

# Prophylactic Effects of Hydrocortisone on Post Dural Puncture Headache after Spinal Anesthesia

Mirmohammad Taghi Mortazavi<sup>1</sup>, Maarouf Ansari Kazaj<sup>2\*</sup>, Reza Movassaghi<sup>1</sup>

**Background:** Post-dural puncture headache is one of the common complications after neuraxial anesthesia. Some researchers have used corticosteroids for treatment of this complication.

We decided to study the prophylactic effect of administering intravenous hydrocortisone before spinal anesthesia in reducing the incidence and intensity of headache after surgery.

**Methods:** This randomized, double-blind, placebo-controlled trial was carried out in 80 patients undergoing abdominal and lower limb surgery without other health problem (ASA I). We randomly put 40 participants in the placebo group and 40 in the hydrocortisone group for study. The placebo group received 2 ml placebo and hydrocortisone group received 2 ml (100 mg) intravenous hydrocortisone. The incidence of PDPH on the recovery, 12, 24, 48 hours and 7 days after surgery was studied, and the severity of PDPH was assessed using a visual analog scale (VAS).

**Results:** The mean intensity of headache in hydrocortisone group after recovery in the first 12, 24 and 48 hours and the first week of surgery were 0.0, 1.27, 2.35, 2.28 and 0.97 mm whereas in placebo group they were 0.0, 2.02, 3.02, 2.92 and 1.47 mm. The difference of headache intensity between two groups was not significant ( $P=1$ ,  $P=0.231$ ,  $P=0.344$ ,  $P=0.351$ , and  $P=0.302$ ). The difference of incidence rate between two groups was not significant ( $P=1$ ,  $P=0.502$ ,  $P=0.633$ ,  $P=0.579$  and  $p=0.576$ ).

**Conclusion:** The results indicated that prophylactic administration of 100 mg hydrocortisone did not have any protective effect against post dural puncture headache.

**Keywords:** hydrocortisone; dural puncture; headache; spinal anesthesia

Headache after puncture of duramater in the spinal anesthesia is one of the common complications, with a prevalence rate of 0.3 to 25 percent [1-2]. Post-dural puncture headache theoretically and primarily is defined due to non closing hole of the needle passage dural and cerebrospinal fluid leak, which caused headache in the patient in a sitting position with the pull of gravity on pain-sensitive elements, including intracranial vessels, meninges and nerves [3]. MRI and manometric studies reported the reduction of cerebrospinal fluid pressure 4 to 15 mm of water [4]. This topic was confirmed by studies that have been conducted on epidural injection of normal saline after spinal anesthesia which was effective in reducing post-dural puncture headache. Compensatory cerebral vascular dilation and reduction of the volume of cerebrospinal fluid can also worsen symptoms [5]. Post-dural puncture headache can occur immediately or after months, but almost 90 percent of

headache occurs in the first 72 hours and often in the first 48 hours after dural puncture [6]. Many patients usually describe post-dural puncture headache in the frontal or occipital with burning sign that spreads to the neck and shoulders. Because spinal anesthesia is easy to do, it is the most common neuraxial block in many surgical procedures, including urology, orthopedics, and gynecology [3]. Post-dural puncture headache can be accompanied by nausea, vomiting, neck stiffness and visual and hearing disturbance, seizures, subdural bleeding and rarely cerebral nerve palsy [7]. For the treatment of this complication many methods including: hydration, oral caffeine, theophylline, corticotrophin, somatropin, blood injection in the epidural space, aminophylline, adrenocorticotrophic hormone and recently pregabalin had been used [8]. Invasive treatments for post-dural puncture headache like injection of blood in the epidural space which is defined as the standard treatment is associated with complications such as worsening pain and infection [9-11]. Severe post-dural puncture headache often is associated by nausea that limits administration of oral medication. That's why intravenous drugs are preferred for quick and effective affects to other methods [12-14]. Risk factors outlined in the studies for the post-dural puncture headache are family history of headache after the dural puncture [15] the tip of the needle, the size of the needle, Bevel of the needle to pass through dura mater, the median approach versus the para median, the type of anesthetic and the clinical experience of the anesthesiologist [16]. Corticosteroids are used to treat post-dural puncture

From the <sup>1</sup>Department of Anesthesiology, School of Medicine, University Medical Sciences, Tabriz, Iran.

