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MINIREVIEWS

Resolution of idiopathic intracranial hypertension after sustained lowering of cerebrospinal fluid pressure

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Abstract

Idiopathic intracranial hypertension (IIH) is a syndrome of headache due to raised intracranial pressure (ICP) where the cerebrospinal fluid (CSF) is normal and there is no alternative pathology on imaging. The aetiology is unknown. This review questions many of the prevailing views regarding aetiology and treatment of IIH. It explores the concept that there is a vicious cycle of fluctuating raised ICP leading to secondary compression of the transverse sinuses and further elevation of ICP. It also raises the question as to whether this vicious cycle could be relieved by prolonged drainage of CSF as seen in Lumbar puncture induced low-pressure headache or alternatively a lumbar drain.

Key words: Lumbar puncture; Cerebrospinal fluid drainage; Idiopathic intracranial hypertension; Low-pressure headache

Core tip: Resolution of idiopathic intracranial hypertension can be achieved by prolonged cerebrospinal fluid drainage as seen with Lumbar puncture induced low-pressure headache.

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INTRODUCTION

Idiopathic intracranial hypertension (IIH) also referred to as benign intracranial hypertension or pseudotumour cerebri is a syndrome of headache due to raised intracranial pressure (> 20 cm H_2O in non-obese patients and > 25 cm H_2O in obese patients) where the cerebrospinal fluid (CSF) is normal and there is no alternative pathology on imaging. Patients present with headache, with or without visual obscuration's and or various cranial nerve palsies most commonly a 6th nerve palsy. In the early stages visual acuity is normal, the blind spot is enlarged and virtually all patients have bilateral papilloedema, although rare cases have been reported where papilloedema is absent[1-3]. The major consequence of untreated or undertreated IIH is visual

loss.

AETIOLOGY OF IIH

The aetiology is unknown with many suggested causes[4-6] most of which to this author do not make sense.

To this author there is only one constant feature present in all patients with IIH and that is the presence of fluctuating raised intracranial pressure. Intracranial pressure (ICP) monitoring has demonstrated the presence of B-waves (rhythmic oscillations occurring every 1-2 min. The ICP rises in a crescendo manner to levels 20–30 mmHg higher than baseline and then falls abruptly)[7,8]. These B-waves almost certainly explain the fluctuations of CSF pressure measurements seen with a Lumbar puncture (LP) and I would like to suggest the intermittent compression of the transverse venous sinuses that King and his colleagues elegantly demonstrated is secondary to and not the primary cause of the raised ICP[9].

What triggers the initial elevation of CSF pressure is unclear. The majority (but not all) patients are obese and females of child bearing age (there are occasional reports of males affected by IIH[10]). It is feasible that the demonstrated elevation of right atrial pressure in obese individuals transmitted to the cerebral venous system[11] could be the very initial trigger[12]. If this is the mechanism then the obvious question is why does this not occur in obese males and why do non obese females develop IIH? The answer is unknown; could it be that female hormones present in premenopausal women reduce the stiffness of the venous walls and predispose them to compression? The author has not been able to find any literature to support such a hypothesis.

The fact that obesity is not present in every patient would indicate that it is not the primary cause of IIH, but increases the risk of developing this condition. There are many other suggested causes of IIH[13,14], the fact that they are not present in every patient must raise significant doubt about their primary role in the aetiology of this condition.

An identical clinical picture is seen in some patients with cerebral vein thrombosis, leading to the suggestion that obstructed venous drainage may play a role in IIH. In recent years stenting of transverse sinuses has also led to a resolution of IIH[15-19], despite the fact that it is well established that the narrowing in the transverse sinuses is secondary to the raised pressure[9]. There is one simple clinical observation that rules out transverse sinus narrowing as the cause of IIH, it not present in every patient and it is not a constant feature in patients in whom it is seen. If the transverse sinus narrowing is secondary to the raised pressure then the question is how does stenting lead to a resolution of IIH in some cases? Pickard *et al*[20] have suggested on the basis of CSF and venous sinus pressure measurements that, in many cases of IIH, there is functional obstruction of venous outflow through the dural sinuses. Raised pressure of CSF (Pcsf) partly obstructs venous sinus outflow, thereby increasing sagittal sinus pressure (pss) which, in turn, leads to a further rise in Pcsf, et sequor. They further suggest that this vicious cycle can be interrupted by draining CSF. Is it possible that stenting helps break this cycle of fluctuating ICP and intermittent venous compression, allowing venous drainage and subsequent normalisation of ICP? Supporting this concept is the observation by McGonigal *et al*[21] of resolution of IIH and transverse sinus stenosis in a patient following a lumbo-peritoneal shunt where the patient developed a low-pressure headache.

