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Original Article

Electron J Gen Med 2018;15(4):em64
ISSN:2516-3507
https://doi.org/10.29333/ejgm/93132

Comparing the prophylactic effect of ondansetron and dexamethasone in controlling headaches caused by spinal anesthesia among women candidated for caesarean A randomized controlled trial

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ABSTRACT

Introduction: Spinal anesthesia is one of the most popular methods of anesthesia for caesarean. One of the major side effects of this method is the headache that the patients would experience as a result of spinal anesthesia. Ondansetron and dexamethasone have been reported to be very useful in reducing these headaches. The present research seeks to study the effects of these two types of medicine in reducing the headaches caused by spinal anesthesia among women candidated for caesarean.

Materials and Methods: This is a double-blind clinical trial conducted on 120 mothers candidated for elective, second time caesarean. They were divided into the following groups with 40 participants in each one: dexamethasone, ondansetron, and placebo. 8 milligram of IV dexamethasone was used for the first group, while the second group was given 8 milligram of IV ondansetron, and the third group was given the same amount of IV distilled water. After the operation, patients' pain scores were measured at 12, 24, and 48 hours following the operation and the average amount of painkiller used 24 hours after the operation was recorded. SPSS 19 was used to analyze the data.

Results: A significant difference was observed between the three groups in terms of the frequency of post-spinal anesthesia headache. This frequency was significantly higher in placebo group compared to what was observed in the other two groups (P = 0.01).

Conclusion: Finally, it turned out that both dexamethasone and ondansetron are very effective in reducing headaches caused by spinal anesthesia. Statistics show that dexamethasone is much better and more effective than ondansetron.

Keywords: spinal anesthesia, headache, caesarean, ondansetron, dexamethasone

INTRODUCTION

Caesarean operation has experienced a dramatic rise in developing countries over the last 30 years (1 & 2). Spinal anesthesia is one of the most popular methods of anesthesia for caesarean operation (2, 3, 4). However, Post-dural-puncture headache (PDPH) is one of the well-known complications of spinal anesthesia. Various factors such as age, gender, pregnancy, and the needle size influence the headache level. This headache is usually felt on both sides and in frontal region or behind the eyes, on the back of the head and influences the neck (3-6). The main mechanism of this headache is the leak of Cerebrospinal fluid (CSF) which is caused by the hole formed in dural by spinal needle. If the needle sent inside the epidural space ruptures dura strings and results in CSF leakage, the meningeal receptor will be stimulated and it will culminate in a headache (3,7). This type of headache is not cured using usual painkillers (2, 7, 8). This makes the period of hospitalization longer and results in further physical and mental problems for mother (4, 9). Ondansetron is usually used to control nausea and vomiting. Various studies have pointed to the fact that ondansetron is very useful to reduce post-spinal anesthesia headache (2, 4, 10). Ondansetron is a selective antagonist for 5-hydroxytryptamine 3 (2, 10, 11). Dexamethasone is a strong corticosteroid with anti-inflammatory and analgesic effects. It has, therefor, been studied for controlling and reducing headache caused by spinal anesthesia (5-7, 12). Considering the importance of such headaches, some attempts have been made to reduce PDPH. As the effectiveness of dexamethasone and ondansetron in reducing the headaches caused by spinal anesthesia has not been thoroughly

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Received: 5 Feb 2018, Accepted: 29 May 2018

compared against one another and considering the high prevalence rate of caesarean operation over recent years (1, 12, 13), we decided to study the effect of adding these two drugs during spinal anesthesia in reducing PDPH among women candidated for elective caesarean.

MATERIALS AND METHODS

This is a double-blind randomized clinical trial study. Our study was done on pregnant women referring to Taleghani hospital in Arak. Patients were randomly divided into three groups: ondansetron, dexamethasone and placebo and after surgery, they were compared in terms of headache.