<sup>2</sup>Department of Anesthesiology, Faculty of Paramedical, University of Medical Sciences, Tabriz, Iran.

Received: 5 October 2017, Revised: 28 November 2017, Accepted: 14 December 2017

The authors declare no conflicts of interest.

\*Corresponding author: Maarouf Ansari Kazaj, MSc. Department of Anesthesiology, Faculty of Paramedical, University of Medical Sciences, Tabriz, Iran. E-mail: marof\_ansari@yahoo.com  
Copyright © 2018 Tehran University of Medical Sciences

headache associated with the known side effects in the long-term usage, including: increased risk of infection, glucose tolerance, increased healing time of wounds, superficial wounds in the stomach and adrenal suppression [6]. The mechanism of corticosteroid effect on post-dural puncture headache is not well known. It seems that it makes the reabsorption of cerebrospinal fluid from the extradural space better, that increases cerebrospinal fluid [17-18]. To assess pain threshold of pain tolerance and variety of psychological methods are used. In this study, according to the results of previous studies on the effect of corticosteroids in the treatment of post-dural puncture headache, we decided to examine the preventive effect of corticosteroids before spinal anesthesia on the incidence and severity of headache after the surgery.

## Methods

In a double-blind, randomized clinical trial, 80 patients who had undergone the abdominal and lower extremity surgeries without other health problem (ASA I), at Imam Reza hospital in Tabriz, Iran, since July 2015 to March 2016 that required spinal anesthesia, were included in the study. The patients were randomly divided into two groups (group A, 40 patients and group B, 40 patients). The patients were trained on the measurement of pain to manner visual analog scale (VAS). After ethics committee's approval and all the patients' written consent to the use of hydrocortisone, the patients were divided into two groups with simple random sampling. Group A received 2 ml (100 mg hydrocortisone 15 minutes before spinal anesthesia, and group B received 2 ml placebo instead of hydrocortisone. The patients in both groups had similar premedication with fentanyl (1µg/kg) and midazolam (0.02 mg/kg), the postoperative analgesic regimen was similarly chosen in the ward. The patients' post-dural puncture headache was recorded by one medical student who was unaware of the group of patients, in recovery, 12-24-48 hours and one week after surgery, and data were collected by questionnaires.

### Statistical analysis

The data were analyzed using descriptive statistics such as mean, standard deviation, median and percentage. The mean pain intensity at different times in the two groups was used in cases where there was matching of T-test and evaluation parametric test for qualitative-quantity variables of Pearson's chi-square test, Fisher's exact test and Monte Carlo. In case where there wasn't matching non-parametric tests like fisher exact test, x2 test and SPSS 23 software Monte Carlo were used. If  $P=0.05$  or less then it was considered statistically significant.

In order to study qualitative variables  $X^2$ , and quantitative variables t-test was employed. For data analysis, SPSS version 15 was used. If  $P=0.05$  or less then it was considered statistically significant. Data obtained from the study by descriptive statistics (frequency-percentage -mean and standard deviation) were analyzed and the mean difference test for independent groups was employed. For normality of distribution of data Kolmogorov-Smirnov test and Q-Q charts was used.

## Results

Eighty patients were included in this study. The patients in the groups A and B were ASA of physical status

classification I. Among them, 67 patients (83.75%) were males and 13 (16.25%) were female. The gender of patients in the group A was 34 males and 6 females and 33 males and 7 females in group B. No statistically significant difference was found between the genders in the two groups ( $P=0.762$ ). The minimum and maximum age of the patients in the group A was 21 years and 60 years and in the group B was 20 years and 60 years. The mean age of patients was  $40 \pm 13.11$  years in group A and  $38.70 \pm 13.04$  years in group B. There was no statistically significant difference between the mean age of patients in the two groups ( $P=0.658$ ). Information (demographic) related to the patients' general characteristics are presented in (Table 1).

Prevalence of post-dural puncture headache in patients of both groups was measured by a medical student by using VAS in recovery and then in 12, 24, and 48 hours and a week after surgery. None of the patients in both groups had headache in the recovery ( $P=1$ ).

