Original Article

Is epidural dexamethasone effective in preventing postdural puncture headache?

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Abstract

Background: Postdural puncture headache (PDPH) is one of the common complications of spinal anesthesia; it is observed in 1−40% of cases involving spinal anesthesia. It can cause considerable morbidity and 40% of cases may require invasive treatments such as epidural blood patch. With the exception of invasive treatments such as an epidural blood patch, current standard treatment modalities have not proved efficacious. There had been some research done that indicated successful prophylaxis and/or treatment of PDPH by administration of intravenous steroids. Based on those findings, we hypothesize that a direct injection of corticosteroids to the anesthesia puncture site could increase the amount of corticosteroid that accumulates in the puncture site, and will be more effective in decreasing dural inflammation and incidence of PDPH than that of parenteral steroids. We formulated our study to evaluate the effect of dexamethasone directly injected into spinal anesthesia puncture sites.

Methods: A total of 268 patients undergoing spinal anesthesia were randomly allocated into two groups; one group received a prophylactic epidural injection of dexamethasone (2 mL, 8 mg) and the other group received 2 mL of normal saline. The incidence and intensity of PDPH and puncture site backache were each measured at 24 hours, 72 hours, and 7 days after spinal anesthesia. The intensity of the headache was graded according to the meningeal headache index.

Results: The overall incidence of headache during the 7-day period was 5 patients (3.7%) in the control group and 11 patients (8.2%) in the study group, which is not statistically significant (X^2 = 2.393 and p = 0.122). The severity of headache also shows no statistical significance (2.2% in cases versus 6% in controls; z = 1.53, p = 0.126). The intensity of headache reported at the 24 hours (z = 0.698; p = 0.485), 72 hours (z = 0.849; p = 0.396), and 7 days (z = 0.008; p = 0.994) was not different. There also was no difference in the incidence of backache in the two groups.

Conclusion: In contrast to other studies that showed the efficacy of intravenous dexamethasone in the prevention and treatment of PDPH, our study did not show any significant effect of prophylactic epidural injection of dexamethasone in prevention of PDPH. However regarding the low number of PDPH in routine cases, evaluation of this intervention in groups with a high incidence of PDPH by using of particulate steroids is recommended to confirm these preliminary findings.

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1. Introduction

In 1899, when August Bier devised the spinal anesthesia procedure, he also described post-dural puncture headache (PDPH) as an untoward complication. Currently, PDPH is defined by the International Headache Society as a positional bilateral headache that first presents within 5 days after a dural puncture. The pain usually presents within 15 minutes after standing upright and is alleviated within 15 minutes of assuming a supine position; it can be accompanied by neck stiffness, photophobia, tinnitus, hearing loss,
or nausea. In 95% of cases, the PDPH will abate within 1 week without any treatment, or within 48 hours after treatment of a cerebrospinal fluid (CSF) leak, usually by administration of an epidural blood patch (EBP). This pressure phenomenon results in a shift of the contents of the skull and changes the tension of meningeal nerve fibers and other pain receptors, causing pain sensations particularly in the upright position. Excessive loss of CSF after spinal anesthesia can be attributed to the puncture of the dura with a large-bore needle; large-bore needles tend to make larger puncture openings that can be more difficult to close quickly and thus leave an opening for CSF leakage. At the dawn of the 20th century, when large-bore needles were first used for this newly developing procedure, the incidence of PDPH was >50%, and in 1989, when large-bore needles were still in use, the figure stood at 70%. Currently, with the advent of smaller bore needles, the incidence of PDPH has dramatically declined to 2–10% for 26-gauge needles and <2% for 29-gauge needles. Of the 1–40% of patients who are affected with PDPH after spinal anesthesia, 40% require intensive treatments such as EBP. In the remaining 60%, pain is controlled using standard analgesic treatments until PDPH is completely resolved (1 week in 70% of patients and 6 weeks in 96% of patients). Although 18% of the patients in this group were only bound by a mild restriction of physical activities, 31% of patients were unable to perform their normal daily activities and 51% of patients were in need of complete bed rest. Currently, several pathogenic mechanisms have been proposed for PDPH. According to the most long-standing theory, a decrease in volume or pressure of CSF as a result of CSF leak from the puncture site is the cause of headache. This theory is supported by the fact that normal CSF pressure, which amounts to 5–15 cmH2O in the supine position and rises to 40 cmH2O in the upright position, can drop to <4 cmH2O following the procedure. A second theory of the PDPH mechanism is based on activation of adenosine receptors caused by an abrupt change in volume and pressure of CSF, which may result in vasodilation and pain. In view of the high prevalence of this condition, especially among parturating women, development of effective measures to control or prevent this condition is considered a medical priority. The current approach to PDPH is composed of symptomatic relief of pain, bed rest, and EBP as needed. There is a general consensus among anesthesiologists regarding the effectiveness of EBP for the treatment of PDPH; however, almost all other treatments (other than symptomatic pain relief) are limited both by a dearth of randomized clinical trials (RCT) and the intensely conflicting results of the few existing studies.

