

# Comparison of the Effect of Ondansetron and Dexamethasone on Postoperative Shivering After Cesarean Section in Patients Undergoing Spinal Anesthesia

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## ABSTRACT

**Background:** Shivering is one of the most common problems after spinal anesthesia, which can cause many complications. Various methods and drugs have been used to prevent and treat postoperative shivering. In the present study, the pretreatment effect of ondansetron and dexamethasone in reducing the incidence of shivering after elective caesarean section by the spinal method has been investigated.

**Methods:** In this study, 78 patients undergoing elective cesarean surgery who were eligible to enter the study were evaluated and randomly divided into two groups: 8 mg of ondansetron and 4 mg of dexamethasone 15 minutes before the end of surgery. Then, the incidence of shivering was measured at specific time intervals after surgery. Statistical analysis was done using SPSS software.

**Results:** The two groups were similar in terms of age, height, weight, and BMI (p-value > 0.05). The incidence of shivering at the time of entering the recovery, 10, 20, and 30 minutes in the ondansetron group was 23.1%, 20.5%, 12.8% and 0% and in the dexamethasone group was 20.5%, 15.4%, 5.2% and 0%, respectively. Statistical analysis showed that these differences are not significant at the significance level of 0.05. These two drugs have the same effectiveness in controlling shivering after cesarean section under spinal anesthesia (p-value > 0.05).

**Conclusion:** Dexamethasone and ondansetron will be able to control shivering after caesarean section with spinal anesthesia.

**Keywords:** Caesarean section, dexamethasone, ondansetron, spinal anesthesia.

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## 1. INTRODUCTION

One of the most important side effects of surgery and anesthesia is postoperative shivering. Its association with other side effects such as nausea and vomiting causes the patient discomfort and dissatisfaction with the treatment results and has risks such as hypoxia, ischemia, infarction, and lengthening the healing time of the surgical wound. Therefore, reducing its incidence can lead to very good results for the patient [1], [2]. Although this complication is not related to the inflammatory markers of the patients, sometimes drugs that affect the inflammatory function of the body cause changes in its incidence [3]. The incidence of postoperative shivering depends a lot on the time of

anesthetic drug administration and its type and time [4]. In general, about 11.6% of patients undergoing surgery experience post-operative shivering [5]. So far, several methods including various drugs such as corticosteroids, narcotics and some painkillers have been investigated to reduce shivering after surgery [6].

Postoperative shivering is the most common complication after surgery, which occurs between 6.3% and 65% of patients who show involuntary movements of one or a group of muscles. Shivering after surgery causes complications such as increased oxygen consumption, CO<sub>2</sub> production, heart rhythm changes, and blood pressure which leads to the exacerbation of ischemic heart diseases,

increased intracranial pressure, intraocular pressure, pain during surgery and patient discomfort [7]. The prevalence of shivering in the recovery room after general anesthesia is 60% and after epidural anesthesia is reported at 30% [8]. Postoperative shivering usually lasts 2 to 60 minutes, and its pathogenesis is not exactly clear [9].

Shivering following spinal anesthesia is due to impaired body temperature regulation and increases tissue oxygen consumption and cardio-pulmonary activity. In addition to the discomfort of the patient, the shivering following spinal anesthesia increases the recovery time as well [10]. Various causes for post-operative shivering, including spinal reflexes, reduction of sympathetic activity, suppression of adrenal gland, respiratory alkalosis or response to hypothermia have been stated [11]. Shivering is a factor that increases postoperative complications, which increases the risk of cardiac ischemia and increases intraocular pressure and brain pressure through increased oxygen consumption, especially of the heart myocardium, and leads to postoperative problems and increased costs [12]. Postoperative shivering increases oxygen consumption by 500%. It also increases the production of carbon dioxide and the rate of metabolism and increases sympathetic tone and cardiac output. Therefore, it increases the incidence of ischemia and myocardial infarction [13]. The use of warm liquids is also effective in maintaining body temperature during and after surgery [14]. So far, several drugs have been introduced to prevent and treat shivering after surgery, including morphine and meperidine, which have anti-shivering properties, and it has been speculated that this effect will be applied mostly through the  $\mu$  receptor [13]. Fentanyl is also used along with bupivacaine  $\mu$  receptor in the spinal cord, which prevents shivering after caesarean section [15]. It has been shown that ketamine with a dose of 5 mg/kg in major cardiac operations, reduces post-operative shivering [16]. Tramadol with a dose of 2–3 mg/kg and pethidine with a dose of 0.4 mg/kg can prevent shivering [17].

