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How to find and overcome reason of the pain - an overview of the possible approaches in intracranial hypotension treatment

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Abstract

Introduction: Intracranial hypotension syndrome develops following cerebrospinal fluid (CSF, cerebrospinal fluid) leakage as a result of iatrogenic or spontaneous interruption of the meninges. The main clinical manifestation of intracranial hypotension, whether spontaneous (SIH, spontaneous intracranial hypotension) or iatrogenic, is a chronic headache of the orthostatic type, which may be accompanied by symptoms of neurological deficits. Despite the usually benign course, subdural haematomas developing following SIH or cerebral venous sinus thrombosis can cause deterioration of the patient's condition and may even be life-

threatening. An important role in the diagnosis of SIH is played by imaging studies (mainly magnetic resonance imaging) of the brain and spinal canal, sometimes supplemented by CSF pressure testing. If conservative treatment fails, consideration should be given to surgical management and epidural blood patch. SIH is dangerous, so it is important to know how to diagnose and treat it.

Purpose: The aim of this scientific paper is to review the current knowledge on the diagnosis and treatment of intracranial hypotension.

Review Methods: We conducted our study as a literature review based on information gathered from PubMed, Embase, GoogleScholar using combinations of the following

Keywords: Spontaneous intracranial hypotension, orthostatic headache, epidural blood patching, CSF leakage, surgery

The state of knowledge: Spontaneous intracranial hypotension (SIH) is a condition that presents with orthostatic head and neck pain due to spontaneous cerebrospinal fluid (CSF) leakage or CSF-venous fistula in the spinal region. Recent advances in neuroradiological techniques have facilitated the understanding of the pathophysiological basis and clinical diagnosis, and the development of more effective methods of investigation and treatment.
The diagnosis of spontaneous intracranial hypotension (SIH) usually involves a combination of different methods to confirm the reduction in CSF pressure and identify any leaks. Treatment options may include initial conservative management with bed rest, caffeine and fluids, steroids and analgesia, interventions such as an epidural blood patch or surgical closure of the leak. Application of a surgical blood patch reinforced with a dural replacement membrane through an anterior single level discectomy may be a successful treatment option.

Conclusion: While diagnosing SIH can be challenging, pinpointing the exact location of the CSF leak is crucial as it greatly informs the selection of an appropriate treatment method. Invasive procedures, like EBP or surgery, have a bigger successful rate in relieving all the symptoms of intracranial hypotension. However, conservative treatment may be a great support in management of this condition.

Introduction

Spontaneous intracranial hypotension (SIH) is a clinical and radiological syndrome caused by spinal leakage of cerebrospinal fluid (CSF) due to a dural tear, leaking meningeal diverticulum or CSF venous fistula. In the USA, it is estimated to occur at a rate of 3.8 cases per 100,000 people annually, roughly equivalent to 2500 new cases of SIH each year in the UK [1]. The syndrome develops more frequently in women than in men (2-5:1), usually in the third or fourth decade of life, but can also occur in children or older people [2]. The etiology of SIH is not fully understood and is thought to be multifactorial [3]. It is thought that CSF leakage may occur as a result of localised weakness or damage to the dura in the region of nerve root exits or within meningo-venous fistulas, as well as compression from disc herniations and osteophytes [4, 5]. Minor injuries, mainly related to falls, are reported in 80% of patients [2]. It has been suggested that certain connective tissue diseases or defects (including Marfan syndrome, polycystic kidney disease, Ehlers-Danlos syndrome type II, neurofibromatosis and Lehman syndrome) may predispose to meningeal diverticula [6]. Meningeal damage is further promoted by manual therapy (chiropractic) [7]. CSF leakage is the most common feature of intracranial hypotension and the vast majority of cases had a cervical or thoracic location of CSF leakage [8, 9]. SIH is most commonly associated with orthostatic headache (i.e. headache that begins or significantly worsens on standing up and improves soon after lying down). Orthostatic headaches manifest in roughly 92% of individuals with SIH [10]. Headache usually improves within 30 minutes of lying down [11]. A minority of patients with radiological evidence of SIH have either non-orthostatic headache (5%) or no headache (3%) [10]. SIH can lead to a variety of other symptoms, which are not specific, including vertigo, ringing in the ears, hypoacusis, tinnitus, nausea and vomiting, photophobia, posterior neck pain, ataxia and root syndrome, fatigue and cognitive impairment (usually non-specific difficulty concentrating) [3,10]. Rarely, SIH can present with a complication such as a subdural haematoma, superficial siderosis or venous sinus thrombosis [12, 13]. Several potential diagnoses can be considered for orthostatic headaches. Due to the similarity in symptoms post-dural puncture and those arising from cerebrospinal fluid leakage due to surgical or traumatic causes, it is imperative to inquire about a patient's history of lumbar puncture, epidural or spinal anaesthesia, and spinal surgery when suspecting SIH. Orthostatic headache may occur in patients with postural tachycardia syndrome or orthostatic hypotension, both of which should be considered in cases