Treatment of spinal column referred pain by epidural steroid injection (ESI) had long been established. In the United States it is now the most common invasive treatment for pain of the spinal column.

The question that arose based on the common usage of ESI for pain relief is whether ESI can be useful for the prevention or treatment of PDPH; therefore, this study was conducted to evaluate the effect of epidural dexamethasone injection in prevention of PDPH.

According to a 2011 study by Dorudian et al., 8 mg intravenous (IV) dexamethasone was able to reduce the severity of PDPH; in 2007, Ashraf et al. demonstrated that IV hydrocortisone can significantly decrease the intensity of PDPH in women who underwent cesarean section under spinal anesthesia in the 48 hours following surgical delivery. Similarly, in a case series of three women undergoing vaginal delivery or cesarean section, IV cortisone caused a dramatic response to PDPH. In this study, they suggested that clinical trials are necessary to establish the role of steroids in treatment of PDPH. Three years later, in 2005, Neves et al. reported one woman with cesarean delivery who experienced complete relief (after conventional treatments of PDPH failed) and two cases in whom PDPH did not develop when IV hydrocortisone was administered prophylactically. Moreover, De Matteis and Pisano revealed that epidural administration of 1.5 mg diluted betamethasone may prevent PDPH effectively. The preventive effect of corticosteroids against PDPH can be caused by their anti-inflammatory effect on the inflammatory process initiated at puncture site. Because these drugs suppress the synthesis of inflammatory mediators in immune cells, these inflammatory mediators will be released to a lesser extent into CSF and decrease the number of stimulated pain receptors in the central nervous system as well.

For the aforementioned reasons, we planned our study to evaluate the effect of dexamethasone directly injected in puncture site to prove or reject this hypothesis.

### 2. Methods

This clinical trial was recorded on [www.irct.ir](http://www.irct.ir) with IRCT ID: IRCT201112178441N1. After obtaining approval from the Ethical Board of the Department of Anesthesiology, Tehran University of Medical Sciences, Tehran, Iran on April 20th, 2010, a total of 268 patients who were referred to the anesthesiology clinic of Sina Hospital in Tehran, Iran for preoperative assessments were included in this study. Written informed consent was obtained from all patients, who were selected from general, orthopedic, urology, and gynecology services.

The patients’ ages ranged between 18 years and 40 years; based on the criteria of the American Society of Anesthesiology (ASA), they were all in ASA Class 1 or Class 2. Patients with a history of a headache disorder, which could confound the prevalence of PDPH, and those in whom steroids were contraindicated were excluded from the study. Patients were randomized by using random allocation software for parallel group randomized trials. Patients were blinded to the group to which they were assigned. The anesthesiologist who performed the procedure was aware of the injection type; however, the anesthesiologist who evaluated the patients’ outcomes was blinded.

#### 2.1. Pilot study

Spinal anesthesia was performed using the barbotage method to evaluate the epidural injection technique, after intrathecal injection of the local anesthetic agent that was used in this study in three patients. Spinal anesthesia was followed by injection of a radiopaque material into the epidural space by pulling the needle 5 to 8 mm out of the subarachnoid space (where there is no flow of CSF at the hub of the needle). After pulling the needle out, iohexol was injected and spread into the epidural space. As visualized by C-arm fluoroscopy in the sitting position, there was no spread of dye to the subarachnoid space.

Fig. 1 shows the patient’s lumbar spine in the sitting position. Fig. 2 demonstrates epidural spread of radiopaque solution following subarachnoid injection of local anesthetic. Epidural spread of iohexol (2 cc) was observed after spinal anesthesia with a 27-gauge Quinke needle.

Fig. 3 shows the spread of iohexol in the epidural space in the supine position. The needle is withdrawn and the patient lies supine; there is no spread of dye into the subarachnoid space.

#### 2.2. Preoperation arrangements

All patients were fasting for 8–10 hours preoperatively. Inside the operating room the patients were monitored with a three-lead echocardiogram, noninvasive blood pressure monitoring, and pulse...
oximetry. Intravenous access was obtained with a 16-gauge IV catheter and 500 cc of normal saline was infused for every patient.

