Update on the Diagnosis and Treatment of Idiopathic Intracranial Hypertension

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Abstract

Advances in ophthalmic diagnostics and results of interventional clinical trials are shifting diagnosis and management of idiopathic intracranial hypertension (IIH) to be more technology- and evidence-based. In this article, the evidence supporting current diagnostic criteria, evaluation, and medical and surgical management of IIH are reviewed.

Keywords

- Idiopathic intracranial hypertension
- pseudotumor cerebri
- papilledema

After the concept of unexplained high intracranial pressure (ICP) resulting in neurological and ophthalmic symptoms and signs was first described by Quincke as serous meningitis in the 1890s,[1] our conceptualization of the disease has continued to evolve over the years. In 1904, "pseudotumor cerebri" was coined by Nonne, and in 1937, Walter Dandy described 22 patients with "intracranial pressure without brain tumor."[2] In the 1950s, "benign intracranial hypertension" was introduced, although this term fell out of favor due to the possibility of non-benign outcomes.[3] "Idiopathic intracranial hypertension" (IIH) was introduced by Corbett and Thompson in the late 1980s.[4] The term IIH focuses on the idiopathic forms, excluding all the nontumor secondary causes of intracranial hypertension, such as venous sinus thrombosis and meningitis, which are included under the broader term pseudotumor cerebri syndrome.[5] Pseudotumor cerebri remains a commonly used term, although there is some controversy over whether this nomenclature is of clinical utility over dividing intracranial hypertension into its primary (i.e., idiopathic) and secondary forms.[5,6] From our perspective, pseudotumor cerebri (i.e., including nontumor secondary causes of intracranial hypertension) is advantageous from a diagnostic perspective because it focuses on identification of the intracranial hypertension syndrome and maintains a broad differential diagnosis of secondary causes. On the other hand, IIH is advantageous from the perspective of targeted treatment, including clinical trials, since it explicitly excludes all secondary causes.

Identifying Intracranial Hypertension

Identifying the syndrome of intracranial hypertension is important for three reasons. The first is to prompt diagnosis of secondary causes such as brain tumors, venous sinus thrombosis, and infectious causes that require directed therapy. The second is to identify and address a pathophysiological state that puts patients at risk of blindness through compressive forces exerted on the optic nerve by high cerebrospinal fluid (CSF) pressure in the optic nerve sheath. The third is to identify a treatable cause of a patient's symptoms such as headache, double vision, and pulsatile tinnitus.

Clinical suspicion for intracranial hypertension is mainly based on symptoms described by the patient. However, some asymptomatic patients come to medical attention when papilledema is observed on routine ophthalmic examination or changes typical of high ICP are detected on neuroimaging studies done for other reasons. Symptoms, medications or past medical history associated with secondary causes of intracranial hypertension may also raise suspicion for this condition.[7] As most patients with IIH are females who are overweight or obese,[8–10] and an increase of weight by 5 to 15% is often sufficient to increase the risk of developing IIH,[11] some providers triage based on demographics and body habitus. However, this is imperfect since IIH does occur outside these demographics, and secondary intracranial hypertension can occur in patients with typical IIH demographics.

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Table 1 Symptoms present at time of patient enrollment in the IIHTT[14]

Symptom	Prevalence ($n = 165$)
Headache	84%
Vision changes	
Transient visual obscurations Vision loss[a] Diplopia photophobia	68% 32% 18% 48%
Tinnitus	
Pulsatile Nonpulsatile	52% 23%
Dizziness	52%
Neck pain	42%
Back pain	53%
Cognitive disturbances	20%

[a]All patients in the trial had bilateral papilledema and mild vision loss on formal visual field testing as a trial entry criterion

Symptoms of Intracranial Hypertension

Our knowledge of the characteristics of symptoms in patients with IIH was informed by the IIH Treatment Trial (IIHTT).[12] This trial included 165 IIH patients with mild vision loss,[13] comprising the largest cohort of IIH patients rigorously studied to date. The baseline profile of IIHTT participants illustrates the prevalence of common symptoms (►**Table 1**).[14] Many of these symptoms are nonspecific, making clear that a diagnosis of secondary intracranial hypertension or IIH cannot be established based on symptoms alone.

