Painless childbirth? Epidural and spinal techniques in obstetric anesthesia

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Chapter 7

Postdural puncture headache: Revisited

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ABSTRACT

Postdural puncture headache (PDPH) may develop after an unintended (accidental) dural puncture, after deliberate dural puncture for spinal anaesthesia or during diagnostic dural punctures performed by other medical specialties.

PDPH may sometimes be predictable (patient characteristics, inexperienced operator or comorbidities), is almost never immediately evident during the procedure, and sometimes presents late, after discharge. Specifically, PDPH severely restricts activities of daily living, patients may be bedridden for several days and mothers may have difficulty in breastfeeding.

Although an epidural blood patch (EBP) remains the management technique with greatest immediate success, most headaches resolve over time but may cause mild-severe disability. Failure of EBP after the first attempt is not uncommon, and major complications may occur but are rare.

In the current review of the literature, we discuss the pathophysiology, diagnosis, prevention and management of PDPH following accidental or intended dural puncture, and present possible therapeutic options for the future.

INTRODUCTION

Postdural puncture headache (PDPH) has puzzled clinicians ever since its first case description by August Bier in 1898 because underlying mechanisms are still not completely understood. Since it is iatrogenic in nature it is important to understand the pathophysiology of PDPH to offer better treatment options. Many prophylactic and therapeutic options were explored, however none of these could be recommended for routine use until the epidural blood patch (EBP) was first used by Gormley in the 1960s, which is today considered by many to be the best choice, specifically in patients with severe PDPH.[1]

PDPH after neuraxial anaesthesia or analgesia procedures continues to affect many obstetric and non-obstetric patients, including about 0.5-1% of mothers receiving epidural analgesia during labour. This is primarily due to the loss of CSF following a meningeal puncture, either intentional or accidental. Smaller diameter spinal needles and better design have reduced the incidence and severity of PDPH after spinal anaesthesia. However, PDPH after accidental dural puncture (ADP) in obstetrics or after diagnostic lumbar puncture continues to be a problem, while novel neuraxial interventional procedures in oncology, pain medicine and neurology contribute to an increased incidence of PDPH. The term PDPH may be considered a misnomer, as not just the dura mater, but also the arachnoid membrane containing the CSF must be breached.

Causes of PDPH

Postdural puncture headache can occur after various neuraxial procedures which are listed in Box 1. Today, the commonest cause of PDPH is an accidental puncture of the meninges during insertion of the epidural needle for labour analgesia. ADP may be evident immediately due to the return of cerebrospinal fluid (CSF) in the epidural needle (>50% of patients) or later when classical symptoms of PDPH manifest without observed CSF. PDPH may also result from a deliberate neurologic diagnostic or therapeutic meningeal puncture or following spinal anaesthesia. Smaller-sized spinal needles with improved atraumatic design have reduced the incidence of PDPH after spinal anaesthesia, but not everywhere, as atraumatic needles are often unavailable or unaffordable. Perioperative lumbar spinal drains to prevent ischemia of the spinal cord in vascular surgery, diagnostic myelogram, CSF drainage in idiopathic intracranial hypertension, intrathecal drug provision and epidural/intrathecal implantation of neuromodulation devices can all cause PDPH.[2-5] Finally, a small group of patients may develop spontaneous intracranial hypotension (SIH) due to leakage of CSF in the cervical-thoracic or lumbar region, which also causes headaches resembling PDPH.[6]

Box 1. Causes of PDPH

Accidental
- Following epidural anaesthesia or analgesia (obstetric or non-obstetric)
- Following epidural lead implantation in neuromodulation

Interventional
- Following spinal anaesthesia for surgery
- Following spinal analgesia in CSE

Diagnostic
- Diagnostic lumbar puncture in neurological or infectious diseases

Therapeutic
- Injection of cytotoxic drugs or antibiotics intrathecally
- Lumbar CSF drainage for vascular surgery
- Intrathecal leads implanted for neuromodulation
- Intermittent CSF drainage in Idiopathic Intracranial Hypertension

Spontaneous
- Spontaneous Intracranial Hypotension

Incidence of PDPH

Depending on the cause of PDPH, the incidence varies considerably. After spinal anaesthesia it occurs between 0.3% and 40%, depending on several factors such as age, gender, needle size and needle type. Sharp traumatic spinal needles result in PDPH significantly more often, regardless of needle size.[7,8] In wealthy countries, the incidence of PDPH after spinal anaesthesia has dropped to as low as 0.16% in non-obstetric and 1.2-3% in obstetric patients due to the use of non-traumatic pencil-point needles.[9,10] The current incidence of ADP following epidural analgesia in labour is <1% and approximately 50-80% of these patients with an ADP develop PDPH.[11] After a diagnostic lumbar puncture, PDPH rates of up to 50% are described, which have decreased to <6% following the introduction of atraumatic needles.[12,13] The use of neuroprotective spinal drains in thoracoabdominal aortic repair causes PDPH in approximately 18% of patients, while the incidence of PDPH after epidural lead placement for spinal cord stimulation was 0.8% per lead insertion.[2,3] In paediatric anaesthesia, the incidence of PDPH has increased as spinal anaesthesia has become more popular, even in very young children.[14]

