JOURNAL of ANESTHESIA and PERIOPERATIVE MEDICINE

Case Report

Intractable Post-Dural Puncture Headache (PDPH): A Challenging Case Report

Hanwool Ryan Choi, Daniel Fernandez, Alexander Hincker, and Chris Lee

ABSTRACT

Post-dural puncture headache (PDPH) is a debilitating condition that can complicate a woman's postpartum course. PDPH is commonly known to present as a positional headache in a fontal-occipital distribution that is associated with photophobia and tinnitus. However, making the diagnosis of PDPH is not always so clear-cut, and various diagnoses for postpartum headache should be ruled out prior to initiating PDPH treatments. The gold standard treatment for post-dural puncture headache is an epidural blood patch. Nevertheless, performing a blood patch may be contraindicated or may even be ineffective. Thus, it is crucial to be aware of alternative treatment modalities, ranging from pharmacologic to interventional options. In this report, we present a case of a 31-year-old woman with a prolonged course of postpartum headache that was difficult to treat. Our aim is to review and discuss the latest updates on PDPH, including its risk factors, differential diagnosis, and treatment modalities.

From the Department of Anesthesiology, Washington University School of Medicine in St. Louis, MO, USA.

Correspondence to Dr. Hanwool Ryan Choi at hchoi22@wustl.edu.

Citation: Hanwool Ryan Choi, Daniel Fernandez, Alexander Hincker, Chris Lee. Intractable Post-Dural Puncture Headache (PDPH): A Challenging Case Report. *J Anesth Perioper Med* 2019; 6: 28- 34.

doi: 10.24015/JAPM.2019.0008

Since the advent of neuraxial analgesia, the complication of a post-dural puncture headache has proven a challenge to diagnose and manage. While neuraxial anesthesia is usually a quick and efficacious solution for multiple situations, the complication of a post-dural puncture headache can haunt patients. Developments on needle design have reduced the incidence of post-dural puncture headache, but it remains an important complication from the technique. This case report details a particularly challenging case of postpartum headache and the importance of a broad differential diagnosis and familiarity with multiple management strategies.

Case Presentation

The patient is a 31-year-old woman, gravida 7 para 5, 98 kg, 63 inches, and body mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 38, with a history of migraines and papillary thyroid cancer status post total thyroidectomy who presented for 5th repeat cesarean delivery at 36.2 weeks of gestational age due to concern for recurrent uterine dehiscence and breech presentation. Given her history of four prior cesarean deliveries, she was offered combined spinal epidural anesthesia

(CSE). A 17-gauge Tuohy needle was advanced at the L3-4 level. A loss of resistance was obtained at a depth of 8 cm, then a 25 g Whitacre spinal needle was advanced through the Tuohy needle. However, there was no return of cerebral spinal fluid through the spinal needle. Therefore, an epidural catheter was threaded, followed by an 18 mL bolus of 2% lidocaine in divided doses. A surgical block was obtained to the T4 level. The remainder of the cesarean delivery and bilateral tubal ligations was unremarkable.

On postoperative day (POD) 3, the patient reported a numerical rating scale (NRS) pain score of 8/10 severity positional headache. A headache was described as bilateral pressure with more prominent throbbing in the right parietal region. It was increased in intensity when sitting, standing, or ambulating, and improved quickly when lying supine. She noted associated photophobia but denied phonophobia, nausea, or vomiting. Her initial vital signs were within normal limits. Conservative management consisting of intravenous fluid, caffeine, acetaminophen, and ibuprofen failed to provide any relief. Subsequently, a sphenopalatine ganglion block was performed with 10 mL of 0.25% bupivacaine by pain management team without any relief on POD 4. On POD 5, the patient received an epidural blood patch with 20 mL of autologous blood, and her headache improved from NRS of 10/10 to 6/10. She was discharged on the same day with a residual, but tolerable, headache.