Although presentations of IIH are typically subacute and some are chronic, a minority of patients (<5%) have a fulminant presentation with rapidly progressive vision loss over the course of days to weeks. Identifying patients in this group and acting quickly to establish the diagnosis and institute appropriate therapy is of particular importance, since visual outcomes are poor (in one series, 50% remained legally blind, with visual acuity less than 20/200 in both eyes or severe visual field constriction despite aggressive treatment).[15]

Headache

Headache is an important cause of morbidity in IIH, with IIHTT patients reporting substantial to severe headache disability at baseline (mean score of 60 on the Headache Impact Test questionnaire, which surveys the frequency and impact of headache and ranges from 6–78).[12] One-quarter of patients reported constant daily headache.[16] While there are some headache features that suggest intracranial hypertension, including being worse in the morning and while lying flat, these characteristics are neither sensitive or specific to be clinically helpful.[17] In the IIHTT, headaches commonly fit the phenotype of primary headache disorders including migraine (52%) or tension-type headache (22%).[16]

Visual Symptoms

Visual loss is the main source of chronic morbidity in IIH.[18] Central vision loss is rare except in advanced presentations, and most vision loss begins at the periphery. There can be a considerable range of visual deficits at presentation, most detectable on automated perimetry.[14,18,19] However, some patients report nonspecific blurry or dim vision in the setting of normal visual function testing. This is likely due to impairment relative to personal baseline that remains within population normative data.[14]

Transient visual obscurations are short, lasting seconds to minutes, and characterized by monocular or binocular fogginess, black, white or gray out, usually triggered by head or eye movement.[17] Some patients report episodic brief visual sparkles or flashes distinct from visual migraine aura.[20] Position- and gaze-evoked symptoms are thought to originate from ischemia of the optic nerve that is induced by movement of the swollen optic nerve head.[21] Similar symptoms occur in association with other causes of optic nerve head elevation, including pseudopapilledema due to optic nerve head drusen. Dimming or sparkles in vision induced by exposure to bright light is similar to what occurs in severe unilateral carotid stenosis, and may represent ischemia due to increased metabolic demand that is not adequately met by the vascular supply to the retina or optic nerve.[22]

Constant or intermittent horizontal diplopia, resolved by occluding either eye, can occur due to unilateral or bilateral cranial nerve (CN) VI (abducens) palsy. This is a false localizing sign of high ICP states, occurring because of tension on the abducens nerve(s). Symptoms are more pronounced in lateral gaze and with distance focus. Unilateral or bilateral CN VI palsy can sometimes be subtle with esotropia or esophoria without clear abduction deficits. Other patterns of diplopia have been reported in IIH, but these are rare and should prompt additional investigation if they are present.[23]

Pulsatile Tinnitus

This consists of hearing either a unilateral or bilateral whooshing, whistling, humming, marching noise or heartbeat, and is thought to represent auditory perception of turbulent pulsatile flow in intracranial vessels. Although 52% of patients in the IIHTT reported this symptom, it is not specific for intracranial hypertension and also occurs due to underlying vascular abnormalities (including arteriovenous malformations, arterial stenoses, or arterial aneurysms), eustachian tube dysfunction, and other benign causes.[24]

Asymptomatic

A minority of patients with IIH may be asymptomatic.[25–27] Some patients may have mild visual dysfunction they have not recognized, while others may be asymptomatic because there is no detectable vision loss.[28] In the IIHTT, which required papilledema and mild visual impairment on automated perimetry to enroll, 68% patients reported no visual symptoms.

