study, ondansetron, aminophylline and normal saline did not significantly affect the incidence of PDPH in any of the three groups (P=0.89) but Fattahi et al. reported a significance decrease (P=0.001) in PDPH incidence in the group receiving ondansetron compared to control group (4.71% vs. 20.75%). The incidence of PDPH at 24, 48 and 72 h after spinal anesthesia in three groups were similar. Therefore, we found that neither ondansetron nor aminophylline had any effect on the incidence of PDPH. There are no further studies on the effect of ondansetron on PDPH. Therefore, further studies are required to investigate the effect of ondansetron on the incidence or severity of PDPH.

In a study conducted by Sadeghi et al. a single dose of intravenous aminophylline 1 mg/kg significantly decreased the incidence of PDPH in the patients undergoing elective cesarean compared to control group (5% vs. 23.3%) (P<0.004). Our study was different from Sadeghi et al. Our sample size was greater (300 vs. 60 patients), our needle was narrower (size 25 vs. 23) and the patients were studied up to 72 h instead of 48 h. Naghibi et al. evaluated the dual effect of aminophylline and dexamethasone on PDPH and found similar results to Sadeghi et al. Our results indicated that intravenous aminophylline had no effect on the incidence and severity of PDPH. Another study by Ismail Sirit et al. showed similar results. They found that aminophylline had no effect on PDPH incidence in cesarean [20] which is similar to the result we achieved.

In our study, the incidence of PONV in each group was very low which was not measurable or comparable statistically. However, in the Fattahi et al.'s study [12], PONV that followed during three days in the group receiving ondansetron was significantly lower than control group (P<0.05).

In our study, the changes in blood pressure and heart rate were significantly different between the three groups in operating room (P<0.001). The lowest and highest hypotension was

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observed in group B (receiving ondansetron) and A (receiving aminophylline), respectively. Also, the lowest need for ephedrine (to maintain blood pressure) was in group B (received ondansetron) and the highest was in group A (received aminophylline) ( $P < 0.001$ ). The highest change in heart rate (decrease more than 20%) was observed in group B (receiving ondansetron) ( $P = 0.02$ ). Fattahi et al. found similar results on the effect of ondansetron to increase mean arterial pressure (MAP) compared to control which indicated lower hypotension in the ondansetron receiving group. They did not find any relation between changes in heart rate and drug groups. Also, in another study by Owczuk et al. the ondansetron receiving group had higher systolic blood pressure and MAP than control group during spinal anesthesia. They did not find any difference between HR of the groups [21].

Sahoo et al. found that the administration of ondansetron prior to spinal anesthesia led to hypotension and decreased the need for vasopressor in the pregnant women undergoing cesarean surgery. They concluded that ondansetron, as a 5HT<sub>3</sub> antagonist; increase the venous return to the heart by inhibition of vasodilation and decreases reduction of MAP and systolic blood pressure [22]. In a study [23], it was observed that hypotension and heart rate decline following spinal anesthesia decreased due to use of ondansetron. Also, 2, 4 and 8 mg of intravenous ondansetron have not affected hemodynamic parameters and hypotension in patients who underwent elective cesarean section under spinal anesthesia [24].

Ondansetron is generally used for prophylactic management of postoperative nausea and vomiting. It is a selective 5-HT<sub>3</sub> receptor antagonist that directly prevents vasodilation in brain *via* blocking the 5HT<sub>3</sub> receptors. Also, ondansetron indirectly inhibits compensatory vasodilation of arteries in brain through maintaining the mean arterial pressure due to auto-regulation. It also inhibits compensatory vasodilation in the intracranial arteries resulting from CSF loss and reduces PDPH [12]. Moreover, the data showed that significant hypotension occurred during operating time results in twice as much PDPH ( $p = 0.009$ ).

### **Conclusion**

This study showed that although 0.15 mg/kg ondansetron does not affect the incidence of PDPH, it decreases the severity of the headache. In addition, it helps to maintain the blood pressure of the patients in the operating room, decreases hypotension occurrence and the need of vasoactive drugs such as ephedrine. This study also suggests that aminophylline has no effect on the incidence or severity of PDPH. It seems that prevention of hypotension may also be effective to reduce the incidence of PDPH. Moreover, the data showed that significant hypotension occurrence during operation time, results in twice as much of PDPH ( $p = 0.009$ ).