PATHOPHYSIOLOGY OF PDPH

The one factor presumed to be essential for the development of PDPH is loss of CSF. However, this does not always result in PDPH, nor is PDPH always preceded by identified CSF loss, as in many instances PDPH can occur after uneventful epidural labour analgesia without any evidence of ADP. Two underlying mechanisms for PDPH are thought to be involved: traction/compression of pain-sensitive intracranial structures and intracranial vasodilation. CSF loss from the spinal intrathecal space to the epidural compartment increases CSF flow from the intracranial to the extracranial space. This reduces intracranial CSF volume which affects the

cushioning of the intracranial cerebral components and causes traction/pressure on pain-sensitive intracranial structures leading to headache and other associated symptoms. The other potential source of headache is vasodilation, which is either compensatory, to retain balance within the intracranial space in accordance with the Monro-Kellie doctrine, or reflex vasodilation resulting from traction on intracranial vessels.[15,16] In the early 20th century, many experimental studies showed that extraction of CSF led immediately to headache symptoms, which disappeared once CSF was returned to the intrathecal space. However, this alone cannot explain the mechanism as some patients suffer from severe PDPH after uneventful spinal anaesthesia with small gauge atraumatic needles and minimal CSF loss. Furthermore, patients having continuous CSF loss via a subarachnoid-cutaneous fistula or patients with radiological signs of intracranial hypotension do not always present with PDPH.[17,18] Patients with spontaneous intracranial hypotension (SIH) undergoing repeated lumbar punctures show varying lumbar CSF opening pressures unrelated to the presence/absence of headache symptoms, which suggests that a decreased CSF volume instead of CSF pressure could be considered pathognomonic.[6,19,20] To increase knowledge of the underlying pathophysiology and challenge presumed concepts, one has to better understand the anatomy and physiology of mechanisms involved in PDPH.

Anatomy

Although dural puncture suggests that the dura mater has to be penetrated to cause CSF leakage, it is actually the middle layer, the arachnoid mater containing the CSF that has to be punctured to cause loss of CSF. Therefore, a more appropriate name would be post-meningeal puncture headache or post-arachnoid puncture headache.[11,21] The spinal dura mater begins at the foramen magnum and ends caudally in the coccygeal membrane, its thickness varies between individuals and decreases over a lifetime. The dura is considered a predominantly supportive membrane, but it is also a complex vascularized and innervated structure, with poorly understood contributions to the homeostasis of the CNS.[22] It is the arachnoid mater which contains CSF in the intrathecal space. Once breached CSF loss occurs, the magnitude depending on the size of the hole and the extent of damage and subsequent repair of the arachnoid lesion.[23] The arachnoid consists of two layers, the inner trabecular layer providing a mesh-like spider web and the outer layer which consists of tightly connected arachnoid cells and collagen fibres lining the inside of the dura mater.[23]

CSF

CSF, consisting of 99% water, provides cushioning protection for vulnerable brain components and also plays an important role in brain parenchymal homeostasis.[24] It facilitates metabolite/waste exchange throughout the CNS, which is essential for optimal neuronal functioning. CSF volume is higher than previously thought, approximately 250 ml, its production is not limited to the choroid plexus and resorption occurs even away from the arachnoid granulations.[25] Microscopic water/solute/waste exchange also occurs in the

perivascular spaces surrounding subarachnoid blood vessels, and instead of a unidirectional bulk flow in the spinal subarachnoid space, there is a significant multidirectional oscillatory CSF flow resulting from respiratory and hemodynamic pressure variations. Additionally, gravity and body position contribute to craniospinal motion.[24,26-29]

SYMPTOMS AND SIGNS

Irrespective of the cause of PDPH, symptoms are similar although intensity and duration may differ. PDPH presents as a dull, throbbing, bilateral headache which appears within 5 days of a lumbar/spinal procedure, often frontal and/or occipital located and accompanied by neck pain, audiovisual symptoms and nausea (See box 2).

Box 2. Common symptoms and signs of PDPH

Headache (frontal, occipital, neck, temporal) that is mostly, but not invariably, postural in character
Auditory symptoms (tinnitus, hearing loss)
Visual symptoms (diplopia)
Dizziness
Nausea and/or vomiting
Symptoms and signs resulting from involvement of cranial nerves

Symptoms may increase during sneezing or coughing, are worse in the upright position and usually, but not invariably, improve in the supine position, although atypical presentations occur, both in SIH and after meningeal puncture.[30,31] The intensity of headache can be very severe (NRS 7-10) and is often disabling, especially after meningeal puncture with a large traumatic needle. In a large observational study on PDPH after ADP in obstetrics the most common symptoms, other than headache and neck pain were dizziness (24%), nausea and/or vomiting (22%), auditory symptoms (18%) and visual symptoms (13%).[32] Nausea, vomiting, vertigo and dizziness can be related to vestibulocochlear disturbances, traction on the vagus nerve resulting in stimulation of the chemoreceptor trigger zone, or caused by pain and discomfort.[33] Changes in hearing acuity and tinnitus appear within days and sometimes have a postural component. These auditory symptoms are the result of transmission of abnormal CSF pressure to perilymph in the cochlea, causing an imbalance between peri- and endolymph which affects the relationship between hair cells and basement membrane.[33,34] Diplopia results from stretching of the abducens nerve over the bony structures of the skull. The ensuing neuropraxia causes symptoms that appear after a few days but sometimes may persist after the headache has resolved.[33] Unilateral facial or tongue numbness, related to trigeminal and facial nerve injury or palsy may occur following PDPH.[33] Physical examination usually does not reveal further information except that the patient prefers lying down as this reduces the severity of symptoms. In case of cranial nerve compromise, symptoms are seldom permanent but resolve, though much slower than headache symptoms, over a period of weeks/months.[33]

