Clinical Neurology and Neurosurgery 186 (2019) 105552

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

CSF volume provocation maneuvers during lumbar puncture as a possible predictive tool for diagnosing spontaneous intracranial hypotension

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ARTICLE INFO

Keywords:
Spontaneous intracranial hypotension
Headache
Cerebrospinal fluid

ABSTRACT

Objectives: Spontaneous intracranial hypotension (SIH) is a pathologic state of low CSF volume caused by a CSF to venous fistula or CSF leak. It is diagnosed based on symptoms, imaging, and CSF pressure but is often a diagnostic challenge because no single test is highly sensitive. Physician-induced changes in CSF volume may result in changes in patient symptoms, as has been shown with idiopathic intracranial hypertension (IIH). The purpose of this study is to determine the sensitivity of CSF volume provocation maneuvers in the diagnosis of SIH.

Patients and Methods: We reviewed consecutive patients that underwent lumbar puncture from January 2015 to January 2017. Patients were included if they met ICHD3 criteria for SIH and CSF volume provocation maneuvers were performed. Cases were considered concordant if there was improvement of symptoms with addition of CSF.

Results: 1084 patients underwent 2250 CT-guided lumbar punctures from January 2015 to January 2017. 92 patients with SIH were identified and 62 of these patients underwent CSF volume provocation maneuvers. 58% (36/62) had concordant lumbar puncture encounters with symptom improvement upon addition of artificial CSF.

Conclusion: CSF volume provocation maneuvers demonstrate 58% sensitivity for identifying patients with SIH, better than those reported for CSF opening pressure and myelography. A positive symptomatic response to CSF volume provocation maneuvers was independent of the other objective tests used for SIH and may aid in the often-challenging diagnostic workup of these patients. Future prospective case-controlled studies are needed.

1. Introduction

Spontaneous intracranial hypotension (SIH) is characterized by a pathologic state of low CSF volume. This low CSF volume is caused by spinal pathology in the form of either a CSF to venous fistula or CSF leak, the latter arising from meningeal diverticula or dural tears due to calcified disks [1]. SIH is more common in women and has an annual incidence of approximately 5 cases per 100,000 people [2]. SIH patients often experience headaches that worsen while standing and improve when recumbent. Other symptoms can include nausea, vertigo, tinnitus, paresthesias and diplopia.

Establishing a diagnosis of SIH can be challenging since no single laboratory value or imaging exam can reliably identify all patients. For example, CSF pressures in SIH patients are often variable, with only one third of patients demonstrating low CSF pressure (< 6 cm H2O) [3]. Furthermore, 40% of patients with known SIH do not have an identifiable CSF leak on myelography [4]. Finally, the characteristic findings of SIH on brain MRI are sometimes absent [5]. For instance, 20% of SIH patients do not demonstrate pachymeningeal enhancement and only 60% have findings of brain sagging (Fig. 1) [5]. SIH is therefore diagnosed based on a combination of factors including patient symptoms, imaging findings, and CSF pressure. Current diagnostic criteria, such as the International Classification of Headache Disorders, 3rd ed (ICHD-3), take into account the need for multiple individual diagnostic components [6]. Given that there is no single test that has been shown to be highly sensitive for SIH, additional diagnostic tests could prove useful in helping to establish the diagnosis.

Since SIH has pathophysiology based on low CSF volume, physician-induced changes in CSF volume may result in changes in patient symptoms. This has been demonstrated in idiopathic intracranial hypertension (IIH), which is a pathologic state of increased CSF volume and pressure. Prior work has shown that removal of CSF in patients with IIH is associated with symptom improvement [7]. We hypothesize that patients with SIH may also experience a change in symptoms with analogous volume provocation maneuvers, specifically the addition of artificial CSF, and that response to these provocation maneuvers may be

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https://doi.org/10.1016/j.clineuro.2019.105552
Received 16 May 2019; Received in revised form 11 September 2019; Accepted 4 October 2019
Available online 07 October 2019
0303-8467/