Optic Nerve Changes in Intracranial Hypertension

Funduscopic exam showing bilateral optic disc edema is very concerning for papilledema due to intracranial hypertension (►**Fig. 1**). The observation of this finding, either incidentally or in a patient with otherwise unexplained headaches, should prompt urgent diagnostic evaluation. It is important, however, to note that optic disc edema is a nonspecific finding that can occur in other neurological and ophthalmic diseases. Other nonspecific findings of intracranial hypertension on fundus exam include venous stasis, hyperemia, hemorrhages, infarcts, cotton wool spots, choroidal and retinal folds, and absence of spontaneous retinal venous pulsations.[18,29–31] In chronic untreated cases, optic disc edema can be replaced by optic atrophy due to damage to the retinal ganglion cells.

Neuroimaging Changes in Intracranial Hypertension

A diagnosis of IIH is considered in some patients when findings associated with high ICP are found on magnetic resonance imaging (MRI) or computed tomography (CT) of the brain done for other reasons. These include globe flattening, optic nerve protrusion into the vitreous, optic nerve widening with increased CSF spaces in the optic nerve sheath, empty sella, and transverse venous sinus changes (►**Fig. 1**).[32] While suggestive, these findings are not diagnostic of active intracranial hypertension due to their occurrence in normal individuals[33] as well as only partial normalization following treatment.[34]

Confirming Intracranial Hypertension

In cases of suspected intracranial hypertension, pathological elevation of intracranial pressure is confirmed by measurement of opening pressure following lumbar puncture, so long as there is no mass lesion to preclude this procedure being carried out safely. For the purposes of diagnosing IIH, an opening pressure of $\geq$ 250 mm water is considered elevated and diagnostic in adults. This cutoff was established in a 1983 paper by Corbett and Mehta, which obtained opening pressure measurements from 4 groups of patients: healthy non-obese, healthy obese, acute pseudotumor cerebri, and chronic (previously diagnosed) pseudotumor cerebri.[35] About 90% of the acute pseudotumor cerebri patients had an opening pressure greater than or equal to 250 mm water. Some healthy obese (26%) and nonobese (7%) patients had an opening pressure of 200–250 mm water, and there was no correlation between the degree of obesity and opening pressure. These findings were in agreement with other studies of ICP in different populations.[36,37] A more recent prospective study of lumbar puncture opening pressures obtained in the lateral decubitus position of over 200 outpatients without a high ICP-associated diagnosis defined a normal range from 100 mm water (2.5 percentile) to 250 mm water (97.5 percentile).[38] A similar study in children found a higher 97.5 percentile of 280 mm water.[39] However, it is important to note that these cut-offs are not absolute, with 2.5% of normal adults having ICP above 250 mm water in the population study,[38] and 10% of patients with acute pseudotumor cerebri having ICP less than 250 mm water in the study of Corbett and Mehta,[35] leading to the possibility of both over- and underdiagnosis of intracranial hypertension based on lumbar puncture alone.