Approximately two weeks from the first blood patch, the patient presented to OB/GYN triage at Washington University Medical Center with nausea and worsening positional headache. She endorsed that her headache felt very different than her usual migraines, which were more throbbing and diffuse in nature. Neurology was consulted to help to determine if headaches represent recurrent post-dural puncture headache after blood patch. Neurology consults recommended a magnetic resonance angiogram (MRA), which was unremarkable, and her headache was still deemed to be related to the epidural placement. She then received a second blood patch with improved symptoms.

Three days from the second epidural blood patch, she presented again to the OB/GYN triage at Washington University Medical Center with a recurrent headache accompanied by blurry vision and subjective fevers. Her vital signs on admission, including a blood pressure of 132/74 mm Hg, heart rate of 85 beats per minute, respiratory rate of 18 breaths per minute, and temperature of 36.4 degrees Celsius, were within normal limits. At this point, we speculated that her recurrent headache might not be from the dural-puncture, as it did not resolve after repeat blood patches. Instead, a new presentation of her prior migraines, in the setting of medication changes and subjective fevers, was considered as a top potential diagnosis. Subsequently, the neurology team recommended treating her headache with intravenous prochlorperazine 10 mg every 6 hours, venlafaxine 37.5 mg daily, ketorolac 30 mg, and magnesium as well as acetaminophen 650 mg PO every 6 hours. A comprehensive fever workup, including a lumbar puncture with cerebrospinal fluid (CSF) analysis, was unremarkable. A normal opening pressure of 21 cm H2O on lumbar puncture ruled out any etiologies involving intracranial hypertension or hypotension. Repeat imaging was deferred given her very recent unremarkable MRA result. Her headache resolved soon after the initiation of medical therapy and she was discharged with follow-up in the neurology headache clinic.

Despite the improvement of her headache, she continued to have fevers at home and began having purulent discharge from the incisional site. Therefore, a computed tomography (CT) scan of the abdominal was performed which demonstrated a rim-enhancing fluid collection in the subcutaneous tissues of the anterior abdomen/pelvis wall along the incision, representing a postoperative seroma versus abscess. She was taken to the operating room for a washout, and her fever resolved, as well. See the Figure for a summary of the case events.

Discussion

Post-dural puncture headache (PDPH) typically occurs after a dural puncture resulting in CSF loss, causing intracranial hypotension and a reduction of overall CSF volume (1, 2). This leads to decreased cerebral cushion, which causes traction on intracranial structures and results in the classic positional headache. The cerebral vascular may also