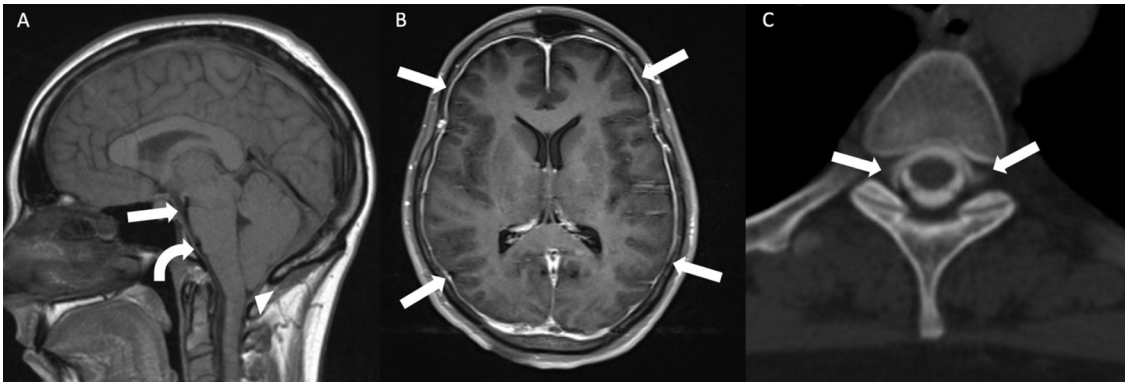

Fig. 1. Common imaging findings in spontaneous intracranial hypotension. (A) Sagittal T1-weighted MRI showing narrowing of the mammillopontine distance (arrow), sagging of the midbrain (curved arrow), and inferior cerebellar tonsillar ectopia (arrow head). (B). Axial T1-weighted post contrast MRI showing diffuse pachymeningeal enhancement (arrows). (C) Axial CT myelogram showing ventral extradural contrast collection (arrows).

a useful diagnostic tool. The purpose of this study is to determine the sensitivity of changes in patient symptoms in response to the addition of artificial CSF in patients with confirmed SIH.

2. Materials and methods

2.1. Study population

We conducted a retrospective review of consecutive patients that underwent a lumbar puncture from January 2015 to January 2017 at a quaternary care center in the United States. Patients were referred to our spine service for lumbar puncture as a part of a headache workup for known or suspected disorders of CSF volume and pressure including SIH and IIH. The medical records were reviewed to identify those that met ICHD-3 criteria for SIH (Fig. 2). Patients were excluded if they did not undergo CSF volume provocative maneuvers, were asymptomatic at the time of the procedure, or were thought to be in rebound high pressure after a prior epidural blood patch for a CSF leak [8]. This study was approved by the Institutional Review Board and was compliant with the Health Insurance Portability and Accountability Act.

2.2. Lumbar puncture

All patients referred to our quaternary care institution for evaluation of headache receive a lumbar puncture to assess their CSF pressure as part of routine standard of care. If patients have clinical symptoms suggestive of SIH or prior imaging findings confirming SIH, they also receive a myelogram to determine the site of CSF leak and to thereby determine the location of epidural blood patches. In this study, all included patients underwent a CT-guided lumbar puncture that was performed in the same way by one of three attending neuroradiologists with or without the help of a physician assistant. All three physicians hold certificates of added qualification in Neuroradiology and have at least 11 years of experience performing lumbar punctures. The patient was placed in the left lateral decubitus position on the CT gantry and an interlaminar space in the lumbar spine was identified using the scout images and limited axial images. A 24-gauge atraumatic Gertie Marx spinal needle (International Medical Development, Park City, UT, USA) was placed into the lumbar thecal sac under CT fluoroscopic guidance.

ICHD-3 criteria for SIH

- Headache has developed in temporal relation to the low CSF pressure or CSF leakage
- Headache accompanied by one or both:
  a) CSF pressure <6 cm H20
  b) evidence of CSF leakage on imaging
- Absence of a procedure or trauma known to be able to cause CSF leakage

Fig. 2. ICHD-3 diagnostic criteria for spontaneous intracranial hypotension (SIH).

Opening pressure was measured in the same manner for all cases using an analog manometer with the patient resting quietly in the left lateral decubitus position with legs extended.