Incidence of post-dural puncture headache was 14 patients (35%) in group A and 12 patients (30%) in group B 12 hours after surgery ( $P=0.633$ ). Incidence of post-dural puncture headache was 20 patients (50%) in group A and 23 patients (57.5%) in group B 24 hours after surgery ( $P=0.579$ ).

Incidence of post-dural puncture headache was 19 patients (47.5%) in group A and 22 patients (55%) in group B 48 hours after surgery ( $P=0.576$ ). Incidence of post-dural puncture headache was 10 patients (25%) in group A and 13 patients (32.5%) in group B a week after surgery ( $P=0.502$ ). There was no statistically significant difference in prevalence of pain at different times after surgery (Table 2).

Rate of mean severity of post-dural puncture headache was measured by VAS in the recovery and the hours of 12- 24 - 48 and a week after surgery.

None of the patients were complaining of post-dural puncture headache in calculating the mean headache severity in patients of both groups in recovery ( $P=1$ ).

The mean severity of post-dural puncture headache was  $1.27 \pm 1.85$  in group A and  $2.02 \pm 3.46$  in group B 12 hours after surgery respectively ( $P=0.231$ ). The mean severity of post-dural puncture headache was  $2.35 \pm 2.71$  in group A and  $3.02 \pm 3.44$  in group B 24 hours after surgery respectively ( $P=0.344$ ). The mean severity of post-dural puncture headache was  $2.28 \pm 2.85$  in group A and  $2.92 \pm 3.22$  in group B 24 hours after surgery respectively ( $P=0.351$ ). The mean severity of post-dural puncture headache was  $0.97 \pm 1.99$  in group A and  $1.47 \pm 2.27$  in group B a week after surgery respectively ( $P=0.302$ ). There was no statistically significant difference in pain severity average at different times after surgery (Table 3).

In the patients of group A, none of the known side effects of hydrocortisone, including anaphylactic reaction, blurred vision, and shortness of breath and or symptoms of meningitis were seen.

**Table 1- Some demographic characteristics of patients in both groups.**

Parameters	Group A	Group B	P values
Patients (n)	40	40	
Male (%)	85.5	82.5	0.762
Female (%)	14.5	17.5	0.762
Total	100	100	0.762

**Table 2- Mean \*severity of headache after spinal anesthesia in both groups**

Parameters	Group A	Group B	P values
Recovery	0	0	1
12 hours after surgery	1.27±1.85	2.02±3.46	0.231
24 hours after surgery	2.35±2.71	3.02±3.44	0.344
48 hours after surgery	2.28±2.85	2.92±3.22	0.351
A week	0.97±1.99	1.47±2.27	0.3.2

\*Results are shown as Mean ± SD.

**Table 3- Prevalence of headache in different times in both groups**

Parameters	Group A (With headache, n)	Group B (With headache, n)	P value
Recovery	0	0	1
12 hours after surgery	14	12	0.633
24 hours after surgery	20	23	0.579
48 hours after surgery	19	22	0.576
A week	10	13	0.502

## Discussion

In this study, despite the selections of random samples and avoiding the impact of gender selection, in order to avoid selection bias, the majority of patients in both groups were male, but there was no statistically significant difference gender distribution between the two groups ( $P=0.762$ ). Distribution of surgery between two groups has not statistically significant difference ( $P=0.289$ ). In the present study the prophylactic effect of intravenous hydrocortisone was examined. The results showed that prophylactic administration of intravenous hydrocortisone had no effect on the prevention of headache after spinal anesthesia in comparison with placebo ( $P= 0.502$ ). In a study that was conducted by Yang B, and colleagues [19], which showed that prophylactic administration of intravenous dexamethasone had no effect in protecting against post-dural puncture headache.

In the Yang B, and colleagues [19], study dexamethasone not only did not reduce headache in the 24 hours after surgery, but also it increased headache. In this study, the incidence of headache was higher in the intervention group in 12 hours after surgery than placebo group, but the difference was not statistically significant ( $P=0.91$ ). It seems that corticosteroids inhibit inflammation at the site of perforation of duramater in the acute phase, causing more leakage of cerebrospinal fluid and exacerbate headaches. In the study of Manouchehrian and colleagues, the prophylactic effect of intravenous dexamethasone in the prevention of headache after spinal anesthesia was assessed, 12.2 percent of the intervention group and 23.6% of placebo group had headache ( $P=0/03$ ). Yousefshahi and colleagues [16] reported that prophylactic administration of dexamethasone increases the severity and incidence of the post-dural

puncture headache, but Hamzei and colleagues [6] reported that prophylactic dexamethasone was significantly effective in reducing the incidence of the post-dural puncture headache in 24 hours ( $P=0/01$ ) and a week later ( $P= 0/001$ ).

