Update on Idiopathic Intracranial Hypertension

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KEYWORDS

• Idiopathic intracranial hypertension • Pseudotumor cerebri • Acetazolamide
• Optical coherence tomography

KEY POINTS

- Acetazolamide when used in patients with idiopathic intracranial hypertension (IIH) with mild visual loss produces a modest improvement in perimetric mean deviation on visual field testing over 6 months. The improvement is much greater in patients with moderate- to high-grade papilledema.
- Acetazolamide has its greatest effect on visual field function and papilledema in the first month of escalating dosage.
- In the IIH treatment trial, treatment failure was much less common in the acetazolamide-plus-diet group compared with the placebo-plus-diet group, and risk factors for treatment failure were presence of high-grade papilledema and lower visual acuity measures at baseline.
- Positive acetazolamide-related effects on quality of life seemed to be primarily mediated by improvements in visual field, neck pain, pulsatile tinnitus, and dizziness/vertigo that outweighed the side effects of acetazolamide.
- High cerebrospinal fluid pressure decreases the size of the entire dural sinus tree and also results in increasing size of skull foramen, canals, and ostia.

Idiopathic intracranial hypertension (IIH) is a disorder of overweight women in the childbearing age characterized by increased intracranial pressure with its associated signs and symptoms in alert and oriented patients. Neuroimaging and cerebrospinal fluid (CSF) analysis is normal except for increased intracranial pressure and its associated symptoms and signs. Also, no secondary cause of intracranial hypertension is apparent. This set of criteria comprises the modified Dandy criteria (**Box 1**). In the last 3 years, there has been an explosion of publications on IIH, with a PubMed search revealing more than 500 articles. In this review, the authors discuss the most important of these articles, especially those generated from the Idiopathic Intracranial Hypertension Treatment Trial (IIHT).

Before 3 years ago, a Cochrane review concluded: "*There is insufficient information to generate an evidence-based management strategy for idiopathic intracranial*

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Box 1
The modified Dandy criteria for idiopathic intracranial hypertension used in the Idiopathic Intracranial Hypertension Treatment Trial

1. Signs and symptoms of increased intracranial pressure
2. Absence of localizing findings on neurologic examination
3. Absence of deformity, displacement, or obstruction of the ventricular system and otherwise normal neurodiagnostic studies, except for evidence of increased CSF pressure (>200 mm water) (Abnormal neuroimaging except for empty sella turcica, optic nerve sheath with filled-out CSF spaces, and smooth-walled non–flow-related venous sinus stenosis 106 should lead to another diagnosis.)
4. Awake and alert
5. No other cause of increased intracranial pressure present

hypertension. There is inadequate information regarding which treatments are truly beneficial and which are potentially harmful. Properly designed and executed trials are needed."[1] In April 2014, the IIHTT results were published in the *Journal of the American Medical Association*.[2] This trial gave us the first evidenced-based approach relating to a protocol that significantly improved visual function in IIH.

THE IDIOPATHIC INTRACRANIAL HYPERTENSION TREATMENT TRIAL

In 1897, Quincke reported the first cases of IIH shortly after he introduced the lumbar puncture into medicine. It was named *pseudotumor cerebri* in 1904 but was not well delineated clinically until the 1940s when cerebral angiography was added to pneumoencephalography to identify cases of cerebral mass lesions. Foley coined the term *benign intracranial hypertension* in 1955; but reports from the 1980s demonstrated a high incidence of visual loss,[3,4] and the term *benign* is no longer appropriate.

Lubow and Kuhr[5] reported a series of patients with IIH, many of whom were treated successfully with acetazolamide and weight reduction.[6] The latter, another mainstay of medical therapy, was further shown to be a viable treatment by others. Gücer and Viernstein[7] used intracranial pressure monitoring and showed gradual CSF pressure reduction in patients receiving acetazolamide once they reached a dosage of 3 to 4 g/d. These uncontrolled studies were the basis for using acetazolamide in the maximally tolerated dosage to treat IIH.

The IIHTT is a multicenter, double-blind, randomized placebo-controlled study of acetazolamide in subjects with IIH with mild visual loss.[2,8] The trial structure and flow is found in **Fig. 1**. All subjects received a lifestyle modification program that included weight reduction with a low-sodium diet. The purpose of the trial was to determine the effect of acetazolamide in reducing or reversing visual loss after 6 months of treatment.

Subjects needed to meet the modified Dandy criteria for IIH and be aged 18 to 60 years. They needed to have reproducible mild visual loss (−2 to −7 dB perimetric mean deviation [PMD]). Participants needed to have bilateral papilledema, have an elevated CSF opening pressure, be untreated with regard to IIH, and have no secondary cause of increased intracranial pressure present.

Subjects were randomly assigned to receive a supervised lifestyle modification program that included a low-sodium weight-reduction diet either with acetazolamide or with matching placebo. The initial dosage of the study drug was 4 tablets daily in 2 divided doses, followed by dosage increases of 1 tablet every week up to a maximum