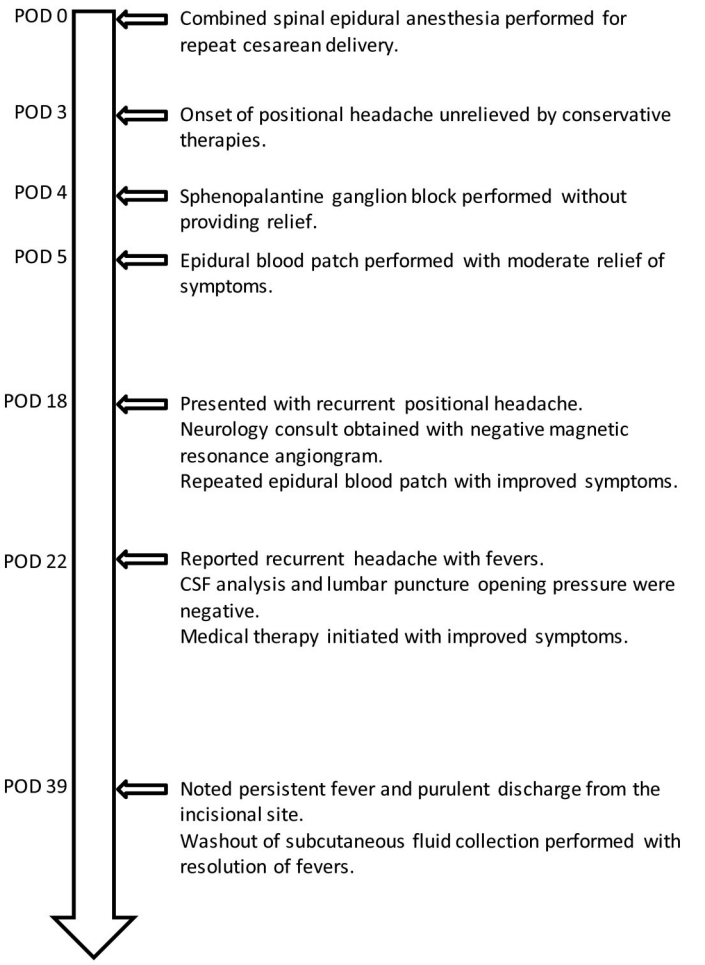

Figure. Timeline of Important Clinical Events During Management of The Patient.
postoperative day, POD; cerebrospinal fluid, CSF.

play a role, as CSF loss causes a compensatory increase in intracerebral blood volume due to the pressure gradient (1, 2). These disruptions can explain the secondary features. Visual disturbances result from traction on the cranial nerves responsible for ocular movement, most notably cranial nerve six (CN VI) as it has a long intracranial course. Tinnitus is an effect from the communication between the perilymphatic space and the subarachnoid space with resulting low inner ear pressure after the CSF reduction (1).

Risk Factors

Our patient possessed multiple classic risk factors for PDPH, including female sex, pregnancy, young age, and history of migraines. Some of the reported patient risk factors, such as low BMI (3, 4), non-smokers (5), and less experienced providers performing the procedure (6), are controversial. In contrast, needle size and design are well-established factors influencing the likelihood of PDPH formation after a dural puncture. Cutting needles (Quincke) are associated with a higher incidence of PDPH compared to non-cutting needles (Sprotte and Whitacre). Smaller diameter needles that create a smaller dural puncture can reduce the incidence of PDPH, though this relationship is more definitive with cutting than with pencil-point needles (7). Additionally, inserting the needle with the bevel facing parallel to the dural fibers and spreading them, rather perpendicularly inserting the needle and cutting the fibers, can reduce the incidence of PDPH (8).

Differential Diagnosis

Our patient had a case of postpartum headache with abnormal presentations, thus posing some challenges in making a clear diagnosis. Table 1 illustrates other considerations in the differential diagnosis when approaching this and similar patients. A classic presentation of PDPH is a dull or a throbbing headache in a frontal-occipital distribution. The headache is positional, i. e., relieved by lying down and exacerbated by standing or sitting. It can be associated with neck stiffness, photophobia, dizziness, auditory disturbances, and nausea. Typically, PDPH presents within 72 hours of the dural puncture and resolves within 1 week even without any treatment. If a blood patch is performed, the headache should resolve within 48 hours after the intervention.

Our patient's headache with pronounced right-temporal predominance that emerged 7 days after the epidural placement did not resemble the classic frontal-occipital PDPH distribution. Furthermore, she had an unusually long course of a headache that was resistant to conservative treatments and repeat blood patches. On the other hand, the headache was clearly positional in nature and did respond briefly to blood patches. She concurrently had an occult post-cesarean section incisional abscess which produced fevers and could thus itself cause headache. In light of this, it is likely that this patient's headache was multifactorial, with the initial headache likely having a

Table 1. Differential Diagnosis for Post-Dural Puncture Headache.
Post-Dural Puncture Headache (PDPH) • Dull, throbbing; front-occipital • The hallmark is **positional** (**improved supine, worse sitting/standing**) • Neurological symptoms: **nuchal rigidity, photophobia, dizziness,** and **auditory disturbances**
Tension Headache • Typically bilateral, non-throbbing, no aura
Migraine Headache • Typically unilateral, throbbing; photophobia and/or phonophobia, +/- aura (visual disturbances, numbness, weakness, speech disturbances)
Meningitis • Nuchal rigidity, photophobia, fever
Pre-eclampsia (in peripartum period) • Hypertension, proteinuria, +/- hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome
Cerebral Venous Thrombosis • Positional, seizures, visual disturbances, focal neurologic deficits
Pneumocephalus • Sudden appearance of headache symptoms, spontaneous resolution within several hours, loss of resistance to air technique during epidural placement
Post-partum Depression • Post-partum headache, depressive mood changes, anhedonia, fatigue, psychomotor slowing
Rebound Intracranial Hypertension • Severe nausea and vomiting, blurred vision, worse lying down, onset 24-48 hours after epidural blood patch papilledema and/or opening pressure > 20 mm Hg

