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Spinal fluid evacuation may provide temporary relief for patients with unexplained widespread pain and fibromyalgia

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A B S T R A C T

Fibromyalgia (FM) exhibits characteristics of a neurological disorder, and similarities have been identified between FM and idiopathic intracranial hypertension (IICH). When intracranial pressure rises, the drainage of excess cerebrospinal fluid (CSF) through the subarachnoid space of the cranial and spinal nerves increases. Higher CSF pressure irritates nerve fibers inside nerve root sheaths and may consequently cause radicular pain, as was reported in patients with IICH. Moreover, the cut-off of 20–25 cm H_20 used to define IICH may be too high, as has been suggested in patients with chronic fatigue syndrome. We hypothesize that the neurological symptoms of FM are caused by the dysregulation of cerebrospinal pressure (CSP) and that spinal fluid drainage can relieve this pain.

Exploring the processes underlying increased CSP may provide an alternative explanation for the generation of unexplained widespread pain (WSP) and FM as opposed to central sensitization.

Additionally, when performing a lumbar puncture for diagnostic reasons, it is useful to measure opening pressure in patients with chronic WSP.

Introduction

Chronic pain is highly prevalent in the general population and is associated with a high rate of disability and poor quality of life. Although unexplained chronic widespread pain (WSP) and fibromyalgia (FM) are considered centralized pain disorders, the exact pathophysiology of these conditions remains unknown. Because of the neurological signs and symptoms and several similarities with other pressure dysregulation disorders, these conditions have been hypothesized to be caused by impaired cerebrospinal pressure (CSP) regulation [1–3].

Similarities exist among FM, WSP and CSP dysregulation syndromes, such as idiopathic intracranial hypertension (IICH), idiopathic normal pressure hydrocephalus (INPH) and symptomatic Tarlov cysts (TCs) [4].

Cerebrospinal fluid (CSF) is produced in the ventricular choroid plexus. It circulates inside the ventricles and enters the intracranial subarachnoid space via the cisterna magna before entering the cranial and spinal subarachnoid spaces. CSF is absorbed through cranial arachnoid granulations directly into the veins or through the lymphatic system of the cranial and the spinal nerves [5].

When intracranial pressure increases, drainage of excess CSF through the cranial and the spinal nerves increases [6]. Increased CSP inside the nerves irritates the nerve fibers and consequently causes widespread radicular pain [7,8]. Higgins et al. [9] previously suggested that using 20 or 25 cm H_20 is probably too high a cut-off to define abnormal intracranial pressure.

We hypothesize that the neurological symptoms of FM and chronic unexplained WSP may be caused by CSP dysregulation [4]. Consequently, withdrawal of spinal fluid might relieve pain in patients suffering from FM and unexplained WSP.

Cerebrospinal pressure (CSP) measurements obtained during a diagnostic lumbar puncture and results of CSF drainage in 30 FM patients were retrospectively reviewed, and pilot data supporting the above hypothesis are presented.

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CSP regulation

IICH, INPH and symptomatic TCs are CSP dysregulation disorders, all of which are largely underdiagnosed [10–13].

When the human body moves from a supine to an upright position, the cerebrospinal fluid pressure in the lower part of the body rises, and pressure in the upper part drops. From an evolutionary point of view, CSP regulation mechanisms were initially designed for quadrupeds. Thus, due to the upright position of bipeds and especially combined with the predominance of sitting activities of our society, the CSP regulation mechanisms are more under stress [14].

Therefore, in some individuals, CSP regulation mechanisms may fail to properly regulate pressure in the upright position.

CSP versus blood pressure

No clear reference values exist for CSP, and controversies exist regarding the OP cut-off value to diagnose IICH (> 20 cm H_2O in non-obese and 25 cm H_2O in obese patients). This threshold is likely too high [9,15]. The effect of chronic or intermittent moderately increased CSP on the brain and the peripheral nerves is unknown. The effects of CSP on the brain and the peripheral nerves can be compared to the effects of blood pressure on the heart and blood vessels. The American Heart Association has long considered a systolic blood pressure < 140 mmHg and a diastolic blood pressure < 90 mmHg as normal values. However, in 2003, updated recommendations were issued. Based on epidemiological studies, it was estimated that the risk of cardiovascular disease begins at a blood pressure of 115/75 mmHg and doubles with each increment of 20/11 mmHg [16].

Unfortunately, unlike arterial pressure, assessing CSP poses methodological problems. First, CSP measurement requires an invasive technique as opposed to the non-invasive technique used to measure blood pressure. Second, measuring CSP or blood pressure represents only one moment in time. When assessing blood pressure, several measurements or monitoring are required for an appropriate diagnosis of arterial hypertension. Similarly, assessing static cerebrospinal OP during a lumbar puncture may reveal a normal value, as has been observed in patients with INPH [11]. However, when using invasive CSP monitoring in patients with INPH, abnormal fluctuations of the CSP [17] and/or inadequate adaptation of the CSP upon position changes have been recorded [18].