Inclusion Criteria

1- All pregnant women candidated for elective caesarean who did not agree to undergo spinal anesthesia. 2- All pregnant women candidated for emergency caesarean. 3- Patients who were abusive drug users.

Exclusion Criteria

1- All pregnant women candidated for elective caesarean whose spinal anesthesia had failed and were applying for general anesthesia. 2- Mothers allergic to dexamethasone or ondansetron. 3- All pregnant women candidated for elective caesarean under spinal anesthesia who had undergone spinal anesthesia more than twice.

In this research, 120 mothers candidated for second-time caesarean were equally divided into three groups using randomized numbers table: dexamethasone, ondansetron, and placebo. Having obtained patients' informed consent and their agreement with spinal anesthesia and upon confirmation of anesthesiologist, the patients were taken to the operation room. All patients underwent basic monitoring. IV (Intravenous) dexamethasone was used for the first group, while the second group was given 8 milligram of IV ondansetron, and the third group was given the same amount of IV distilled water. All medicines were prepared by resident of anesthesiology and given to the project anesthesiologist who was blind about the types of drugs. The project anesthesiologist who gave patients IV injections of medicines knew nothing about the content of syringes. Using the IV installed, 3-5 cc crystalloid fluid was given as CVE (Compensatory Volume Expands). Following hemodynamic registration, the patients were asked to assume a sitting position. After prep and drape, they underwent spinal anesthesia from the L4-L5 or L5-S1 space using 25g B-Brawn spinal needle made in Germany. 75 mg Marcaine 0.5% was used for spinal blocking. All those patients who had undergone spinal anesthesia more than twice and those who didn't meet the inclusion criteria were removed from analysis. If the spinal anesthesia was unsuccessful and the patient underwent general anesthesia, she would be excluded from research. When the hemodynamic operation was over, the patients were taken to the recovery room and the project intern used a special status scale to check patients for headache and pain score. The average amount of painkiller used by patients was recorded in special questionnaires by project intern. Finally, SPSS 19 and t-test, anova, and chi-square were used for statistical analysis of information.

SAMPLING AND SAMPLE VOLUME (BASED UPON REFERENCE 14)

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

$$Z_{1-\alpha/2} = 1.96 \; \delta_1 = 1.85$$

$$Z_{1-\beta} = 2.33 \; \delta_2 = 1.46$$

$$\mu_1 = 2.46 \;\; \mu_2 = .68$$

N= 40 subjects in each group

As many as 120 participants were chosen. Based on the research type (R.C.T. i.e. Randomized Clinical Trial), randomized sampling method based upon randomized numbers table was utilized and, finally, 120 patients were randomly divided into 3 equal groups (ondansetron, dexamethasone, and placebo) each including 40 participants. SPSS 19 and t-test, anova, and variance analysis were used to analyze the results and present them in the form of tables and charts.

RESULTS

As P ≥ 0.05, no significant difference was observed between the three groups in terms of patients' average age. The mean age was approximately similar (30 years old) across all three groups (P ≥ 0.05). As P ≥ 0.05, no significant difference

Table 1: *A comparison between mean age, week of pregnancy and mean weight of patients*

Groups	Ondansetron	Dexamethasone	Placebo	P-value
Mean age (years)	30.9 ± 4.1	31.3 ± 3.9	30.8 ± 4.7	P = 0.46 Not significant
Week of pregnancy (weeks)	38.8 ± 2.1	38.5 ± 2.9	38.7 ± 2.4	P = 0.69 Not significant
Mean weight (KG)	79.2 ± 5.1	78.9 ± 4.9	78.8 ± 5.6	P = 0.52 Not significant

Table 2: *A comparison between mean blood pressure and heart rate of patients*

Groups / mean blood pressure and heart rate	Ondansetron	Dexamethasone	Placebo	P-value
Mean blood pressure during operation	68.3 ± 9.9	68.5 ± 10.1	67.9 ± 9.2	P = 0.38 Not significant
Mean heart rate during operation	70.9 ± 8.5	71.4 ± 9.7	71.6 ± 8.7	P = 0.42 Not significant