large contribution from PDPH and the later headaches having less or no such contribution. This case thus illustrates how in situations where the diagnosis of PDPH is unclear, alternative diagnosis needs to be considered for a proper treatment course. In other words, the differential diagnosis of PDPH is broad, and the providers should promptly rule out competing diagnoses in order to avoid more devastating consequences.

Either a tension headache or migraine is responsible for as high as 47% of postpartum headaches (9). Migraine was a top differential for our patient given her previous history of migraines. A migraine headache is characterized by a unilateral headache that is throbbing and often associated with photophobia and phonophobia. Migraines are also sometimes accompanied by auras, such as flashing lights, zigzag lines, temporary blindness, numbness, tingling, limb weakness, and speech disturbances. Although our patient' s initial headache was unilateral without any aura, migraines were a less likely diagnosis because the character of this headache differed from her typical migraine and because it was positional in nature.

Given our patient's febrile episodes, meningitis was considered as a potential culprit of her headache. Meningitis typically presents as a headache with neck stiffness, nuchal rigidity, photophobia, and fever. The diagnosis was ruled out with a negative CSF culture via lumbar puncture.

Pre-eclampsia should be considered when a patient presents with a throbbing headache secondary to cerebral edema that is associated with hypertension, proteinuria, or HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome (9, 10). Furthermore, a CT scan should be performed when a headache secondary to intracranial mass, bleeding, or cerebral infarct is suspected. Of note, our patient did not exhibit any focal neurologic deficits that often accompany the mentioned intracranial etiologies, and her scan showed no evidence of cerebral edema.

Very rarely (less than 1: 10, 000 of pregnancies), cerebral venous thrombosis can cause headaches which can be positional in nature, similar to PDPH. However, it is also typically accompanied by seizures, visual disturbances sec-

Table 2. Summary of Effective Symptomatic/Definitive Treatments for Post-Dural Puncture Headache.
Conservative Measures
• Bed Rest
Methylxanthines
• Caffeine
• Theophylline
Hypothalamic-Pituitary-Adrenal (HPA) Axis Medications
• Hydrocortisone
• Adrenocorticotropic hormone (ACTH) / Cosyntropin
Neuromodulators
• Gabapentin
Invasive Therapies
• Epidural Blood Patch
• Epidural Saline Injection
• Epidural Morphine*
• Acupuncture*
• Greater Occipital Nerve Block*
• Sphenopalatine Ganglion Block*

Treatment modalities found to have some efficacy for symptom management or definitive treatment by our literature review.
*denotes a modality which requires further study.

Table 3. Summary of Post-Dural Puncture Headache Prevention Techniques.
Spinal Needle
• Non-cutting (i.e. Sprotte, Whitacre)
• Diameter (smaller size, i.e. 25 G, 26 G, 27 G)
• Bevel Direction (parallel to dural fibers)
After Recognized Unintentional Dural Puncture
• Epidural Blood Patch
• Epidural Morphine
• IV Cosyntropin
• IV Neostigmine and Atropine

Intravenous, IV.

ondary to papilledema, and focal neurologic deficits (10). Our patient did not have any of these symptoms, and cerebral venous thrombosis was able to be definitively ruled out with a negative MR angiogram (MRA).