where imaging results are normal. In the diagnostic process of SIH, occipital neuralgia should be considered and ruled out, due to the fact that in SIH the headache is most often localized in this area. Orthostatic headaches may be mistaken for movement sensitivity in migraines or position-related headaches in cervicogenic headache. Thus, it's crucial to verify that the headache is triggered by an upright position, not movement or neck position. It's essential to keep in mind that migraine and SIH can coexist [14, 15].

Review methods

We conducted our study as a literature review based on information gathered from PubMed, Embase, GoogleScholar and explored the methods of diagnosis and management to overcome intracranial hypotension.

The State of Knowledge

Spontaneous intracranial hypotension (SIH) is a condition presenting with orthostatic head and neck pain due to spontaneous cerebrospinal fluid (CSF) leakage or CSF-venous fistula in the spinal region. Recent advances in neuroradiological techniques have facilitated the understanding of the pathophysiological basis and clinical diagnosis, and the development of more effective methods of investigation and treatment [14]. The diagnosis of spontaneous intracranial hypotension (SIH) usually involves a combination of methods to confirm the reduction in CSF pressure and to identify any leaks. SIH can be diagnosed clinically by orthostatic headache and associated symptoms and radiologically by contrast-enhanced MRI of the brain [16]. Treatment options may include initial conservative management with bed rest, caffeine and fluids, steroids and analgesia, interventions such as an epidural blood patch or surgical closure of the leak [17]. Placement of a surgical blood patch reinforced with a dural replacement membrane through an anterior single level discectomy may be a successful treatment option. If there is no response to non-targeted epidural blood patch(s), dynamic CT myelography or digital subtraction myelography should be used to localise the site and cause of the CSF leak in the spinal cord for targeted surgical treatment [16].

Diagnostic criteria and diagnostic algorithm for SIH

To improve the diagnostic and treatment situation and refine the relevance of the guidelines, the International Headache Society developed in 2013 a third diagnostic criteria

(Table 1) for spontaneous intracranial hypotension (SIH) based on criteria developed earlier [18]. Other conditions such as postpartum, venous sinus thrombosis and subdural haematoma, which are known to cause positional headache, must be excluded.

Table 1. International Classification of Headache Disorders (ICHD) diagnostic criteria for SIH [18].

International Classification of Headache Disorders (ICHD) diagnostic criteria for SIH	
A	Any headache fulfilling Criterion B
B	Headache has developed in temporal relation to low CSF pressure or CSF leakage, or has led to its discovery
C	Low CSF pressure (<6 cm H2O) and/or evidence of CSF leakage on imaging
D	Not better accounted for by another ICHD-3 Diagnosis

