RESEARCH ARTICLE

Effect of Intravenous Meperidine in Controlling Post Dural Puncture Headache

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Background: Spinal anesthesia is usually applied for urologic surgeries. Postdural puncture headache (PDPH) is among common complications which has not been reduced during last years despite all advances in the field of medicine. Therapeutic effects of conventional therapy (paracetamol and novaphen) are being compared to intravenous meperidine in patients suffering from PDPH.

Methods: One hundred patients, with PDPH following spinal anesthesia for transurethral lithotripsy were enrolled and randomly allocated to receive conventional (group C) or intravenous meperidine (group P) (20 mg every 5min up to 120mg or when the pain was decreased to less than 3/10).

Results: Time interval to reach acceptable headache was 3 hours in group P compared to 8 hours in group C. Group P patients received statistically significantly less amount of paracetamol and novaphen, and experienced fewer episodes of severe headaches in 48 hours after the start of treatment, compared to group C.

Conclusion: Short term intravenous meperidine compared to conventional therapy resulted in more rapid and effective outcomes.

Keywords: meperidine; acetaminophen; post-dural puncture headache

Post dural puncture headache (PDPH) is an excruciating and non-radiating headache that involves up to 40% of patients after spinal anesthesia [1]. In most cases headache does not initiate right after spinal puncture, but begins at 24-48 hours after spinal puncture. The location of pain is most commonly at frontal or occipital area. Headache is aggravated by sitting or standing [1]. Many theories exist regarding the pathophysiology of PDPH such as loss of cerebrospinal fluid into the epidural space with a decrease in cerebrospinal fluid pressure and downward movement of the brain and traction on the dura, but it is still controversial [2-3]. There are several risk factors contributing to the post-lumbar puncture headache [4]. Pressure on abdomen by hand in standing position, may transiently decrease headache due to intra cranial pressure rising [5]. Spontaneous recovery within 5 days occurs in most cases, but PDPH could last up to many months [6]. However, during this time patient is forced to stay at home due to severe positional headache or risk of falling down. This will decrease patients' ability to work and increase work days off and have a significant effect on the patient's postoperative wellbeing [7]. By using current treatments, the course of disease will decrease to 2 weeks.

Numerous pharmaceutical drugs have been proposed to treat PDPH but there are still some uncertainties about their clinical effectiveness [8]. Most popular treatments are extra liquid intake, regular pain killers and Cosyntropin which may decrease headache severity to less than 50% in 1 week [9]. The effect of regular pain killers on rate and amount of decreasing pain score have not been compared to the effect of short term meperidine therapies. The rational of this research is the high incidence rate of PDPH after spinal anesthesia, patients' loss of work days; side effects of blood patch, and cost effectiveness and simplicity of administering meperidine instead of long term ineffective regular pain killers. We compared the effect of oral acetaminophen and novafen with intravenous meperidine in decreasing post-dural puncture headache in this study.

Methods

The study was reviewed and approved by the Shahid Beheshti University of medical sciences ethics committee and performed accordingly. Information about the study was given comprehensively both orally and in written form to all patients or their accompanying adult. They gave their informed written consents prior to their inclusion in the study. This study was designed as a double blinded randomized clinical trial. One hundred cases were randomly assigned to two groups of study, each had 50 cases based on accidental numbers assigned by computer to each case. In a randomized double blinded clinical trial, patients with spinal

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anesthesia were enrolled in the study and randomly assigned to one of groups of study.

Inclusion criteria were patients candidate for elective trans-uretheral lithotripsy (TUL) surgery, American Society of Anesthesiology physical status classification (ASA) 1 and 2, no history of drug abuse, no severe underlying disease, and age between 30-60 years. Exclusion criteria were headache after 72 hours post spinal and patients' lack of cooperation.