Table 3: *A comparison between mean blood pressure and heart rate of patients*

Groups / mean blood pressure and heart rate	Ondansetron	Dexamethasone	Placebo	P-value
Mean blood pressure in recovery	74.2 ± 8.8	73.5 ± 10.4	75.2 ± 12.2	P = 0.36 Not significant
Mean heart rate in recovery	84.9 ± 8.9	83.6 ± 9.2	85.5 ± 10.9	P = 0.51 Not significant

Table 4: *A comparison between the mean period of patients' hospitalization*

Groups / mean period of hospitalization	Ondansetron	Dexamethasone	Placebo	P-value
Mean period of hospitalization (days)	2.1 ± 0.8	2.01 ± 1.1	2.2 ± 0.9	P = 0.63 Not significant

Table 5: *A comparison between occurrence of post-spinal headache*

Groups / frequency of headaches	Ondansetron	Dexamethasone	Placebo	P-value
Frequency of headaches	10%	7.5%	20%	P = 0.001 Significant

was observed between the three groups in terms of patients' average age of pregnancy. The mean age of pregnancy was approximately similar (38.5 weeks) across all three groups (**Table 1**).

The groups were similar in terms of average weight and no significant difference was reported between them (P ≥ 0.05).

According to **Table 2**, no significant difference was observed between the three groups in terms of mean blood pressure and heart rate during the operation. The mean blood pressure in recovery was 68 mmhg for all three groups and the mean heart rate was 71 (P ≥ 0.05).

According to **Table 3**, no significant difference was observed between the three groups in terms of mean blood pressure and heart rate in recovery. The mean blood pressure in recovery was 74 mmhg for all three groups and the mean heart rate was 84 (P ≥ 0.05).

According to **Table 4**, no significant difference was observed between the three groups in terms of mean period of hospitalization and the mean hospitalization period was 2 days (P ≥ 0.05).

According to **Table 5**, a significant difference was observed between the three groups in terms of post-spinal headaches. The frequency of such headaches in placebo group was significantly more than what was observed in the other two groups (P = 0.01).

According to **Table 6**, a significant difference was observed between the three groups in terms of headache score. This score in placebo group was more than the other two groups within 12,24,48 hours following the operation, and this score in ondansetron group was more than what was reported for dexamethasone group within the same period (P = 0.02, p=0.03). (This comparison was naturally conducted between patients suffering from post-spinal headache. All patients with headache scores VAS ≥5 were given painkillers).

Table 6: *A comparison between headache scores following spinal anesthesia in various times*

Groups / headache score	Ondansetron	Dexamethasone	Placebo	P-value
VAS 12 hours	5.01 ± 1.1	3.6 ± 0.9	5.5 ± 1.8	P = 0.02 Significant
VAS 24 hours	5.03 ± 1.4	4.6 ± 1.7	5.8 ± 2.1	P = 0.03 Significant
VAS 48 hours	2.01 ± 0.7	1.01 ± 0.6	2.9 ± 1.1	P = 0.03 Significant

Table 7: *A comparison between the dose of medicines used to control headache within 48 hours following the operation*

Groups / dose of the medicine	Ondansetron	Dexamethasone	Placebo	P-value
Average dose used (mg)	112.5 ± 7.6	100.8 ± 8.2	150.7 ± 9.1	P = 0.01 Significant

According to **Table 7**, a significant difference was observed between the three groups in terms of the amount of drug taken within 48 hours following the operation in order to control headache. The average dose of the drug in dexamethasone group was less than what was reported for the other groups, and this dose in ondansetron group was less than placebo group.