2.3. Spinal anesthesia

First, 1 mL of a 2% lidocaine solution was injected through a 29-gauge needle to anesthetize the skin and subdermal tissues. Next, a 27-gauge Quinke spinal needle was introduced into the space between the L3 and L4 vertebrae. After the position of the needle in the intrathecal space was confirmed by a gush of CSF, 2 mL (10 mg) of 0.5% bupivacaine solution was injected as the local anesthetic.

2.4. Epidural injection

When the bupivacaine injection was completed, the spinal needle was withdrawn while performing barbotage for 0.5 cm or until cessation of CSF flow (which indicates entry into the epidural space). Next, 2 mL of dexamethasone (8 mg) or 2 mL of normal saline was injected into the patient’s epidural space (case and control groups, respectively). The needle would then be completely withdrawn and patients remained in the recumbent position.

2.5. Intraoperative monitoring

All patients were administered O2 5 L/minute via face mask. Blood pressure was checked every 5 minutes; if a 20% decrease from baseline blood pressure was observed, prompt IV infusion of normal saline and ephedrine 5–10 mg were administered intravenously. Bradycardia (<60 bpm) was treated by 0.6 mg of atropine.

2.6. Follow-up for PDPH and back pain

Fig. 4 illustrates the methods of evaluation and management of patients after surgery. Patients were discharged at the discretion of the attending physician 24 hours after the surgical procedure in the absence of headache, backache, or other surgical complication. The patients were followed up by telephone for the presence of headache, back pain, and the intensity of pain on Day 3 and Day 7 after the surgical procedure. Headache pain was scored based on the meningeal headache criteria, and the presence or absence of back pain was recorded for every patient (Table 1). Patients who were found to have mild PDPH were advised to take paracetamol 325 mg, caffeine 40 mg, and ibuprofen 200 mg every 6 hours as needed and to increase their fluid intake. Patients who were found to have severe PDPH or PDPH that was nonresponsive to treatment were advised to follow up in person at the anesthesiology clinic. Intractable pain after 24 hours of pain onset was treated with EBP in the operating room. All patients who remained hospitalized 24 hours after surgery, whether because of headache within 24 hours after surgery or for any other reason, were followed up inside the hospital in concert with attending physicians.

The data were analyzed by SPSS version 18 software (SPSS Inc., Chicago, IL, USA). The t test was used for quantitative comparisons between the two study groups. For qualitative variables, the Chi-
square test (for nominal data) and the Mann-Whitney U test (for ordinal data) were used, and the error was set at 0.05.

3. Results

Both the control and intervention groups had 134 patients; each group contained 102 men (76.12%) and 32 women (23.88%). The mean patient age in the control group was 27.8 ± 6.1 years (standard error = 0.56), and mean patient age in the intervention group was 28 ± 5.9 years (SE = 0.48); this is not significantly different between the two groups (t = 0.252, p = 0.801). The incidence of headache and back pain at any time during the 1st week following all the different surgical procedures is listed in Table 2. The incidence of headache shows no statistical difference regarding the surgical procedure (X² = 1/414, p = 0.702).

The overall prevalence of headache at any time within the 1st week following the surgical procedure was five cases (3.7%) and 11 cases (8.2%) in the control and case groups, respectively, which was not found to be significantly different (X² = 2.393 and p = 0.122 using the Chi-square test). The control group had three cases of mild headache (2.2%) and two cases of severe headache, whereas the case group had eight cases of mild headache (6%) and three cases of severe headache (2.2%). The Mann-Whitney U test revealed no statistically significant difference in the severity of headache between the two groups (z = 1.53, p = 0.126).

The overall incidence of back pain at any time within the 1st week following the operation was 15 patients in the control group (11.2%) and 11 patients in the intervention group (8.2%); this was not found to be significantly different (X² = 0.682 and p = 0.409 using the Chi-square test).

The prevalence of headache and back pain at 24 hours, 72 hours, and 1 week after the surgical procedure did not differ significantly between the two groups (see Table 3). The Mann-Whitney U test revealed that the intensity of headache was not significantly different between the two study groups at any recorded point (z = 0.698, p = 0.485 for 24 hours; z = 0.849, p = 0.396 for 72 hours; and z = 0.008, p = 0.994 for 1 week).

