

Low CSF pressure headache

*SR Thanthulage**

*Consultant in Anaesthesia and Pain Medicine, Mid Essex
Hospitals NHS Trust, Broomfield Hospital, Chelmsford, Essex, UK*

**Corresponding author: subodha@btinternet.com*

Orthostatic headaches following dural puncture are well known to anaesthetists as well as other physicians who perform lumbar punctures. However, due to the progression of medical knowledge and newer diagnostic capabilities, many other causes of low pressure headaches have been recognised. Even though low pressure headache is largely under-diagnosed at present, with increased awareness it may become a common finding in the future. This article includes symptoms, diagnostic problems, and treatment options available for patients with low CSF pressure headache including post dural puncture headaches.

Keywords: low pressure headache; spontaneous; iatrogenic; intracranial hypotension; cerebrospinal fluid leak; low cerebrospinal fluid pressure.

Introduction

The normal intracranial pressure (ICP) depends on age and body posture. In a healthy adult this could range between 7-15mmHg supine to -10 to -15mmHg in vertical position. According to the Monroe- Kellie doctrine, the total intracranial volumes which consist of brain, blood, CSF and other pathological entities such as tumours remain fixed.¹ The dynamics of ICP is maintained by changing volumes of blood or CSF. While cerebral blood flow (CBF) depends on cerebral perfusion pressure (CPP), the CSF production, absorption and circulation play a key role in ICP.² Normal production of CSF in an adult is around 500ml a day and its pressure in the lumbar spine could vary between -5 to-15 mmHg on horizontal and around 40mmHg in sitting positions.³ The most common neurologic symptom associated with CSF pressure change is headache. Low pressure headaches, which are due to low CSF pressure or volume, are increasingly implicated as a cause of daily persistent headache.^{1,2,3,4} Low pressure headache could be provoked (following lumbar puncture or breaching of the dura following a neurosurgical procedure) or spontaneous (CSF leak). Low pressure headache without any clear provocation is termed as spontaneous intracranial hypotension (SIH).^{5,6,7}

Causes of spontaneous and iatrogenic CSF leak (Box 1)

Spontaneous CSF leak generally neither present with any local symptoms nor carry any risk of

infection, as the CSF leak is into a sterile environment. This is unlike the CSF leak following a surgical procedure or traumatic injury. Causes of the leak are largely unknown but the predisposing dural weakness such as dural or arachnoid diverticula or trivial trauma are hypothesised as contributing factors and are commonly found in patients with connective tissue disorders.^{7,8,9} One of the postulated complications of weak dural tissue is possible CSF leak around those areas (nerve root sheath, epidural cyst or diverticula) due to cough, minor trauma or severe exercise or even dural tear caused by a spondylitic spur.^{7,8,10,11,12} Anatomical location of the CSF leaks need to be actively investigated on a suspected patient.^{4,8,10,12} The commonest anatomical sites are at the cervico-thoracic junction or at the thoracic spine. The skull base is the least common place to have CSF leaks.^{8,10,11}

Iatrogenic CSF leaks in anaesthetic practice mainly occur following lumbar puncture or neurosurgical interventions.

The anatomy and pathophysiology of low pressure headaches

The spinal dura mater starts at the foramen magnum and can extend up to the lower limit of S2 which consist of dense connective tissue matrix of collagen. Nevertheless there are tight fibrous connective tissues being identified connecting the posterior spinal dura at the atlanto

–axial and atlanto–occipital levels to nuchal ligament.^{6, 13,14}

Box 1: Potential risks factors for low CSF pressure headaches^{7,8}

Risk factors for spontaneous CSF Leak	Risk factors for iatrogenic (lumbar puncture) CSF leak
Marfan Syndrome Ehlers-Danlos Syndrome Autosomal dominant polycystic kidney disease Isolated joint hypermobility Isolated skeletal features of Marfan syndrome Joint hyper mobility with facial thinning Spontaneous retinal detachment	Age 18-40 Female sex Low BMI History of chronic headaches Size of the needle Shape of the needle Bevel orientation Failure to replace stylet before removal of the spinal needle Poor hydration

The pathophysiology of the disease was first described by Augustus Bier in the 1890s as being due to a CSF leak. The pain generators of the low pressure headache are not entirely certain. The best theoretical explanation is, that the imbalance between the CSF leak through the dural defect and the production, give rise to depletion of CSF volume. Firstly this will generate reflex vasodilation of pain sensitive cerebral vessels to compensate intra cranial volumes; secondly there will be traction on pain sensitive meninges and cranial and spinal nerves. Furthermore another causative factor of headache is neuronal hypersensitivity to substance P which is released in high quantities in up to 30% of the dural puncture patients.

