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EC NEUROLOGY
Review Article

Idiopathic Intracranial Hypertension (IIH) a Possible Paradigm Shift in Management

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Received: April 01, 2019; **Published:** May 31, 2019

Abstract

The underlying pathogenesis of idiopathic intracranial hypertension (IIH) is unknown. Spontaneous resolution can occur in mild cases and with weight loss. Lumboperitoneal shunt and stenting of transverse sinuses ameliorates symptoms but recurrence can occur when they occlude. Intracranial pressure fluctuates significantly resulting in intermittent constriction of the transverse sinuses. Despite the fact that this constriction is secondary to the raised intracranial pressure stenting can lead to a resolution of symptoms. This implies that the transverse sinus constriction must contribute to persistent elevation of the raised intracranial pressure.

Why IIH sometimes resolves after a lumbar puncture (LP) is uncertain. Current guidelines discourage repeated lumbar puncture and recommend initial pharmacological management with Acetazolamide, Topiramate, Frusemide or Octreotide. Insertion of a lumboperitoneal shunt or transverse sinus stenting is recommended when medical therapy fails. If vision is threatened optic nerve fenestration or a temporary lumbar drain is recommended.

This chapter discusses a potential paradigm shift in management. It is based on our observations in a small number of patients where immediate resolution[1] of IIH occurred in the setting of prolonged cerebral spinal fluid (CSF) drainage at low-pressure. The repeated observation of immediate and sustained resolution is not what is encountered in patients with IIH treated with currently recommended therapy.

It is important to stress that the approach outlined in this chapter although based on sound logic is not currently accepted by the scientific community.

Keywords: *Idiopathic Intracranial Hypertension; CSF Drainage; Lumbar Puncture; Low-pressure Headache*

Introduction

Idiopathic intracranial hypertension (IIH) is the syndrome of headache due to raised intracranial pressure (> 25 cm H_2O in adults and > 28 cm H_2O in children) where the cerebrospinal fluid (CSF) is normal and there is no alternative pathology on imaging [1]. These criteria have supplanted the Dandy criteria [2] since Whiteley *et al.* demonstrated that normal CSF pressure is up to 25 cm H_2O [3]. Although it is more common in young overweight females it can occur in the absence of obesity and rarely in males. The major consequence of untreated or undertreated IIH is visual loss.

In his paper of 1937 [2] Dandy elegantly argued that the only place that the increased pressure could be was in the substance of the brain. We agree with Dandy for the following reasons. The pressure inside a closed space reflects the rigidity of the wall (in this case the

[1]Resolution is defined as asymptomatic with resolution of papilloedema confirmed by an ophthalmologist.

rigid skull) and the contents within that space. The ventricles are slit like and there is no CSF collection over the hemispheres thus it cannot be excess CSF within the ventricular system or subarachnoid space. The intermittent constriction of the veins is a physiological narrowing secondary to raised intracranial pressure [4] and the proximal venous sinuses are not dilated. Increased arterial blood flow is secondarily increased due to the raised pressure [5]. The logical conclusion is that the only possible place the increased fluid volume causing raised pressure can be is within the substance of the brain. Recent insights into the CSF circulation provide support for this concept.

Cerebral spinal fluid circulation

The traditional view of CSF physiology is that the majority of CSF is produced by the choroid plexus, circulates through the ventricles, the cisterns, and the subarachnoid space to be absorbed into the blood by the arachnoid villi. It is now recognised that there is a two-way flow of CSF between the subarachnoid space and the extracellular space within the cerebrum via the Virchow Robin spaces [6]. In IIH this trans-ependymal movement of CSF results in increased fluid within the extracellular space.

Clinical observations that provide insights into IIH

Our understanding of the pathophysiology and treatment of IIH has evolved over several years. Interest in IIH was triggered when we encountered a patient with low-pressure headache after an LP in the setting of clinically definite IIH. It was as if someone had thrown a switch from very high to very low-pressure. It occurred to us that a low-pressure headache represents a CSF leak where the rate of leakage must be greater than CSF production.

