ACCIDENTAL DURAL PUNCTURE DURING NEURAXIAL ANAESTHESIA – POSTDURAL PUNCTURE HEADACHES AND POTENTIAL NEUROLOGICAL DEFICITS: AN OVERVIEW

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SUMMARY

The cerebrospinal fluid surrounding the spinal cord and brain and contained within the subarachnoid space and ventricles has essential roles in support of these central nervous system structures. From the inception of spinal anaesthesia in the late 19th century, the iatrogenic generation of postdural puncture headaches after accidental dural and subarachnoid dural puncture during spinal and epidural procedures and subsequent cerebrospinal fluid leak, has been problematic, not only in terms of prevention but also in terms of treatment. This brief overview of the literature considers the nature and incidence of the problem of postdural puncture headache (PDPH), the theories relating to the central nervous system mechanisms that occur with cerebrospinal leaks leading to PDPH, the symptoms and other possible complications associated with cerebrospinal leaks, the need for differential headache diagnoses in some cases, and current recommendations for treatments of cerebrospinal leaks and prevention of PDPH. Brief discussion also includes deliberate dural punctures such as lumbar puncture procedures to extract CSF, since these procedures also carry a high risk of PDPH.

INTRODUCTION

In 1898, Karl August Bier, the German surgeon, a pioneer in spinal anaesthesia, had the experience of a severe postdural puncture headache (PDPH) after a spinal anaesthetic with loss of cerebrospinal fluid (CSF).[1] PDPH and its prevention after accidental dural puncture during epidural or spinal procedures remains problematic today particularly in epidural or spinal anaesthesia for obstetric surgery and labour. In the world literature, the topic continues to be discussed, especially as there are few adequate randomized controlled trials on different preventative techniques after accidental dural puncture, In South Africa, however, there is scant literature on the topic. This literature review considers the nature of the problem, the complications that may arise after accidental dural puncture during epidural or spinal anaesthesia, the putative mechanisms of PDPH, the types of conservative and invasive treatments applied both for prevention and in treatment of PDPH, particularly regarding PDPH in obstetric anaesthesia, and the efficacy of such procedures for resolution of PDPH.

NATURE OF THE PROBLEM: PDPH

Accidental dural puncture leads to leak of CSF which causes altered hydrostatic and haemodynamic pressures in the mechanical support and protection of the brain.[2] Such alterations are assumed to play an important role in the development of PDPH. However, no correlation has been found between the volume of CSF loss and the degree of headache after dural puncture.[3]

PDPH can be distinguished from other types of headache, such as migraine. The bilateral headache may be frontal, occipital, or in both areas, and pain may also be experienced from stiffness in the neck and upper shoulders. Headache onset occurs within 15 minutes of assuming an upright position and is relieved within 30 minutes of lying flat.[4] Onset usually occurs within 48 hours of the accidental dural puncture but in 25% of cases develops later than 3 days after the event.[4] In the largest study on duration of PDPH in which 8460 patients were followed up, in 72% of the patients the PDPH resolved within 7 days and by 6 months in 87% of the patients.[5] Slipman et al. (2005), however, report a case of PDPH that persisted for 3 months despite two previous intralaminar blood patches being applied, and was finally relieved by a fluoroscopically-guided transforaminal cervical blood patch.[6] This case is interesting in that the fluoroscopic-guided blood patch was successful where the blind application of the previous blood patches had not been successful).6 Furthermore, MacArthur et al. (1992) report a case where the PDPH lasted for 8 years. [7]

During the PDPH, the severity of the headache makes it very difficult for mothers to care for their newborns since the lying prone is the only position that relieves the headache intensity. PDPH also potentially increases costs to the patient by prolonging hospitalizations. Fortunately, in most cases, the PDPH is self-limiting, resolving within 7 to 14 days, although this time may be very painful and an initial dysfunctional period for new mothers. However, the risk for more serious complications is present after accidental dural puncture and need to be borne in mind.

In a recent review on the topic, the rate of accidental dural puncture after epidural catheter placement is reported to vary between 0.19% and 3.6%, as found in a number of surveys.[8] After such an incident, it has been shown also that over 50% of parturient patients develop PDPH.[9] It is also worth noting that untreated, persistent PDPHs may lead to subdural haematoma, herniation and death.[10]

PHYSIOLOGICAL CHANGES DURING PREGNANCY AFFECTING REGIONAL ANAESTHESIA

Pregnancy induces important physiological changes that require consideration in obstetric anaesthesia.

