Section A -Research paper

Brief Overview about Post-Dural Puncture Headache

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Abstract:

Background: The German surgeon, Augustus bier was the first to introduce spinal anesthesia over 100 years ago; using himself as a subject, local anesthetic cocaine was injected into the subarachnoid space. In the next morning he suffered from a headache - now widely known as post- dural puncture headache (PDPH). He attributed this headache to continuous leakage of CSF from the subarachnoid space through the dural puncture; furthermore he reported six cases of PDPH after spinal anesthesia for lower limb surgeries in 1889. The needles used back then were large cutting Quincke- type spinal needles. Post- dural puncture headache (PDPH) is a common and disabling complication that occurs after intentional puncture of the dura-arachnoid whether for purposes of diagnosis, therapy, spinal anesthesia or unintentionally during epidural anesthesia. CSF leak is defined as the escape of CSF from any tear or hole in the meninges. The direct consequence of CSF leak is the drop of CSF volume and then pressure. Indeed, leakage of the CSF is the most common cause of spontaneous intracranial hypotension. Based on the findings that pregnancy and the immediate postpartum period are associated with the lowest CSF density and the particular high incidence of PDPH in obstetric setting, the CSF density changes during the chronic leakage of CSF was also considered as a potential risk factor for PDPH.

Keywords: Post-Dural Puncture Headache

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Introduction

The German surgeon, Augustus bier was the first to introduce spinal anesthesia over 100 years ago; using himself as a subject, local anesthetic cocaine was injected into the subarachnoid space. In the next morning he suffered from a headache - now widely known as post- dural puncture headache (PDPH). He attributed this headache to continuous leakage of CSF from the subarachnoid space through the dural puncture; furthermore, he reported six cases of PDPH after spinal anesthesia for lower limb surgeries in 1889. The needles used back then were large cutting Quincke- type spinal needles **(1)**.

The incidence of PDPH in the year (1898) was 66% as reported by Wulf. The average incidence of PDPH in the early 1900s were about 50% of all patients undergoing spinal anesthesia .In 1951 pencil-point spinal needles were developed by Whitacre and resulted in a significant decrease in the incidence of PDPH .Over the years using small gauge needles also helped in decreasing the incidence of this undesirable complication after spinal anesthesia **(2).**

Definition

Post- dural puncture headache (PDPH) is a common and disabling complication that occurs after intentional puncture of the dura-arachnoid whether for purposes of diagnosis, therapy, spinal anesthesia or unintentionally during epidural anesthesia.

The International Headache Society (IHS) defines PDPH as a headache that meets all four of the following criteria **(2):**

1- Occurs after dural puncture.

2- Develops within 5 days of dural puncture.

3- Worsens within 15 minutes after sitting or standing and improves within 15 min after lying down and is associated with neck stiffness, tinnitus, hypoacusia, photophobia, or nausea.

4- Either resolves spontaneously in one week or within 48 hours after effective treatment.

However, there are some issues with this definition because, nearly 33% of all PDPH patients don't meet these criteria due to lack of associated symptoms or having a headache that lasts more than one week. So PDPH should be highly suspected after dural puncture especially in high risk patients such as pregnant women even in absence of all these qualifying diagnostic criteria**(3)**.

Leibold et al., (4) reported that PDPH can develop up to 2 weeks after the dural puncture, or very rarely, it can occur immediately.

Pathophysiology of PDPH

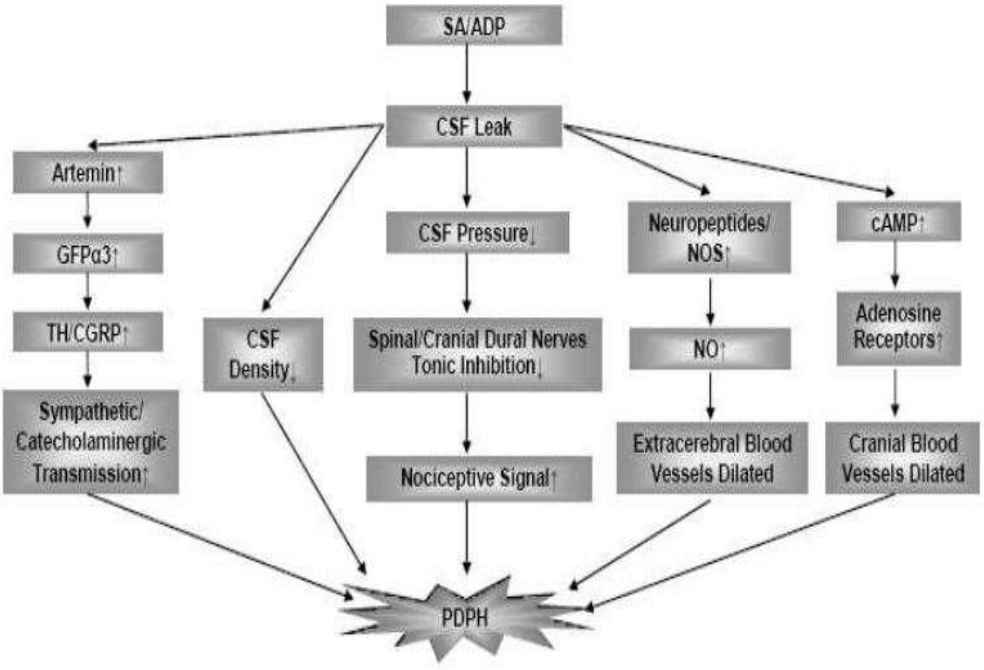
There are two theories that may explain how PDPH develops:

1-Dural Puncture and loss of CSF (Leak Theory) (figure 1).

CSF leak is defined as the escape of CSF from any tear or hole in the meninges. The direct consequence of CSF leak is the drop of CSF volume and then pressure. Indeed, leakage of the CSF is the most common cause of spontaneous intracranial hypotension. Theoretically, lumbar puncture-induced CSF leak consists of acute and chronic phases. The acute phase largely results from the abrupt outflow of CSF from the broken dura within minutes to several hours, during which the CSF pressure dives down to a lower level (3-4 cmH_2O) that eventually leads to shifting of intracranial contents and gravitational traction on pain sensitive structures causing a headache that worsens when the patient is upright and subsides on lying down. On the other hand, the chronic phase starts from the formation of a new CSF pressure balance (several hours after dural puncture) to the complete resolution of the dural puncture site (1-6 weeks). This phasic alteration in CSF leakage can explain, at least in part, the variability of PDPH onset and duration in different patients **(5)**.

In addition, the loss of CSF may activate adenosine receptors that subsequently dilate intracranial arteries and veins; hence clinical manifestations of PDPH. Based on the findings that pregnancy and the immediate postpartum period are associated with the lowest CSF density and the particular high incidence of PDPH in obstetric setting, the CSF density changes during the chronic leakage of CSF was also considered as a potential risk factor for PDPH. Functional immunohistochemistry found that neuropeptides and nitric oxide synthase (NOS) are expressed in the nerve fibers of the supratentorial dura mater, and the structural alterations of nitroxidergic axons innervating blood vessels of the dura mater support the idea that nitric oxide (NO) is involved in the induction of headache. Artemin, a member of the glial cell line-derived neurotrophic factor family, is a vasculature-derived growth factor shown to regulate migration of sympathetic neuroblasts and targeting of sympathetic innervation. The expression of artemin was detected in the smooth

muscle of dural vasculature, and its receptor glial-cell-line-derived neurotrophic factor family receptor alpha-3(GFRα3) was found present in nerve fibers that is closely associated with tyrosine hydroxylase (TH) or calcitonin gene-related peptide (CGRP). Given TH functions as the precursor of catecholamine (norepinephrine and epinephrine), a potential interaction exists among artemin, sympathetic regulation, and catecholaminergic transmission in nerves located in cranial dura mater, and this interaction may underlie the occurrence of PDPH **(6).**



SA: spinal anesthesia; ADP: accidental dural puncture; CSF: cerebrospinal fluid; GFPα3: glial-cell-line-derived neurotrophic factor family receptor alpha-3; TH: tyrosine hydroxylase; CGRP: calcitonin gene related peptide; NOS: nitric oxide synthase; NO: nitric oxide; cAMP: cyclic adenosine monophosphate; PDPH: post-dural puncture headache.

Figure (1): CSF leak and pathogenesis of PDPH (leak theory)(7).

2-The Air Theory (Dural puncture and pneumocephalus)

Pneumocephalus (PC) is defined as a pathological collection of gas within the cranial cavity. Most cases of PC following epidural techniques have been associated with the Loss of Resistance Technique (LOR). The LOR technique is widely used either with air or saline to identify the epidural space. Pneumocephalus is a rare complication of inadvertent dural puncture and injection of air into the subarachnoid or subdural space. It is assumed that the symptomatic headache arises from irritation of the spinal roots by air migrating cranially in the sitting patient. Diagnosis can be done by imaging modalities such as CT and MRI showing air trapped in the spine and brain**(9)**.