We then observed the effect of lowering CSF pressure on bilateral transverse sinus narrowing in a young female with IIH. When the CSF pressure was reduced to 11 cm H_2O one transverse sinus became patent, both became patent when the CSF pressure was reduced with a 2nd LP to 8 cm H_2O [7].

John King and colleagues from the Royal Melbourne Hospital elegantly demonstrated that the transverse sinus narrowing is secondary to the raised pressure [4]. If the transverse sinus narrowing is secondary to the raised pressure and yet stenting relieves the symptoms of IIH [8-12], the only logical conclusions is that it cannot be the cause but must play a role in perpetuating the raised pressure in IIH [13,14].

With these observations in mid we wondered whether we could possibly induce resolution of IIH by decreasing CSF pressure low enough to reverse the transverse sinus narrowing. This proved not to be the case. Several patients had the CSF pressure reduced by LP to < 10 cm H_2O and the IIH did not resolve unless they developed a low-pressure headache [15]. There were other patients where the CSF pressure was not lowered to < 10 cm H_2O and yet when they developed a low-pressure headache the IIH resolved. IIH resolved in 1 patient in the setting of malfunction of an L-P shunt and a 2nd in the setting of lumbar drainage as a prelude to insertion of an L-P shunt. We are not the only ones to observe resolution of IIH in the setting of low-pressure headache [13]. The reduced pressure with an LP is usually transient but more prolonged with a CSF leak complicating an LP.

We believe that the likely mechanism that caused resolution of IIH in our patients (and others who have observed the same phenomena) was a prolonged CSF leak, reducing the CSF pressure low enough to allow the transverse sinuses to become patent. This reduces the backpressure in the venous system and allows the CSF within the extracellular space to diffuse back into the ventricular system and subarachnoid space thus normalising intracranial pressure. The reduction in pressure induced by an LP resulting in resolution may or may not be sufficient enough to produce the symptoms of a low-pressure headache. Not all cases of resolution have reported a low-pressure headache.

Although there is no large prospective series describing the natural history of IIH; except in very mild cases it is usually a protracted course lasting months to years [16-19]. An immediate and sustained resolution of IIH as seen in our cases does not reflect the "natural history" of patients treated with drugs, optic nerve fenestration, lumboperitoneal shunt or transverse sinus stenting. Recurrence of symptoms often occurs with cessation of drug therapy, occlusion of the shunt [20] or recurrent stenosis adjacent to the stent [21].

We are not the first to observe resolution of symptoms in the setting of low-pressure headache [13,14], the reversal of transverse sinus narrowing with an LP [14,22,23] nor to suggest that IIH consists of a vicious cycle of raised pressure perpetuated by secondary transverse sinus compression [22]. Pickard *et al.* [24] have also suggested that the vicious cycle can be interrupted by draining CSF.

A word of caution

There are several cases in the literature [25-27] and a case reported to us by a colleague where coning occurred following an LP in patients with IIH. In all cases there was significant tonsillar herniation (not a Chiari malformation) [26] prior to the LP possibly representing critically elevated intracranial pressure. Tonsillar herniation detected on MRI should be regarded as a contraindication to LP.

Current therapeutic guidelines

There is no consensus regarding optimal management of IIH [28]. Current treatment guidelines [34,35] recommend weight loss that is often difficult to achieve and pharmacological therapy with Acetazolamide at doses of up to 4 gm per day, a dose that many patients cannot tolerate. Second line drug therapy includes Topiramate 100-150 mg per day. Case reports describe the use of Frusemide up to 2 mg per kilogram per day in children and [31] Octreotide, a somatostatin analogue at doses up to 1000 μg per day [32]. Neither Frusemide nor Octreotide have been subjected to rigorous randomized trials.

Bariatric surgery is recommended in morbidly obese individuals who are unable to lose weight [33].

When medical therapy fails, temporary lumbar drain in fulminant IIH, lumboperitoneal shunt, transverse sinus stenting [11] or optic nerve fenestration if vision is threatened is recommended. There are no trials to assist in choosing the most appropriate therapy.