As mentioned above in the International Classification of Headache (ICHD-3) criteria, the diagnosis of SIH is based on an opening pressure of less than 60 mm H2O, which is measured by a lumbar puncture performed with the patient in the supine position, or on the demonstration of CSF leakage on imaging [18]. The 'loss' of CSF is almost always localised in the spine, usually as a result of a ventral vertical tear of the dura, a laterally localised diverticulum of the nerve root or a veno-venous fistula of CSF [19]. Only about one third of patients with SIH have a CSF opening pressure of less than 60 mm H2O. The CSF opening pressure may actually be normal or even elevated, especially in patients with a long history of SIH or a large abdominal girth [20]. This fact only emphasises the importance of demonstrating CSF leakage (or the indirect consequences of such leakage) with imaging studies and other ancillary investigations to confirm the diagnosis of SIH. At present, there is no single, absolutely reliable test that establishes the diagnosis of SIH. Magnetic resonance imaging

(MRI) of the brain before and after intravenous contrast agent administration is the primary study recommended in patients with suspected SIH. It is important to note that a normal brain MRI does not exclude SIH - up to 20-30% of patients with clinically confirmed intracranial hypotension syndrome show a normal brain image [5]. The diagnosis of SIH can be established by several types of studies with complementary indications. The diagnostic algorithm presented in the table 2 has been developed, and is currently used, in several centres with a large number of cases.

Table 2. Diagnostic algorithms for SIH [21]

Type of diagnostic study	Goal of study and pathological findings
Head MRI	Demonstration of SIH signs and potential complications (SIH: homogeneous, linear pachymeningeal contrast enhancement, subdural hematoma or hygroma, dilated dural venous sinuses, mamillopontine distance <6.5 mm, narrowing of the suprasellar cistern to <4 mm and of the prepontine CSF space to <5 mm, kinking of the midbrain with respect to the pons, diminished interpeduncular angle, enlarged pituitary gland, low cerebellar tonsils)
Spinal MRI	Demonstration of epidural fluid and/or meningeal diverticula
Possibly, transorbital ultrasonography	Measurement of the optic nerve sheath diameter in the lying and standing positions (SIH: >5% decrease of diameter)
CSF pressure measurement	Measurement of the CSF opening pressure (SIH: <60 mm h2o) (beware: only in one-third of cases)
Possibly, CSF infusion test	Measurement of CSF outflow resistance, Rcsf (SIH: <5 mmhg/ml × min in the first 3 months)
Dynamic myelography	Demonstration of a CSF leak with contrast medium egress into the epidural space

Myelo-CT	Demonstration of epidural contrast medium
Possibly, dynamic CT myelography	Precise localization of the CSF leak • Prone positioning if myelo-CT has revealed epidural contrast medium • Lateral decubitus positioning in case of prominent nerve root diverticula with or without surrounding contrast medium
Possibly, dynamic subtraction myelography	Demonstration of a CSF-venous fistula (study performed with patient in the lateral decubitus position)

Non-invasive options for treatment

Treatment for spinal CSF leaks can be divided into conservative therapy, epidural patching, and surgery. Conservative treatment includes bed rest, irrigation, steroids, analgesia and caffeine preparations [5]. Some authors have suggested that most cases of SIH will resolve with conservative therapy [22]. However, it is unclear how often this happens and how long conservative treatment should be used before other therapies are tried. In a recent systematic review and meta-analysis of 144 articles, D'Antona et al. [10] summarised the evidence on SIH. They found that successful conservative management was reported in only 28% of cases. This consisted mainly of bed rest and hydration in 88% and 83% of the included patients, respectively. The effect of other types of conservative treatment on the success rate was significantly lower, which may underestimate the overall effectiveness. Oral medications play only an adjunctive role in the management of SIH, and there are no pharmacological therapies specifically designed to treat this condition. Caffeine is the most commonly used agent and can be administered in the form of caffeinated beverages or caffeine tablets. Some patients report improvement with caffeine, although the relief provided is usually minor. Anecdotal improvement has been reported with other medications, including corticosteroids, indomethacin and theophylline, although these agents are not usually curative and may carry a

