

# Effect of dexamethasone on incidence of headache after spinal anesthesia in cesarean section

## *A single blind randomized controlled trial*

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### ABSTRACT

**الأهداف:** دراسة أثر عقار ديكساميثازون في التقليل من حدوث آلام الرأس.

**الطريقة:** أجريت دراسة عشوائية على 160 مريضة خضعن لعملية قيصرية في مستشفى بهمان، إيران خلال الفترة من مارس 2010م حتى مارس 2011م. تم تقسيم المرضى عشوائياً إلى مجموعة الشاهد ومجموعة التجربة. تم دراسة معدل آلام الرأس خلال الأربع وعشرين ساعة الأولى والأسبوع الأول بعد تخدير العمود الفقري. تم تقدير معدل الإصابة بالآلام الرأس بمقياس رقمي باستخدام مقياس أنالوج البصري. كما تم جمع البيانات وتحليلها باستخدام برنامج الإحصائي نسخة 11.5 واستخدام الاختبارات الإحصائية الوصفية (اختبار كاي، واختبار مان ويتني).

**النتائج:** تمت ملاحظة صداع ثقب فوق الجافية في 2.5% من مجموعة التجربة و12.5% من مجموعة الشاهد في الأربع وعشرين ساعة بعد الجراحة  $p=0.016$  و11.3% في مجموعة الحالة و32.5% في مجموعة التحكم في الأسبوع الأول بعد الجراحة ( $p=0.001$ ).

**خاتمة:** أظهرت نتائج الدراسة أن حقن عقار الديكساميثازون يقلل من صداع ثقب فوق الجافية في الأربع وعشرين ساعة الأولى وخلال الأسبوع الأول بعد تخدير العمود الفقري في المريضات اللاتي خضعن لعملية قيصرية.

**Objectives:** To investigate the effect of dexamethasone in reducing the incidence of headache.

**Methods:** This randomized controlled trial was carried out in 160 cesarean patients with physical conditions-1 and emergency-1 at 22-Bahman Hospital, Iran between March 2010 and March 2011. Patients were randomly divided into sample and control groups. The women were studied for incidence of headache in the first 24 hours and the first week after spinal anesthesia. The mean severity of

the headache was evaluated on a quantitative scale using the visual analog scale (VAS). Data were gathered and analyzed using the SPSS software Version 11.5, descriptive statistical test, Chi-square, and Mann-Whitney U test.

**Results:** The incidence of post-dural puncture headache was observed in 2.5% of the sample group and 12.5% of the control group in the first 24 hours after surgery ( $p=0.016$ ); and 11.3% in the sample group and 32.5% in the control group in the first week after surgery ( $p=0.001$ ).

**Conclusion:** The findings of this research illustrate that intravenous dexamethasone reduces the incidence of post-dural puncture headache in the first 24 hours and the first week after spinal anesthesia in cesarean section patients.

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Spinal anesthesia involves the blocking of the spinal nerves by the injection of a local anesthetic into the subarachnoid space.<sup>1</sup> As it is easy to perform, this anesthetizing method is the most common nerve blocking procedure in urologic, orthopedic, obstetric and gynecological operations. Complications of this method are divided into 2 groups: during and after

anesthesia.<sup>2</sup> Complications during anesthesia include a fall in blood pressure, dyspnea, nausea and vomiting, and so forth. The most common complications after or post anesthesia consist of a neuro-toxic effect on the nervous system, infection of the central nervous system, headache, and backache.<sup>3,4</sup>

First reported in the year 1898,<sup>5</sup> post-dural puncture headache (PDPH) is a debilitating condition appearing after the puncturing of the dura mater and the most important of the delayed complications following spinal and epidural anesthesia. Risk factors for PDPH include: young age, female gender, history of previous PDPH, and size and type of needle used. Post-dural puncture headache is more prevalent in pregnant women who undergo spinal analgesia for cesarean section or normal delivery. The symptoms of this sickness (PDPH) generally appear in the first 7 days after the dura has been punctured and persist for 7 days after.<sup>6,7</sup> The symptoms of this ailment include, hearing loss, visual impairment, and headache. The headache is worsened by sitting up, is aggravated by coughing, moving suddenly or standing, and is improved by lying in a supine position or by increasing intra-abdominal pressure. Different theories have been put forward to explain the cause of PDPH. It was reported that the culprit was thought to be the leakage of cerebrospinal fluid (CSF), and currently it is the difference of pressure between the subarachnoid space and the epidural space, which is considered to be responsible.<sup>8</sup> The treatment of PDPH comprises of 300 mg caffeine taken orally or 500 mg in one liter infusion intravenously for one to 2 hours, and bed rest. In case no response to the treatment is observed, an epidural blood patch is performed.<sup>3,9,10</sup> Although proven that caffeine influences vasoconstriction of blood vessels in the brain, this condition is temporary. Moreover, it seems that caffeine is more effective, when the headache is caused by thin needles (as in spinal anesthesia), whereas epidural blood patch is more effective in cases where thicker needles are used. One of the negative effects of caffeine is that it causes restlessness and insomnia. Further, seizure and cardiac arrhythmia have also been reported from caffeine consumption. A small amount of caffeine is found in mother's milk but no unfavorable effects have been observed in the suckling infant.<sup>8</sup> The long-term administration of dexamethasone,