Pregnancy also induces changes in the epidural structure during pregnancy. In a epiduroscopic study in which a 17-Tuohy needle and loss-of-resistance to air followed by injection of 5ml of air into the epidural space was used, and comparing women who were non-pregnant, pregnant in the first trimester and pregnant in the third trimester, Igarashi *et al.* (2000) found that:

"... the epidural pneumatic space, after injection of a given amount of air, was narrower and the density of the vascular network greater in the third-trimester group than in the other two groups. The amount of engorged blood vessels was greater in the third and first trimester groups than in the nonpregnant group. The amount of bleeding at the needle tip and the amount of fatty and fibrous connective tissue did not differ among the three groups. ..." [11]

These authors concluded that the above changes in the epidural space may increase the spread of local anaesthetic during pregnancy, therefore resulting in lower doses of local anaesthetic being required for analgesia in epidural or spinal regional analgesia during pregnancy. The risk of additional bleeding in the dural spaces due to needle rupture of engorged blood vessels would seem to be also greater during regional anaesthesia in the third-trimester of pregnancy, although no differences in this respect were found between the three groups in the above study.[11]

In the experience of the author (JR), the physiological changes leading to general softness of tissues and narrowing of the epidural space during pregnancy, result in difficulty during regional anaesthetic procedures in assessing when the needle tip has entered the dural spaces as there is generally less resistance than normal in the ligamentum flavum to such entry. There is therefore greater risk of causing tears in the dura resulting in CSF leakage. For this reason, inexperienced anaesthetists need to exercise greater care in performing neuraxial anaesthetic procedures on pregnant patients.

MECHANISMS OF CSF LOSS LEADING TO PDPH

There are three dural layers consisting of collagen and elastic fibres surrounding the brain and spinal cord – the dura mater, the arachnoid mater and the pia mater. These layers extend from the

foramen magnum to the second sacral spinal segment.[10] In the horizontal position, the lumbar CSF pressure is between 5 and 15 cm H_2O, and when sitting or standing upright, this pressure increases to 40 cm H_2O.[1] Imaging studies show that these dural lamellae have no consistent pattern, but that the fibres of the outer dura mater lamella generally run parallel (longitudinal) to the spinal cord while the inner lamellae are more transverse.[12, 13] Gaiser (2010) points to the finding that the thickness of the "posterior dura" (at different spinal segment levels) varies across individuals, and such variability is not predictable.[4] These findings imply that dural puncture in thicker portions of the dura are less likely to produce CSF leak and PDPH.[4] The cerebrospinal fluid (CSF) in the spinal subarachnoid space and ventricles of the brain provides buoyancy and protection to these structures. Normal volume of CSF in an adult is 150ml, with 80% in the ventricles. CSF is produced at 0.35ml per min (approximately 20 ml per hour) and the full volume is replaced 3.7 times per day.[14]

While it is generally accepted that, after accidental needle punctures, PDPH results from the loss of CSF through the hole in the compromised dura, there is still debate about which subsequent mechanisms produce postdural puncture headaches. Since several specific sequelae have been shown to follow loss of CSF, a number of different related mechanisms have been proposed. PDPH and the accompanying symptoms seem to involve the effects of several such mechanisms, perhaps with differential applicability across patients.[5]

The consequences of excessive loss of CSF through a dural tear as they relate to the main hypothesized mechanisms of PDPH may be summarized as follows:-

1. *intracranial hypotension* with concomitant reduction in CSF volume and reduction of adult subarachnoid pressure from the normal 5-15 cm H_2O to 4 cm H_2O or less.[1] These authors point out that studies have shown that the rate of CSF loss of 0.084-4.5 ml per second is greater than the rate of CSF production of 0.35ml per min, especially with a dural tear from a large needle (25G); as already noted, however, the development of PDPH does not necessarily correlate with the amount of CSF lost.[3]

2. *reduced CSF protection and buoyancy* of the spinal cord and brain, which, together with the reduced intracranial pressure, causes traction of and subsequent *"sagging"* of sensory innervated intracranial structures which then produce the pain of the PDPH and symptomatic transient cranial nerve palsies – the cranial nerves most affected are the 3rd, 4th, 6th, 7th and 8th. [15]

3. *venodilatation*, whereby, as compensation for the loss of CSF, there is an acute distension of the venous sinuses and increased blood flow.[1,16] The proposal for this mechanism is based on the Monro-Kellie hypothesis, according to which the "sum of volumes of the brain, CSF, and intracranial blood is constant";[1] acute distension of the venous sinus complexes have also been shown to produce pain; 16 this consequence has led to the proposal that PDPH have similarities to a vascular-type headache, and the use of medications such as the triptans in prevention and treatment of PDPH.