Clinical presentation and diagnosis of low CSF pressure headache¹⁰

The commonest clinical presentation in low CSF pressure headache is orthostatic headache which occurs or worsens within 15 minutes on upright position and improves within 30min of ‘lying down’ or within 3 days of epidural blood patches, although this could be variable.^{7,8} Iatrogenic low CSF pressure headaches are followed by the event and 66% to 90% dural puncture related CSF leaks become symptomatic in 2 to 3 days respectively.⁷ Onset of spontaneous CSF leak headaches could be abrupt or sub-acute, reaching maximum intensity overtime or may be very vague and become apparent over time.¹⁰⁻¹⁵ Typically the pain locations are frontal (5th cranial) occipital, temporal (9th and 10th cranial) neck and shoulders (C1, 2, 3).^{8,9}

Description of headache may be throbbing, or non-throbbing, pulling the head toward the neck, feeling of an ice cube in an empty glass and it is rarely unilateral.^{4,8} Although postural headache is the hallmark of low CSF pressure headache, in untreated patients the posture related component may become less prominent. Headache may become lingering and persistent and unrelated to posture or completely absent.^{7,8,12,15} The most common accompanying symptoms according to literature reports are nausea, neck stiffness and photophobia which suggest meningeal irritation. The symptoms such as tinnitus and hyperacusis (extreme aversion and hypersensitivity to sounds) or hypoacusia (slightly diminished acuteness of the sense of hearing) with a sense of losing balance are associated with irritation of 8th intra cranial nerve complex.^{4,8,9,12,15} An ophthalmological symptom such as diplopia after spinal anaesthesia was described by Augustus Bier for the first time 100 yrs ago. The ophthalmological effects such as visual blurring or visual field defect and diplopia are due to the effects on 2nd, 3rd, 4th and 6th cranial nerves. The common and rare clinical manifestations of CSF leak in otherwise healthy adults are summarised in Box 2. Subtle cognitive changes may fail to be recognised until the successful treatment of the CSF leak. Spinal manifestation of the CSF leak can be shoulder, inter scapular pain, radicular symptoms or local back pain at the site of the injections.^{8, 9,12,15}

As with any other disease, diagnosis should start with listening to the patient’s history and a thorough examination. Low pressure nature could be easily missed as the presentation symptoms could be vague, especially in spontaneous CSF leak, however such patients may also present with acute symptoms.¹⁶ Although 90% of PDPH patients present within first 3 days, presentation could be delayed up to 12 days or if untreated headache can remain with long term CSF leak.^{17, 18,19,20}

Box 2: Common and rare clinical manifestation of CSF leaks^{10,15} (These symptoms have been reflected in the International Headache Society (IHS) Diagnostic Criteria (**Box 3**) caused by low ICP.^{4, 5, 8})

<p>Common symptoms</p> <p>Headache Neck stiffness or pain (meningeal irritations) Shoulder and interscapular pain (traction on cervical 123 nerve roots) Nausea with or without vomiting Altered hearing (Echoed, distant noise, muffled noise) Disturbed sense of balance or dizziness Photophobia (meningeal irritations) Visual blurring (11,111, IV,VI, cranial nerves palsy) Horizontal diplopia (unilateral or bilateral cranial nerve VI palsy)</p> <p>Uncommon</p> <p>Non horizontal diplopia (cranial nerve 111 or 1V palsy) Encephalopathy, obtundation, coma, stupor Visual field defects Upper limb numbness, weakness or spasm Menieres syndrome like symptoms (labyrinthine hydrops) Fronto-temporal dementia Parkinsonism, ataxia, bulbar manifestations Dorsal mid brain syndrome Unsteady gait Bladder and bowel control difficulties Quadriplegia Chorea Decrease growth hormone secretion, galactorrhoea (due to the distortion of pituitary gland) Amnesia Psychic akinesia (hypoactive hypo alert behaviour) Transient herniation Acute respiratory failure Cerebella haemorrhages</p>

If the clinical diagnosis of CSF leak has been suspected, radiological investigation and diagnostic studies will greatly facilitate the confirmation of the cause as well as its anatomical location.

Magnetic Resonance Imaging (MRI) has greatly improved the understanding of the features of intracranial hypotension as well as reduces the time needed to confirm the diagnosis. (Figure 1) On the other hand poor understanding of the MRI changes or variable findings, may prevent the patient been diagnosed with low pressure headache. Diagnostic studies and typical features seen are summarised in Box 4.