Ondansetron is a serotonin antagonist that has anti-shivering properties and the mechanism of its anti-shivering effect is by inhibiting the reuptake of serotonin in the anterior hypothalamic area. Currently, ondansetron is the choice drug within prophylaxis for nausea and vomiting after chemotherapy [18], [19]. In general, more interventional studies are needed to choose the best treatment. Considering the importance of this issue, in this study, we investigate the effect of ondansetron and dexamethasone on shivering after caesarean section by spinal method.

## 2. METHODS

This study was designed as a double-blind randomized clinical trial. After obtaining the permission and decision of the Research Committee of Tehran University of Medical Sciences, 78 patients with American Society of Anesthesiologists (ASA) grade 1 and 2 candidates for elective caesarean section with the spinal method, whose surgery lasted 60–180 minutes, were entered. The general exclusion criteria were as follows: BMI 27 or below 20, people above 40 or below 20 years, patients who have received

vasodilator drugs (such as blood pressure drugs) during the operation, taking alfentanil or intraoperative pethidine, unconventional bleeding, and intraoperative vasoconstrictor or vasodilator use. The samples were collected in the years 2019 to 2020 at Amirul Mominin Hospital in Tehran. All patients were randomly divided into two groups: the first group received 4 mg of ondansetron and the second group received 8 mg of dexamethasone 15 minutes before surgery. The incidence of shivering upon entering the recovery room, 10, 20, and 30 minutes was assessed. The drug used for anesthesia in this study was Marcaine 0.5% in the amount of 2.5 to 3 cc, 15 minutes before caesarean surgery. Spinal block was performed at t4 or t5 level. Shivering was checked at the time intervals after the end of the surgery.

### 2.1. Statistical Analysis

Based on the following formula and considering alpha (error of the first study) as 0.05, beta (error of the second study) as 0.2, P1 (Efficacy of Ondansetron) as 0.3 and P2 (Effectiveness of Dexamethasone) as 0.6, 78 people were included in the study in two groups of 39 people, ondansetron, and dexamethasone. Data analysis is done using SPSS version 24 statistical software and absolute and relative frequency will be recorded for qualitative variables. An appropriate statistical test is selected based on the type of variables and their distribution. If the data distribution does not follow the normal distribution, non-parametric equations are used.

$$N = \frac{[P1(1 - P1)] + [P2(1 - P2)] \times (Z1 - \alpha/2 + Z1 - \beta)^2}{(P1 - P2)^2}$$

$$N = \frac{(0.3 \times 0.7) + (0.6 \times 0.4) \times 7.8}{(0.3)^2}$$

$$N = 39$$

## 3. RESULTS

The demographic characteristics are shown in [Table I](#). The results obtained from the tests of Kolmogorov Smirnov and Shapiro-Wilk showed that the distribution of data related to the variables of age, height and weight of the patients does not follow the normal distribution. However, the BMI of people is subject to normal distribution.

The average age of patients in the ondansetron and dexamethasone groups was reported as  $27.59 \pm 4.68$  and  $26.4 \pm 4.43$  years, respectively. Mann-Whitney test showed that these differences are not significant and the two

TABLE I: DESCRIPTIVE INDEXES (MEAN  $\pm$  STANDARD DEVIATION) OF AGE, WEIGHT AND HEIGHT OF PEOPLE ACCORDING TO STUDY GROUPS

Group	Age	Height	Weight	BMI
Ondansetron	27.58 $\pm$ 4.68	162.05 $\pm$ 4.10	66.36 $\pm$ 7.29	26.95 $\pm$ 2.81
Dexamethasone	26.41 $\pm$ 4.43	163.20 $\pm$ 5.75	64.09 $\pm$ 6.87	25.84 $\pm$ 2.58
p-value	0.185	0.892	0.534	0.073