Box 3. Diagnostic criteria for PDPH (ICHD-3)

A. Headache fulfilling criteria for 7.2 Headache attributed to low CSF pressure*
B. Dural puncture has been performed
C. Headache develops within 5 days of dural puncture
D. Not better accounted for by another ICHD-3diagnosis

It is usually accompanied by neck stiffness and/or subjective hearing symptoms. It remits spontaneously within 2 weeks, or after sealing the leak with an autologous epidural blood patch
**Modified in 2018 to add that the headache is "usually but not invariably orthostatic"*

Diagnosis

The diagnosis of PDPH, irrespective of the nature of the meningeal puncture is clinical and based on the diagnostic criteria of the ICHD-III listed in Box 3.[35] The ICHD-3 states PDPH should be fulfilling the criteria of headaches attributed to low cerebrospinal fluid pressure i.e. demonstration of either low CSF pressure (<60 mmHg) or evidence of CSF leakage on imaging. However, in clinical practice, this criterion is seldom fulfilled since CSF pressure is not measured and routine radiological imaging is not performed. Instead, the clinician relies upon the presence of headache symptoms appearing within 5 days of a suspected or intended meningeal puncture, not better accounted for by another diagnosis for confirming PDPH, especially if neck stiffness or hearing symptoms are present. The most important diagnostic feature of PDPH, worsening of symptoms within 15 min of sitting/standing and improving within 15 min after lying down, has recently been changed to 'often but not invariably' since some patients, despite a confirmed PDPH, have no or minimal orthostatic component.[30,32] This makes a definite diagnosis of PDPH challenging, especially after an intended meningeal puncture or during epidural insertion where PDPH can occur without evidence of a definite ADP (CSF in epidural needle), as in up to 40% of patients where other causes of postpartum headache are present.[36,37] (see differential diagnosis box 4).

Box 4. Differential diagnosis of postpartum headaches

Common causes	Uncommon causes
Tension headache	Subarachnoid bleeding
Lack of sleep	Cortical/sagittal vein thrombosis
Dehydration	Pre-eclampsia/Eclampsia
Migraine	Reversible cerebral vasoconstriction syndrome
Caffeine	Withdrawal other drugs/substances

Radiological imaging may be useful in ruling out other pathology or corroborating an unclear presentation. MRI findings typical of PDPH, although not always present, include dural venous engorgement that may result in pressure-driven extravasation of fluid, seen as abnormal pachymeningeal enhancement of the innermost dural layers. Other characteristic features may be decreased size of subarachnoid cisterns and cerebral ventricles, downward

displacement of the brain ('sagging') and pituitary gland enlargement.[38] Once the diagnosis of PDPH is confirmed, a changing presentation such as increased severity, disappearance of the initial positional component, lateralization of symptoms, new onset of nausea, vomiting, neurologic focal symptoms or sedation and coma require immediate additional diagnostic studies and multidisciplinary management.

RISK FACTORS FOR PDPH

The incidence of PDPH decreases with age, which may be due to changes in elasticity of the dura mater, a reduced response of cerebral vessels to loss of CSF or smaller epidural space.[39,40] Regardless of pregnancy, women are at higher risk of PDPH, probably due to the increased amount of circulating oestrogens that may affect the tone of the cerebral vessels and their response to a decrease in CSF pressure; differences in nociception processing between men and women might contribute to this higher risk as well.[39,41] During pregnancy, several factors contribute to an increased risk, such as further elevation of oestrogen levels, increase in intra-abdominal pressure, increased CSF pressure during second-stage pushing and dehydration secondary to NPO status, blood loss or post-partum diuresis.[42] A history of chronic headaches or PDPH results in a higher risk of developing PDPH. However, a history of migraine is not related to an increased risk of PDPH.[13,16] Obesity is thought to be protective in the development of PDPH since increased intra-abdominal pressure increases epidural pressure, which limits CSF loss after meningeal puncture. Data on PDPH after ADP in the obstetric population are conflicting, but following lumbar puncture, a low BMI is associated with an increased incidence of PDPH.[12,13,43,44]