(a synthetic glucocorticoid) may cause undesirable adverse events such as an increased risk of infection, glucose intolerance, delayed wound healing, superficial ulceration of gastric mucosa, and adrenal suppression.<sup>11</sup> A review of the randomized trials conducted between 1996 and 2001 using preoperative single-dose steroid administration, showed that dexamethasone had antiemetic and analgesic effects in various types of operations.<sup>12</sup> However, these adverse events were not related to a single-dose of dexamethasone at 8-10 mg.<sup>13</sup> In spite of the same, spinal anesthesia has become the most common anesthetizing method in cesarean section as it has reduced mortality from general anesthesia in such surgeries,<sup>8</sup> moreover it has also proven less detrimental to mother and infant compared to general anesthetics; the mortality rate is 16 times higher in pregnant women who are candidates for cesarean section and receive general anesthesia compared to those undergoing spinal anesthesia.<sup>8</sup> As spinal anesthesia is becoming more common, steps should be taken to improve this procedure by reducing the complications arising from it. The aim of this study is to examine the effects of administering intravenous dexamethasone during surgery (headache is the most prevalent complication of spinal anesthesia) for elective cesarean delivery.

**Methods.** The present study is a parallel randomized controlled trial that was carried out for a period of 13 months in the 22-Bahman Training Hospital, Gonabad, Iran in 160 patients in 2010. The samples consisted of patients who had consented to and were deemed fit for cesarean section under spinal anesthesia according to the anesthesiologist and intensive care specialist. According to comparative ratios formula for 2 independent population and the results of pilot study, the sample size was estimated 80 women for each group, level of power considered 80% and 95% confidence level. Due to possible decrease of samples, we allocated 90 samples for each group. This research was approved by the Ethics Committee of the Research Council of Gonabad Medical University, Gonabad, Iran under code no. 89.49 and has been registered by IRCT.

The samples were selected objectively and at the beginning 194 women entered the study. Inclusion criteria were willingness to participate in the study and an age of 20-40 years; having undergone cesarean section under spinal anesthesia, having no history of chronic headaches or migraines, or no known emotional or mental illness; and falling within the American Society of Anesthesiologists (ASA)<sup>14</sup> physical condition class of emergency-1 (E1) and condition-1. At first, researchers draw a chart including 180 rows (001-180). Then, we

**Disclosure.** This study was registered under code no. 89.49 by the Iranian Registry of Clinical Trials (IRCT: 201201095445N2).

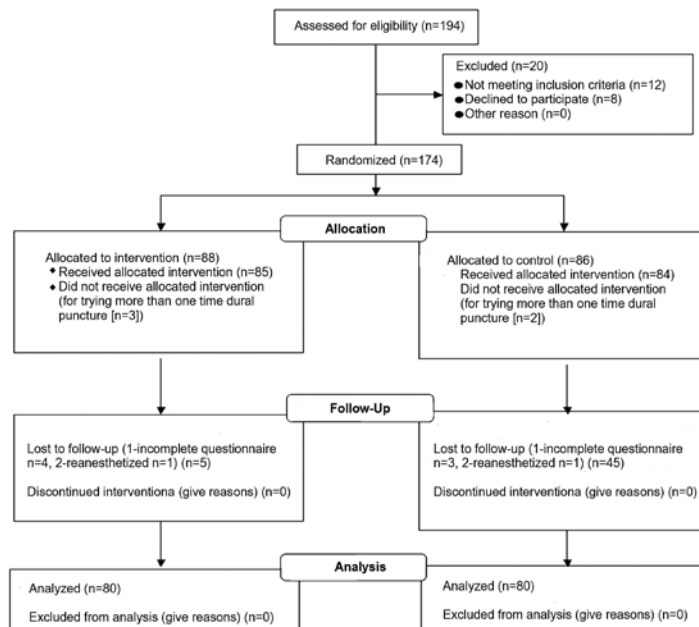
carried out an allocation to the control and sample group using the table random numbers. Patients were divided into 2 groups: control group (n=90) and sample group (n=90). Names and characteristics of patients were allocated to each groups, and only the researchers were aware of this table, and the patients do not know about the injected drug. Also, the anesthesiologists were not aware of the groups before allocation of participants. Moreover, the supervisor responsible for registering the severity of headache did not know which patients are in which group (sample or control). For all patients, only one anesthesiologist performed the spinal anesthesia with only one try, and if it was necessary to more than one time that sample were excluded from the study. Furthermore, participants who underwent 2 anesthetic during the period were excluded.