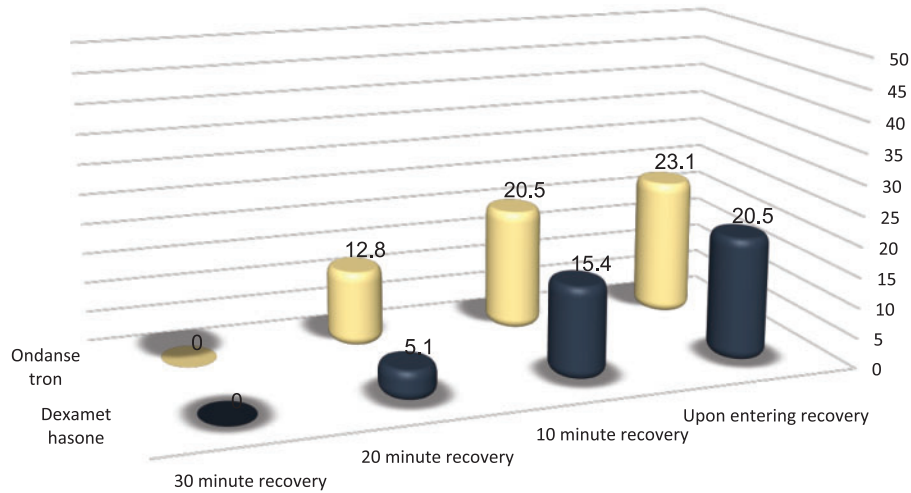


Fig. 1. Comparison of the incidence of shivering in the studied groups.

groups are similar in terms of age (p-value = 0.185). The average weight of the patients in the ondansetron and dexamethasone groups was  $66.37 \pm 7.29$  and  $64.1 \pm 6.88$  kg, respectively. The Mann-Whitney test showed that the weight distribution of mothers in the investigated groups was not different (p-value = 0.534). The average height of the patients in the ondansetron group was  $162.05 \pm 4.10$  and in the dexamethasone group was  $163.20 \pm 5.75$ , and the difference was evaluated as non-significant (P-value = 0.892). The average BMI of the subjects in the ondansetron and dexamethasone groups was  $26.95 \pm 2.81$  and  $25.84 \pm 2.58$  kg/m<sup>2</sup>, respectively. Independent t-test showed that these differences were not significant and the two groups were similar in terms of BMI (p-value = 0.073).

The incidence of shivering at the beginning of recovery, 10, 20 and 30 minutes in the ondansetron group was estimated as 23.1%, 20.5%, 12.8% and 0%, respectively. In the dexamethasone group, it was estimated to be 20.5%, 15.4%, 5.2% and 0%, respectively (Table II, Fig. 1). The chi-square test showed that these differences are not significant at the significance level of 0.05, and these two drugs have the same effectiveness in controlling shivering after cesarean section under spinal anesthesia (p-value > 0.05). The effects of ondansetron and dexamethasone on shivering after cesarean spinal surgery was not different based on age and BMI of the patients in any of the investigated time intervals (p-value > 0.05).

#### 4. DISCUSSION

Prevention and treatment of shivering after surgery is an important part of patient care after surgery, because

TABLE II: INCIDENCE OF SHIVERING IN THE DEXAMETHASONE GROUP COMPARED TO THE ONDANSETRON GROUP

Group	Upon entering recovery	10-minute recovery	20-minute recovery	30-minute recovery
Dexamethasone	8	6	2	0
Ondansetron	9	8	5	0
P-value	0.5	0.38	0.21	1.00

severe damage may occur due to sympathetic stimulation, increased oxygen consumption or carbon dioxide production in the patient. To choose the appropriate treatment to control this complication, it is necessary to conduct comparative interventional studies. Based on this study, the effect of ondansetron and dexamethasone on shivering after cesarean section was compared. The incidence of shivering at the beginning of recovery, 10, 20 and 30 minutes of recovery in the ondansetron group was estimated to be 23.1%, 20.5%, 12.8% and 0%, respectively. It was estimated 20.5%, 15.4%, 5.2% and 0% for the dexamethasone group, respectively. If we consider the highest reported percentage for each group, we can state that the average incidence of shivering in the ondansetron group with a 95% confidence interval is between 10% and 36% and in the dexamethasone group between 7.9% and 26.9%. The results obtained from our research also showed that the effectiveness of these two drugs in controlling shivering is the same, and regardless of the age and BMI of the patients, both drugs are able to control the shivering of patients after cesarean section with spinal anesthesia. This result is in line with the findings of Hirmanpour et al. [20]. They compared dexamethasone, ondansetron and ketamine in the prevention of shivering after cesarean section with general anesthesia. The incidence of shivering at the beginning, 10 and 20 minutes of recovery in the dexamethasone group was estimated to be 30%, 10% and 7.5%, respectively. This was estimated in the ondansetron group at 42.5%, 17.5% and 7.5%, respectively. The results showed that dexamethasone and ondansetron have the same and acceptable effectiveness in controlling shivering after a caesarean section [20]. In our study, the effectiveness of ondansetron in controlling shivering was reported in the range of 10% to 36.4%. This result is in contrast to the findings of Teymourian et al. who assessed 80 patients, aged 20 to 60, undergoing elective craniotomy surgery, and reported the occurrence of tremors in 7.5% of ondansetron patients [21].