risk of side effects with prolonged use [23]. There is great heterogeneity in the type, route and dose of steroids used in previous reports, with treatment duration ranging from days to several weeks. Adverse effects are both dose and time dependent. Ecchymosis, cushingoid features, parchment-like skin, leg oedema and sleep disturbance typically follow a linear dose-response pattern [24]. However, above a certain threshold dose, weight gain, nose bleeding, glaucoma, depression and hypertension occur. Analgesics such as paracetamol and non-steroidal anti-inflammatory drugs may be tried, and occasionally, opioid medication is required, but their routine use should be avoided. Antiemetics may be required for symptomatic management of nausea and vomiting [14]. Prospective, randomized studies are needed to establish the safety and effectiveness of steroids to avoid the need for more invasive treatments [25].

Epidural blood patch (EBP)

The preferred invasive procedure is an epidural blood patch (EBP), which can be either targeted or non-targeted. It is the infusion of the small amount of the patient's own blood into the epidural space with the aim of sealing off any small leaks or tears in the dura mater and stopping the leakage of cerebrospinal fluid by forming a clot [26]. This also leads to an increase in CSF pressure. It is said that this dual mechanism has a synergistic effect elucidating both the lasting and immediate therapeutic effects of the EBP [27].

Although direct blood infusion into the lumbar spinal cord is still known as the standard procedure, now we know that most spontaneous CSF leaks emerge in the cervicothoracic or thoracic spine and in these cases targeted EBP is technically advantageous [28].

An epidural blood patch can be administered using the loss-of-resistance technique without imaging, where the physician identifies a rupture in the epidural space by the needle encountering decreased resistance after crossing the ligamentum flavum. Alternatively, and more commonly, it can be done under fluoroscopic or CT guidance [21]. Recent studies indicate that the quantity of material used could be the primary indicator of the success of EBP. In a publication involving 150 cases of spontaneous intracranial hypotension, Wu et al. found that injecting a larger volume of blood (≥ 22.5 ml compared to < 22.5 ml) was linked to a higher success rate (67.9% versus 47.0%) [29]. In 2018 a big retrospective review was conducted on 165 patients with cerebrospinal fluid (CSF) leaks who did not respond to conservative treatments such as bed rest and increased fluid intake within a two-week timeframe. All patients achieved a satisfactory recovery following one (145 patients), two

(12 patients), three (7 patients), or four (1 patient) targeted epidural blood patches administered

during their initial hospital stay. Furthermore, no significant complications occurred during the placement of EBPs or in the subsequent follow-up period, which ranged from 3.3 years, with an average duration between 1 and 7 years [30]. A limited-scale investigation involving the retrospective review of medical records from 14 patients diagnosed with SIH (aged 25–69 years) revealed that a single EBP injection resulted in symptom and radiological resolution in 85% of cases. Notably, 85% of patients experienced symptomatic improvement, with 64% achieving complete symptom resolution and 21% showing moderate improvement [31]. According to D'Antona et al., the success rate of a single EBP was documented at 64% with a confidence interval of 95% ranging from 56% to 72%. No significant adverse events were recorded following EBP treatments [10]. All of the above shows us that EBP is an effective, well-tolerated treatment, despite being an invasive procedure associated with the potential for iatrogenic complications. Side effects are reported by a small number of patients. In all studies, the most frequently notified were back pain, paraesthesia, bradycardia, dizziness. [10, 26, 30]. It is uncommon, but more dangerous complications such as pneumocephalus, spinal subdural haematoma or iatrogenic subarachnoid haemorrhage, are sometimes also linked to the usage of this method [32].