4. Specifically referring to lumbar puncture headache (LPH)], Levine et al. (2001) propose the hypothesis that CSF loss leads to *"abnormal craniospinal elasticity"*, in which:-

   "...Lumbar puncture increases the compliance of the caudal spinal portion of the CSF space relative to the rostral intracranial portion. This increase in caudal compliance changes the distribution of hydrostatic pressure in the CSF, causing an abnormally low intracranial CSF pressure in the erect position. As a result, there is acute intracranial venous dilation on sitting or standing, over and above any venodilation caused by CSF hypotension in recumbency." (p. 2) [16]

These authors draw on the analogy of hydrostatic pressure in a closed water-filled tube with elastic top and bottom seals to illustrate the hydrostatic pressure changes that occur when the tube is horizontal and perpendicular, and which they propose as explanation for the orthostatic nature of postdural puncture headaches produced by CSF leakage.

Summary: Theories of the mechanisms of PDPH

Accidental dural and arachnoid mater needle punctures with subsequent CSF leaks from the subarachnoid space disrupt the hydrostatic and haemodynamic pressures maintained within the CSF-containment areas of the spinal cord and the brain, leading to intracranial hypotension and compensatory venodilation, traction and pressures on intracranial structures with accompanying neurological disturbances of normal neural sensory and motor functions. The combined effects of these sequelae result in the symptoms accompanying CSF leakage. These are better explained by reference to the integrated effects of such leakage, rather than reliance on one effect alone.

RISK FACTORS

Specific demographic factors seem to be associated with PDPH, although the reasons are not clearly understood.[10] The following demographic characteristics are considered to be risk factors for PDPH:-

- **Patient age:** below the age of 13 years, children seldom experience PDPH, probably due to CSF pressures in children, while adolescents increasingly experience PDPHs similar to those of adults. The highest risk age range is between 18 and 40 years, with risk 3-4 times greater at 25 years than at 65 years.

- **Female sex:** irrespective of age, is a risk factor for PDPH, but the reasons are not known. Women have twice the probability of PDPH than men.

- **History of chronic or recurrent headache or previous PDPH:** are reported in about 60% of patients with PDPH, and previous history of PDPH predisposes to subsequent PDPH on further postdural punctures.

- **Pregnancy:** by itself, has not been shown to be a cause of PDPH. Accidental dural puncture during epidural anaesthesia for labour significantly increases the risk for PDPH, but the risk is also elevated for pregnant women receiving spinal anaesthesia alone.

- **Low body mass:** young, thin women appear to be at highest risk for PDPH.[10]

Differences in incidence of PDPH between females and males may relate to the brain size differences between the genders.[17]

NEEDLE SIZE AND DESIGN

For regional anaesthesia involving delivery of epidural or spinal anaesthetics, either during surgeries or for pain management, the needles used for drug delivery are essential in reducing the risks of creating punctures that produce excessive CSF leakage after accidental dural punctures. Since the extraction of CSF in procedures like lumbar punctures deliberating produce punctures of the dura and subarachnoid mater with consequent occurrence of PDPH, consideration in such procedures should also be given to the needles used so as to reduce the risks of PDPH. The most important needle factors relate to the size and shape of the needle tip and level of orientation of the needle tip to the dura during procedures.[10,18] Many studies have been conducted on these needle features in both anaesthetic and lumbar puncture procedures. While these factors are familiar to anaesthesiologists, they may not have the same significance to other physicians or specialists who use of needles during their spinal procedures.[18]

Amount of CSF loss from a subarachnoid and dural hole and the shape of the puncture holes are directly related to the size of the needle used - the larger the needle, the greater the CSF loss and the more frequent and severe the PDPH.[10,18] In this respect, cutting edge (Quincke) needles carry a higher risk of larger CSF leakage than atraumatic pencil-point or non-cutting needles (Sprotte and Whitacre), because these latter needles produce smaller dural holes.[10,18] These authors also point to studies that show that the incidence of PDPH is greater than 80% with 16-guage needles as opposed to 5% with 26-guage needles, and that the smaller pencil-point spinal needles have reduced the incidence of PDPH between 0.02-1.5%. It is therefore recommended that 24-guage pencil-point needles have favourable results, and avoid the epidural failure rate with very small-guage needles.[10]

Candido *et al.* (2003),[18] citing the study by Dittman *et al.* (1988),[12] who, in reporting on the variability of the thickness of the dura, also described the "tin can lid" phenomenon, in which:

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its base. The hole tends to be ellipsoidal when the needle is inserted through a thick section of dura. By contrast, when a needle of the same gauge and design perforates a thinner section of dura, the resultant orifice is larger, and it closes much more slowly. A hole left in the dura resembles an opened tin can rather than a neat punched out hole. The resulting

flap may fall back into place, virtually sealing the hole. ... Quincke needles produce an oval or ellipsoidal hole, as opposed to Whitacre or Sprotte needles, which produce a more rounded hole".[18]

In addition, bevel orientation of the needle tip is important to the nature of the puncture hole produced. While the dural fibers do not have a consistent orientation, the size of the opening in the elastic fibres is minimized when the Quincke cutting bevel of the needle is inserted parallel to the longitudinal axis of the spine, causing the dural hole to be smaller because fewer fibres are cut than if the needle tip were in the perpendicular orientation. There is therefore less CSF leakage through such a hole. This consideration does not arise with pencil-point needles, as the tip tends to separate the dural fibres rather than cutting them, and they return to their original position with decreased CSF leakage.[10,18]

Frank (2008) also mentions that the study by Strupp et al. (2001) showed that replacing the needle stylet before removal of the needle reduced PDPH from 16% to 5% with 21-guage Sprotte atraumatic needles.[10,19] The stylet replacement may therefore prevent the needle tip from pulling a strand of arachnoid mater into the dural rent thereby maintaining an opening that allows greater CSF leakage. Although not formally studied, if the needle tip strikes bone on insertion and is then damaged, it has been hypothesized that the same effect as above may occur with a subsequent CSF leakage.[10]

The cost of pencil-point needles may be prohibitive in developing countries, as reported by Nafiu *et al.* (2007) from a tertiary teaching hospital in Ghana.20 In their obstetric setting and in other West African obstetric/anaesthetic practices, these authors report that the most commonly used needle for spinal anaesthesia is the 22-guage Quincke needle. In their study, they compared the use of the 22-guage needle in 12 patients (12.5% of the population), 25-guage needle in 46 patients (47.9%) and the 26-guage needle in 38 patients (39.6%) in the production of postdural headaches. They report that PDPH developed in 8 patients – an overall incidence of 8.3% - but that 50% of these patients were in the smallest group for whom spinal anaesthesia was performed with the 22-guage cutting-edge Quincke needles, although these patients comprised only 12.5% of the study population. Based on these findings, they recommend that the 22-guage Quincke needle should be stopped for obstetric spinal anaesthesia, when the risk of PDPH is considered, but, where alternative pencil-point small-guage needles are unavailable due to prohibitive cost, the risk of PDPH should be explained to the patients. [20]

Citing the study by Sharma *et al.* (1995) in which more postdural puncture paraesthesias were found with dural punctures produced by 25-guage Whitacre needles compared to the Atraucan 26-guage needle, Turnbull *et al.* (2003) postulate that the reason for this finding may be that the tip of pencil-point needles have to be inserted at least 0.5 mm into the subarachnoid space before the needle orifice enters the subarachnoid space, and the tip may thus impinge on the stretched cauda equina. [21, 1]

POSTPROCEDURAL COMPLICATIONS

POSTDURAL PUNCTURE HEADACHES DUE TO PNEUMOCEPHALUS

Although fortunately rare, according to the literature, and distinguished by the headache not being a positional related as in PDPH and the headache and not being relieved in the supine position, another risk factor is pneumocephalus, which requires a differential diagnosis from that of PDPH. Pneumocephalus is associated with the use of the "loss of resistance" technique for identifying the subarachnoid space using air rather than saline or a liquid medium. The air introduced into the subarachnoid space travels intracranially causing post-procedural symptoms, including headache, which usually resolve with absorption of the air.

Velickovic IA *et al.* (2007) report an illustrative case of a parturient 23-yr old female on whom they performed a combined spinal epidural in the sitting position using the loss of resistance to air technique and a Tuohy needle.[22] The patient complained immediately after the delivery of a shooting severe headache. A CT scan three days after the procedure confirmed pneumocephalus in the frontal horn of the right lateral ventricle, interhemispheric fissure, and superior cerebellar cistern. Because the symptoms then decreased, the patient was discharged home the following day, but returned to the hospital 6 days later with "typical symptoms of postdural puncture headache". While repeat CT scan showed that the intracranial air had been absorbed, an epidural blood patch improved the headache after 5-6 hours.