Consequently, epidemiological studies on the link between moderately or intermittently increased CSP levels and disease are difficult to perform. To date, the most prominent signs of CSP dysregulation are papilledema in IICH patients presenting with vision loss; enlarged ventricles in patients with INPH presenting with dementia, gait problems, and incontinence; or large TCs in patients presenting with radicular pain. These obvious symptoms and signs may be the end stages of pressure dysregulation that have progressed over previous years or decades.

Opening pressure

An OP > 20 cm H_2O has been found in 19% of patients with chronic unresponsive migraine. Moreover, a higher prevalence of WSP has been reported in both IICH and chronic unresponsive migraine patients [8,15]. IICH without papilledema mimicking chronic migraine is probably much more prevalent than believed, is often misdiagnosed as chronic migraine and is refractory to preventive treatments [19]. In patients with IICH and headache without papilledema, lower mean OPs have been reported than in those with IICH with papilledema [20].

A mean OP of 19.0 cm H_2O was measured in patients with CFS suffering from severe headaches, indicating that increased cranial pressure may be responsible for fatigue, headaches and cognitive dysfunction in CFS patients [9].

The authors suggest that a cut-off of 20–25 cm H_20 may be too high to define Idiopathic Intracranial Hypertension (IICH).

Remarkably, the mean OP of 19.7 cm H_2O measured in our chronic pain patients (mean age 42.0 ± 11.2 years – range 21–61 years) is very similar. Furthermore, 6 of our chronic pain patients were also diagnosed with chronic fatigue syndrome (CFS).

The characteristics of the patients and the results of spinal fluid drainage are presented in Table 1

Table 1
Patient characteristics and lumbar puncture data.

	Sex	Age	BMI kg/m^3	FM	EDS	TCs	CFS	EMG L3-S4 myotomes	OP	Symptom improvement after lumbar puncture
1	m	57		x				0	23	Yes
2	f	37	> 25			x		DA + AA reflex	15	Yes
3	f	38	> 25	x	x	x		DA + AA reflex	16	Yes
4	f	34		x				0		Yes
5	f	44				x		DA + AA reflex	11	Yes
6	m	41	> 30	x			x	0	17	Yes
7	f	57				x		DA	18	No
8	m	30				x		0	32	No
9	f	51		x			x	0	18	Yes
10	f	45				x		DA + AA reflex	21	Yes
11	f	45		x	x	x	x	DA + AA reflex	15	Yes
12	f	23		x	x			DA + AA reflex	15,5	Yes
13	f	42		x		x	x	0	23	Yes
14	f	56						0	18	Yes
15	f	32	> 30	x				0	28	Yes
16	m	31		x				0	22	No
17	m	29		x				0	20	Yes
18	f	38		x		x		0	15	Yes
19	f	51				x		0	24	Yes
20	m	40				x		DA + AA reflex	13	No
21	f	29	> 30	x				DA	23	Yes
22	m	52		x				0	19,5	No
23	f	48		x		x	x	0	24	Yes
24	f	63		x		x	x	normal	14	No
25	m	29		x				0	21	No
26	m	55						0	23	No
27	m	21						normal	23	Yes
28	m	45	> 25	x		x		0	24	Yes
29	m	36						DA	23	No
30	f	61				x		0	12	Yes

FM = Fibromyalgia, EDS = Ehlers-Danlos Syndrome, TC = Tarlov cysts, CFS = Chronic Fatigue Syndrome, EMG = Electromyography, OP = Opening Pressure.
DA = denervation activity, AA reflex = delayed ano-anal reflex.

Spinal fluid taps

Diagnostic spinal fluid tap tests have been used in patients with INPH. Cognitive impairment, gait problems and urine incontinence improved despite an OP < 20 cm H_2O in most patients [11].

Diagnostic spinal fluid taps have also recently been used in patients with CFS and chronic migraine. In CFS, withdrawal of spinal fluid temporarily improved fatigue symptoms in all 5 patients with an OP > 20 cm H_2O and in 12 of 15 patients with an OP between 12 and 20 cm H_2O (in total 85%) [21]. Similarly, in patients with chronic unresponsive migraine, withdrawal of CSF relieved headaches in 3 of 6 (50%) patients with a CSP > 20 cm H_2O [9,22].

In our cases, 50% of the chronic pain patients had a CSP < 20 cm H_2O. Nevertheless, 70% of the patients felt relief of their symptoms following spinal fluid withdrawal during a few hours to 8 weeks,