Surgical management

Surgical closure of the spinal CSF leak is recommended for patients for whom less invasive treatments such as blood patches have proven ineffective in alleviating symptoms of SIH and if the leak site has been conclusively localized [21]. Surgeons typically utilize various sealing materials, such as a fat patch, muscle piece, fibrin glue, or cyanoacrylate-based preparations, for closing the leak [33]. During surgery, the spinal leak can be addressed through microsurgical techniques, including simple suturing or the application of an adhesive patch onto the dura mater. The specific location and direction of the leak relative to the dural sac significantly influence the choice of surgical approach. Advanced neurosurgical methods enable the closure of nerve root diverticula, direct CSF-venous fistulae, and dural tears located laterally or ventrally with minimal invasiveness [34]. Access to these areas can be achieved through a dorsal approach utilizing interlaminar fenestration or hemilaminectomy. For ventral dural tears, a transdural approach is necessary, involving detachment of the denticulate ligaments to allow safe mobilization of the spinal cord under intraoperative neuromonitoring [35]. A comprehensive literature review research regarding the surgical treatment of patients diagnosed with SIH, conducted by Sobczyk et al., revealed that the majority of patients

remained symptom-free after neurosurgical treatment. The success rate for surgical intervention in SIH ranged from 82.6% to 100% [35]. These findings are consistent with other prospective, single-arm, cross-sectional investigation, in which Wang et al. recently documented significant improvement in objective headache severity among a group of 20 patients who underwent surgical ligation of CSF-venous fistulas. Furthermore, no short- or long-term complications were observed [36]. Another retrospective, observational case–control study, which was focused on what the primary determinant of positive outcomes following surgical intervention for SIH is, showed that a shorter duration of preoperative symptoms holds the greatest significance. While initial conservative treatment may be warranted, the study suggests that early definitive treatment within a 12-week timeframe, particularly in cases of persistent symptoms, is advisable [37]. The most commonly mentioned side effects in the literature are recurrent or persistent CSF leak requiring re-operation, postoperative infection, postoperative epidural hematoma and a new, but transient neurological deficit. It's important to note that none of the patients included in the aforementioned studies experienced any new, persistent neurological deficits following surgery [34, 35, 37]. This literature review indicates that surgical treatment for SIH is infrequently pursued, yet highly effective. However, given the limited research available on this topic, treatment decisions should always be personalized to the individual patient [38].

Conclusions

Spontaneous Intracranial Hypotension (SIH) poses a significant risk as it can manifest with a range of non-specific yet troubling symptoms, often leading to confusion with less severe conditions like migraine. This underscores the importance of recognizing the symptoms of SIH and exploring appropriate diagnostic avenues. While diagnosing SIH can be challenging, pinpointing the exact location of the CSF leak is crucial as it greatly informs the selection of an appropriate treatment method. Conservative treatments such as bed rest, hydration, steroids, pain relief, and caffeine preparations remain a great support in managing intracranial hypotension, and in some cases, they may suffice as the sole treatment. However, in many instances, these measures alone prove insufficient. In such scenarios, a treatment approach for intracranial hypotension must also incorporate invasive procedures such as epidural blood patch (EBP) or surgery. Both of them have demonstrated effectiveness and tolerability, despite their invasive nature and the potential for iatrogenic complications, which are rare. It is essential to bear in mind that due to the scarcity of research in this area, treatment choices should always

be tailored to the unique needs of each patient. This involves taking into account factors like limitations, adherence to treatment, and the goal of achieving lasting outcomes.

Disclosures

Author's contribution

Conceptualization:Jan Piotrowski, Izabela Hądzlik Methodology:Julia Biały-Karbowniczek, Izabela Hądzlik and Blanka Łuczak Software: not applicable; Check: Klaudia Bulska, Patrycja Brzozowska and Bianka Nowińska Formal analysis: Konrad Sławek, Andrzej Piela Investigation:Katarzyna Słychan, Jan Piotrowski Resources: not applicable; Data curation:Andrzej Piela, Konrad Sławek Writing - rough preparation: Jan Piotrowski, Izabela Hądzlik Writing - review and editing: Katarzyna Słychan, Julia Biały-Karbowniczek Visualization: Klaudia Bulska, Patrycja Brzozowska Supervision:Blanka Łuczak, Bianka Nowińska Project administration: Izabela Hądzlik
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