In our study, the incidence of shivering in the dexamethasone group was estimated between 7.94% and 26.9%. This is in line with Asl et al. who conducted as a clinical trial on 120 patients undergoing surgery under general

anesthesia to compare the effects of dexamethasone and pethidine in preventing shivering after surgery. Eligible patients were randomly divided into three groups: placebo, dexamethasone and Pethidine were divided. The incidence of shivering was 47.5% in the placebo group, 10% in the dexamethasone group, and 37.5% in the pethidine group. The results indicated significant differences in the incidence of shivering between the groups. The dexamethasone group had the lowest shivering rate and the control group had the highest shivering rate [7].

In a study by Browning *et al.*, they conducted a clinical trial, by examining 118 patients undergoing surgery and dividing them into two groups; the ondansetron and the placebo, which did not show a statistically significant difference [22]. In a study conducted by Abdulahi et al. 90 patients undergoing surgery were examined in three groups ondansetron, meperidine and placebo. The results showed that the rate of post-operative shivering in the meperidine group was 46.5%, ondansetron 31.2% and placebo 60.8%, which had a statistically significant difference [23]. In another study conducted by Asl *et al.*, 90 patients underwent cord surgery and were examined in three groups: ondansetron, meperidine, and placebo. The results showed that the incidence of shivering after surgery in the meperidine group, was 20%, ondansetron 13.3%, and placebo 50%, which had a statistically significant difference [24]. In a study by Shakya *et al.*, 120 patients were examined in three groups: ondansetron, ketamine and placebo. The results showed that the amount of post-operative shivering in the ketamine group was 2.5%, ondansetron 10% and placebo 42.5%, which had a statistically significant difference [25]. In another similar study, Nemat Shahi *et al.* showed that there is no significant difference between the incidence of postoperative shivering in the two groups of ondansetron and meperidine [26].

In a study in 2006, Kelsaka *et al.* compared the preventive administration of 0.4 mg/kg meperidine and 8 mg ondansetron in reducing shivering after spinal anesthesia in three groups of 25 patients. In their study, the shivering rate was 36% in the control group, 8% in the meperidine and 8% in the ondansetron. There was no significant difference between the meperidine and ondansetron groups [19].

## 5. CONCLUSION

Dexamethasone and ondansetron will be able to control the occurrence of shivering after cesarean section with spinal anesthesia. Our findings revealed that dexamethasone is more effective in controlling shivering although this efficacy was not statistically significant.

## CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

## REFERENCES

[1] Alfonsi P. Postanaesthetic shivering: epidemiology, pathophysiology, and approaches to prevention and management. *Drugs*. 2001;61(15):2193–205.

[2] Bagi M, Amjad F, Ghoreishian SM, Shahsavari SS, Huh YS, Moraveji MK, *et al.* Advances in technical assessment of spiral inertial microfluidic devices toward bioparticle separation and profiling: A critical review. *BioChip J*. 2024. doi: 10.1007/s13206-023-00131-1.

[3] Kawaguchi M, Inoue S, Sakamoto T, Kawaraguchi Y, Furuya H, Sakaki T. The effects of prostaglandin E1 on intraoperative temperature changes and the incidence of postoperative shivering during deliberate mild hypothermia for neurosurgical procedures. *Anesth Analg*. 1999 Feb;88(2):446–51.

[4] Mato M, Pérez A, Otero J, De Antonio P, Márquez C, Torres LM. Incidence of postoperative shivering in relation to the time of sevoflurane discontinuation. *Rev Esp Anestesiol Reanim*. 2002 Apr;49(4):197–200.

[5] Eberhart LH, Döderlein F, Eisenhardt G, Kranke P, Sessler DI, Torossian A, *et al.* Independent risk factors for postoperative shivering. *Anesth Analg*. 2005;101(6):1849–57.

[6] Kranke P, Eberhart LH, Roewer N, Tramèr MR. Single-dose parenteral pharmacological interventions for the prevention of postoperative shivering: a quantitative systematic review of randomized controlled trials. *Anesth Analg*. 2004 Sep;99(3):718–27.

