EDITORIAL VIEW

What works for the management of PDPH; is the current evidence enough?

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ABSTRACT

Post Dural Puncture Headache (PDPH) is apparently not an uncommon occurrence and in most cases need serious attention. Conservative, supportive non-pharmacological management to interventional invasive and pharmacological treatment of PDPH are reported in the literature. The PDPH treatment strategies can be divided into *symptom management* and *mechanism directed* therapies, both of which complement each other. *S*upportive management for symptom relief includes soft pain killers, non-steroidal anti-inflammatory drugs, oral hydration and caffeinated drinks. If PDPH does not resolve then epidural blood patch is considered a definitive intervention. Novel pharmacological therapies tested and reported include use of triptans. Over two decades, sumatriptan has been used in a staggered manner and some reports of its success and lack of effectiveness appeared in the literature. In this issue Riaz A. et al have reported the first successful use of Zolmitriptan for PDPH. Although recent Cochrane review is not supportive of triptan use in PDPH but the review could not include Zolmitriptan therapy in PDPH since the original research article in this issue is the first reported use of it. This editorial view discusses the PDPH prevention, current therapeutic strategies, and novel pharmacological management with triptans. Future research and reporting is encouraged for PDPH management and the clinicians might welcome '*whatever works strategy', if* supported by clinical reasoning, scientific evidence and in practice safely without causing any harm.

Key words: PDPH; Symptom directed therapy; Mechanism directed therapy; Epidural blood patch; Triptans

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Dural puncture in the spinal region could be intentional or inadvertent (accidental). The intentional therapeutic dural puncture is undertaken to induce spinal analgesia or anaesthesia, to obtain CSF for diagnosis or to inject chemotherapeutic medications.

Post dural puncture headache (PDPH) in obstetric anaesthesia practice is of major concern for the operator (anesthetist) and debilitating and disabling for the patient. Karl August Bier in 1898 reported the first spinal anesthetic and he also experienced himself the disabling headache after receiving one. In his opinion headache occurred because of excessive loss of cerebrospinal fluid (CSF) which disappeared on lying flat and came back when upright position was assumed.[1]

Accidental unintentional dural puncture commonly referred as dural taps may occur during the performance of labour epidural with large 18 or 16 G tuohy needles and is immediately recognised on most occasions. PDPH incidence varies from 1.5% to 11.2% and is related to the type and size of the needles.[2] Headache normally occurs within first 72 hours (3 days) after dural puncture. In parturient, the collective risk of unintentional dural puncture with an epidural needle is described as 1.5%, and of these, 52.1% will experience PDPH.[2] Provider seniority decreases the relative risk of headache by 1.02 per year difference in experience.[3] The incidence of PDPH following an Emergency department (ED) lumbar puncture appears to be in the range of 5% to 10%.[4]

Nonetheless about 38% of PDPH can arise after a seemingly uneventful spinal anesthetic.[5] According to the available pooled data 85% of PDPH seems to have resolved within 6 weeks of its occurrence,[1] and therefore, it is usually considered as a self-limiting but debilitating and serious condition. In ASA closed claims analysis of mid-nineties and also in recent data, PDPH appeared to be the third most common cause of litigation in obstetric anesthesia.[6]

The young obstetric patients are at risk of intractable PDPH especially when an accidental dural puncture occurs with a large-bore epidural needle. Management requires immediate acknowledgement, offering complete explanation with treatment options to the parturients suffering with PDPH.

The question arises, is every headache in a parturient, a PDPH? Several causes of *postpartum headaches* are discussed by Sabharwal & Stocks (2011) who proposed that anesthetists must be familiar with the possible differential diagnoses of *postpartum* headaches and the management options available.[7] The contemporaneous existence of PDPH with subclinical migraine, tension or cluster and vascular headache blurs the clinical picture by its apparent relief with drugs effective for the latter entities.