Table 1
Classification of severity of meningeal puncture headache.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Postural headache slightly restricting daily activities patient is not bedridden at any time during the day. No associated symptoms</td>
</tr>
<tr>
<td>Moderate</td>
<td>Postural headache that significantly restricts daily activities. Patient is bedridden part of the day. Associated symptoms may or may not be present</td>
</tr>
<tr>
<td>Severe</td>
<td>Postural headache severe enough to stay in bed all day. Associated symptoms always present. Associated symptoms of meningeal puncture headache*</td>
</tr>
</tbody>
</table>

* Vestibular: nausea, vomiting, dizziness; cochlear: hearing loss, hyperacusis, tinnitus; ocular: photophobia, teichopsia, diplopia, difficulty with accommodation; and musculoskeletal: neck stiffness, scapular pain.

Table 2
The prevalence of headache and back pain at any time during the first postoperative week for all types of surgeries.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Headache</th>
<th>Back pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>1 (2.4)</td>
<td>2 (4.8)</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>7 (7.6)</td>
<td>11 (12.0)</td>
</tr>
<tr>
<td>Otoologic</td>
<td>5 (5.8)</td>
<td>10 (11.6)</td>
</tr>
<tr>
<td>Gynecologic</td>
<td>3 (6.3)</td>
<td>3 (6.3)</td>
</tr>
<tr>
<td>Statistical test</td>
<td>X² = 1.414</td>
<td>X² = 2.721</td>
</tr>
<tr>
<td>p = 0.702</td>
<td>p = 0.437</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as n (%).
Dexamethasone in postdural puncture headache

Table 3
The prevalence of headache and back pain at 24 hours, 72 hours, and 1 week after the surgical procedure.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Time</th>
<th>Normal saline</th>
<th>Dexamethasone</th>
<th>X²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>24 h</td>
<td>3 (2.2)</td>
<td>5 (3.7)</td>
<td>0.473</td>
<td>0.722</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>5 (3.7)</td>
<td>8 (6.0)</td>
<td>0.394</td>
<td>0.571</td>
</tr>
<tr>
<td></td>
<td>7 d</td>
<td>2 (1.5)</td>
<td>2 (1.5)</td>
<td>0.392</td>
<td>0.522</td>
</tr>
<tr>
<td>Back pain</td>
<td>24 h</td>
<td>14 (10.4)</td>
<td>10 (7.5)</td>
<td>0.301</td>
<td>0.583</td>
</tr>
<tr>
<td></td>
<td>72 h</td>
<td>8 (6.0)</td>
<td>6 (4.5)</td>
<td>0.076</td>
<td>0.137</td>
</tr>
<tr>
<td></td>
<td>7 d</td>
<td>9 (6.7)</td>
<td>3 (2.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as n (%).

4. Discussion

In this study, epidural injection of dexamethasone had no positive effect in the prevention of PDPH. It also was ineffective in reducing the prevalence of back pain.

A literature review showed that almost no other RCT had evaluated the effects of a prophylactic epidural injection of steroids simultaneously with a subarachnoid block on the incidence of PDPH. One similar study is an Italian study in 1991 where an epidural injection of 1.5 mg of betamethasone was shown to reduce the incidence of PDPH in 74 patients. Other anecdotal studies on this issue are limited to the evaluation of intravenous steroids, only two of which were RCTs. In the limited case reports that do exist, only one steroid has been found to be effective in treatment of PDPH.10,11

Such reports are not just limited to PDPH, rather, they also address the headache caused by spontaneous intracranial hypotension (SIH), which assimilates PDPH without LP.16–19

However, because the total number of patients studied in all of these reports is 10 and the steroids that have been studied in these reports differ in their pharmaceutical properties, the results may not necessarily be used for extrapolations.

The experimental studies regarding preventing and treating PDPH were all conducted in Iran and consist of two RCTs and a self-controlled trial.8,9,20 In the first RCT,9 the effect of IV hydrocortisone on PDPH was evaluated; the study found that 6 hours after treatment with hydrocortisone a significant decrease in the intensity of headache was observed and by repeating the dose six times, the headache was completely resolved after 48 hours.9

The self-controlled trial by Tavakol et al10 evaluated the therapeutic effects of IV dexamethasone on PDPH; it was composed of 35 patients with PDPH in the intervention group and did not have a separate control group. These patients responded favorably to treatment with IV dexamethasone after unsuccessful conventional treatments.10 Although the study produced impressive results, the study is flawed because it lacks a control group for comparison. Moreover, the patients received other PDPH treatments without determining the proportion of the response that is attributable to each treatment. Furthermore, Tavakol et al’s10 study defined a favorable response as “improvement in headache 2 hours after intravenous infusion of dexamethasone”; it did not evaluate parameters such as response to treatment in relation to the time elapsed, sustainability of the response and possible need for multiple doses of dexamethasone.