Schier *et al* (2005) conducted a meta-analysis to test the hypothesis that the use of a liquid medium "loss of resistance" technique, compared to the use of air, reduces the complications with epidural placement, they found that, in 5 studies with 4422 patients of which 4 were obstetric and 1 large nonobstetric study of chronic pain patients, there was no statistical difference in the overall risk for adverse outcomes in the obstetric population.[23] There was a small, statistical significant risk difference for PDPH when fluid was used during epidural placement for chronic pain management, being 1.5% lower in chronic pain patients. While recognizing the limitation of their study in that only 1 large study of chronic pain patients was found, they conclude that using the liquid technique reduces the incidence of PDPH in chronic pain patients. Two further case reports reflect this finding for pneumocephalus after lumbar epidural steroid injections with the "loss of resistance" technique using air in elderly chronic back pain patients.24,25 Post-procedural symptoms mimicked a stroke in the second case reported.25 In both cases, CT scans confirmed the diagnosis of pneumocephalus, and treatment with increased inspired oxygen resolved the headache and symptoms.

The potential complications of postdural puncture may be considered in terms of an event-time perspective, in which complications may be immediate as a consequence of CSF leakage (within 24 hours), intermediate (occurring between 24 hours and 72 hours) and long-term (occurring from 72 hours onwards).

Table 1 below summarizes some of the other potential complications that may follow inadvertent dural punctures.[10,26]

Table 1: POSTDURAL PUNCTURE COMPLICATIONS

>24 HOURS	24 – 72 HOURS	>72 HOURS
Cerebral Hypotension	Postdural Puncture Headache	- PDPH usually resolves in
Spread of local anaesthetic	Symptoms associated with	+/- 1 week, but can rarely lead
(increased level of block)	PDPH: nausea, vomiting	to prolonged headache
Increased risk of infection	dipoplia, hearing loss,	needing medical treatment
Bacterial meningitis	Cranial nerve palsies	- sometimes onset delayed
	(Sacadai *et al.* 2010; and	with full recovery from 2 weeks
	Nishi *et al.* 2004)	to 8 months
	Subdural haematoma	
	Increased cost of hospitalization	

CASE REPORT: POSTDURAL PUNCTURE, HEADACHE AND DIPLOPIA

A 36 year old male, due for surgical knee ligament repair, underwent lumbar epidural anaesthesia (L3-4), performed with an 18-guage needle and loss of resistance with air. Anticoagulation was not administered. The dura was inadvertently punctured. It decided to thread an epidural catheter in the subarachnoid space and a mixture of spinal bupivacaine 0.5% (1.5ml) plus 10μg fentanyl was introduced. The ligaments were repaired successfully under a thigh tourniquet. At the end of surgery, a further dose of 10μg fentanyl plus 2.5ml saline was introduced into the subarachnoid space.

Postoperatively, the patient complained of postdural puncture headache and bilateral diplopia. To avoid the headache, he moved his head to look to either side rather than moving his eyes. CT scan was normal. The headache resolved before the diplopia about which the patient was more concerned. Referral to the Professor of Ophthalmology resulted in a diagnosis of 6th nerve palsy with a recommendation for conservative treatment. The patient was at first quite litigious, but calmed down with regular phone call follow-ups and consistent reassurances that the symptoms would resolve without further treatment. There was a marked improvement at 6 months with complete recovery at 9 months.

Dipoplia, also termed extraocular muscle paralysis (EOMP), has been reported infrequently in the literature as occurring after dural punctures.[27] Forty reported cases were reviewed, reflecting the international literature from 1966 to 2002, in which the incidence of EOMP varied from 1 in 400 to 1 in 8000, being most prevalent after either spinal anaesthesia or diagnostic lumbar punctures where larger spinal needles were often used. On the type of procedures after which EOMP had been reported, Nishio *et al.* (2004) summarize their findings, as follows:-

"Spinal anesthesia was found to be the most frequently reported procedure involved (47%), followed by myelography (18%), diagnostic lumbar puncture (12%), epidural anesthesia/injection (11%), continuous spinal anesthesia (4%), and other dural puncture procedures (9%)".[27]

While lumbar puncture may induce other temporary cranial nerve palsies, Nishio et al. (2004) also point out that:

- in 92-95% of cases the abducens nerve (cranial nerve VI) is affected;
- in 80% of cases this abducens palsy is unilateral and can co-exist with oculomotor (cranial nerve III) or trochlear (cranial nerve IV) nerve palsies;
- such multiple co-existence with a large esotropia causes difficulty in exact diagnosis;
- the pathophysiological mechanism is unclear but the generally accepted mechanisms are either nerve lesion causing neuropraxia or nerve stretch with or without nerve compression from intracranial hypotension resulting from the CSF leak;
- VII nerve palsy may fully recover any time between 2 weeks and 8 months, although there are rare reports of permanent symptoms. [26, 27]

From the above, it can be seen that our case had typical features of postdural puncture headache and prolonged sixth nerve palsy.