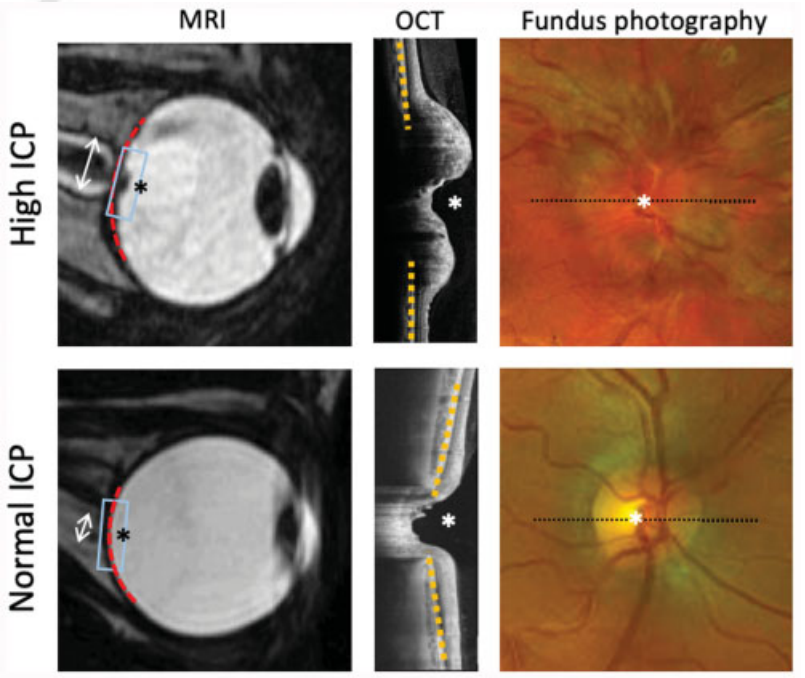

Fig. 1 Findings associated with intracranial hypertension (top) compared with normal ICP (bottom) on ancillary testing, including MRI (left), OCT (center) and fundus photography (right). Box on MRI indicates region of OCT. Dashed line on fundus photography indicates cross-section of OCT. Optic nerve head (*), optic nerve sheath width (double arrow), globe flattening (red dashed line), and eye shape change (yellow dashed line).

Further uncertainty is introduced by the concern that normal ICP ranges established with lateral decubitus positioning may not apply for different lumbar puncture techniques. While a previous study suggested that prone CSF pressure measurement may overestimate ICP by approximately 20 mm water compared with lumbar decubitus positioning,[40] a 2014 study suggested that there was no statistically or clinically significant difference between opening pressures measured in the prone and lateral decubitus positions, and that body mass index (BMI) did not affect measurements in either position.[41] What is likely most important is that the manometer zero is positioned level with the foramen magnum regardless of patient positioning. This is underscored by a study of invasive ICP monitoring that demonstrated relatively stable ICP (within 5 mm Hg) in supine versus seated and standing positions in normal patients.[42] Interestingly, IIH and hydrocephalus patients had larger changes in ICP, with supine and lateral decubitus ICP being higher than when sitting or vertical.

CSF pressure measurement via lumbar puncture is a point measurement of a fluctuating system. This, and challenges with CSF pressure measurement procedures related to both procedural (e.g., needle positioning) and patient factors (e.g., the Valsava), raises the possibility of false positive and false negative ICP measurements. As with any medical test result, the measured pressure must be interpreted in the context of the patient's symptoms, examination, and other diagnostic test results.

Diagnosis of Idiopathic Intracranial Hypertension

Dandy's original suggestion of separating IIH from other causes of raised intracranial pressure, including brain tumors, was formalized as the "modified Dandy criteria" by Smith in 1985.[43] Neuroimaging to exclude tumor and venous sinus thrombosis, CSF analysis, and review of medications and past medical history is typically undertaken to exclude secondary causes (►**Table 2**).[7] Cross-sectional imaging of the brain (MRI or CT) is necessary to assess for secondary causes such as tumors and hydrocephalus. Venous sinus thrombosis cannot be distinguished from IIH on the basis of history,[44,45] and though it may be evident on brain MRI, MR or CT venography (MRV or CTV) are more sensitive.[46] Venous imaging may have an additional role in identifying impaired outflow, and arterial imaging may help to identify dural arteriovenous contributing to intracranial hypertension.[47] Spinal imaging can identify spinal lesions, which is a rare secondary cause of intracranial hypertension.[48] While there are some conditions, such as hydrocephalus, brain tumors, and venous sinus thrombosis, as well as some medications, such as steroid withdrawal or tetracycline antibiotics, for which a causal relationship with intracranial hypertension is likely, the causal relationship for other conditions and medications reported in association with intracranial hypertension is murkier.