Box 3: IHS Diagnostic criteria caused by low CSF pressure headaches^{4,5}

Criteria	Post-dural puncture headache Diagnostic criteria	CSF fistula headache	Headache attributed to spontaneous (or idiopathic) low CSF pressure
A	neck stiffness tinnitus hypoacusia photophobia nausea	neck stiffness tinnitus hypoacusia photophobia nausea	neck stiffness tinnitus hypoacusia photophobia nausea
B	Dural puncture has been performed	A known procedure or trauma has caused persistent CSF leakage with at least one of the following: 1. evidence of low CSF pressure on MRI (e.g., pachymeningeal enhancement) 2.evidence of CSF leakage on conventional myelography, CT myelography or cisternography 3. CSF opening pressure <60 mm H ₂ O in sitting position	1. evidence of low CSF pressure on MRI (e.g., pachymeningeal enhancement) 2. evidence of CSF leakage on conventional myelography, CT myelography or cisternography 3. CSF opening pressure <60 mm H ₂ O in sitting position
C	Headache develops within 5 days after dural puncture	Headache develops in close temporal relation to CSF leakage	No history of dural puncture or other cause of CSF fistula
D	Headache resolves either spontaneously within 1 week within 48 hours after effective treatment of the spinal fluid leak (usually by epidural blood patch)	Headache resolves within 7 days of sealing the CSF leak	Headache resolves within 72 hours after epidural blood patching
Confirmation of the diagnosis	Headache that worsens within 15 minutes after sitting or standing and improves within 15 minutes after lying, with at least one of the Criteria A and fulfilling criteria C and D	Headache that worsens within 15 minutes after sitting or standing, with at least one of the Criteria A and fulfilling criteria C and D	Diffuse and/or dull headache that worsens within 15 minutes after sitting or standing, with at least one of the Criteria A and fulfilling criterion D

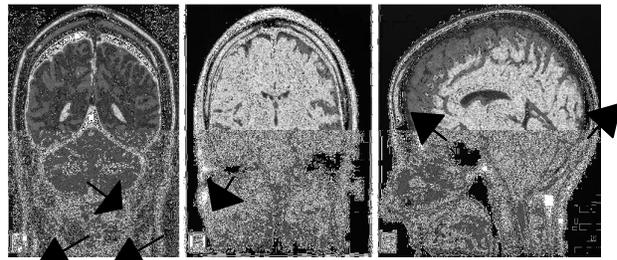
Box 4: Diagnostic studies

Diagnostic study	Findings	Remarks
MRI	Subdural collections, Pachymeningeal enhancement Engorgement of venous structures Pituitary hyperaemia, Sagging of the brain	Pachymeningeal enhancement is the most well documented abnormality, could be identify as diffuse, non-nodular enhancement in supra and infratentorial compartments. Nevertheless around 20% of the patient this may be negative. Improvement of MRI changes could identify within days to weeks of the successful treatment for the CSF leak. Patient who does not have specific treatment may still have the MRI changes despite their clinical improvements.
Cranial computed tomography	Subdural fluid collections Obliteration of subarachnoid cisterns and ventricular collapse	May not be conclusive but has a diagnostic value in emergency department setting.
Myelography	Location of the leak Extent of the leak, Meningeal diverticula	In combination with enhanced MRI thin cut myelography allows most accurately identify the leak in the entire spine. Fear of cerebral herniation due to the myelography not yet documented and risks exacerbation of existing symptoms are around 5%.
Radinucleotide scintigraphy	Early accumulation of tracer in kidneys and bladder Slow ascent along the spinal axis Paucity of activity over the cerebral convexities Parathecal activity at the level or approximate site of leak	This remains useful when the diagnosis of CSF leak in doubt with normal myelography results. May not show exact site of the leak and may remained incomprehensible in one third of patients.
Spinal MRI	Dilated epidural and intra dural veins Dural enhancement Meningeal diverticular Nerve root sleeve ectasia Extrathecal CSF collections Syringomyelia Retrospondyl fluid collections.	In the presence of extradural fluid will helpful to identify the location of the leak, but this is very rare to be effective.
Lumbar puncture and CSF opening pressure measurements	Low CSF pressure (less than 60 mm water)	Can be persistently normal
CSF analysis	Lymphocytic pleocytosis Normal or elevated proteins content up to 1000mg/dl Xanthochromia	CSF appearance may be normal, xanthochromia is probably due to increased permeability of dilated venous complexes but it could be due to blood tap.