ANTICOAGULATION DURING PREGNANCY AND SUBDURAL HAEMATOMAS

Although associated more with potentially serious neurological deficits in the perioperative period than with postdural puncture headaches, the rare occurrence of subdural haematoma after neuraxial anaesthesia and increased risks with the frequent use of anticoagulation to counteract the hypercoagulable state during pregnancy needs to be considered briefly. Tryba (2003) points out that incidence of bleeding during neuraxial anaesthetic procedures has been estimated to be less than 1/150,000 for epidural and less than 1/220,000 for spinal anaesthesia.[29] There is the possibility of bleeding in the spinal canal during needle or catheter placement or removal.[30] In the general surgical population, after uncomplicated epidural needle puncture or catheter insertion, slight bleeding in the epidural space may occur in 2.8-11.5% of patients.[30] Narchi (2004) also points out that, while such bleeding is usually self-limited, in cases with a clotting abnormality (either spontaneous or drug-induced), and where difficult needle or catheter placement occurs, the bleeding may lead to formation of epidural haematomas.[30]

In his analysis of 613 cases of spinal and epidural haematomas reported between 1826 and 1996, one of the findings by Kreppel (2003) was that over 50% of the cases reported occurred after 1989.31 Allopi (2009) comments that this apparent increase in reported cases may be due to the use of modern imaging techniques such as MRI for diagnostic purposes and ease of electronic publication.32 For example, Zeidan et al. (2006) report a case of a 39 year-old parturient who underwent caesarean section with spinal anaesthesia, performed with a 26-guage traumatic needle.[33] Postoperatively she developed severe non-postural headache with right-eye tearing, fifth cranial nerve palsy and left hemiparesis. The diagnosis of subdural haematoma was confirmed by CT scan. With conservative treatment, full recovery occurred after 12 weeks. In their literature review, these authors found 46 patients who had developed a postdural puncture headache complicated by development of subdural haematoma. It may be concluded that, after accidental postdural puncture, careful follow-up is needed for early diagnosis and management of possible subdural haematomas for patients in whom postdural puncture headaches are not relieved by appropriate measures and whose headaches change from postural to non-postural with concomitant neurological deficits.

Therapeutic anticoagulation represents the major risk factor for epidural haematoma after neuraxial anaesthesia.[34] Anticoagulation therapy during pregnancy is prescribed as prevention for thrombotic complications due to hypercoagulability, venous stasis, and vascular damage – the three elements of Virchow's triad.[34,35] Anticoagulant medications can be divided broadly into anti-platelet drugs and anticoagulation drugs, which have different pharmacological actions on the clotting processes. In the first group of drugs are included aspirin and the non-steroidal anti-inflammatory medications, adenosine receptor antagonists of which clopidogrel and ticlopidine are the main agents, and GPIIb/IIIa antagonists of which there are three quite different agents – aboximab, tirofban and eptfbatid.32,35 In the second anticoagulant group are unfractionated heparin, the mainstay of anticoagulation in the past, warfarin (coumarins – Vitamen K antagonists), and the low molecular weight heparins (LMWHs), which have become the preferred anticoagulants during pregnancy for the past 10 years, although it should be noted that physiological changes during pregnancy alters the metabolism of this class of medications leading to higher doses needed during pregnancy, and that their cost is higher than unfractionated heparin.[35] Direct thrombin Inhibitors (DTIS) are yet again newer anticoagulant drugs that have been developed.[32]

In South Africa, where it is estimated that up to 80% of the population uses both traditional medicines and conventionally-prescribed medications in their healthcare, the anaesthetist planning regional anaesthesia for parturients needs to be aware that some herbs, such as garlic, gingko and ginseng, are active in causing anticoagulation, although research is still needed on the extent of this risk factor.[37, 32]

Coumarin is known to exist widely in plants, and its derivative constitutes the anticoagulant, Warfarin, widely used for thrombophylaxis in potentially thromboembolic conditions. It has particular contraindications during pregnancies of women with mitral valve replacements, although it is often used prophylactically outside pregnancy for such patients.[38] If found to be prescribed during pregnancy, warfarin should be converted to heparin for the duration of the pregnancy, subject to peripartum interruption.