Rarely, epidural placement can cause complications other than PDPH, such as pneumocephalus (11). It may result from a large quantity of air inadvertently being injected in the subdural or subarachnoid space with an air-filled loss of resistance syringe. A pneumocephalus headache appears suddenly and spontaneously resolves within several hours, in contrast to the chronic course of this headache (11). As with PDPH, it is worse with sitting, improved with lying down. For our patient, normal saline was used for loss of resistance, thus making the diagnosis of pneumocephalus very unlikely.

Although its symptoms can sometimes be more insidious than other diagnoses listed above, postpartum depression should be considered in a patient presenting with a postpartum headache. Presentations vary widely between patients, but the headache can be the sentinel reported symptom. Per this patient and her physicians, however, her mood was stable, and she lacked other symptoms of a depressive episode such as anhedonia, psychomotor retardation, or fatigue, making the postpartum depression unlikely.

Lastly, rebound intracranial hypertension is a rare complication of epidural blood patching that may often fail to be recognized and may rather be misdiagnosed as refractory post-dural puncture headache (12). The headache is associated with severe nausea, vomiting, and blurred vision. Furthermore, the headaches are worse with lying down, unlike in post-dural puncture headache where the headache improves with lying down (12). The onset of symptoms is usually within 24-48 hours of blood patching. Rebound intracranial hypertension can be diagnosed with objective findings of CSF opening pressure greater 20 cm H_2O and/or papilledema (12).

Treatment in the Setting of Suspected Post-Dural Puncture Headache (PDPH)

Definitive management of post-dural puncture headaches (PDPH) has typically been the application of an epidural blood patch. However, it is important to be aware of other techniques and modalities as an alternative, as epidural blood patches are not benign. These range from conservative, pharmacologic, and invasive treatments such as epidural injections, nerve blocks, and even acupuncture. Being familiar with a variety of therapies, as detailed in Table 2, can aid in the management of PDPH, especially in difficult cases.

Treatment for post-dural puncture headache is important, not only to improve patient quality of life and satisfaction as well as provide symptomatic relief, but because untreated PDPH has rarely associated with complications such as cortical venous thrombosis and subdural hematoma (13). Typically, PDPH is treated conservatively

within the first 24 hours, especially since most cases of PDPH typically resolve within 1 week (1). When managing PDPH, it' s important to evaluate patients daily if admitted, or provide them with contact information and symptoms that would be alarming for a PDPH if managing as an outpatient.

Conservative management focuses on counteracting proposed mechanisms of PDPH pathophysiology, including CSF loss causing traction and caudal displacement of intracranial structures (14) and cerebral vasodilation (13). Hydration therapy was theorized to counteract this loss by increasing CSF production. However, the evidence does not support hydration therapy as an effective treatment modality (15). The prone position or using an abdominal binder is thought to increase intra-abdominal and epidural space pressure, providing some symptomatic relief, however these can be uncomfortable and data does not show a decrease in the length of PDPH (13). Bed rest was only found effective for symptomatic relief but not for treatment of PDPH (15).

Pharmacologic management has produced varied results in the literature but there are a few therapies that have gained favor due to positive study results. Oral analgesics, such as acetaminophen, oxycodone, or combination medications such as butalbital/acetaminophen/caffeine are typically recommended along with the conservative treatment phase since some of these can be obtained over the counter. However, they typically have low success rates at providing relief (13).

The methylxanthines, such as caffeine and theophylline, have been proposed to counteract cerebral vasodilation causing increased cerebral vascular resistance, and decreasing cerebral blood flow and cerebral blood volume (16). Caffeine has been found to reduce pain scores in PDPH (17), but caution should be used in patients with seizure disorders or hypertension. Theophylline has a similar mechanism of action to caffeine, and similarly has been shown to reduce pain scores (17). Thus, it is typically employed in the earlier stages of treatment, even along with some conservative treatment strategies. In addition, recent evidence suggests gabapentin reduces PDPH severity and duration in parturients undergoing cesarean delivery under spinal anesthesia without significant adverse effects on the mother or the newborn (18).