2.3. CSF volume provocation maneuvers

Patients who met ICHD-3 criteria for SIH and underwent CSF volume provocation maneuvers were included for analysis. In all cases, a total of 10 mL of artificial CSF (Elliotts B solution, Baxter Laboratories, Morton Grove, Illinois) was injected into the thecal sac slowly over two minutes. After completion of the injection, patients were observed for another two minutes in order to allow for CSF equilibration. Subsequently, patients were asked to rate their symptoms as “better”, “worse”, or “the same” after the addition of fluid. Patients’ response to the addition of artificial CSF was considered concordant if symptoms improved with addition of fluid, unchanged if their symptoms were unaffected, and discordant if symptoms worsened.

2.4. Statistics

Descriptive statistics including means and standard deviations were used to present patient demographics. For continuous data, t-tests were used to assess for differences in means between groups including volume of CSF used in cases with and without concordance. Chi-squared tests were used to assess for associations between the individual covariates MRI brain findings and myelogram findings with response to CSF volume provocation maneuvers. Commercially available software (Version 3.4.1; R Statistical and Computing Software, http://www.r-project.org) was used for statistical analyses and a significance threshold was set at $p < .05$.

3. Results

3.1. Study population

A total of 1084 patients underwent 2250 CT-guided lumbar punctures from January 2015 to January 2017. Using ICHD-3 criteria, 92 patients with SIH were identified. Among those, 62 patients underwent provocative maneuvers and were included in the final study cohort for analysis (Fig. 3). Not all of the physicians at our institution routinely performed CSF volume provocation maneuvers, which accounts for the additional 30 SIH patients for which these maneuvers were not performed.

Patients were more commonly female (61%) with a mean age of 52 ± 13 years (range 20–81 years). All patients in the cohort met ICHD-3 criteria for SIH by either having a brain MRI positive for findings of SIH or a myelogram exhibiting a CSF leak. Pre-procedural

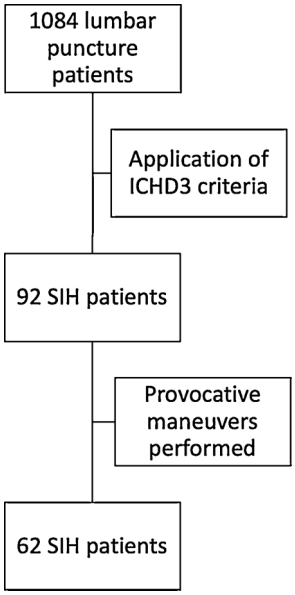

Fig. 3. Flowchart of spontaneous intracranial hypotension patient inclusion and exclusion.

brain MRI was positive in 77% (48/62) of patients and 43% (27/62) of patients had evidence of a leak on myelography (Table 1). In 26% (16/62) of the patients both the brain imaging was positive and a leak was identified on myelography.

3.2. Lumbar puncture

The mean opening pressure was 11.8 ± 5.7 cm H2O (interquartile range [IQR] 7.5–15.6). Opening pressures were less than 6 cm H2O in 10% (6/62) of SIH patients.

3.3. Response to CSF volume provocation maneuvers

Among SIH patients in this study cohort, 58% (36/62) of lumbar puncture encounters exhibited symptomatic changes that were concordant (improved) after the addition of Elliot's B solution. A total of 34% (21/62) of patients had no change in symptoms. Only 8% (5/62) of patients had a discordant (worsened) response. There was no association between positive symptomatic response to CSF volume provocation maneuvers and the CSF opening pressure ($p = 0.65$), presence of SIH findings on the brain MRI ($p = 0.16$), or the presence of a CSF leak on myelography ($p = 0.97$). There were no complications from the provocative maneuvers.

4. Discussion

SIH remains a diagnostic challenge due to the inconsistent imaging findings and variable CSF pressures. Our results demonstrate 58% sensitivity for the diagnosis of SIH with CSF volume provocation maneuvers, more specifically the addition of artificial CSF to increase the volume. This sensitivity is greater than that of CT myelography, which detected a cause of SIH in 43% of cases in our study, similar to rates found in the prior literature [4]. CSF volume provocation maneuvers were also markedly more sensitive than low opening CSF pressures, which only had 10% sensitivity in this study and ranges from 21 to 55% in other series [5,9,10]. These findings suggest that CSF volume provocation, via the addition of artificial CSF, may be a useful adjunctive diagnostic test in patients with suspected SIH.