To reduce the risk of peripartum bleeding during neuraxial anaesthesia and minimize the associated risks, including that of subdural haematoma, the American Society of Regional Anesthesia (2002) has laid down guidelines for mandatory interruption of oral heparin anticoagulation in the peripartum period. In these guidelines, a distinction is made between unfractionated heparin and LMWH drugs. Gibson *et al.* (2009) summarize these guidelines as follows:-

"...To facilitate use of regional anesthesia in these women, therefore, options include:

- Electively stopping LMWH 24 hours before planned induction of labor
- Electively stopping prophylactic-dose LMWH or unfractionated heparin at about 38 weeks of gestation, to await spontaneous labor, or

- Switching therapeutic or prophylactic LMWH to unfractionated heparin at about 36 weeks of gestation, with instructions to discontinue the injections in the earliest stages of spontaneous labor. This aims to shorten the heparin-free period required before neuraxial anesthesia while minimizing maternal thrombotic risk. ..."[35]

Allopi (2009) points out that there is an increased risk of spinal haematoma when antiplatelet or oral anticoagulant medications are administered in combination. (Studies on the newer anticoagulants in respect of subdural haematomas still need to be performed).[32]

PREVENTION OF PDPH

In attempts to prevent the development of PDPH, both conservative and invasive procedures have been employed with varying levels of reported efficacy.

Conservative Interventions

Table 2 lists some of the reported conservative means for PDPH prevention, and indicates the reported effectiveness for prevention and associated shortcomings.

Invasive Procedures

Table 3 below lists the published invasive procedures that are applied for prevention of PDPH.

In their systematic review on prevention of PDPH, Apfel *et al.* (2010) point out that no clear agreement exists as to which prophylactic invasive procedure is most effective, because the reported results of these interventions are mixed, and there is a lack of randomized controlled trials, In addition, there is a plethora of non-randomised studies and a publication bias towards reporting positive outcomes in small populations in such studies.[8]

In the South African literature, Lamacraft (2004) provides a good overview of the topic of complications of regional anaesthesia for caesarean section, including postdural puncture headaches.[38] This review covers the same aspects as discussed in this paper regarding the incidence, nature and treatment of PDPH, with the exception that the author points out that intrathecal morphine may lead to the reactivation of herpes simplex in patients.

As can be seen in Table 3 above, the greatest percentage difference between the UK and the USA in the use of a prophylactic invasive procedure exists in the use of epidural blood patches.

Summary: Efficacy of Invasive prophylactic procedures for prevention of PDPH

1. **Intrathecal catheters:** Apfel et al. (2010) point out that the results of studies in which an intrathecal catheter is threaded through the dural hole are "highly heterogenous" in that several small studies show that leaving the catheter in place for at least 24 hours is more preventative of PDPH than shorter term placement (>24 hours), but that no preventative effect was found in a larger study.[8]

2. **Epidural saline bolus:** In their analysis of three studies using epidural saline, Apfel et al. (2010) found that these studies failed to reach statistical significance with a relative risk (RR) of 0.65 (95% CI – 0.40-1.05), and that the one study on intrathecal bolus of 10mg of saline also failed in this respect. In addition, from the pooled results of non-RCTs and RCTs, there was evidence of publication bias for small non-RCTs with positive results.[8]

3. **Epidural blood patch:** Apfel et al. (2010) analyzed 9 published studies – 5 non-RCTs and four RCTs in respect of this prophylactic procedure – they found that, in the non-RCTs, there was a significant reduction in PDPH (RR = 0.48, 95% CI – 0.23 – 0.99), but that overall the RCTs did not show statistical significance (RR = 0.32 95% CI = 0.10-1.03), although again the results showed significant heterogeneity.8 In the non-RCTs analyzed, the volume of the blood patch varied between 5-20ml, while in the RCTs, the volume varied between 15-20ml, and this difference in volume may be important.[8]

Oedit RR et al. (2005) provide a comprehensive study protocol for their RCT of epidural blood patch application for PDPH treatment after lumbar puncture, including a diagramme of the method of application.39 In the published results of this study, van Kooten et al. (2008) report that 17 patients were randomly allocated to epidural blood patch and 23 patients to conservative treatment.40 There were 2 drop-outs from the epidural patch group before application of this treatment, and 7 drop-outs from the conservative treatment group. Seven days after blood patch application, 3 of these patients (16%) still had a mild headache, but were able to return to daily activities, while 18 patients in the conservative treatment group still had headaches, in 10 of whom the headache was classified as moderate or severe. On the basis of these results, the authors conclude that epidural blood patch is an effective treatment for PDPH, resulting in complete resolution of headache in a large proportion of patients, and reducing the severity of headache in the remaining patients.[40]