In meperidine group, 1.5 mg/kg meperidine was administered as a titrated dose of 20 mg every 2 hours. Two liter of normal saline was also infused. If patient had nausea and vomiting, 4 mg of ondansetrone was administered. Thereafter, patients were advised to use acetaminophen as pain killer and report the amount of acetaminophen intake to us. Patients in this group were not allowed to use novafen if pain lingered. In conventional group, patients were advised to ingest oral acetaminophen every 6 hours and novafen every 8 hours. Two liter of normal saline was administered to the patient. Patients with Numerical Rating Scale (NRS) >5 in meperidine group received rescue dose of morphine with respiratory monitoring. In both groups, blood patch treatment was considered if patients were unable to tolerate the pain during next 24 hours.

PDPH was diagnosed based on international headache society (IHS) definition. PDPH was diagnosed as a headache that was post dural puncture and started 15 minutes after standing up and diminished 15 minutes after lying down. It is accompanied with one of signs of tinnitus, neck stiffness, photophobia, or nausea vomiting.

Patients candidate for elective TUL were admitted to the unit and after complete history taking, patients were scheduled for spinal anesthesia. Appropriate IV line was taken and 500 cc of normal saline was administered before spinal anesthesia. Patients monitoring included ECG, heart rate and oxygen saturation with pulse oxymetery. Atropine 0.07 mg/kg was administered as premedication. Spinal anesthesia was performed using a Quinke 25 gage needle at L3-4 or L4-5 lumbar spine level, after clear CSF. Drug was bupivacaine 3 cc of 0.5% concentration.

Patients with PDPH and NRS >3 were advised to return to clinic for further assessments and treatments and then patients were admitted to ward. NRS is a measure of pain scale from 0 to 10 where 0 is the least and 10 is the worst pain [10].

The onset of pain relief was measured from start of treatment and when NRS<3. The number of times when NRS>3 in next 24 and 48 hours was also recorded. Amount of acetaminophen used during next 24 and 48 hours was also recorded in both groups. Failure rate was also measured if patient's headache did not respond to the considered therapy. All demographic variables were extracted from patient's file and patient's own interview in preoperative visit. All variables were recorded in a data sheet.

Statistical calculations were conducted using SPSS 22 (Chicago, IL, USA). The parametric variables were presented as mean±SD and were analyzed by t-test; non-parametric variables were analyzed by Chi-Square, Fisher Exact test, or Kruskal-Wallis -test. P<0.05 was considered as statistically significant. Sample size was estimated using sample size calculator software with 95% confidence interval, p=0.05 and power of 80% and difference between two groups of 30% in primary outcome based on pilot study.

Results

Total number of 100 patients was enrolled in the study and divided randomly into two groups of meperidine and conventional. Interestingly, all patients enrolled were male patients. Other demographic variable are depicted in (Table 1) which were not significantly different between two groups of study.

Time to achieve NRS< 3 was 3 hours in meperidine group and 8 hours in conventional group which was significantly different in two groups (Table 2). None of the patients in meperidine group had headache with NRS>5 and did not receive morphine. Number of times patient had a headache with NRS>3 (Frequency of headache) during next 24 hours was significantly lower in meperidine group compared to conventional group (p=0.003). Frequency of headache with NRS>3 occurrence during next 8 hours was also significantly lower in meperidine group compared to conventional group (p=0.016) (Table 2).

Total dose of acetaminophen per 24 hours was also significantly lower in meperidine group compare to conventional group (p=0.002) (Table3). Total dose of novafen per 24 hours administered was also significantly lower in meperidine group compared to conventional group with no side effects (p=0.001) (Table 3).