Prevention

Patient-related factors for PDPH include age (younger), gender (female), pregnancy and a previous history of headaches. The main modifiable factor that has been demonstrated to reduce the incidence of PDPH after spinal anaesthesia is the spinal needle design.[9,45] Atraumatic pencil point needles result less often in PDPH. They cause blunt irregular tearing and more damage to the dura/arachnoid membrane, in contrast to the clean crescent-shaped cut resulting from a puncture with a sharp traumatic needle.[46] Why this extended damage leads to a reduced incidence and severity of PDPH has not been determined, does it contribute to a quicker healing process? While needle size seems quite irrelevant for pencil point needles, when traumatic sharp needles are used, smaller needles result in less PDPH.[9,45] Spinal needle insertion parallel to the spinal axis has been associated with a reduced risk for PDPH if traumatic needles are used, although this cannot be explained by the previously incorrectly assumed longitudinal orientation of dural fibres.[47,48] Paramedian spinal approaches to reduce PDPH have shown conflicting results, but greater experience of the provider might reduce multiple attempts or ADP.[12,49-51] Bed rest after lumbar puncture does not reduce the incidence or duration of PDPH.[52] A recent practical guideline recommends using

atraumatic needles for neurologic diagnostic and therapeutic lumbar punctures, which show equal efficacy to conventional needles but reduce the incidence of PDPH by >50%.[53,54] Can PDPH be prevented once an ADP occurs? Following an observed ADP many preventive measures have been proposed, ranging from re-siting the epidural at another level for labour analgesia (sometimes followed by injecting autologous blood (prophylactic EBP) or epidural morphine through the catheter before removal), to inserting the epidural catheter intrathecally and providing spinal analgesia.[21,55-57] Assisted vaginal deliveries and elective caesarean sections have been associated with a reduced incidence and severity of PDPH.[42,44] The use of a 'prophylactic blood patch' in patients with ADP has been attempted but is no longer recommended.[58,59] Injection of epidural morphine in order to prevent PDPH after ADP has been shown to indeed reduce the incidence of PDPH and the need for an EBP.[57]

The insertion of an intrathecal catheter (ITC) through the epidural needle that caused the ADP is considered a strategy to reduce the incidence and severity of a subsequent PDPH.[56,60] The are several advantages of an ITC: the need to perform a new epidural with the risk of a new ADP is avoided, patients can get immediate relief of labour pain using the spinal catheter and one could use it for spinal anaesthesia if needed for a caesarean section. However, there are attendant risks, since the catheter may be accidently used as an 'epidural' catheter, and there is also a potential risk of infection. ITC prevents further CSF loss, and although inert, allows time for an inflammatory response, which facilitates rapid closure of the breach once the catheter is removed. Whether an ITC reduces the risk of a subsequent EBP has been explored and some studies seem to support this belief, but the evidence remains inconclusive.[56,60,61] For a more comprehensive review of ITC, readers are referred to an excellent review published recently.[62] Randomized studies are urgently needed in the literature to determine the use of this technique as a proactive management strategy when ADP is clearly evident during epidural needle insertion. The most important step to reduce the incidence of PDPH is to prevent ADP. Supervised training in obstetric anaesthesia followed by frequent performance to increase the 'volume' of epidurals inserted are prerequisites for maintaining a low frequency of ADP in training institutions. The use of ultrasound techniques should be encouraged so as to identify the midline, the level of the lumbar puncture and the depth of the epidural space.[63] This may be specifically useful in patients with vertebral column pathology, obese patients and those in whom there was previous difficulty in establishing an epidural block. Finally, experienced anaesthesiologists should either perform or supervise labour epidurals in complex patients to prevent the occurrence of an ADP. Using smaller 18 G Tuohy needles instead of 16 G, air instead of saline for detecting loss of resistance, inserting the epidural at L2-L3 compared to L3-L4, and inserting an ITC after ADP have all been associated with a reduced risk of subsequent EBP to treat PDPH in a recent prospective observational study.[32]

COMPLICATIONS

The self-limiting character of PDPH, either spontaneously or after an EBP, should be questioned: chronic symptoms have been reported as early as 60 years ago when 6%-13% of patients had persistent symptoms after spinal anaesthesia.[35,64] Recent studies describe chronic headache and backache symptoms with widely varying incidences, depending on the cause of PDPH, the definition of headache used and the duration of symptoms. Headaches lasting longer than 6 weeks have been reported in 28-58.4% of obstetric patients after ADP, with almost similar incidences at 18 months.[65-68] In a large database study, PDPH was associated with an increased adjusted OR of 7.7 for a diagnosis or readmission for chronic headache or migraine, and OR of 4.4 for chronic back pain.[69] A recent systematic review and meta-analysis found an increased risk of headache, backache and neckache at 12 months after ADP in obstetric patients, with the authors unable to demonstrate a significant reduction after EBP.[70,33] 2 retrospective studies identified an association between PDPH and postpartum depression, which also needs further investigation.[69,71] These long-term consequences of PDPH, occurring at higher rates in obstetric patients than previously thought, can no longer be ignored, as they affect maternal well-being and may result in chronic ailment with potential socio-economic consequences. Optimizing neuraxial techniques, material and efforts to prevent ADP and PDPH are mandatory to avoid chronic sequela. Furthermore, patients should be informed during the consent process of the potential complications of various neuraxial procedures. Subdural haematoma (SDH) is the most feared complication of PDPH. Recent database studies using hospital admission records provide staggering insights into the relationship between PDPH and subdural haematoma. Moore reported an OR of 199 after neuraxial anaesthesia in childbirth, while Guglielminotti described an OR of 19 for the composite outcome of cerebral venous thrombosis/subdural haematoma in PDPH patients compared to women without PDPH.[69,72] Both publications reported comparable incidences of SDH after elective caesarean or vaginal deliveries. The diagnosis of SDH may be difficult as symptoms may be attributed to PDPH and do not change substantially before subdural haematoma is detected.[73-75] SDH is not always related to severity of PDPH. A recent review suggested that most subdural haematomas reported in the literature occurred after intentional dural puncture, with <50% of cases originating from the obstetric population.[73,74] The underlying mechanism is thought to be the rupture of thin-walled subdural veins between the dura and arachnoid membrane after CSF loss and subsequent brain sagging. Other factors such as coagulation disorders, intracranial vascular abnormalities and second-stage pushing might contribute to its occurrence in a minority of obstetric patients.[75] Early recognition of SDH is essential in order to initiate treatment, but diagnosis is not always easy. Sensory disturbances, motor deficit and reduced level of consciousness may be present in some cases, but Cuypers identified focal neurologic symptoms in 69% of cases, with persistent headache losing its postural component as a common symptom.[73-75] Therefore, undetected cases of SDH might accompany PDPH.