[7] Entezariasl M, Isazadehfar K. Dexamethasone for prevention of postoperative shivering: a randomized doubleblind comparison with pethidine. *Int J Prev Med*. 2013;4:818–24.

[8] Horn EP, Werner C, Sessler DI, Steinfath M, Schulte am Esch J. Late intraoperative clonidine administration prevents postanesthetic shivering after total intravenous or volatile anesthesia. *Anesth Analg*. 1997;84(3):613–7.

[9] Rosenberg H, Clofine R, Bialik O. Neurologic changes during awakening from anesthesia. *Anesthesiol*. 1981;54(2):125–30.

[10] Reynolds Beckmann J, Kurz A. Perioperative complications of hypothermia. *Best Pract Res Clin Anaesthesiol*. 2008 Dec;22(4):645–57.L.

[11] Sessler DI, Rubinstein EH, Moayeri A. Physiologic responses to mild perianesthetic hypothermia in humans. *Anesthesiol*. 1991;75(4):594–610.

[12] Sessler DI. Thermoregulatory defense mechanisms. *Crit Care Med*. 2009;37(7 Sup):S203–210.

[13] Ronald DM, Lee A, Fleisher, Young WL. *Miller Anesthesia*. 6th ed. Churchill Livingstone; 2005.

[14] Alfonsi P. Postanaesthetic shivering: epidemiology, pathophysiology and approaches to prevention and management. *Drugs*. 2001;61(15):2193–205.

[15] Woolnough M, Allam J, Hemingway C, Cox M, Yentis SM. Intraoperative fluid warming in elective caesarean section: a blinded randomised controlled trial. *Int J Obstet Anesth*. 2009;18(4):346–51.

[16] Mahmood MA, Zweifler RM. Progress in shivering control. *J Neurol Sci*. 2007;261(1–2):47–54.

[17] Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section. *BMC Anesthesiol*. 2005;5(1):5.

[18] Roy JD, Girard M, Drolet P. Intrathecal meperidine decreases shivering during cesarean delivery under spinal anesthesia. *Anesth Analg*. 2004;98(1):230–4.

[19] Kelsaka E, Baris S, Karakaya D, Sarihasan B. Comparison of ondansetron and meperidine for prevention of shivering in patients undergoing spinal anesthesia. *Reg Anesth Pain Med*. 2006;31(1):40–5.

[20] Hirmanpour A, Talakoub R, Mohammad-Salehi N, Taghian M. A comparative study on the effect of intravenous dexamethasone, ondansetron, and ketamine in preventing postoperative shivering in cesarean section under general anesthesia. *Journal of Isfahan Medical School*. 2017 Apr 21;35(423):310–7.

[21] Teymourian H, Mohajerani SA, Bagheri P, Seddighi A, Seddighi AS, Razavian. Effect of ondansetron on postoperative shivering after craniotomy. *World Neurosurg*. 2015 Dec;84(6):1923–8. doi: 10.1016/j.wneu.2015.08.034. Epub 2015 Sep 3.

[22] Browning RM, Fellingham WH, O'Loughlin EJ, Brown NA, Paech MJ. Prophylactic ondansetron does not prevent shivering or decrease shivering severity during cesarean delivery under combined spinal epidural anesthesia: a randomized trial. *Reg Anesth Pain Med*. 2013 Jan–Feb;38(1):39–43.

[23] Abdollahi MH, Forouzannia SK, Bagherinasab M, Barzegar K, Fekri A, Sarebanhassanabadi M, *et al.* The effect of ondansetron and meperedin on preventing shivering after off-pump coronary artery bypass graft. *Acta Med Iran*. 2012;50(6):395–8.

[24] Asl ME, Isazadefar K, Mohammadian A, Khoshbaten M. Ondansetron and meperidine prevent postoperative shivering after general anesthesia. *Middle East J Anesthesiol*. 2011 Feb;21(1):67–70.

- [25] Shakya S, Chaturvedi A, Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. *J Anaesthesiol Clin Pharmacol*. 2010 Oct;26(4):465–9.
- [26] Nematshahi M, Sahebanmaleki M, Moodi Z, Enayati H, Asade A. A comparison of prophylactic effect of ondansetron and meperidine in reducing shivering prevalence following elective c/s by spinal anesthesia method. *Horizon Med Sci*. 2011;17(3):15–20. Available from: <http://hms.gmu.ac.ir/article-1-1280-fa.html>.