Medications interacting with the hypophyseal-pituitary-adrenal (HPA) axis have also been evaluated as a treatment option, potentially via aldosterone-induced blood volume increase, dural edema, increasing CSF production, or via increasing b-endorphins (13). While hydrocortisone did show a decrease in pain scores (17), it was not shown to decrease the need for an epidural blood patch (13). Adrenocorticotropic hormone (ACTH) and cosyntropin were not found to be effective in treating PDPH (17), though they can decrease the incidence of PDPH development when given prophylactically after a dural puncture, as further discussed below.

Often considered the gold-standard treatment for PDPH, epidural blood patch has been shown to be effective in most cases. There is clear evidence that an epidural blood patch can treat PDPH more definitively than conservative treatments when used after headache develops (1, 2). Symptoms can be expected to resolve within approximately 48 hours after an epidural blood patch (1). However, it is important to be aware of the risk of back pain, radicular pain secondary to epidural inflammatory response with nerve compression, and, more rarely, chronic adhesive arachnoiditis and subdural hematoma (14).

Given the success of epidural blood patches, other epidural injections have also been investigated. Epidural saline has been shown to provide relief, also providing a tamponade effect, but less effective and with higher recurrence rates as compared to an epidural blood patch (13). Hydroxyethyl starch and fibrin glue have also been attempted as epidural injections, however both of these have also had limited effectiveness and require more study (13).

Other emerging therapies have also been investigated as treatment. Acupuncture has shown some effectiveness in small studies, but more study is needed (13). Nerve blocks have also been investigated for efficacy in treating PDPH. Given that the greater occipital nerve is responsible for sensory innervation in the occipital region and often useful for occipital neuralgia, it is a reasonable treatment path and has shown a reduction of pain scores and even cessation of PDPH (19). Sphenopalatine ganglion blocks have also been studied for PDPH treatment, postulated to coun-

Take Home Messages
· While the epidural blood patch remains the gold standard for post-dural puncture headaches (PDPH), there is certainly a variety of treatment options when it comes to patients with PDPH.
· Patients may require a repeat epidural blood patch for treating PDPH.
· Even with a multi-modal approach, as in the case of our patient, PDPH can still be a difficult entity to treat.
· It is important to consider the wide differential diagnosis and to consider assembling a multi-disciplinary team to help aid in the diagnosis and treatment process in difficult to treat cases.

teract cerebral vasodilation via the parasympathetic blockade. This can be done non-invasively with cotton-tip applicators trans-nasally; with 69% of patients not requiring an epidural blood patch after sphenopalatine ganglion block, this is a promising treatment modality (13).

Prevention of Post-Dural Puncture Headaches (PDPH)

In addition to selecting and utilizing needles according to the criteria previously mentioned, including using pencil point versus cutting needles, using smaller gauge needles, and aligning the bevel of the needle with the dural fibers, there are multiple approaches which have been investigated to prevent the development of PDPH. These are summarized in Table 3.

For instance, epidural blood patches (EBP) may decrease PDPH as compared to placebo and epidural saline when used prophylactically, though further study is still warranted (2). Trials of prophylactic epidural steroid injections were not found effective preventing PDPH (20). Epidural morphine was found to reduce the incidence of PDPH and the need for EBP when used prophylactically and therapeutically, but it has not been examined as a stand-alone therapy for PDPH (13).

Lastly, intravenous (IV) medications, such as IV cosyntropin, have demonstrated to reduce PDPH incidence after recognized, unintentional dural puncture (1). Furthermore, a recent study showed that administration of neostigmine and atropine to patients lowered pain scores and avoided the need for epidural blood patch (21). This was postulated to act via antagonization of cerebral vasodilation and stimulation of CSF production. This and other methods above still require more investigation but provide encouraging avenues for future preventive measures.

The authors declare no conflicts of interest.