CONSERVATIVE (NON-INTERVENTIONAL) MANAGEMENT OF PDPH

When the diagnosis of PDPH is confirmed, irrespective of aetiology, most anaesthesiologists prefer conservative management initially, unless the headache is very severe and disabling. In most patients, symptoms subside gradually over time and an EBP was shown to be more successful if applied after 24-48 h.[76] However, conservative treatment without reduction of symptoms may eventually lead to intracranial bleeding due to stretching of the meninges from a 'sagging' brain. Patients need close surveillance to identify either worsening symptoms or the appearance of new symptoms. These patients require either an early EBP or further diagnostic procedures to exclude other intracranial pathology. Common strategies used for conservative management are shown in Box 5, the evidence behind these strategies is discussed below.

Box 5. Conservative management strategies

Hydration and fluid therapy (orally/intravenously)
Bed rest/delayed mobilisation
Analgesics
Caffeine
Others
(good evidence for most of the above strategies is either limited or lacking)

Hydration

It was believed by some that dehydration may be a factor influencing the incidence of PDPH since it is high in pregnant women after delivery when fluid intake is low and fluid losses high. Therefore, it became common practice to rehydrate patients prior to spinal anaesthesia. Although volume preloading reduced the incidence and magnitude of spinal anaesthetic-induced sympathetic blockade, evidence is inconclusive regarding the incidence of PDPH.[52,77] Today it is recommended that normal hydration of the patient should be maintained. Extra hydration does not alleviate the headache but dehydration makes symptoms worse.

Bed rest or delayed mobilization

Placing a patient horizontally for a period of time after a dural puncture does not affect the incidence or duration of PDPH but delays the onset of the PDPH until mobilization.[52,78] Due to the severe headache in the upright position, patients nevertheless prefer bed rest initially to avoid the discomfort associated with an upright position. A lateral horizontal position produces less tension on the dural injury than a supine position and may result in less leakage of CSF. In one study in patients having spinal anaesthesia for surgery, the authors found a lower incidence of PDPH in the group that was maintained in the prone position postoperatively compared to the supine position.[79] Today, early mobilization is

recommended to the extent that the patient can be out of bed. This has the additional benefit of reducing the risk of deep vein thrombosis when immobilized.

Analgesics

Irrespective of the cause of the headache (PDPH), pharmacological management is commonly initiated, specifically during the 'observation period' of 24-48 h before a definite decision is made as to how to proceed. Analgesics commonly used by oral or intravenous routes provide varying degrees of pain relief and are a first line for management. No specific analgetic is better than another, physicians tend to use mild analgesics such as paracetamol or NSAIDs for the mild headache going over to stronger (opioid-based) analgesics for more severe cases. Box 6 shows a summary of the common analgesics used today.

Box 6. Analgesics used to relieve PDPH

Paracetamol
Non-steroidal anti-inflammatory agents (NSAIDs)
Opioid-analgesics (oral, intravenous, epidural, intrathecal): Morphine
Other drugs: Steroids, ondansetron, dexmedetomidine, magnesium, ketamine
Regional blocks: Sphenopalatine ganglion block, greater occipital nerve block

Many drugs have been considered for treatment, with gabapentin, amino/theophylline and hydrocortisone showing some decrease in pain severity scores, while data on other drugs such as sumatriptan and ACTH are more inconclusive.[80] There are many publications in the literature on the use of caffeine to relieve the symptoms of PDPH with mixed results. The evidence today seems to point towards a lack of efficacy, possibly a placebo effect. Its therapeutic benefits therefore seem questionable and caffeine in any form cannot be recommended as a routine management technique for PDPH.[80,81] Several uncommon prophylactic and therapeutic strategies have been recently tried to reduce the incidence and severity of PDPH after various neuraxial procedures, such as ketamine, magnesium, dexmedetomidine, neostigmine, ondansetron etc., but the evidence is limited and recommendations cannot be given yet. A recent observational case series described patients with severe PDPH who were given high-flow oxygen through a non-rebreathing mask and experienced immediate relief without return of symptoms, can this be confirmed in prospective randomised studies?[82] Similarly, sphenopalatine ganglion blocks (SPGB) and greater occipital nerve blocks have been used to resolve PDPH symptoms, sometimes successfully, but the evidence remains unconfirmed until more studies are performed.[83-85]