The concept of provocative testing for evaluation of SIH has been previously proposed. Amoozegar et al suggested using provocative maneuvers that promote extradural CSF leakage (e.g. Valsalva maneuver or upright positioning) to potentially increase the sensitivity of diagnostic tests for detecting CSF leaks [11]. However, this was never formally studied and they did not consider the effect of CSF volume provocation on patient symptoms during lumbar puncture as a method for SIH diagnosis. CSF volume provocation maneuvers were established as part of our routine clinical care in the evaluation of SIH patients in 2015. This was started because physicians noted that IIH patients improved with removal of fluid and because we felt that SIH patients with CSF leaks were better visualized with higher volumes of fluid in the subarachnoid space during myelography. We found that a positive symptomatic response to CSF volume provocation maneuvers was independent of the other objective tests used for SIH including myelography, brain MRI and opening pressure, suggesting it is a useful adjunctive test in patients that may not exhibit all the classic imaging features.

It is unknown why some patients with confirmed SIH responded positively to addition of artificial CSF and why others had unchanged or worsened symptoms but we suspect that dural compliance may play a role. Dural compliance is known to be a contributing factor in IIH, another disorder of CSF volume and pressure [12,13]. Prior work has shown that symptom improvement upon CSF removal in IIH patients is due to increased spinal canal compliance, supporting the hypothesis that CSF pressure, volume and compliance are interrelated [13]. Others have hypothesized that compliance contributes to the pathophysiology of CSF leaks [14,15]. Given the connection between CSF compliance, volume and pressure, it is possible that alterations in spinal compliance may influence how patients respond to provocation maneuvers. Specifically, in patients with chronic aberrations of CSF volume and pressure, it may take extended periods of time before they experience a change in symptoms from CSF volume provocation maneuvers.

CSF provocative testing has been performed in patients with idiopathic intracranial hypertension (IIH), which is a pathologic state of increased CSF volume and pressure. Prior work has shown that removal of CSF in patients with IIH is associated with symptom improvement [7,16–19]. Yri et al were the first to perform a prospective, case-control study in which they were able to calculate a sensitivity of 72% and specificity of 77% for symptom improvement upon CSF removal in patients with IIH [7]. They suggested that provocative maneuvers be included in the diagnostic ICHD criteria for IIH. Given that SIH is also a pathologic state of CSF volume and pressure, it is logical to hypothesize that addition of CSF in these patients may also result in symptom improvement. To our knowledge, this is the first study confirming that hypothesis.

There are several limitations to this study. First, there was no control group, and therefore specificity cannot be calculated based on the current data. This provides the opportunity for further prospective research assessing the specificity and diagnostic accuracy of CSF volume provocation maneuvers for SIH. Ideally future work would include provocation maneuvers performed in patients without disorders of CSF

Table 1
Imaging features of patients with SIH and their response to provocative maneuvers.

Imaging features	Number of patients	Concordant response to provocative maneuvers
Brain MRI: Positive for SIH	48/62 (77%)	22/48 (46%)
Myelogram positive for CSF leak	27/62 (43%)	14/27 (52%)
Both brain MRI and myelogram positive	16/62 (26%)	6/16 (38%)

volume and pressure. Second, closing pressures were not routinely obtained after volume provocation maneuvers. Recording closing pressures in these patients would be valuable in determining how volume provocation maneuvers affect CSF pressures as it may help us to assess the compliance of the CSF system. A better understanding of compliance may provide information helpful in explaining why some patients exhibited discordant responses. Finally, future studies would ideally include patients with SIH that undergo a sham CSF volume provocation maneuver to account for possible placebo effect.

In conclusion, CSF volume provocation maneuvers demonstrate a 58% sensitivity for identifying patients with SIH, which is better than a low CSF pressure and CT myelogram. Furthermore, a positive symptomatic response to CSF volume provocation maneuvers was independent of the other objective tests used for SIH including myelography, brain MRI and opening pressure. Therefore, this new tool may aid in the often-challenging diagnostic workup of these patients. Future prospective case-controlled studies are needed.

Sources of funding

None.

Declaration of Competing Interest

The authors have no potential conflicts of interest to disclose.

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