In Yousefshahi and colleagues [16] study 4 different anesthesiologists had done spinal anesthesia and in some patients was performed more than once trying to puncture of duramater, and Hamzei and colleagues [6] study was not double-blind. The previously mentioned problems could lead to disproportionate results. In this study, patients with more than two attempts of spinal anesthesia were excluded from the study; the study was conducted as a double-blind.

The effect of corticosteroids on intracranial hypotension syndrome has been demonstrated. This syndrome is usually known with low cerebrospinal fluid pressure and severe froto- occipital headache and worse with standing and improves with the consumption of analgesics. Headache quality and response to treatment is very similar to the post-dural puncture headache. Pascual and colleagues [20] study has shown that headache of patients with intracranial hypotension within 2 to 4 weeks after treatment with prednisone is better. Mechanisms of corticosteroids are not entirely clear for treatment of post-puncture headache and intracranial hypotension headache. Patients with intracranial hypotension are marked with variable amounts of cerebrospinal fluid in extradural space and dilated epidural veins in the upper area of neck [21]. Steroids may improve the absorption of cerebrospinal fluid from extradural space and increased the volume of cerebrospinal fluid [22]. Short-term use of short-acting corticosteroids may exhibit an allergic reaction just like other drugs but there have been no long-term side effects and as a result, they are

more acceptable for injection [23]. It seems that analgesic effect of steroids on the post-dural puncture headache are related to anti-inflammatory effects at the site of duramater puncture. Inflammatory mediators secreted by immune cells in the recovery phase of the duramater in perforated place, spread in the cerebrospinal fluid and stimulate pain receptors. Steroids may reduce headaches by reducing inflammatory mediators. Steroids reduce the production of arachidonic acid through inhibition of phospholipase activity, which ultimately reduces the production of prostaglandins such as PGE<sub>2</sub>, PGI<sub>2</sub> and the leukotrienes [24]. Corticosteroids also reduce the production of inflammatory cytokinins such as IL2 and IL1 or TNF [25]. It seems that corticosteroids with this mechanism extended the inflammatory process caused by leakage of cerebrospinal fluid and the headache.

Suggestions: Due to the low number of patients in this study and the same dose of drug for all patients and perhaps low used dose, it is recommended that to achieve better results, the studies are done with more patients and with higher doses of medication or dose in milligrams per kg.

## Acknowledgement

We would like to express our sincere gratitude to Tabriz University of Medical Sciences for financing (grant number 5/4/1446) this study.10.5.2014.

## References

1. Jacobus CH. Does Bed Rest Prevent Post-Lumbar Puncture Headache? *Ann Emerg Med.* 2012; 59(2): 139-40.
2. Frank RL. Lumbar Puncture and post – dural puncture headaches: implications for emergency physician. *J Emerg Med.* 2008;