INTERVENTIONAL MANAGEMENT

Epidural blood patch (EBP)

The use of autologous blood injected in the epidural space as treatment for PDPH was first considered around 1960 when James B. Gormley, a surgeon, observed that after a bloody spinal tap (for spinal anaesthesia) patients rarely developed any PDPH. Subsequently he successfully introduced the intrathecal injection of saline followed by epidural injection of 2-3 ml of autologous blood during needle withdrawal.[1] Continuing work of DiGiovanni, Crawford, Paech and others eventually led to the current use of 20-30 ml blood, as the epidural mass effect is considered to be the most important factor driving the success of EBPs.[76] It took a while longer before EBP was introduced to treat PDPH resulting from other procedures and SIH, with varying success.[86-88]

Why are EBPs successful?

The precise underlying working mechanism is thought to be two-folded. First, the instant relief of symptoms after application of the EBP is considered to be the result of the epidural injection of a certain volume of blood and its immediate epidural mass effect. Second, the injected blood will clot adjacent to the dural damage and prevent further leakage of CSF while the dural/arachnoid membrane repairs. The epidural mass effect has been demonstrated in SIH patients, with subarachnoid spinal and intracranial pressures and its surrogate, the optic nerve sheath diameter (ONSD) measured by ultrasound, responding immediately with parallel relief of symptoms.[89,90] This immediate increase in intracranial CSF volume and pressure may reduce traction on pain-sensitive structures and vasodilation. As compliance of the epidural space is highly variable between patients, the volume needed to achieve an initial mass effect is difficult to predict, which has led to the practice of injecting blood until the patient complains of symptoms such as back ache or radiating pain.[91,92] The injected epidural blood spreads circumferentially with a preference for cephalad distribution, the resulting dural sac compression still visible on MRI 3 h after injection.[93,94] The second effect of an EBP is the formation of an epidural blood clot adjacent to the meningeal damage. This mature clot tissue is thought to contribute to the repair of the lesion in the meningeal membranes, and appears to be present locally till at least 18 h after application of the EBP.[94] Permanent repair of the meningeal opening is dependable on the local inflammatory reaction, with more damaged tissue produced by non-cutting needles resulting in faster closure of the traumatic lesion.[46] Other unknown factors might be involved, as the following questions remain unanswered. Why is it that EBPs at lumbar levels are also successful in treating PDPH in SIH resulting from dural tears at cervical or thoracic levels?[95,96] Why do EBPs in obstetric patients with PDPH provide complete initial relief in only one in three patients, and why are other factors, especially the timing of an EBP, related to its success or failure?[32,97]

Indications for an EBP

Conservative management without an EBP may be a good alternative in many patients since the natural course is generally one of a gradual reduction of symptoms. Without active intervention in obstetric patients experiencing PDPH, >80% have mild or no headache one week after ADP.[32] However, with serious symptoms which do not subside or increase in severity over time, an early EBP might be indicated, even if it implies a second EBP, as PDPH is related to severe disability and suffering, temporary damage to cranial nerves and subdural haematoma. Delayed application of an EBP has been associated with an increased incidence of subdural haematoma in the obstetric population.[72] Other indications for an EBP are PDPHs after other neuraxial procedures and patients experiencing PDPH-like headaches resulting from SIH.

Contraindications for EBP

The same contraindications apply as for epidural needle placement, such as local skeletal and/or neurological abnormalities, myelomeningocele, tethered cord, patient refusal, the presence of coagulopathy or the use of coagulants and signs of infection, either systemic or local at the proposed injection site and lastly the risk of CNS herniation in patients with an intracranial space-occupying lesion.[98]

Why do EBPs fail, and can this be avoided?

There is no consensus in the literature regarding the definition of a failed EBP. While some studies consider persistent headache or recurring headache, whatever its intensity, as a failed EBP, others define it as the need for a second EBP.[76,91] EBPs have also been classified as partial or complete failures or described as initial success with permanent relief or initial success and subsequent failure.[99-101] Depending on the definition, a failed EBP may occur in 7-66% of patients.[76,100,102] In a recent large observational study, the authors classified headaches after EBP as mild (NRS <3), moderate (3-6) and severe (>6).[101] Using this definition, moderate-severe headache post-EBP was seen in >30% of patients and approximately 20% received a second EBP. Considering that application of an EBP is an invasive procedure associated with complications, failure rates are quite high and therefore it is important to understand the reasons for EBP failure.