Lumboperitoneal shunts were 1st described by Vander Ark *et al.* in 1971 [34] and despite the potential for significant complications [35,36] have been widely employed in refractory cases of IIH. The IIH often recurs when they occlude indicating that they do not cure the problem but only ameliorate the symptoms. We believe that the likely explanation for this is that the shunt pressure is set to approximately 15 cm H_2O [37,38]. This is sufficiently low enough to alleviate symptoms but not low enough for reversal of the transverse sinus narrowing.

The problem with all currently accepted treatments is that by and large they don't lead to resolution of the raised intracranial pressure and ongoing treatment is required for months and in some cases years, often with devastating consequences of visual impairment.

Proposed alternative approach to management

Once again we wish to reiterate that this recommended approach is not accepted by the scientific community.

Low-pressure headache is characterized by two features; (a) a marked reduction in CSF pressure (0 - 6 cm H_2O) [39,40] and (b) a sustained period of CSF drainage. Which of these two mechanisms is responsible for the resolution of IIH is uncertain, but we suspect it may be both. Prolonged drainage alone occurs with shunts, but when shunts occlude symptoms recur. We have observed that an LP induced short period of CSF pressure reduction to < 10 cm H_2O alone does not lead to a resolution of IIH in all patients.

Our current approach is to use a non-pencil point needle at the time of the initial lumbar puncture in patients with clinical definite IIH. The needle is inserted at right angles in order to split the fibres and increase the chances of developing a CSF leak and the pressure is lower to less than 10 cm H_2O. At this stage we have not put repeated holes in the dura, something recommended to one of us (PG) in 1977 by John Billings, (better known for the rhythm method of contraception) when we were a resident in neurology. If the first lumbar puncture fails then the patient is offered a 2nd lumbar puncture using the same technique [41].

Subsequent management depends on patient preference and the severity of IIH. In mild cases weight loss and pharmacological treatment with Acetazolamide are instituted. In more severe cases we insert a temporary lumbar drain [42], draining the CSF at a rate equal

to that of production (approximately 20 mL per hour) for a period of 12 hours and then clamp the drain. The pressure is re-measured approximately 2 and invariably it has been < 10cm H_2O. The CSF is drained for 48-72 hours.

Over the last 5 years using this approach we have avoided the insertion of a lumboperitoneal shunt. We are aware of 2 patients who have relapsed years later, both in the setting of significant weight gain. One was cared for by another neurologist and tragically suffered severe visual loss, the other has only recently been seen. There IIH had resolved after an LP induced CSF leak. This patient is currently in the process of undergoing further MRI and LP. There is third patient who has ongoing symptoms of whistling tinnitus but not headache following documented normalisation of the CSF pressure using a lumbar drain. An ophthalmologist has confirmed improvement in the degree of papilloedema and it is uncertain whether this patient has persistent elevation of their CSF pressure.

Much work still needs to be done, the number of patients thus far studied in small but many of them have remained symptom-free for years. The optimal period of drainage is uncertain, how many patients will respond to this approach is uncertain, whether the approach really results in sustained resolution in the great majority of IIH patients is unclear, although most of the individuals observed over the last 15 years have remained symptom free. The safety of this approach and what % of patients will be willing to endure a low-pressure headache is unclear. Having said this repeated LP's have been employed without long-term deleterious effects.

Conclusion

The combination of a critical level of reduced CSF pressure and more prolonged CSF drainage as occurs with low-pressure headache might be the explanation why an LP leads to resolution in some patients with IIH. If these observations are correct patients with IIH may respond to a sustained lowering of CSF pressure to a critical level using a lumbar drain where both the CSF pressure and period of drainage can be varied and monitored.

If our observations are confirmed this approach would represent a paradigm shift in the management of IIH.

It is hoped that this paper may stimulate others to collaborate and establish whether the observation in the small number of patients can be extrapolated to the greater population of those suffering from IIH.

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Volume 11 Issue 6 June 2019