Table 1- Age, headache NRS score and time to initiate headache after spinal anesthesia

Characteristics	Meperidine (n=50)	Conventional (n=50)	p-value
Age (y)	35.6±15	36.6±9	0.6
Headache NRS score before drug administration	6.2±1.4	6.1±1.1	0.7
Time to initiate headache after SA (h)	19±7	20±8	0.5

SA: spinal anesthesia; NRS: Numerical rating scale

Table 2- Time to achieve NRS<3 and frequency of headache in 24 and 48 hours after administration of drug

Characteristics	Meperidine (n=50)	Conventional (n=50)	p-value
Time to achieve NRS<3	3±1	8±3	<0.0001
Frequency of headache with NRS>3 /24 h	0.5±0.6	1±1	0.003
Frequency of headache with NRS>3 /48 h	0.08±0. 2	0.3±0.4	0.016

Table 3- Total dose of Acetaminophen and Novafen (mg) intake per 24 hours after drug

Characteristics	Meperidine (n=50)	Conventional (n=50)	p-value
Total dose of Acetaminophen (mg) /24 h	912±388	1232±575	0.002
Total dose of Novafen (mg) intake/24 h	0.5±0.2	0.9±0.7	0.001

Discussion

The interesting results showed that severe headache (NRS> 3) in meperidine group could be relieved in shorter time compared to conventional therapies. Duration of headache relief was 3 hours in meperidine group compared to 8 hours in conventional group.

Number of times patient had a headache with NRS>3 was significantly lower in meperidine group compared to conventional group. This demonstrated that patients could have a headache with NRS>3 in both groups but meperidine could be more effective in controlling PDPH. This indicates that even in meperidine group some patients had NRS>3 during next 24 hours, and meperidine is not a treatment with hundred percent success rate. Although epidural blood patch (EBP) is a treatment with higher success rate of approximately 90% [11], however there are some reports of adverse effects of epidural patch. In addition, it has the same side effects as every epidural technique. On the contrary, there are some reports of low success rate of EBP in which following treatment with one epidural blood patch 33% of patients obtained complete and permanent relief, 50% partial relief and 12% no relief [12]. Patients vary tremendously in their response to EBP and clinicians have been disinclined to use it routinely. These facts and considering the sterility and timing needed for EBP procedure, we introduce meperidine as a therapy with higher success rate than conventional modules. Nevertheless, respiratory monitoring due to risk of respiratory depression is advised for every patient administering opioids.

One interesting result was that meperidine was effective enough to control pain as none of patients needed morphine. This may be due to the fact that meperidine has affinity to μ receptor [13]. In addition, previous research suggests that the action of meperidine is in part mediated by non–μ-opioid receptors. Meperidine possesses considerable κ activity and also has central anticholinergic activity [12].

Some research showed the efficacy of prophylactic epidural morphine while fentanyl did not. However, this is an invasive procedure and needs the precautions of an EBP. Several other studies have focused on treatment options. Basurto et al. showed effectiveness of caffeine for treating PDPH compared to placebo. Gabapentin, theophylline and hydrocortisone have also shown a decrease in pain severity scores when compared with placebo or conventional care. However, they found no conclusive evidence for sumatriptan and ACTH [14]. Ten years later, the same group explained that none of the new included studies have provided additional information to change the conclusions of the last published version of the original cochrane review [15]. Patients who received pregabalin had significantly lower visual analog scale scores after the second day of treatment, and had significantly lower diclofenac sodium requirements [16].

It is unknown whether opioids could diminish PDPH headache. In a report, authors successfully treated refractory post-dural puncture headache with low doses of the strong opioid piritramide (equal to 10 mg of morphine) [17]. They proposed that opioids should be included in the guideline of PDPH treatment and may represent a promising tool in the management of PDPH. Other study indicated that opioids block the nociceptive neurotransmission within the trigeminal nucleus caudalis and in addition inhibit neurogenic dural vasodilation via an action on mu-opioid receptors located on trigeminal sensory fibres innervating duralblood vessels. These peripheral and central actions are similar to those of the 'triptan' 5-HT (1B/1D) agonists and could account for the anti-migraine actions of opioids [18]. All included patients in our study were male and therefore inadvertently this could be a possible source of bias [19]. Besides, we only used Quinke needle and generalization of our results to other type of spinal needle is not appropriate.

In conclusion, meperidine could be a suitable alternative for conventional therapies in diminishing PDPH. Intravenous meperidine is an applicable and easy to use therapy for management of PDPH; besides, time to decrease in severity of headache was shorter and frequency of severe headache was lower in meperidine compared to conventional pain killers. However, meperidine should be used for short time and under respiratory monitoring.