History of spinal anesthetic administration and postural element of headache requires a little further evidence to start treating postpartum headache as PDPH. It is more or less a clinical decision before PDPH is labelled. C*an you please tell me the treatment of Post dural puncture headache (PDPH)*? I (KS) asked my third year anesthesia resident on an operating list. *Bed rest, hydration, caffeine*… she replied. This confirms that not a lot has changed for many decades and the literature is inundated with conflicting evidence that shows *not everything works* consistently. A meta-analysis that could build consensus would be a challenge since most studies on PDPH lack scientific rigour. Many trials were not prospective, randomized, or blinded, and follow-up and outcome criteria were not standardized.[8] Turnbull and Shepherd laments the lack of large randomised controlled trials and statistically insignificant results of inadequately powered designed studies responsible for lack of agreement on a definitive treatment or management of PDPH.[1]

A large prospective randomised placebo controlled trial involving accidental dural punctures with Tuohy needles may not clear ethics approval. Quality assurance demands the prevention of such incidences rather than focusing on treating one. The shift on using small bore needles (>25 to 29 G) and the needle tip shape modification has considerably reduced the incidence of PDPH after spinal anesthetic. However the technical difficulties and failure of spinal anesthesia in 29 G spinal needle groups has been reported in the literature.[1] Pencil point needles are no guarantee to eliminate PDPH altogether. The apprehension over the lack of rapid appearance of clear and free CSF flow through the small gauge spinal needles may result in multiple attempts in haste. Therefore CSF leak through perhaps multiple unrecognized dural holes may result in PDPH after an apparently naïve and uneventful spinal anesthetic.

The technique modification of spinal needle insertion and orientation parallel to the longitudinally running dural fibres suggested to have reduced the incidence of PDPH as well. However, Turnbull & Shepherd[1] presented opposing evidence in their review where clinical teaching is being contested by light and electron microscopic studies of human dura mater which revealed inconsistent thickness throughout its length.[9] Therefore the effect of needle orientation may be different at different level of spinal insertion with differing outcomes.

PDPH manifests itself as complain of frontal or occipital headache accompanied by its postural component. The severity increases on sitting or standing, coughing or straining, and improves on lying down. The associated symptoms are neck stiffness, nausea, vomiting, visual disturbances, photophobia and auditory symptoms such as hearing loss, hypacusis and tinnitus. In severe cases, when CSF volumes are low, the 6th (abducent) cranial nerve palsy may occur as this is susceptible to traction owing to its length but more so fixed and tight course.

Bier's prescient hypothesis that PDPH occurs as a result of continuous CSF leak leads to PDPH turned into the leak and traction theory Kunkle proposed in 1943. Loss of CSF and low subarachnoid pressure results in sagging of the brain and meninges resulting in traction on pain-sensitive structures like blood vessels and cause severe headache and pain in the nuchal region of the neck, shoulder and upper back.

Sechzer (1979) proposed that the low CSF pressure or volume per se is not primarily responsible for the

disabling headache and it is the *loss of intracranial volume* which activates adenosine receptors directly, causing compensatory dilation of cerebral veins and venous sinuses and cause 'vascular type' headache.[10] Vascular headaches respond to cerebral vasoconstrictors such as caffeine, theophylline and triptans.[11] The vascular type headache forms the basis of using triptans (5-HT 1 d brain adenosine receptors blockers) an appropriate treatment strategy for PDPH.

PDPH treatments are either '*mechanism based*' or '*symptom directed*'. In both the cases either attempt to seal the hole or to reverse cerebrovascular dilatation is targeted. Currently conservative to interventional management are simultaneously planned to achieve both the aims, with a view, *whatever works, will eventually work*.