Factors related with the success and failure of an EBP

Timing

There is no consensus regarding the timing for application of an EBP. When only considering the risk of failure, waiting 24-48 h seems appropriate, as early provision is associated with increased failure.[76,101] However, in patients with severe symptoms, evidence of 'sagging' on CT examination or signs of cranial nerve involvement (ocular, auditory, abducens nerves), it may be wise to proceed earlier with an EBP. Prophylactic EBP's have been used in the past in obstetric patients after ADP, using a second epidural catheter inserted after the first EDA attempt resulted in an ADP. Sealing the dural damage after delivery with autologous blood

before symptoms arose, was considered to prevent further CSF loss and the occurrence of PDPH. Until now evidence is not supporting the use of prophylactic EBP, as it does not decrease the incidence of PDPH significantly, with its failure associated with potential dilution of the injected blood by either local anaesthetic or CSF, which both may affect clot formation and clot stability.[58,103-105] Contrary to the USA, where an early EBP after ADP in patients with severe PDPH is not uncommon even though the risk for a second EBP is high, in Europe the tendency is to start with conservative measures first and wait to see if symptoms decrease before application of an EBP.[55,101,106] Late EBP provision, apart from causing prolonged suffering and pain, might be associated with an increased risk of cranial nerve compromise and subdural haematoma resulting from continuous low CSF pressure.[72] Moore demonstrated that women with PDPH in childbirth who received an EBP during a hospital re-admission (late), had an adjusted absolute risk increase of 130 per 100.000 deliveries of having a subdural haematoma, although the precise timing was not specified in this study.[72]

Location

The current recommendation is to administer the EBP below the level of the original dural puncture to enhance success, but Gupta et al. recently failed to demonstrate an association between EBP success and the level of insertion of the EBP in relation to the level of the initial dural puncture.[93,94,101] Only the level of the initial ADP was relevant to the success/failure of the EBP; the higher the initial ADP, the greater the risk of failure of a subsequent EBP.[101] In SIH it was thought that an EBP targeted near the meningeal lesion had a higher success rate, but a recent study demonstrated similar efficacy when targeted and non-targeted levels for an EBP were used. A distant lumbar EBP might be preferable and effective in patients with challenging cervical or thoracic lesions.[96,99,107]

Volume

The role of volume in the working mechanism of EBPs is incompletely understood. Pratt et al. have demonstrated that, although there is a curvilinear relationship between the volume of blood injected and the epidural pressure, there is a wide variety of epidural pressures generated, unrelated to the success of the EBP.[92] The current advice is to use up to 20 ml unless symptoms occur earlier, based on one of the few RCTs on EBP volume in women experiencing PDPH after ADP, which concluded that using 30 ml provided no additional benefits while causing more often pain during injection.[76,97] In patients with SIH, higher volume was the only factor significantly related to a higher success rate of the EBP.[96,99] There is limited data regarding EBP volume in children. While generally 0.3 ml/kg has been suggested, Kokki et al. reported that 0.2 ml/kg resulted in permanent relief in 85% of patients who experienced PDPH either after lumbar puncture or spinal anaesthesia.[108] Whatever volume is chosen, one should stop injecting once the patient complains of back pain, neck pain or radicular symptoms.

Does EBP reverse the accompanying symptoms of PDPH?

Most cranial nerve symptoms accompanying PDPH are relieved within weeks/months after an EBP, apart from the auditory symptoms, which resolve rapidly.[33,34] But several years after having received an EBP for PDPH in obstetrics, a minor hearing loss can still be found with pure tone audiometry (<5 dB) at low frequencies.[34] Some cranial nerve disturbances actually appear only after application of the EBP, which is thought to result from compromised vasa nervosum surrounding cranial nerves due to sudden increases in intracranial pressure after EBP.[33]

How to patch?

Imaging is not necessarily recommended when classical symptoms of PDPH are present in relation to a recent neuraxial procedure unless a sudden change in presentation demands exclusion of other causes. The same precautions and preparations as for an epidural injection should be applied, and standard monitoring and intravenous access are advised as some patients will respond with bradycardia to injection of fluids in the epidural space.[97]

Once the epidural needle is advanced to the epidural space, autologous blood (up to 20 ml) should be drawn through a second intravenous needle under strict aseptic conditions, which can then be injected through the epidural needle until patients complain of backache, discomfort or radiating pain.[76,97] Ultrasound might improve correct identification of the epidural space, while fluoroscopic guided EBP has shown to result in a higher success rate and the use of a lower volume.[107,109,110] Duration of immobilization appears to be unrelated to EBP success/failure; only one small study associated longer immobilization (2 h) with success of EBP, while Gupta rather found a tendency towards more complete failures in patients mobilized later (>4 h).[97,101,111] Patients should be advised to avoid heavy exercise, lifting and bending after the procedure, as this might interfere with closure of the dural injury.

Are there any complications of an EBP?

An EBP, although an invasive technique, is considered a safe procedure, but complications can occur. Risks are comparable to all neuraxial procedures such as the risk of another accidental dural puncture, nerve root irritation by the needle and infection. Spreading of the blood along the nerve roots can cause temporary radicular irritation, and back pain is often described, resulting from subcutaneous, muscular and/or tissue irritation due to the presence of blood.[112,113] Although seldom occurring, more severe complications such as spinal subdural or intrathecal haematoma have been reported.[114] After an EBP in SIH patients Ferrante et al. visualized subarachnoid blood in 8.5% of patients, unaccompanied by arachnoiditis or clinical symptoms.[115] Both cerebral venous thrombosis and subdural intracranial haematoma have been described during PDPH, with an unknown association with EBPs.[69,72,116] Arachnoiditis, transient bilateral paraplegia and retinal haemorrhage have also been reported after EBP treatment.[117-120] Recent studies have shown a relationship between development of chronic symptoms such as backache or headache and PDPH, without evidence of the EBP contributing to a significant reduction, with one study

actually demonstrating an increased incidence in chronic low back pain occurring after EBP.[70,71,113,121]

How to proceed after a failed EBP?