References

1. Thomas SR, Jamieson DR, Muir KW. Randomised controlled trial of atraumatic versus standard needles for diagnostic lumbar puncture. BMJ. 2000; 321(7267):986–90.
2. Vallejo MC, Mandell GL, Sabo DP, Ramanathan S. Postdural puncture headache: a randomized comparison of five spinal needles in obstetric patients. Anesth Analg. 2000; 91(4):916–20.
3. Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. Br J Anaesth. 2003; 91(5):718-29.
4. Bateman RJ, Morris JC. Factors Contributing to the Post-Lumbar Puncture Headache. JAMA Neurol. 2015; 72(7):835.
5. Robert L. Frank, MD, FAAEM, Lumbar Puncture and Post-Dural Puncture Headaches: Implications for the Emergency Physician. J Emerg Med. 2008; 35(2):149-157.
6. Barbosa FT. [Post-dural headache with seven months duration: case report]. Rev Bras Anestesiol. 2011; 61(3):355–9.
7. Jabbari A, Alijanpour E, Mir M, Bani Hashem N, Rabiea SM, Rupani MA.Post spinal puncture headache, an old problem and new concepts: review of articles about predisposing factors. Caspian J Intern Med. 2013; 4(1):595-602.
8. Choi T-LP. Management of Postdural puncture headache. Techniq reg anesth pain. 2001; 5(1):41-5.
9. Wight JM, Kalidindi R. Management of post-dural puncture headache in late pregnancy before the onset of labour. Int J Obstet Anesth. 2016; 25:92-3.
10. Gharaei B, Jafari A, Aghamohammadi H, Kamranmanesh M, Poorzamani M, Elyassi H, edt al. Opioid-sparing effect of preemptive bolus low-dose ketamine for moderate sedation in opioid abusers undergoing extracorporeal shock wave lithotripsy: a randomized clinical trial. Anesth Analg. 2013; 116 (1), 75-80.
11. Boonmak P, Boonmak S. Epidural blood patching for preventing and treating post-dural puncture headache. Cochrane Database Syst Rev. 2010; (1):CD001791.
12. Williams EJ, Beaulieu P, Fawcett WJ, Jenkins JG. Efficacy of epidural blood patch in the obstetric population. Int J Obstet Anesth. 1999; 8(2):105-9.
13. Kurz M, Belani K, Sessler DI, Kurz A, Larson MD, Schroeder Mm, et al. Naloxone, meperidine, and shivering. Anesthesiology. 1993; 79(6):1193-201.
14. Basurto Ona X, Martínez García L, Solà I, Bonfill Cosp X. Drug therapy for treating post-dural puncture headache. Cochrane Database Syst Rev. 2011; (8):CD007887.
15. Basurto Ona X, Osorio D, Bonfill Cosp X. Drug therapy for treating post-dural puncture headache. Cochrane Database Syst Rev. 2015; 7:CD007887.
16. Huseyinoglu U, Huseyinoglu N, Hamurtekin E, Aygun H, Sulu B. Effect of pregabalin on post-dural-puncture headache following spinal anesthesia and lumbar puncture. J Clin Neurosci. 2011; 18(10):1365-8.
17. Rachinger-Adam B, Kraft E, Luchting B, Woehrle T, Hasbargen U, Krueger W, et al. Treatment of refractory post-dural puncture headache with low doses of the strong opioid piritramide. Br J Anaesth. 2013; 110(3):490-1.
18. Williamson DJ, Shepheard SL, Cook DA, Hargreaves RJ, Hill RG,

Cumberbatch MJ. Role of opioid receptors in neurogenic dural vasodilation and sensitization of trigeminal neurones in anaesthetized rats. Br J Pharmacol. 2001; 133(6):807-14.

19. Wrobel M, Volk T. Post-dural puncture headache. Anesth Pain Med. 2012; 1(4):273-4.