The available PDPH symptom management options are: *bed rest*, hydration (to replace lost CSF), *mechanical* approaches to minimise CSF leak through dural rent by assuming *prone position*, applying *abdominal binders* and *avoiding* Valsalva maneuver, violent coughing, straining or sneezing. Abdominal compression or application of firm pressure around abdomen may sometimes improve the headache (Gutsche's test) but may not be too practical in post-caesarean delivery patients. Active management of second stage of labour in vaginal deliveries is recommended to avoid pushing and straining after a witnessed dural taps with tuohy needles.[12]

Conservative treatment may be effective if small bore spinal needles were used but may fail in young obstetric patients especially when a dural puncture occurs accidentally with a large-bore tuohy needle.

Bed rest is recommended only for *symptom control* rather than a definitive treatment. The evidence is directed towards its failure as a cure of PDPH. The long term argument against bed rest is that it masks the real problem instead of solving it. They argue that early ambulation unmasks the problem sooner and helps commencement of PDPH therapy. However, early ambulation and assumption of upright position might have seriously damaging effects because of apparently unseen and indescribable by the patient processes in the cranium and spinal cord. A balanced approach is recommended here.

Following a witnessed dural puncture, measures to prevent PDPH include siting intrathecal (IT) catheters, bolus or infusion of epidural saline, epidural morphine and intrathecal normal saline.[13,14]

A study by Charsley & Abram found that the injection of intrathecal normal saline reduces the severity of PDPH. The supposed mechanism might have been the rise in subarachnoid pressure to normalize pressure gradient and achieve deactivation of adenosine receptors with consequent reversal of cerebral vasodilatation. The similar mechanisms help while the patient assumes lying position. The first response to postural headache is to lie down which help achieve some symptomatic relief through the same mechanism. The approximation of cut dural fibres because of intrathecal saline infusion and consequent rise in pressure is also proposed in this study.[14]

Siting and leaving IT catheters on witnessed dural tap with Tuohy needles has several premises. It provides immediate analgesia, avoids the possibility of further dural puncture and may help reduce the incidence or the severity of PDPH. In a recent questionnaire survey by Baysinger et al[13] sent to North American Obstetrics anesthesiologists, respondents reported to have placed epidural 75% and intrathecal catheter 25% of the time following accidental dural puncture. This practice commonly reflected in less than 10 years of experience anesthetists however the threshold of abandoning conservative measures within 24 hours in favour of EBP was as high as 80% amongst the survey respondents.[13] Ayad et al reported decrease in PDPH incidence when intrathecal catheter was left in situ for 24 hours.[15] A recent study by Russell did not show any reduction in incidence of PDPH if the intrathecal catheter is left in situ when compared with re-sited epidurals.[3] According to a meta-analysis, significant reduction in the incidence of PDPH from 66% to 51% and requirement for EBP from 59% to 33% noted after intrathecal catheter placement.[5]

The infusion of saline (saline patch) and Hartman or single bolus of low molecular weight dextran 40 has also been tried but are now of historical interest only. However their effectiveness might have been achieved due to the pressure equalizing effect of the infusion of epidural saline or Hartmann. The application of fibrin glue and gelatin powder to seal the hole is also attempted in the past.

The invasive and interventional therapies to treat PDPH include epidural blood patch (EBP) which

may be performed prophylactically in witnessed dural taps or deferred until the symptoms of PDPH appear. The evidence of performing prophylactic epidural blood patch (PEBP) within first 24 hours and its effectiveness is documented in witnessed accidental dural taps where only 10% went on to develop headache. Failure in PEBP group might be due to a wet and soaked epidural space as a result of continuous infusion of large volumes of local anesthetic in obstetric population. This can be argued that it may hinder the blood to form a strong clot in PEBP because of dilution of CSF that otherwise has pro coagulant properties.[16] The argument against PEBP is to weigh risk and benefit of the procedure and not subject the patient to possibly another dural tap or another complication. A case reported 3 accidental dural punctures in one patient in which EBP was abandoned in favour of Sumatriptan treatment that finally worked.[17]

Gormley's observation led to the development of popular treatment of EBP for PDPH.[18] More interesting is the debate whether or not it is the physical presence of blood clot which simply behaves like a patch for dural rent or the actual rise in epidural volume creating mass effect with consequent elevation of subarachnoid pressure that works? Due to less or slow dissipation of blood from the space, first and foremost immediate relief of severe headache could have been due to reversal of cerebral vasodilatation because of reversed pressure changes. Later blood clots and seals the dural rent and stop the CSF leak.