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Figure 1: Diagnostic investigations in CSF leaks



A, Brain MR images showing typical findings in spontaneous intracranial hypotension with a coronal T2-weighted image showing subdural fluid collections; B, a coronal gadolinium-enhanced T1-weighted image showing enhancement of the pachymeninges; and C, a T1-weighted sagittal image showing sagging of the brain ⁴ (Published with permission of Professor W.I. Schievink)

Incidence and differential diagnosis (Box 5)

Low pressure headaches associated with spontaneous intracranial hypotension and fistula leaks are rare (5 in 100,000, female to male ratio 1:2). On the other hand incidence in post dural puncture headache (PDPH) is not uncommon and could vary (10-30%).^{2,8,20,21,22}

Box 5: Differential diagnosis in low pressure headaches^{8,17,20}

Primary headaches

Migraine

Tension headaches

Secondary headaches

Low CSF pressure headaches

Subarachnoid haemorrhage

Cerebral vein thrombosis

Meningitis

Intracerebral bleed

Eclampsia

Cerebral tumour

Non-specific headache

Sinusitis

Treatment

Although there are several methods of treatment available for low CSF pressure headaches most of the iatrogenic and spontaneous CSF leaks resolve spontaneously with bed rest and hydration. Symptoms of PDPH may improve within one week, but duration for resolution of spontaneous leaks is unknown.^{7,8,11}

Conservative treatment

Patients who seek medical treatment should initially be treated with conservative methods. The key is to reassure the patient and provide emotional support, bed rest, regular analgesics and hydration. Even though bed rest has been advocated it can only postpone the headache in some PDPH patients. Oral and intravenous hydration remain key to avoid dehydration, as poor hydration is associated with headaches, although it has not shown to increase the CSF production.^{7,8,9}

Caffeine

Effect of caffeine is due to cerebral vasoconstriction and stimulating the CSF production. Intravenous injection of caffeine may be 70 to 80% effective in the initial stage of the treatment of PDPH, but unfortunately headache may return after 48 hours.^{7,9, 11}

Theophylline

As with caffeine intravenous theophylline causes cerebral vasoconstriction.

Adrenocorticotrophic hormones

Steroid hormones act by stimulating adrenal gland to increase CSF production and endorphin release, and can be used to treat low CSF pressure headaches.

Epidural saline and colloid infusions

These methods only produce transient effect due to increase in epidural pressure thereby reducing the CSF leak temporarily.

Autologous epidural blood patch (ABP)

In the event of failure to respond to conservative treatment using a targeted epidural blood patch should be considered. The main stay of treatment of CSF leak with autologous epidural blood (ABP) patch was first described by Gromeley in 1960.²¹ Pain relief is usually instantaneous and this often confirms the diagnosis. The mechanism of pain relief is firstly associated with the immediate dural tamponade effect and secondly with sealing of the dural leak. The success rate of persistent pain relief in PDPH could vary between 61 to 95%. Most recommended blood volumes are 15 to 20ml for the 1st blood patch. A second ABP will be able to relieve symptoms in almost all patients.⁷ On the other hand in spontaneous intracranial hypotension, ABP may help only up to 30% of the patients.^{7,8} The discrepancy is likely to be due to the fact that spontaneous leaks could also be in the anterior aspect of the dura, the dural sleeves or could be due to multiple leaks. Furthermore dural holes may be complicated with weak unsupported subarachnoid tissues. In the event of multiple leaks, targeted multiple limited EBPs could be performed at multiple sites.¹¹ If the 1st ABP is not effective the second blood patch with up to 100ml could be injected within 5 days interval. The volume of blood could be restricted due to high risk of infection with large volumes as well as back and radicular pain.^{8,22}

Other techniques

If epidural blood patching fails to reduce pain, placement of percutaneous fibrin sealant should be performed. Surgical repair should be left as the last resort for patients who are refractory to all other methods of treatment. Surgical repair of the CSF leaks are safe and can provide long lasting relief but this needs knowledge of the precise anatomical location of the leak. Accurate diagnosis and treatment of the low CSF pressure headache has very good prognosis of long lasting relief with less than 10% of recurrence in spontaneous CSF leaks.⁸

In conclusion, low CSF pressure headaches while not a life threatening condition may cause considerable lowering of the quality of life.

Iatrogenic causes of low CSF pressure headaches are well recognised and measures to reduce it should be undertaken. Spontaneous intracranial

hypotension often remains under diagnosed. The spectrum of clinical and radiographic manifestations is varied, with diagnosis largely based on clinical suspicion, cranial magnetic resonance imaging, and myelography. Numerous treatment options are available, but much remains to be learned about this disorder.

Acknowledgments

The author wishes to thank Drs. P Tilakaratna, S Liyanage and VN Rathnasiri, for their valuable suggestions and editing of this review.

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