Friedman and Jacobson formalized the cutoff of 250 mm H_2O for high ICP in their diagnostic criteria published in 2002.[49] The 2013 criteria for pseudotumor cerebri syndrome included a cut off of 280 mm water in children.[5] To account for the possibility of patients with the clinical syndrome of intracranial hypertension having ICP below this cutoff, current criteria allow for borderline ICP between 200 and 250 mm H_2O when symptoms (pulsatile tinnitus), ophthalmic examination findings (Frisen's grade 2 papilledema or sixth nerve palsy), or high ICP-associated neuroimaging findings are present (►**Table 3**).[13] Although false normal ICP measures can occur for a variety of reasons, including recently attempted LP with CSF leak, poor needle positioning and physiological fluctuation, caution is urged when making an IIH diagnosis without confirmation of intracranial hypertension, including cases where an LP has not been attempted. Response of symptoms and examination findings to ICP directed treatment can be helpful in indeterminate cases.

Special care is advised when diagnosing intracranial hypertension in the absence of disc swelling due to the possibility of falsely elevated ICP measurement and the common occurrence of primary headache disorders.[7,50] Friedman et al included these cases of IIH without papilledema in a 'probable' diagnostic category,[5] and similar guidelines were included in recently published consensus criteria.[7] While IIH without

Table 2 Secondary causes of intracranial hypertension[a]

Past medical history	Anemia Addison's disease Adrenal insufficiency Acute and chronic inflammatory demyelinating polyneuropathy Down syndrome Head trauma Lupus Obstructive sleep apnea Past subarachnoid hemorrhage or meningitis Renal failure Superior vena cava syndrome Systemic venous hypertension Turner syndrome
Medications	Tetracycline, minocycline, doxycycline Vitamin A and retinoids Corticosteroid withdrawal Growth hormone Lithium Many others implicated but unproven
Laboratory tests (serum)	Anemia
Laboratory tests (CSF)	Meningitis (infections, inflammatory or neoplastic) Elevated protein
Neuroimaging	Intracranial mass lesions Hydrocephalus Venous sinus thrombosis or obstruction Arterio-venous fistula Bilateral jugular venous blockage Subarachnoid hemorrhage Craniosynostoses Spinal cord tumor

Abbreviation: CSF, cerebrospinal fluid.
[a]Presence of a secondary cause of intracranial hypertension is not diagnostic of intracranial hypertension.

Table 3 IIHTT Modified Dandy Criteria for IIH[13]

CSF pressure	> 25 cm H_2O	20–25 cm H_2O *Fulfill all requirements for CSF pressure > 25 cm H_2O plus at least one * item*
Symptoms	Headaches, nausea, vomiting, transient obscurations of vision, papilledema Awake and alert	*Pulse synchronous tinnitus
Neurological exam	Absence of localizing findings on neurologic examination (except unilateral or bilateral cranial nerve VI palsies)	*CN VI palsy *Frisèn Grade II papilledema and no pseudopapilledema
CSF analysis	Normal constituents	
Neuroimaging	Absence of deformity, displacement, or obstruction of the ventricular system No abnormal neuroimaging except for empty sella turcica, optic nerve sheath with filled out CSF spaces, and smooth-walled non flow-related venous sinus stenosis or collapse	*MRV with lateral sinus collapse or stenosis *Partially empty sella with unfolded perioptic nerve CSF spaces
Disclaimer	No other cause of increased intracranial pressure present	

Abbreviations: CSF, cerebrospinal fluid; IIH, idiopathic intracranial hypertension; IIHTT, IIH Treatment Trial; MRV, magnetic resonance venography.

papilledema is physiologically possible, given that unilateral papilledema can occur, this diagnosis should be made with caution, since it is more likely for an ICP measurement to be falsely elevated in a patient with a chronic primary headache disorder than for a patient with intracranial hypertension to not have papilledema. There is also an important prognostic distinction, since IIH without papilledema does not threaten vision.

Monitoring Idiopathic Intracranial Hypertension

Although this chapter focuses on IIH, many of the monitoring techniques are also applicable in patients with papilledema due to secondary causes of intracranial hypertension who are also at risk of visual impairment.