Clinical features of PDPH

PDPH is classically a fronto-occipital headache which sometimes radiates to both

temples, may be felt behind the eyes, and is more diffuse than localized. The headache typically has a postural nature, with the pain exaggerated by sitting or standing and relieved by lying flat. This postural feature differentiates it from other serious intracranial causes of headache such as a subdural hematoma. Any movement that increases intracranial pressure (such as coughing, sneezing, straining, or ocular compression) may also exacerbate symptoms. Signs that may be found on physical examination of the patient include the Gutsche sign; the application of a firm manual pressure around the abdomen of the seated patient produces transient relief. Furthermore, this headache may or may not be associated with other symptoms **(8)**.

Symptoms associated with PDPH may include: Neck stiffness, dizziness, hyperacusis, hearing loss, tinnitus, Nausea and vomiting, diplopia, photophobia, or difficulty in accommodation. **(10)**.

The severity of PDPH can be classified using a modified Lybecker classification (Table 1).

Table (1) : Modified Lybecker classification (11).

Mild PDPH	Moderate PDPH	Severe PDPH
Slight restriction of daily activities.	Significant restriction of daily activities.	Complete restriction of daily activities.
Patient not bedridden.	Patient bedridden most of the day.	Patient is bedridden all day.
No associated symptoms	Associated symptoms may or may not be present.	Associated symptoms present.
Responds well to non-opiate analgesics.	Requires the addition of opiates.	Not responsive to conservative management.

Incidence of PDPH

The incidence of PDPH in the year (1898) was 66% as reported by Wulf. However, with the introduction of 22 G and 24 G needles in (1956), the incidence decreased. It Was reported an overall incidence of PDPH can reach up to 36% with the highest incidence of 36% was found after ambulatory diagnostic lumbar puncture using a 20 or 22 gauge standard Quincke spinal needles**.** The pregnant woman is at particular risk of PDPH because of sex, young age, and the widespread application of neuraxial anesthesia **(1)**.

Risk factors for PDPH

Size of the spinal needle: -

Indeed, the smaller the size of the needle, the smaller the dural defect and consequently the lesser the incidence of PDPH**.** The incidence of PDPH varies greatly according to the size of the spinal neddle as it is reported to be about 40% with a 20 G needle; 25% with a 25 G needle; 2–10% with a 26 G needle, and less than 2% with a 29 G needle. However, technical difficulties are common when spinal anesthesia is attempted with 29 G or smaller needles **(12).**

Design of the spinal needle: -

Cutting needles (Quincke) are associated with a higher incidence of PDPH than pencil point needles (Sprotte and Whitacre) **(13).**

Cutting needles were thought to be more traumatic as they cut across the longitudinal fibers of the dura and prevent the retracting dural fibers from sealing the puncture site when removed. However, microscopic dissection of cadaveric dura mater showed that dura fibers run concentrically around the medulla spinalis **and** that pencil point needles were actually more traumatic to the dura than cutting needles. So it was assumed that the trauma caused by the pencil point needles resulted in a greater local inflammatory reaction that helped seal the dural puncture leak more efficiently **(14)**.

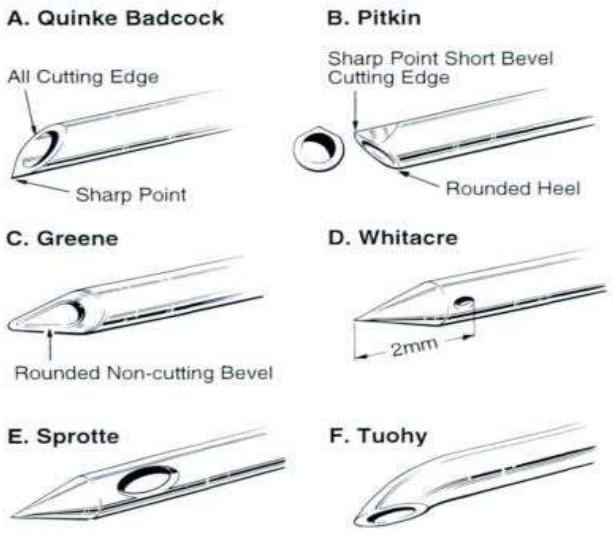


Figure (2): Design of spinal and epidural needles.

Bevel orientation of the spinal needle: -

A longitudinal bevel orientation (bevel orientation parallel to the long axis of the spinal column) is more favorable than perpendicular orientation as it significantly decreased the incidence of PDPH, when compared with the perpendicular (10.9% versus 25.8%) **(15)**.