There is no consensus about what is causing the raised pressure. Logically the pressure within a closed space reflects the contents of the space and the rigidity of the wall. The skull is rigid, the ventricles are slit like, there is no collection of CSF over the hemispheres, the venous sinuses are compressed and arterial pressure is raised secondarily to the raised ICP. It therefore stands to reason that there must be increased fluid in the cerebrum.

The concept that the raised intracranial pressure is related to fluid in the interstitial space is supported by recent studies on CSF dynamics. The traditional view that the majority of CSF is produced by the choroid plexus, circulates through the ventricles and the subarachnoid space to be absorbed by the arachnoid villi has recently been challenged[22]. The CSF circulation also comprises a pulsatile to and fro movement throughout the entire brain with local fluid exchange between blood, interstitial fluid and CSF[23,24]. There is a growing consensus that the interstitial fluid and CSF are mainly formed and reabsorbed across the walls of CNS blood capillaries with aquaporins playing a role[25]. It is now believed that there is a continuous bi-directional fluid exchange at the blood brain barrier and the cell membranes at the border between CSF and the interstitial fluid spaces[24].

The total volume of CSF is estimated to be 150 mL in adults with 25 mL in the ventricles. It has also been estimated that nearly 30% of CSF production may come from the ependyma[23]. CSF production is estimated to be 0.37 mL/min or approximately 500-600 mL/d[24]. If IIH represents a vicious cycle of raised intracranial pressure due to an increase in interstitial fluid with secondary venous compression this could explain why stenting could break the cycle by abolishing the venous compression. It might also explain the observation that an uncomplicated LP would not break the cycle as CSF would re-accumulate rapidly. It could also explain how a low CSF pressure that would occur with a continuous leak of CSF in the setting of a low-pressure headache could also break the cycle. The CSF must be leaking at a greater rate than it is being produced.

TREATMENT OF IIH

There are many review articles[4,26,27] that discuss the current treatment if the initial LP fails to lead to a

resolution, treatment options include serial LP's, medical therapy (weight loss, Acetazolamide, Topiramate or Octreotide) and surgical intervention (bariatric surgery, lumbo-peritoneal drain, transverse sinus stenting or optic nerve fenestration). As Batra and Sinclair comment "the aetiology is poorly understood and there are no evidence-based guidelines on the management of the disease".

It is not the intention of this article to discuss these various treatment options in detail suffice to say that medical therapy tends to be employed for mild cases of IIH and surgical intervention for the more severe cases with a tendency to favour optic nerve fenestration if vision is threatened. Rather I would like to explore the concept of "resetting the abnormally elevated pressure to normal" by prolonged CSF drainage reflecting our own observations[28-30] and a review of the literature.

LP is used to confirm the diagnosis and occasionally a single LP[31,32] or several LP's[33] can result in resolution of IIH but how this occurs is unclear. In the study of children by Weisberg *et al*[33] 20 to 50 mL of CSF was removed each time but they did not comment on the closing pressure or the whether patients developed low-pressure headache. When serial LP's are employed the CSF pressure is reduced to a normal level, 10-20 cm H_2O. We would argue that CSF is replaced very rapidly and unless the pressure is lowered to below normal and or the CSF is drained at a rate higher than it is replaced the vicious cycle of elevated intracranial pressure cannot reverse.

In refractory cases a lumboperitoneal shunt is often recommended. These run the risk of infection and recurrence of IIH when they become occluded. The CSF is often shunted to maintain the CSF at a normal pressure and to avoid a low-pressure headache from over drainage. One case in this series developed a low pressure headache after insertion of a lumboperitoneal shunt requiring removal, following which she experienced a resolution of IIH. We suspect the reason the IIH "recurs" with blockage of the shunt is that it was never reversed in the 1st case by the shunt, but rather the CSF pressure was maintained at a level that leads to a resolution of headache and papilloedema but not low enough to reverse the excess fluid in the intracellular space.