Monitoring Vision

Visual acuity with each eye tested separately with best correction for testing distance is essential but does not replace peripheral vision assessment, since central vision is impacted late in the disease. Confrontation visual field testing is of limited sensitivity for mild to moderate visual field loss.[51] Quantitative visual field testing is preferred for guiding management and can be accomplished with automated perimetry, most commonly a Humphrey Visual Field. This method maps a patient's ability to view varying intensities of stimuli throughout the visual field. This test is critical for establishing visual function and monitoring response to treatment. As such, it has been both an enrollment criterion and primary outcome measure in IIH treatment trials.[52]

Peripheral visual defects are the most common patterns of visual loss that develop from optic nerve dysfunction which is related to compression by high CSF pressure in the optic nerve sheath associated with papilledema.[53,54] Earliest changes are usually seen in the inferior nasal periphery.[55] Blind spot enlargement occurs due to peripapillary hyperopia (a refractive deficit), and less commonly due to chorioretinal folds, as a result of optic nerve sheath distension or fluid tracking beneath the retina from the optic disc.[56] Central vision is not affected until there is advanced optic nerve dysfunction and peripheral vision loss encroaches on fixation, or there is tracking of subretinal fluid from the swollen optic nerve to the fovea. A pattern of central more than peripheral vision loss should prompt consideration of other causes of optic neuropathy.[49] There is also the potential for functional (i.e., nonphysiologic) visual field loss or poor testing performance which impacts testing results. The former should be suspected when there is incongruence between the physical exam and pattern of vision loss on automated testing. The latter should be suspected when test indices show high false positive responses, false negative responses, or fixation errors.

Monitoring Papilledema

Fundus Examination

Papilledema appearance is a useful metric and is generally graded with the Frisen classification despite its poor interrater reliability.[57,58] Use of ophthalmic imaging (see below) has practical applications with regard to documentation and comparison between visits. Optic nerve pallor suggests permanent injury to the optic nerve has occurred.

Fundus Photography

This can be performed quickly and without pupil dilation to generate images of the optic nerve head (►**Fig. 1**). It is widely available in ophthalmic practice and is actively being studied in neurology and emergency room settings.[59] It has a higher sensitivity than direct ophthalmoscopy,[60] and medical students are more accurate in ophthalmic pathology identification using fundus photography compared with direct

ophthalmoscopy.[61] Fundus photography is an effective method of assessing the fundus in an emergency setting in which providers may have difficulty identifying key findings using the direct ophthalmoscope.[62,63] Even for examiners skilled in the ophthalmoscopic physical exam, fundus photos capture many ophthalmic features of IIH and can serve as the basis for comparison between examinations.[64,65]

Optical Coherence Tomography

Optical coherence tomography (OCT) generates noninvasive high-resolution cross-sectional images of the retina using a near-infrared light source through undilated pupils and is widely used in ophthalmic practice (►**Fig. 1**). Many neuro-ophthalmologists incorporate OCT in monitoring of IIH patients, although there remains disagreement whether this is associated with improved outcomes.[66]

The optic nerve contour, which can be difficult to appreciate with non-stereoscopic direct ophthalmoscopy, is readily apparent on OCT. It can identify, classify, and provide longitudinal assessment of optic nerve swelling, although it does not capture some of the qualitative vascular features seen on ophthalmoscopy and fundus photography.[67] There may even be subtle changes in patients with IIH without frank papilledema.[68] Another finding on OCT relevant to IIH management is quantification of the thickness of the retinal ganglion cell layers in the macula, a decrease in which is indicative of irreversible injury to the optic nerve.[69] Detection of such atrophy should alert the provider that the patient is at risk of permanent vision loss.

The shape of the back of the eye and of the scleral opening around the optic nerve, visible on OCT, assumes a concave shape in disc swelling due to intracranial hypertension compared with other causes.[70] Research studies have demonstrated that quantitative OCT parameters of the optic nerve head such as optic nerve head volume and eye shape relate to other optic nerve head measures and CSF pressure.[71,72] Furthermore, OCT measures of optic nerve swelling normalized in association with treatment provided in the IIHTT[73]; however, these are not considered established diagnostic tests as yet.