One hundred seventy-four patients were include in the study (control: n=86 and sample: n=88). Routine care for cesarean section with spinal anesthesia was given in 86 patients of the control group and the same was carried out for the 88 patients in the sample group. But, 6 patients from control group and 8 from sample group were excluded during the allocation and follow-up. Finally 160 patients (control: n=80 and sample: n=80) were studied. An 8mg of dexamethasone was administered intravenously during surgery after delivery. All subjects were anesthetized in a sitting position in the space between the third and fourth lumbar vertebral spaces (L3-L4) and L4-L5 using a number 25 gauge

disposable needle to administer 75mg Lidocaine 5% and 25microg Fentanyl. The patients who had been given dexamethasone were compared with the patients who had not received the same with regards to the manifestation of headaches. After the operation, patients were admitted into the women's surgery ward. In the first 24 hours and the first week after spinal anesthesia differentials were measured through interviewing, and the average severity of headache was evaluated using the visual analog scale (VAS).

Data was analyzed using the Statistical Package for Social Sciences Version 11.5 (SPSS Inc, Chicago, IL, USA). Chi-square, Mann-Whitney U, and a meaningful level of <0.05. Mann-Whitney U was used to compare the mean of severity of headache in the sample and control groups. Chi-square test was used to compare the ratio of headache in sample and control groups, also comparative qualitative demographic variables were carried out using Chi-square in both groups.

**Results.** Figure 1 shows the participants flow. In this study we assessed 194 women but 20 participants were excluded because 12 of them do not meet the inclusion criteria and 8 declined to participate. During intervention and follow up 5 did not receive allocated intervention for more than one time for dural puncture, and 9 did not follow up. Duration of the study was 13 months. All participants were assessed using VAS scale during the first 24 hours and after the first week of



**Figure 1** - Participants flow of 194 participants.

spinal anesthesia for post-dural puncture headache and pain severity variables.

Table 1 summarizes the demographic characteristics of both groups.

Twelve women suffered headaches in the first 24 hours and 35 in the first week. A meaningful statistical difference was seen in both groups with regards to getting headache in the first 24 hours ( $p=0.016$ ) and in the first week ( $p=0.001$ ) after spinal anesthesia; showing that headaches were less common in the sample group than in the control group (Table 2).

Although there was no significant statistical difference in the severity of pain in the 2 groups, the pain was less severe in the sample group, in both first 24 hours and first week (Table 3).

**Discussion.** There is a meaningful statistical relationship between the intravenous injection of

dexamethasone during surgery and manifestation of headaches after surgery ( $p<0.05$ ). The occurrence of headache in the women who had cesarean section and who had been given dexamethasone was less than the women who had not been administered the drug. Javid and Rafeian-Kopaei illustrated that dexamethasone causes an improvement in the symptoms of headache in patients suffering from migraine, the extent of recovery being equal to that of 1 mg dihydroergotamine intravenous administration, the decrease in the severity and length of pain were the same in both groups. However, side effects were occasionally seen in the cases using Ergotamine, where as this was not the case in the patients using dexamethasone.<sup>15</sup> Previous study, showed that intravenous hydrocortisone reduces headache after spinal anesthesia, in our study 30 patients randomly received conventional therapy