The incidence of failure of an EBP varies, and a patient might experience only partial relief or a return of symptoms. A second EBP might be considered after excluding other causes of headache, but only if symptoms and signs are similar and not changing or fluctuating. In case of any doubt, multidisciplinary consultation and additional imaging might be needed before a second EBP is provided. One should consider the use of fluoroscopy or ultrasound to optimize the repeat EBP procedure and demonstrate effective delivery of the autologous blood in the epidural space.[63,109,112] No evidence exists on when to provide a second EBP after failure of the first, individual circumstances should guide the attending physician.

Sphenopalatine ganglion block (SPGB)

The parasympathetic sphenopalatine ganglion (SPG), which is located directly behind the nasal cavity, mediates intracranial vasodilation. Blocking this ganglion bilaterally with two cotton tips soaked in LA is known to reduce symptoms related to cluster headache, migraine and trigeminus neuralgia and is currently considered by some as a good alternative to an EBP in the management of patients with PDPH.[85] The simplicity of the technique is attractive and initial case series and an observational study did find that SPGB reduced PDPH symptoms and the need for an EBP.[85,122,123] Jespersen et al. could not confirm this in a prospective, blinded study comparing local anaesthetics with placebo for SPGB in 40 PDPH patients (70% women); in both groups, only 50% of patients needed a subsequent EBP.[124] Another study comparing early vs. late SPGB found that early application reduced the length of hospital stay, without any other differences, while a pilot meta-analysis on SPGB vs. other treatment modalities could not find a statistically significant difference in headache intensity or adverse effects, and concluded that more studies are needed.[125,126] In conclusion, although this is an interesting and simple procedure, evidence to date is not conclusive of its efficacy compared to placebo.

THE FUTURE

The debate on the management of PDPH following dural puncture (deliberate or inadvertent) continues. Evidence is still lacking if an early EBP, in patients with severe symptoms, also reduces the incidence of intracranial bleeding. Studies are needed that compare maximal tolerated EBP blood volume vs. a maximum of 20 ml or lower and to determine the relation between EBP volume, success rate and the occurrence of side effects, as current practice is based on only one properly designed study. The efficacy and safety of inserting an ITC once ADP occurs need to be further examined in randomized studies.[76,92] The precise mechanism by which an EBP reduces headache immediately after injection needs to be explored, transcranial Doppler can be used to determine if immediate cerebral arterial

vasoconstriction explains the prompt relief of symptoms after receiving an EBP. All future studies should document precisely, using ultrasound, the level of neuraxial procedures to study the observed association between initial ADP level, the severity of PDPH and success rates of EBPs. Do novel strategies such as a SPGB or the provision of high-flow oxygen reduce the need for an EBP in patients with severe PDPH? Finally, increased international collaboration between researchers is needed to accelerate global PDPH research and reduce the duration of clinical trials by enhancing patient recruitment. It will facilitate faster optimization of PDPH management strategies and reduce patient suffering from this iatrogenic complication of neuraxial procedures. Please see Box 7.

Box 7. Research agenda

Late vs. early application of EBP in severe PDPH
Associations between PDPH, EBP and chronic sequelae
Optimal volume of EBP
Safety and efficacy of ITC insertion during ADP to prevent severe PDPH
Underlying pathophysiology of ADP, PDPH and EBP
Ultrasound to study association between level of neuraxial procedures, PDPH and EBP
Significance of SPGB and occipital nerve block in the management of PDPH
High-flow oxygen administration and the need for EBP

CONCLUSIONS

Postdural puncture headache is an uncommon complication of neuraxial anaesthesia and analgesia, resulting from either accidental or intentional puncture of the spinal meningeal membranes, but it also occurs after other diagnostic or therapeutic neuraxial procedures. The intensity of PDPH may be severe depending on various factors, including needle size and design. It is often self-limiting and treatment may be conservative if the headache is not very severe. More severe cases are often treated with an EBP, specifically following ADP, which is successful in about 70-80% of patients after the first attempt. Some patients may need two or more EBPs before PDPH resolves, but chronic residual symptoms are not uncommon. The precise timing for performing EBP depends on the individual patient and physician but initial conservative management is common. There is a small but significant risk that unresolved PDPH after an EBP may be due to other intracranial pathology and this should be investigated early, specifically if the headache character alters. The benefit of intrathecal catheters in the prevention of PDPH needs to be further investigated and promising new therapeutic strategies explored. Patients suffer a lot as a result of PDPH and efforts should be made to provide easy access to atraumatic spinal needles worldwide. International cooperation should intensify to better understand and manage PDPH in both obstetric and non-obstetric populations.

Box 8. Practice points

- Prevention is always better than cure (avoid ADP when possible)
- Initial conservative management for 24-48 h unless symptoms are very severe, when EBP should be considered early
- Aim to administer 20 ml blood if possible during EBP
- Mobilize early, both during conservative management and after EBP
- Consider further diagnostics (CT/MRI) if the headache has an abnormal presentation or changes in character during observation
- Follow-up patients after discharge until resolution of symptoms

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