The second RCT (Dorudian et al’s8) is similar to the current study in that it focused on the prevention rather than the treatment of PDPH (using IV dexamethasone). It involved 178 patients assigned to two groups to be treated with either IV dexamethasone or normal saline. Despite success in reducing the intensity of PDPH, dexamethasone was not shown to reduce the incidence of headache among the patients of this study.8 A shortcoming of both the current study and that of Dorudian et al8 is the limited number of patients with PDPH severe enough to treat with steroids; in Dorudian et al’s8 study only 15 of 34 patients were treated with dexamethasone; in the current study, only 11 of 16 patients with PDPH were treated with dexamethasone.8

By briefly reviewing the aforementioned reports it can be concluded that a higher number of patients in a future study will increase the odds for a more solid result from steroids possibly because of the low incidence of the studied variable. The power of a study on a disease is reduced by low incidence of the disease, and a higher number of patients increases the power of the study to detect differences; with respect to the 4–8% incidence rate for PDPH among the patients of this study, the power of this study is calculated at 0.18. The incidence of PDPH and power of Dorudian et al’s8 study are 16.8% and 0.19, respectively. With such a low power it is difficult to make a precise judgment on the effectiveness of epidural dexamethasone in prevention of PDPH.

Of note, the use of smaller needles reduces the incidence of PDPH to <2%. Such a low incidence rate may not justify risky invasive treatments; however, the use of small needles may not be feasible on all hospital wards. According to one survey, in 85% of neurology wards, diagnostic lumbar punctures (LP) are performed with needles larger than 22 gauge, which may result in an incidence rate of 36% for PDPH.21 On pediatric and neurology wards this figure might be as low as 28%.22,23 Also in view of the 80% incidence rate observed in accidental dural puncture cases, particularly among laboring women, developing effective measures to address this problem is prudent. With this in mind, although this study has been done on patients undergoing LP with small-bore needles, it is useful to consider another study on patients who are more likely to develop PDPH (i.e., women in labor, and patients with lumbar punctures done with large-bore needles). The results of such studies could be used for extrapolation with a higher level of confidence.

As with all pharmacologic studies, the type of steroid used, the dosage given, the frequency of dosages, and time of administration are all important factors in determining the results. Synthetic steroids are categorized as either particulate or nonparticulate steroid formulations. Being of the nonparticulate type, dexamethasone has the advantage of being less likely to cause ischemia by entering the spinal arteries.24,25 However, the higher solubility of dexamethasone is also associated with shorter duration of its action when locally administered. Dreyfuss et al22 showed that epidural triamcinolone is more effective than dexamethasone in treating neck pain, and O’Donnell et al26 obtained the same result for treatment of low back pain. However, Gharibio et al27 in their review of articles, suggest that local administration of nonparticulate steroid such as dexamethasone dose not yield sustainable anti-inflammatory results. They conclude that because of the property of being quickly dispersed, local infiltration of nonparticulate steroids has no advantage over systemic administration.

PDPH normally ensues 24–48 hours after a dural puncture. The main preventive effect of dexamethasone that was seen in this current study may be ascribed to the bulk of the locally infiltrated dexamethasone that is systemically absorbed, keeping in mind that dexamethasone was given at a single 8-mg dose, which happens to be the minimum therapeutic dose for epidural administration.21 It may be argued that for the purpose of achieving long-term therapeutic effects (prevention of headache), particulate steroids would have been a better option.

Dexamethasone was the only steroid that was used in the only existing report, suggesting that a positive result may be elicited from epidural injection of steroids for the prevention of headache.12 Indirect techniques of identifying the epidural space are at best associated with a 25% error rate, which may present another pitfall
of this study. In view of the low incidence of headache among the patients of the current study, such a rate for erroneous infiltration may dramatically alter the final results. With the use of fluoroscopic imaging, this type of error may be decreased by 90%.

5. Conclusion

This study presents the first RCT on the preventive effects of dexamethasone injection on the incidence of PDPH. The results of this study suggest that dexamethasone is not effective in preventing PDPH and back pain. However, considering the direct and indirect effects of steroids in pain reduction and theories on the direct role of steroids in the pathophysiology of PDPH, it seems that designing more studies of this kind with a few amendments are indicated to further evaluate the use of steroids. Points to consider in designing future studies are as follows: (1) inclusion of patients who are more likely to develop PDPH in order to increase the power of the study; (2) use of higher doses of particulate steroids to increase the intensity and duration of the response; and (3) use of a technique as to increase the precision and accuracy of injection into the epidural space especially in low incidence rates.

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