- 35(2):149-57.
3. Turnbull D, Shepherd DB. post – dural puncture headaches: pathogenesis, Prevention and treatment. *Br J Anaesth.* 2003; 91(5):718-29.
  4. Apfel C, Saxena A, Cakmak kaya OS, Gaiser R, George E, Radke O. Prevention of postdural puncture headache after accidental dural puncture: a quantitative systematic review. *Br J Anaesth.* 2010; 105(3):255-63.
  5. Charsley mm, Abram SE. The injection of intrathecal normal saline reduces the severity of postdural puncture headache. *Reg Anesth Pain Med.* 2001; 26(4):301-5.
  6. Hamzei A, Bashiri Moghaddam M, pasban Noghahi S. Effect of dexamethasone on incidence of headache after spinal anesthesia in cesarean section. A single blind randomized controlled trial. *Saudi Med J.* 2012; 33(9): 948-53.
  7. Boyle JA, Stocks GM. Post-dural puncture headache in the parturient – an update. *Anaesthesia & Intensive Care Medicine.* 2010; 11 (8): 302-4.
  8. Alam MR, Raheen MR, Iqbal KM, Chowdhury MRA. Headache following spinal anaesthesia: a review on recent update. *J Bangladesh Coll Phys Surg.* 2011; 29 (1): 32-40.
  9. Ergün U, Say B, Ozer G, Tunc T, Sen M, Tüfekcioglu S, et al. Intravenous theophylline decreases post – dural puncture headaches. *J Clin Neurosci.* 2008; 15(10): 1102-4.
  10. Huseyinoglu U, Huseyinoglu N, Aygun H, Sulu B. Effect of pregabalin on post – dural puncture headache following spinal anaesthesia and lumbar puncture. *J Clin Neurosci.* 2011; 18(10):1365-8.
  11. Rahmawy, Ghada El, Doaa Rashwan, Nashwa NM. The efficacy of preoperative pregabalin on reduction of the incidence and severity of postdural puncture headache after spinal anesthesia. *Egyptian journal of Anesthesia.* 2013; 29 (4): 357.
  12. Basurto Ona X, Uriona Tuma SM, Martinez Garcia L, Sola I, Bonfill Cosp X. Drug therapy for preventing post – dural puncture headache. *Cochrane Database Syst Rev.* 2013; 28 (2): CD001792.
  13. Ghaleb A, Arjang K, Devanand M. post – dural puncture headache. *Int J Gen Med.* 2012; 5: 45–51.
  14. Doroudian MR, Norouzi M, Esmaili M, Tanhaeivash R. Dexamethasone in preventing post – dural puncture headaches: a randomized, double – blind, placebo – controlled trial. *Acta Anaesthesiol Belg.* 2011; 62(3):143-6.
  15. Alam MR, Rahman MA, Ershad R. Role of very short-term intravenous hydrocortisone in reducing postdural puncture headache. *J Anaesthesiol Clin Pharmacol.* 2012; 28 (2):190-3.
  16. 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(4):345-50.
  17. Hong M, Shah Gv, Adams Km, Turner Rs, Foster NI. Spontaneous intracranial hypotension causing reversible frontotemporal dementia. *Neurology.* 2002; 58(8):1285-7.
  18. Gentile S, Giudice R L, Martino PD, Rainero I, Pinessi L. Headache attributed to spontaneous low CSF pressure: report of three cases responsive to corticosteroids. *Eur J Neurol.* 2004; 11(12):849-51.
  19. Yang B, Li DL, Dong P, Zhang XY, Zhang L, Yu JG. Effect of dexamethasone on the incidence of post-dural puncture headache after spinal anesthesia: a randomized, double-blind, placebo-controlled trial and a meta-analysis. *Acta Neurol Belg.* 2015; 115(1):59-67.
  20. Pascual LF, Santos S, Escalza I, Iniguez C, Morales – Asin F. Spontaneous intracranial hypotension: Quick clinical and magnetic resonance imaging response to corticosteroids. A case report. *Headache.* 2002; 42 (5): 359-61.
  21. Bezov D, Lipton RB, Ashina S. post-dural puncture headaches: Diagnosis, Epidemiology, Etiology, and pathophysiology. *Headache.* 2010; 50 (7) 1144-52.
  22. Miyazawa K, Shiga Y, Hasegawa T, Endoh M, Okita N, Higano S, et al. CSF hypovolemia vs. intracranial hypotension in spontaneous intracranial hypotension syndrome. *Neurology.* 2003; 60 (6): 941-7.
  23. Graeme PC, Paterson ED, Keenan F, Nath S, Watt SJ. An unexpected response to intravenous hydrocortisone succinate in an asthmatic patient. *Br J Clin Pharmacol.* 2005; 60 (3): 342.
  24. Gilron I. Corticosteroids in postoperative pain management: Future research direction for a multifaceted therapy. *Acta Anaesthesiol Scand.* 2004; 48(10): 1221-2
  25. Elenkov IJ, Chrousos GP. Stress Hormones, Proinflammatory and Anti inflammatory Cytokines, and Autoimmunity. *Ann N y Acad Sci.* 2002; 966: 290-303.