Management of Idiopathic Intracranial Hypertension

Management of IIH is based on symptomatic and ophthalmic outcomes as described above. Diagnosis of secondary intracranial hypertension does not preclude the use of IIH management strategies, since these can be important to improve symptoms and visual outcomes in addition to, or instead of, treatment of the secondary cause. Examples include directed ICP treatment in patients with venous sinus thrombosis or in patients for whom cessation of a (possibly) causal medication may pose undue risk.

Management should be guided by the following visual function and the optic nerve appearance closely. Any clinical worsening should prompt escalation of therapy and shorter follow-up intervals. A recent set of guidelines includes discussion of controversies and available evidence.[7]

Weight Loss

In the IIHTT, all enrolled patients received a comprehensive weight loss program with dietary, exercise and behavioral interventions. Although there was a greater improvement in the visual field outcome in the group that received acetazolamide, the placebo group also showed improvement in outcomes of vision, headache and quality of life.[12] In a previous study, a weight loss diet was associated with sustained improvement in ICP, symptoms, and papilledema.[74] Bariatric surgery has been associated with CSF pressure reduction and papilledema resolution in non-randomized studies.[75] Weight loss is therefore an important consideration as part of any IIH treatment regimen. In patients without optic nerve injury, weight loss intervention can be considered as monotherapy, but close ophthalmic monitoring is imperative as 6 of 7 treatment failures in the IIHTT occurred in the group that received weight intervention only.[12] However, given that weight loss cannot realistically be accomplished in a short time frame, additional treatment in those with vision loss or severe headache disability is often necessary.

Given the association between weight gain and IIH recurrence,[76] emphasis should be on a long-term, sustainable weight management plan. In the IIHTT, this was accomplished using a telephone-based program in a multidisciplinary collaboration.[77] Bariatric surgery is an option in obese patients and this should be pursued in a bariatric surgery center.[78] A randomized study of surgical and non-surgical approaches to weight loss for IIH treatment is being planned.[79]

Medical Treatment

Acetazolamide is a carbonic anhydrase inhibitor that is thought to reduce CSF production by the choroid plexus. In oral and IV forms, it reduces ICP[80] and has been the first-line therapy for IIH for many years. The IIHTT provided level II evidence by demonstrating that a combination of weight loss intervention and oral acetazolamide was associated with improved vision, papilledema, and quality of life over 6 months.[12] Mediation analysis confirmed a drug effect after accounting for more weight loss in the acetazolamide group. Interestingly, there was no drug effect on headaches, which improved similarly in both groups. In a 6-month extension of the IIHTT, patients who had not improved on placebo were transitioned to open label acetazolamide and subsequently recorded significant improvement in papilledema and headache.[81] Doses of up to 4 g daily were tolerated, with common symptoms reported by patients including paresthesias, dysgeusia, nausea, vomiting, diarrhea, and fatigue. Hypokalemia and metabolic acidosis occurred in 4 and 5% of acetazolamide-treated patients, respectively.[82] Acetazolamide is a diuretic and can put patients with venous sinus thrombosis at risk of clot propagation due to dehydration if hydration is not maintained. While it may play a role in ICP management with regard to cases of venous sinus thrombosis, careful monitoring is necessary. It commonly causes a mild metabolic acidosis, which can exacerbate respiratory and metabolic acidosis resulting from other causes (e.g., myasthenia gravis or diabetes). It can also cause hypokalemia, which can be easily managed with potassium supplementation.

Topiramate is a weak carbonic anhydrase inhibitor that was found to be noninferior in a randomized open label trial against 1 g to 1.5 g of acetazolamide.[83] It also has efficacy in migraine and weight-reduction effects. Although the carbonic anhydrase side effects are milder than with acetazolamide, it may cause cognitive slowing in a subset of patients. A recent study demonstrated topiramate to be more effective at lowering ICP than acetazolamide in healthy rodents[84]; however, it is not known if this translates to humans.