Approach for administering spinal anesthesia: -

Regarding the angle of insertion of the needle, an in vitro study using a model of human dura mater demonstrated a smaller loss of CSF when the needle was inserted using the paramedian approach (0.3-0.4 ml/min), whereas when the midline approach was used the loss of CSF was greater (3.3-1.6 ml/min). One possible explanation would be that the paramedian approach decreases the loss of CSF resulting from perforation of the dura mater and the arachnoid at different angles, producing a valvular mechanism that prevents a greater CSF flow to the epidural space **(16)**.

Age of the patient: -

It was found that patients between 21 and 50 years old have a higher risk for developing PPDH. The incidence of PDPH decreases with the increasing age. Patients above 50 years old are the least likely to suffer from PDPH and this can be attributed to: **(17)**.

- Reduced elasticity of the dura mater, which makes it more difficult for CSF to leak through the puncture hole.
- Weaker reaction of the cerebral vessels to CSF hypotension.
- Reduced vertebral extradural space allowing a small amount of CSF accumulation, thereby arresting the leak of CSF from the subarachnoid space (increased extradural resistance).

On the other hand, PDPH is not common in children, due to less physiological pressure from the CSF and the low hydrostatic

pressure in the lumbar region when these patients sit up, compared with adults **(16)**.

Female gender particularly pregnant women: -

In Wu et al.'s study, women showed a risk of PDPH 2.25 times greater than that of men, while another study demonstrated that the risk of PDPH in women was twice as great as that of men, irrespective of age, needle caliber or design of the bevel. This can be attributed to the following factors**(18)**.

- Physiological, anatomical, social and behavioral characteristics peculiar to women.
- High levels of estrogen can influence the tone of the cerebral vessels, thus increasing the vascular dilatation in response to CSF hypotension especially in the premenopausal phase.
- Women seem to process nociceptive information differently from men, showing greater sensitivity to painful stimulation, which facilitates the central sensitization process, as has been shown in neuroimaging studies.
- The thickness of the dura-arachnoid, which facilitates CSF leakage when the dura is thinner as in women, could possibly account for the susceptibility of women to consecutive episodes of PDPH**(19)**.

Smoking: -

Smoking decreases the incidence of PDPH probably due to the clot-promoting properties of smoking that facilitates the occlusion of the dural puncture **(20)**.

Body mass index of the patient (BMI): -

Patients with lower BMI are more likely to develop PDPH than patients with higher BMI **(21)**.

History of previous PDPH: -

Patients with previous history of PDH have a higher risk for developing it again after spinal anesthesia **(3)**.

Treatment of PDPH

1-Non-invasive treatment:

- **Psychological support**

Postpartum PDPH usually makes it difficult for the mother to take care of her newborn and interact with other family members, which makes her angry, resentful and depressed **(1)**.

Severe PDPH may also delay discharge from the hospital, so psychological support of the mother becomes essential and a detailed explanation of the cause of headache, the anticipated time course, and the available therapeutic options should be discussed with her **(22)**.

- **Posture:**

PDPH is characterized by this postural element in which the headache increases on sitting and standing and is relieved after lying down. So horizontal position is usually preferred by the patients and also should be recommended **(23)**.

- **Hydration**

There is a little or no evidence that increased fluid intake has a therapeutic effect on PDPH. However, increased oral hydration especially with caffeinated drinks remains the popular first step therapy for PDPH **(22)**.

- **Caffeine**

Caffeine is a central nervous system stimulant, which produces cerebral

vasoconstriction. It is available in an oral and intravenous form and it easily crosses the blood-brain barrier and has a long half-life of 3–8 hours. Several studies however, showed that the beneficial effect of caffeine might be transient **(22)**.

- **First line analgesics**

Paracetamol and NSAIDS are usually used to alleviate symptoms of PDPH as they decrease synthesis of pain mediating prostaglandins **(24).**

- **Theophylline**

Theophylline is a member of the methyl xanthine family available in long-acting oral preparations, which might be a suitable alternative to caffeine for the treatment of PDPH. It is a potent cerebral vasoconstrictor**(25)**.

- **Sumatriptan**

Sumatriptan is a serotonin receptor agonist that affects predominantly type D_1 receptors. It promotes cerebral vasoconstriction in a similar way to caffeine. Sumatriptan has been advocated in the treatment of migraine and recently, for PDPH. Nevertheless, this drug is expensive and must be given subcutaneously **(26)**.

- **Gabapentin**

Gabapentin is a structural analogue of gamma-amino-butyric-acid (GABA). Thus it likely increases the concentration of GABA in the brain. Oral (300 - 400 mg) every 8 hrs decreases VAS score of PDPH **(27)**.