Cochrane review (2010) has concluded that *therapeutic* EBP is beneficial compared with conservative treatment for PDPH.[19] There is a concern that its success is over-reported but it remains the gold standard treatment for persisting PDPH. The chance of complete cure from a single EBP is 50%, and, a second EBP may be required in up to 40% of cases if PDPH recurred.[20]

The *pharmacological* treatment includes simple analgesics like acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), oral or intravenous caffeine, theophylline, sumatriptan, DDAVP adrenocorticotrophic hormone (ACTH) .[1]

Caffeine[1] is a central nervous stimulant and cerebral vasoconstrictor known for its symptomatic relief of headache but carries a risk of reducing seizure threshold and must not be prescribed for longer term therapy. Caffeine 500 mg intravenously in 1 L of fluid over 1 hour or 500 mg orally repeated 8 hourly may be prescribed. In practice however, parturients with PDPH are encouraged to drink highly caffeinated beverages to achieve the same effect. Theophylline slow release preparation provides similar effect owing to its longer effect of causing cerebral vasoconstriction. Sumatriptan is a 5-HT1D (serotonin type 1d) receptor agonist and a cerebral vasoconstrictor commonly prescribed to treat migraine and found to be potent in treating vascular headaches.[21] Sumatriptan 6 mg subcutaneously has been successfully used by Carp et al in case studies of six patients in relieving PDPH.[11] After Carp et al study (1994), sumatriptan has been reported to have worked in some,[22] but appeared to be of no benefit in another study.[23] In a small non randomised study 5-HT1b/1d agonist frovatriptan found to be more effective cerebral vasoconstrictor but only if used prophylactically in preventing an anticipated PDPH.[24]

Recent Cochrane review[19] on pharmacological treatment of PDPH included seven RCTs of 200 participants amongst which between 88% and 90.5% were women and mostly parturients (84% to 87%) who suffered headache after a lumbar puncture for regional anesthesia. The treatment drugs assessed were oral and intravenous caffeine, subcutaneous sumatriptan, oral gabapentin, oral theophylline, intravenous hydrocortisone and intramuscular adrenocorticotropic hormone (ACTH). Cochrane review concluded that apart from Sumatriptan and ACTH, rest of the drugs mentioned have shown effectiveness of varying degree against placebo, caffeine being most effective, widely used and studied.

But what if migraine without an aura or trigger present already and remain in the subclinical horizon? It can be argued that migraine or other vascular type headache might coexist with PDPH and may be the reason why triptans are effective in this cohort of patients. It can be suggested that a thorough elective history of pre-epidural migraine or any type of headache may be obtained from the parturient before epidural or spinal anesthetic.

In this issue Riaz A, et al have reported a comparative study of two groups.[25] One group received conservative or supportive treatment (control group) and the other Zolmitriptan. Zolmitriptan is second

generation triptan that has not been used in treating PDPH so far, authors claimed. Their findings are interesting and encouraging as they found noticeable reduction in PDPH in Zolmitriptan group at 6, 12, 24 and 48 hours when compared with control group that only received supportive treatment. However after 72 hours, both groups had similar scores and no noted further change or improvement in Zolmitriptan group was found. Their conclusion though supports the combination of supportive management and zolmitriptan perhaps a combination of symptom management and mechanism directed therapy. This is line with the widely held belief and practice that in PDPH, a multimodal, symptom and mechanism directed therapy needs to be combined to optimize PDPH management. Further and continued research and more importantly sharing and reporting of success or failure of the conventional or novel treatment is highly desirable.

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