In 2009 we observed a young non obese female with IIH who had bilateral narrowing of the transverse sinuses demonstrated on magnetic resonance venography (MRV). MRV (using the same methodology) immediately before and 15 min after the next two LPs showed partial resolution of the transverse sinus narrowing when the pressure was reduced from 50 cm H_2O to 11cm H_2O and complete resolution of the bilateral transverse sinus narrowing when the pressure was reduced from 47 cm H_2O to 8 cm H_2O[28]. On the basis that stenting can lead to a resolution of IIH, we postulated that lowering the CSF pressure lower than usually recommended, could result in a resolution of the transverse sinus narrowing and therefore a resolution of IIH. This proved not to be the case, in several patients where the CSF pressure was reduced to less than 10 cm H_2O (a level where we had demonstrated resolution of the transverse sinus narrowing, see above) the IIH persisted[30].

At about the same time we observed a patient with IIH who had developed a low-pressure headache after an LP. Our initial reaction was to suspect the original diagnosis of IIH was incorrect, how could a patient with markedly elevated pressure develop a low-pressure headache it did not seem to make sense. On review of the patient's medical record it was clear that she fulfilled the diagnostic criteria[34-37].

A low-pressure headache represents prolonged drainage of CSF resulting in a low pressure, usually less than 5 cm H_2O. Clinically the headache of IIH is distinct from that of low-pressure headache with the latter abolished by lying flat with the foot of the bed elevated, but the only way to differentiate with certainty between IIH and low-pressure headache is to measure the CSF opening pressure. We subsequently undertook a review of all cases of IIH seen at the Geelong hospital. One patient had developed a low-pressure headache after the insertion of a lumbo-peritoneal shunt that had to be removed. IIH resolved in this patient but recurred some years later. A second patient developed a low-pressure headache in the setting of a temporary lumbar drain with permanent resolution of IIH. There were 10 other patients who had complete resolution of IIH (average follow-up 3 years (range 3 mo-10 years) following the development of a low-pressure headache. In 2 patients low CSF pressure was confirmed by LP (5 and 7 cm H_2O). There was one patient in whom the IIH persisted and who was clinically suspected of developing a low-pressure headache; the low pressure was not confirmed by LP in this patient[29,30]. One young non obese female patient has subsequently relapsed.

One possible explanation for these observations is that a low-pressure headache represents prolonged drainage of CSF reducing the external pressure on the transverse sinuses, relieving the physiological stenosis of these sinuses and allowing the vicious cycle of raised pressure to normalise. If this interpretation is correct then a way to explore this concept is to undertake a study of patients with IIH using controlled lumbar drainage, a technique that has been employed to control medically refractory increased intracranial pressure[38]. The CSF may need to be drained at a faster rate than has been traditionally recommended and the duration of drainage is uncertain. This could be explored in a multicentre study where the rate of and the duration of CSF drainage could be varied with each centre learning from prior experience. After the period of drainage the CSF pressure could be measured after a period of clamping of the drain for a minimum of 2 h (enough time for the volume of CSF in the ventricles to be restored, *i.e.,* 25 mL with a production rate of 0.37 mL/min). If the CSF remains elevated then one could undertake a further period of drainage at a faster

rate and/or for a longer period, once again measuring the CSF pressure after clamping the drain. An online database could be established to share observations and hopefully establish the ideal rate and duration to drain the CSF.

CONCLUSION

This paper has explored the concept that IIH may represent a vicious cycle of elevated intracranial pressure, triggered by unknown factor(s) that could potentially be interrupted by prolonged drainage of CSF as seen with a post-LP induced low-pressure headache or by prolonged lumbar drainage without the necessity of inserting a permanent lumbo-peritoneal shunt or transverse sinus stenting. The lumbar drain would need to drain CSF at a faster rate than 0.37 mL per minute in order to reduce the CSF pressure to a level low enough for the increased interstitial fluid to diminish back to its normal state.

Until such an approach is confirmed patients with severe IIH particularly if vision is threatened should be managed along conventional lines.

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