### **References**

1. Canningham FG, Leveno KJ, Bloom SL, Spong CH, Dashe JS, Hoffman BL. Williams Obstetr Gynecol (23th Edn.). New York: McGraw-Hill 2010; 438.
2. Spierings EL. Mechanism of migraine and action of antimigraine medications. *Med Clin North Am* 2001; 85: 943-958, vi-vii.
3. Ahmed SV, Jayawarna C, Jude E. Post lumbar puncture headache: diagnosis and management. *Postgrad Med* 2006; 82: 713-716.
4. Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. *Br J Anaesth* 2003; 91: 718-729.
5. Kuczkowski KM. Post-dural puncture headache in the obstetric patient: an old problem new solutions. *Minerva Anesthesiol* 2004; 70: 823-830.
6. Halpern S, Douglas M. Evidence-based obstetric anesthesia. *BMJ* 2005; 330: 256.
7. Silberstein SD. Headache and female hormones: what you need to know. *Curr Opin Neurol* 2001; 14: 323-333.
8. Brown DL. Spinal, epidural and caudal anesthesia. *Millers Anesthesia* (6th Edn.). Philadelphia: Churchill Livingstone 2005; 1653-1679.
9. Reina MA, Lopez A, De Andres J, Martin S, Mora M. An in vitro study of dural lesions produced by 25-gauge Quincke and Whitacre needles evaluated by scanning electron microscopy. *Reg Anesth Pain Med* 2000; 25: 393-402.
10. Choi PT, Galinski SE, Takeuchi L, Lucas S, Tamayo C, Jadad AR. PDPH is a common complication of neuraxial blockade in parturients: a meta-analysis of obstetrical studies. *Can J Anaesth* 2003; 50: 460-469.
11. Shaikh S, Ramesh N. Perioperative management of post dural puncture headache. *Int J Biomed Adv Res* 2015; 6: 78-83.
12. Fattahi Z, Hadavi SM, Sahmeddini MA. Effect of ondansetron on post-dural puncture headache in parturients undergoing cesarean section: a double-blind randomized placebo-controlled study. *J Anesth* 2015; 29: 702-707.
13. Zajac K, Zajac M, Jach R. Is there any point in pharmacological prophylaxis of PDPH (post-dural puncture headache) after spinal anaesthesia for caesaren section? *Przegl Lek* 2012; 69: 19-24.
14. Yousefshahi F, Dahmardeh AR, Khajavi M, Najafi A, Khashayar P, Barkhordari K. Effect of dexamethasone on the frequency of postdural puncture headache after spinal anesthesia for cesarean section: a double-blind randomized clinical trial. *Acta Neurol Belg* 2012; 112: 345-350.
15. Chuanjie W, Lian Y, Guan D, Wang L, Miao Y, Xie N. A multicenter clinical study on treating post dural puncture headache with an intravenous injection of aminophylline. *Pain Phys* 2016; 19: 761-765.

16. Pranjali S, Sajan T. Post-lumbar puncture headache. *Hosp Physician* 2007; 43: 51-54.
17. Sadeghi SE, Abdollahifard G, Nasabi N. Effectiveness of single dose intravenous aminophylline administration on prevention of post dural puncture headache in patients who received spinal anesthesia for elective cesarean section. *World J Med Sci* 2012; 7: 13-16.
18. Motaghi K, Farhad Safari F, Khodabendelou L, Salimi A. Evaluation the efficacy of IV dexamethasone on post puncture headache incidence after cesarian section. *Anesth Pain* 2011; 1: 49.
19. Naghibi K, Hamidi M. Prophylactic administration of aminophylline plus dexamethasone reduces post-dural puncture headache better than using either drug alone in patients undergoing lower extremity surgery. *Adv Biomed Res* 2014; 3: 5.
20. Sirit I, Ozturk I, Yazicioglu D. Aminophylline does not prevent postdural puncture headache in caesarean section. *Int J Anesthetic Anesthesiol* 2015; 2: 31.
21. Owczuk R, Wenski W, Polak-Krzeminska A, Twardowski P, Arszulowicz R, Dylczyk-Sommer A. Ondansetron given intravenously attenuates arterial blood pressure drop due to spinal anesthesia: a double-blind, placebo-controlled study. *Reg Anesth Pain Med* 2008; 33: 332-339.
22. 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: 24-28.
23. Marashi SM, Soltani-Omid S, Soltani Mohammadi S, Aghajani Y, Movafegh A. Comparing two different doses of intravenous ondansetron with placebo on attenuation of spinal-induced hypotension and shivering. *Anesth Pain Med* 2014; 4: 12055.
24. Ortiz-Gomez JR, Palacio-Abizandab FJ, Morillas-Ramirez F, Fornet-Ruiz I, Lorenzo-Jimenez A, Bermejo-Albares M. 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: 138-143.

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