References

1. Gaiser RR. Postdural puncture headache: A headache for the patient and a headache for the anesthesiologist. *Curr Opin Anaesthesiol* 2013;26(3):296-303.
2. Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. *Br J Anaesth* 2003;91(5):718-29.
3. 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.
4. Peralta F, Higgins N, Lange E, Wong CA, McCarthy RJ. The relationship of body mass index with the incidence of postdural puncture headache in parturients. *Anesth Analg* 2015;121(2):451-6.
5. Dodge HS, Ekhator NN, Jefferson-Wilson L, Fischer M, Jansen I, Horn PS, et al. Cigarette Smokers Have Reduced Risk for Post Dural Puncture Headache. *Pain Physician* 2013;16(1):E25-30.
6. Kuntz KM, Kokmen E, Stevens JC, Miller P, Offord KP, Ho MM. Post Lumbar Puncture Headache: Experience in 501 Consecutive Procedures. *Neurology* 1992;42(10):1884-7.
7. Zorrilla-Vaca A, Mathur V, Wu CL, Grant MC. The impact of spinal needle selection on postdural puncture headache. *Reg Anesth Pain Med* 2018;43(5):502-8.
8. Norris MC, Leighton BL, DeSimone CA. Needle bevel direction and headache after inadvertent dural puncture. *Anesthesiology* 1989;70(5):729-31.
9. Stella CL, Jodicke CD, How HY, Harkness UF, Sibai BM. Postpartum headache: is your work-up complete? *Am J Obstet Gynecol* 2007;196(4):318.e1-7.
10. Bleeker CP, Hendriks IM, Booij LH. Postpartum post-dural puncture headache: is your differential diagnosis complete? *Br J Anaesth* 2004;93(3):461-4.
11. Aida S, Taga K, Yamakura T, Endoh H, Shimoji K. Headache after attempted epidural block: the role of intrathecal air. *Anesthesiology* 1998;88(1):76-81.
12. Kranz PG, Amrhein TJ, Gray L. Rebound Intracranial Hypertension: A Complication of Epidural Blood Patching for Intracranial Hypotension. *AJNR Am J Neuroradiol* 2014;35(6):1237-40.
13. Katz D, Beilin Y. Review of the alternatives to epidural blood patch for treatment of postdural puncture headache in the parturient. *Anesth Analg* 2017;124(4):1219-28.
14. Gaiser RR. Postdural Puncture Headache: An Evidence-Based Approach. *Anesthesiol Clin* 2017;35(1):157-67.
15. Arevalo-Rodriguez I, Ciapponi A, Roqué i Figuls M, Muñoz L, Bonfill Cosp X. Posture and fluids for preventing post-dural puncture headache. *Cochrane Database Syst Rev* 2016;3:CD009199.
16. Camann WR, Murray RS, Mushlin PS, Lambert DH. Effects of oral caffeine on postdural puncture headache. A double-blind, placebo-controlled trial. *Anesth Analg* 1990;70(2):181-4.
17. Basurto Ona X, Osorio D, Bonfill Cosp X. Drug therapy for treating post-dural puncture headache. *Cochrane Database Syst Rev* 2015;(7):CD007887.
18. Nofal WH, Mahmoud MS, Al Alim AA. Does preoperative gabapentin affect the characteristics of postdural puncture headache in parturients undergoing cesarean section with spinal anesthesia? *Saudi J Anaesth* 2014;8(3):359-63.
19. Uyar Türkyilmaz E, Camgöz Eryilmaz N, Aydin Güzey N, Moraloğlu Ö. Bilateral greater occipital nerve block for treatment of post-dural puncture headache after caesarean operations. *Braz J Anesthesiol* 2016;66(5):445-50.
20. Najafi A, Emami S, Khajavi M, Etezadi F, Imani F, Lajevardi M, et al. Is epidural dexamethasone effective in preventing postdural puncture headache? *Acta Anaesthesiol Taiwan* 2014;52(3):95-100.
21. Abdelaal Ahmed Mahmoud A, Mansour AZ, Yassin HM, Hussein HA, Kamal AM, Elayashy M, et al. Addition of Neostigmine and Atropine to Conventional Management of Postdural Puncture Headache: A Randomized Controlled Trial. *Anesth Analg* 2018;127(6):1434-9.