DISCUSSION

As the results of data analysis indicated, both ondansetron and dexamethasone were significantly effective in controlling headache, but dexamethasone was far more effective. Mothers receiving dexamethasone had a lower pain scale compared to those receiving ondansetron. A review of previous researches points to results similar to those achieved in our study. Various previous studies have pointed to the positive prophylactic effects of dexamethasone and ondansetron on post-spinal anesthesia headache and they could reduce the rate of this headache (2, 3, 4, 15-19). Some papers have pointed to dexamethasone's therapeutic effects in controlling headaches caused by spinal anesthesia (4, 6, 20-25). In a research by Zainabosadat Fattahi et al (2015) on 210 elective caesarean patients in Iran who had undergone spinal anesthesia, ondansetron was shown to play a major role in relieving headaches caused by spinal anesthesia (2) which is in line with the results of our research. In another research by Azar Danesh Shahraki et al (2013) conducted on 30 women candidated for elective caesarean under spinal anesthesia in Iran, it turned out IV dexamethasone has nausea effects caused by spinal anesthesia and relieves the pain following spinal anesthesia in caesarean operation (5). Both studies have pointed to the significant effect of dexamethasone in reducing headaches caused by spinal anesthesia. In another research by Fardin Yousefshahi et al (2012), 372 pregnant women were studied in dexamethasone and placebo groups. The frequency rate of this headache in dexamethasone group was 10.8%, while this frequency in placebo group was 6.2% indicating a statistically significant difference. They finally arrived at the conclusion that using this medicine is a risk factor in occurrence of headaches after dura rupture (9). These results were not in line with those achieved in our study. Dexamethasone has caused a noticeable reduction in headache scale following spinal anesthesia in our research, but Yousefshahi's results were completely different and had introduced dexamethasone as a risk factor for headaches caused by spinal anesthesia (9). The cause of difference is not clear, but the main point is that nearly all previous studies had confirmed the effectiveness of dexamethasone in reducing the headaches caused by spinal anesthesia. In another research by Doroudian MR et al, 178 patients undergoing orthopedic operations in their lower limbs were studied. In the end, it turned out that Dexamethasone was capable of causing a significant reduction in headache scale of patients (12). Their results were completely in line with those achieved in our research. In a research by Saeid Pasban (2014) in Tarbiat Modarres University, the effects of Dexamethasone on headaches caused by spinal anesthesia among patients candidated for elective caesarean were studied. It was concluded that dexamethasone had a good effect on reducing the headaches following spinal anesthesia (7). These results were also in line with those we have achieved. Mahzad Yousefian et al. (2016) studied 150 pregnant women candidated for caesarean using local anesthesia. The patients were divided into 3 equal groups. The first group received placebo, while the second and third groups received 4 mg ondansetron and 8 mg IV dexamethasone, respectively. The placebo group was observed to have 18% headache caused by spinal anesthesia and 20% nausea and vomiting during the operation. However, symptoms such as headaches following spinal anesthesia, nausea and vomiting during operation in the two groups receiving ondansetron and dexamethasone were not reported and the difference of results across these two groups of intervention was ignorable ($P < 0.05$) (24). These results were in line with those achieved in our research as both researches pointe to the prophylactic positive effect of dexamethasone and ondansetron in reducing headaches caused by spinal anesthesia. Contrary to our

research, no difference was observed between the two interventions groups. However, dexamethasone was shown to be more effective than ondansetron in relieving headaches caused by spinal anesthesia in our research. As a result, a comparison between the results of our research and those achieved in previous studied points to the fact that dexamethasone and ondansetron have a prophylactic positive effect on reducing the headaches caused by spinal anesthesia. However, few researches have compared these two drugs. The results of our research confirm the fact that dexamethasone is more effective than ondansetron in relieving headaches caused by spinal anesthesia.

LIMITATIONS OF THE STUDY

Some pregnant women would not cooperate to take part in the project. Having explained the benefits of spinal anesthesia, a limited number of them did not agree to undergo spinal anesthesia.

CONCLUSION

Dexamethasone and ondansetron are significantly effective drugs to relieve the headaches caused by spinal anesthesia. The data and statistics indicate that dexamethasone is more effective and better than ondansetron.

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