Table 2: Conservative Interventions to prevent or relieve PDPH

Interventions	Reported Efficacy	References
Bedrest	Lessens severity	Gaiser, 2010
Analgesics	Pain relief only	
Intravenous hydration	Overhydration unnecessary	Schwalbe, 2010
Other medications: Triptans	Generally not effective	Frank, 2008
Caffeine (Oral: excessive amounts needed)	Not effective	Schwalbe 2010 Lin 2002
Methylxanthine derivatives (aminophylline)	Reported 90% efficacy	Frank, 2008
Intravenous caffeine sodium benzoate	Mixed reports	Schwalb access 2010
Triptans (sumatriptan) – mixed results	Generally – not effective	Gaiser, 2010
Cosyntropin (ACTH analogue)	Effective (v. text)	Hakim, 2010

Table 3: Common Invasive procedures for prevention of PDPH

Interventions	Reported usage: UK	UK-USA USA	References Surveys in the UK and USA
Catheter placement *(intra-thec)	15%	19%	UK: Baraz *et al*,. 2005
Epidural saline bolus	13%	12-25%	USA: Harrington *et al*., 2009
Epidural Blood Patch	1-2%	10-31%	
Epidural morphine (1 RCT)		Al-Metwalli, 2009	
long-term intrathecal			

4. Epidural morphine:

Apfel *et al.* (2010) found only one small randomized control trial (50 parturient patients – conducted in Saudi Arabia [Al-Metwali, 2008]) of prophylactic epidural morphine applied for the prevention of PDPH after inadvertent dural puncture, although there are a number of uncontrolled other reports in the literature.[8,41] The patients in this RCT were parturients who had an inadvertent dural puncture with a 17-guage epidural needle during epidural analgesia for labour delivery and subsequent epidural catheter placement. Twenty-five patients each were randomly assigned to either the control group (10ml epidural saline) or to the trial group (3mg epidural morphine) after diagnosis of inadvertent dural puncture. Two morphine and saline injections were applied 24 hours apart. The results showed a significant difference in incidence of PDPH between the two groups – 3/25 (12%) in the morphine group and 12/25 (48%) in the saline group ($p = 0.014$). Also six patients in the epidural saline group required a therapeutic epidural blood patch to resolve their headaches, while none of the epidural morphine group required this treatment. Nausea was more frequent in the morphine group as a side effect. The conclusion drawn from the study was that epidural morphine appeared to be a simple and effective method for preventing PDPH after accidental dural puncture in high-risk obstetric patients.[41]

Apfel *et al.* 2008) report that in the above study, a statistically significant relative risk (RR) of 0.25 (0.08-0.78) arose from the reduction in incidence of PDPH in the epidural morphine group. Further and larger studies of epidural morphine for prevention of PDPH after accidental dural puncture are needed to confirm the efficacy of this preventative treatment.[8]

In the South African literature, Lamacraft (2004) provides a good overview of the topic of complications of regional anaesthesia for caesarean section, including postdural puncture headaches.[38] This review covers the same aspects as discussed in this paper regarding the incidence, nature and treatment of PDPH, with the exception that the author points out that intrathecal morphine may lead to the reactivation of herpes simplex in patients. However, complications due to HIV infection are not mentioned in this paper.

Neuraxial blockade and PDPH in HIV-positive patients

Apart from extra caution being taken in the preanaesthetic assessment of HIV-positive parturient patients, the literature indicates that there are no greater risks for neuraxial anaesthesia in HIV-infected patients than in the non-infected population, with the exceptions that HIV-infected patients may be more susceptible to spinal pathologies due to the early spread of infection to the CSF, and that such patients may be at higher risk for complications if the PDPH is not treated early – epidural blood patches being relatively safe in such patients.[42, 43, 44]

CONCLUSIONS

This review has focussed on providing an overview of the problem and its remediation presented by the production of inadvertent postdural puncture headaches after neural anaesthesia, mainly for obstetric analgesia, but with mention of other spinal procedures such as diagnostic lumbar punctures and epidural analgesia for chronic pain. While considerable success in prevention and treatment of PDPH has been reported in the literature for the various conservative and invasive methods, some treatments have been shown to be ineffective. New invasive methods to improve efficacy are being applied and studied with greater rigour, but the search and debate continue. In South Africa, there is still the need for studies to be conducted, particularly in view of our HIV-infected obstetric population.

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