- **Adrenocorticotrophic hormone**

The proposed mechanisms of action of the adrenocorticotropic hormone (ACTH) include increased beta endorphin levels and increased intravascular volume. However, this therapy is not widely used in clinical practice and deserves further investigation **(28)**.

Hydrocortisone

Corticosteroid hormone receptor agonist. IV (200 mg) and then 100 mg three times a day (oral) for 48 hours decreased VAS score by 50% 6 hours later and by 75% 24 hours after treatment **(28)**.

- **Abdominal binder**

Abdominal binder causes an increase in the intra-abdominal pressure, and subsequently an increase in CSF pressure. This may reduce the symptoms of PDPH **(1)**.

2-Invasive treatment:

If the patients don't show improvement after 48 hours of conservative measures the following invasive strategies should be considered:

- **Greater occipital nerve block (GONB)**

Bilateral GONB is a minimally invasive, low-volume, safe peripheral nerve block which can be offered to patients who are suffering from PDPH when conservative management is ineffective. If the patient continues to suffer from PDPH even after bilateral GONB, an epidural blood patch should be considered **(28).**

- **Epidural blood patch (EBP)**

Epidural blood patch (EBP) has become the "Gold Standard" in the treatment of PDPH. It is a relatively simple procedure; sterile autologous blood is injected epidurally at or near the site of the dural puncture. It is thought to work via sealing of the CSF leak by local blood clot formation and increasing intracranial CSF pressure and volume by mass effect **(29)**.

It was reported that blood can serve as a sealing material. In his study he injected 2 - 3 ml of blood to seven patients suffering from PDPH at the site of the puncture. No consensus was reached as to the precise volume of blood required for EBP, but it was

recognized that the 2-3ml of blood originally described by Gormley is inadequate, and that 20-30 ml of blood is more likely to ensure success. However, there was a successful case treated with larger volumes of blood up to 60 ml in patients with spontaneous intracranial hypotension **(30)**.

A systematic review published in 2010 showed that EBP reduced the duration and intensity of PDPH compared with conservative treatment. Indeed, the reported success rate of the EBP technique was 70-98% if carried out more than 24 hours after the dural puncture. However, though it seems a highly effective way of treatment with minor complications, up to 30% of patients would experience recurrence of symptoms requiring a second EBP **(31)**.

On the other hand, EBP can lead to some complications such as:

- Backache which is probably caused by local nerve root irritation and can last up to 5 days.
- Accidental injection of the blood intrathecally, instead of epidurally can lead to blood-borne infections such as arachnoiditis or meningitis and various neurological deficits such as cauda equina syndrome or permanent nerve damage.
- Other complications may include; facial nerve paralysis, spinal subdural hematoma, dizziness, vertigo, and pneumocephalus **(32)**.

- **Epidural saline or colloid injection**

Colloid solutions (dextran 40%, hydroxyl ethyl starch and modified fluid gelatin) and saline injections at the site of the prior lumbar puncture are believed to decrease CSF leakage by restoring the subarachnoid pressure; however, the effect is transient due to their quick dispersion. A few case studies showed relief of the headache in most patients, but with high rate (50%) of recurrence**(33)**.

- **Epidural morphine**

Eldor and others in (1992) (34) were the first to show that injection of 3.5 - 4.5 mg of morphine via an epidural catheter caused total relief of the pain in six patients. A study published later on supported this idea; administration of 3 mg morphine epidurally significantly reduced PDPH and the need for EBP **(35)**.

- **Intrathecal catheter**

This involves placement of a catheter through the dural perforation. The mechanism of action is believed to be a local inflammatory reaction created by the catheter that promotes dural tear healing and reduces the CSF leak **(36)**.

- **Fibrin glue**

Fibrin glue is a biological adhesive made up of fibrinogen and thrombin that is applied to the tissue sites to glue them together or block bleeding by creating a fibrin clot.

There were successful PDPH cases treated with epidural fibrin glue after failure of EBP, injected through percutaneous CT guidance or blindly. There is however, an increased risk of infections, immune reactions and anaphylaxis because fibrinogen is a biological material derived from pooled human plasma and it contains tranexamic acid which can cause severe nervous complications **(37)**.

- **Surgery**

Cases that are unresponsive to the above suggested therapies are subjected to neurosurgery to seal the dural puncture. This is clearly the last resort treatment **(38)**.

<u>Prevention of PDPH</u>

A large meta-analysis was conducted in 2013 and demonstrated that five methods were shown to reduce the incidence PDPH**(38)**:

- Using non-cutting small-gauge pencil-point spinal needles.
- Lateral bevel orientation during insertion.
- Prophylactic epidural blood patch.
- Prophylactic epidural morphine.

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