**Table 1** - Demographic characteristics of the participants in sample and control groups.

Demographic characteristics	Sample n (%)	Control n (%)	P-value	Degrees of freedom	$\chi^2$
<i>Age</i>			0.81	3	0.95
20-25	17 (21.3)	20 (25.0)			
26-30	24 (30.0)	27 (33.7)			
31-35	24 (30.0)	21 (26.3)			
36-40	15 (18.7)	12 (15.0)			
Total	80 (100)	80 (100)			
<i>Length</i>			0.61	3	1.79
140-150	6 (7.4)	4 (5.0)			
151-160	19 (23.8)	26 (32.4)			
161-170	44 (55.0)	39 (48.8)			
>170	11 (13.8)	11 (13.8)			
Total	80 (100)	80 (100)			
<i>Education</i>			0.7	4	2.15
Uneducated	1 (1.3)	1 (1.3)			
Elementary school	23 (28.7)	17 (21.3)			
Guidance	8 (10.0)	12 (15.0)			
High school( diploma)	29 (36.3)	27 (33.7)			
College graduates	19 (23.7)	23 (28.7)			
Total	80 (100)	80 (100)			
<i>Job</i>			0.4	3	2.91
House wife	71 (88.8)	67 (83.8)			
Employee	8 (10.0)	12 (15.0)			
Other	1 (1.2)	1 (1.2)			
Total	80 (100)	80 (100)			
<i>History of cesarean section</i>			0.1	1	1.03
Yes	42 (52.5)	33 (41.3)			
No	38 (47.5)	47 (58.7)			
Total	80 (100.0)	80 (100)			

**Table 2** - Incidence of headache after spinal anesthesia in sample and control groups.

Groups	First 24-hours			First week		
	Yes	No	Total	Yes	No	Total
Sample	2 (2.5)	78 (97.5)	80 (100)	9 (11.3)	71 (88.8)	80 (100)
Control	10 (12.5)	70 (87.5)	80 (100)	26 (32.5)	54 (67.5)	80 (100)
Result of test	$\chi^2= 5.76$ , Df = 1, $p=0.016$			$\chi^2= 10.56$ , Df = 1, $p=0.001$		

Data are expressed as number and percentage (%)

**Table 3** - Comparison of the average of severity of headache in sample and control groups.

Groups	N	First 24 hours Mean± SD	N	First Week Mean± SD
Sample	2	2.5 ± 2.12	9	4.66 ± 2.82
Control	10	2.6 ± 2.55	26	4.7 ± 2.75
Result of test	Mann-Whitney U: $p=1$		Mann-Whitney U: $p=0.95$	

(complete bed rest, hydration, acetaminophen codeine and pethidine) while other 30 patients received intravenous hydrocortisone (200mg first, then 100mg 3 times a day, for 2 days). Further studies are needed to consider steroid therapy as a standard treatment for postural puncture headache.<sup>16</sup> Tavakol et al, found out in a randomized clinical trial in which 35 cases of parturient women, who developed headache (PDPH) due to spinal anesthesia after cesarean section in spite of consumption of NSAID drug, opioid, bed rest, and rehydration. They received intravenously drip dexamethasone 0.2mg/kg (maximum 16mg) in one liter of normal saline for 2 hours, Result showed that mean of VAS pain score before treatment was  $6.5 \pm 1.8$  and decrease to  $1.6 \pm 1.2$  after treatment. We found out that dexamethasone therapy in comparison with routine supportive therapy is the greater rapidity in pain relief and earlier release of patients from hospital.<sup>17</sup> Yousefshahi et al, showed a slightly increase in overall incidence rate of post-dural puncture headache due to intraoperative administration of dexamethasone. This difference can be due to the following factors, they do not controlling the intervention variables, like performing dural puncture by 4 anesthesiologists and a group of anesthesia residents. Further, they do not controlling the number of trying for spinal anesthesia. But in our study we control both of the intervention variables by doing dural puncture by one anesthesiologist and also exclude samples who tried more than once for spinal anesthesia.<sup>18</sup> The results of the present research have verified the efficacy of dexamethasone in preventing PDPH. Furthermore, the probability of the existence of an inflammatory process, besides the change in the subarachnoidal pressure in the pathogenesis of causes headache after spinal anesthesia, has also come to light. Corticosteroid can help reduce pain by inhibiting the conversion of Arachidonic acid into pain producing mediators (Prostaglandin I<sub>2</sub>, E<sub>2</sub> and Leukoterian B<sub>4</sub>) and also by preventing the production of pro-inflammatory cytokines (IL-1, IL-6 and TNF- $\alpha$ ).

**Study limitations.** One of the important limitation of this study is that VAS is a subjective scale and the

results can be different according to the person's tolerance and understanding of pain.

In conclusion, it was observed that administering an 8mg dose of dexamethasone intravenously during spinal anesthesia is effective and useful in preventing headaches that follow this anesthetic procedure. Taking into consideration the results of this research, intravenous dexamethasone is suggested for prevention of headaches in patients who undergo spinal anesthesia and if they are allowed to use corticosteroids. According to the results of this study we suggest other researchers to perform more studies using more subjects and using different designs like double blind.

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