Furosemide was associated with lower CSF pressure when combined with acetazolamide in a small pediatric case series.[85] It is sometimes used as an add-on therapy when acetazolamide response is inadequate. It is included in the medical therapy regimen for the surgical IIH treatment trial (NCT03501966).

Symptomatic headache management may be an important adjunct to improve disability concurrent with ICP-lowering therapy.[7] Among patients who have no subjective or objective visual impairment and no evidence of visual pathway injury, including those without papilledema, symptomatic headache therapy without ICP-lowering therapy may be considered with close ophthalmic monitoring.

Procedural Treatment

This is generally reserved for medically refractory or fulminant IIH, particularly in patients with vision-threatening disease. Enrollment is ongoing for the Surgical IIH Treatment Trial (NCT03501966), which will compare medical management alone, optic nerve sheath fenestration, and ventriculoperitoneal (VP) shunt. A cerebral venous sinus stenting trial is also planned.[86]

Optic nerve sheath fenestration involves cutting slits or a window in the nerve sheath, thereby reducing CSF pressure in the subarachnoid space around the optic nerve in an effort to improve or stabilize vision. A rare although significant complication is vision loss.[87] In a meta-analysis of published cases, vision improved in a majority and worsened in 11%.[88] In some cases, there is reported improvement in headache and fellow eye papilledema following a unilateral procedure.

CSF diversion aims at acutely and directly lowering ICP using VP or lumboperitoneal shunts and is associated with improvement in vision.[89] Long-term outcomes suggest better headache remission in IIH patients with papilledema and shorter term (<2 years) headache duration.[90] There are long-term risks related to indwelling hardware, in addition to immediate procedural complications. Lumbar drains may have application for short-term emergent treatment. Serial LPs are not in routine use but may have application as a temporizing measure in certain cases.[7]

Cerebral venous sinus stenting aims to reduce cerebral venous hypertension and by extension intracranial hypertension by opening a stenosis in one of the transverse sinuses. Stenoses, either primary or secondary to high ICP, can be detected on MRV or CTV. Catheter venography is used to confirm a pressure gradient across the stenosis and deploy the stent. Experience is increasing with this relatively new procedure, which appears to be safe and effective in the short term in carefully selected patients.[91] Long-term follow-up is not yet available. This treatment is discussed in detail elsewhere in this issue.

Delivery of Care

IIH diagnosis and monitoring relies heavily on the ophthalmoscopic examination. Trainees and nonophthalmologists (including neurologists) often perform this with poor proficiency.[92,93] In addition, most emergency, inpatient and non-eye care outpatient facilities lack the necessary equipment for visual field testing, an important IIH outcome. While some of these barriers can be overcome using ophthalmic imaging such as fundus photography, another strategy is partnership with an ophthalmologist or optometrist who is skilled in collection of this data.

In most cases, IIH is managed in the outpatient setting. Thus, effective transitions from emergency and inpatient settings, where the initial diagnostic work up often occurs,[94] are critical to optimize outcomes. Challenges in relation to social deprivation exist among some patients[95] which, in turn, is associated with poorer access to health care. Limited availability of subspecialists with expertise in its diagnosis and management is another important concern.[96]

Conclusion

Symptoms of intracranial hypertension are broad and it is important to maintain a high clinical suspicion to diagnose patients with secondary causes who require treatment and patients who are at risk of irreversible optic nerve injury. Confirmation of the diagnosis through measurement of ICP as well as careful assessment of optic nerve function and structure are important to guide management with the goal of preserving vision and controlling symptoms. Weight loss and medical therapy are well tolerated and effective in IIH. Procedural interventions are generally reserved for medically refractory or fulminant presentations.

Conflict of Interest
None.

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