A Case Study on Idiopathic Intracranial Hypertension Management and Outcome

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ABSTRACT

Background: Pseudo Tumor Cerebri (PTC), also known by the name Idiopathic Intracranial Hypertension (IIH), is a disorder with increased intracranial pressure (ICP) and associated headache, nausea, vomiting, transient visual obscuration, double-vision, and visual field defects.

Material and methods: Thirty-four cases of idiopathic intracranial hypertension reported to our institute, all reported people are female, and all are over twenty years of age, with a diagnosis of IIH according to the Modified dandy criteria were included and treated medically with oral acetazolamide at a dose of 500 mg/day.

Results: All patients are started on oral acetazolamide 250 mg twice daily; all patients got resolved of fundus changes and nerve palsy with the therapy within three months of follow up.

Conclusions: In this study, administration of low doses of acetazolamide 250mg twice daily for a duration of 3 months for all the patients, and there were no signs of recurrence after cessation of acetazolamide and in the further follow-up. Acetazolamide plays an important role in cases of IIH for its best outcome. Early diagnosis and early treatment with acetazolamide gave good outcomes in all cases of Idiopathic Intracranial Hypertension.

Keywords: Idiopathic Intracranial Hypertension, Headache, Acetazolamide, Papilloedema, Optic Nerve Tortuosity.

INTRODUCTION

Pseudo Tumor cerebri (PTC) or Idiopathic Intracranial Hypertension (IIH), is a disorder with increased Intracranial Pressure (ICP) and associated headaches, nausea, vomiting, papilledema, vision changes, pulsatile tinnitus, cerebrospinal fluid (CSF) composition within normal limits and normal brain parenchyma, without any ventriculomegaly or mass lesion. It affects women of child-bearing age and overweight women,[1] however, men, women of all ages and children of both genders are affected.[2] There are multiple hypotheses about the etiology of PTC, including increased CSF production and decreased CSF absorption.[1] Regardless of the etiology, this disorder was debilitating and may lead to a permanent reduction in visual acuity. Therefore early diagnosis and treatment is a must.

MATERIAL AND METHODS

We conducted an observational and ambidirectional study of thirty-four patients diagnosed with idiopathic intracranial hypertension in the GSL General Hospital from December 2016 to November 2018. All the patients attended the ophthalmology outpatient department at GSL Medical College, who satisfy the inclusion and exclusion criteria within the study period taken as the sample.

Inclusion criteria

All patients over 20 years with a diagnosis of IIH according to the modified Dandy criteria were included (Table 1).[3,4]

Exclusion sriteria

Patients with secondary PTCS, such as the history of medications, cerebral venous sinus thrombosis, or systemic disorders associated with increased intracranial pressure (ICP) were excluded from the study.

Methodology

Patients were evaluated by the following parameters:

A detailed history was taken including age, gender, body mass index (BMI). Detailed clinical symptoms with special emphasis on the duration of symptoms, presenting symptoms (type and site of headache, nausea, vomiting, and ocular symptoms such as double-vision, transient visual obscuration, and visual field defects).

General systemic examination

Detailed examination of the nervous system with special emphasis on fundus examination, visual acuity, extraocular movements, systemic hypertension, and diabetes was done. The investigation includes perimetry, magnetic resonance imaging (MRI) brain with orbits. All patients were treated medically with oral acetazolamide at a dose of 500 mg/day.

RESULTS

There were 34 cases reported to our institute, all reported patients being female and age between 20-50 yrs, presented with complaints of headache with a period of 1-week to a 3-month interval, headache associated with nausea vomiting and transient loss of vision in all cases. With best-corrected visual acuity range from 6/9 to 6/6 (figure-1).

Out of the cases reported 7 cases are with diplopia due to abducens nerve palsy, 14 cases are overweight, 7 patients showing enlargement of blind spot, 5 cases showed empty

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How to cite this article: K. Srinivasa Rao, Vamaravalli Krishna Yasaswini, V.S. Gurunadh, K. Satish. A case study on idiopathic intracranial hypertension management and outcome. International Journal of Contemporary Medical Research 2019;6(10):J1-J4.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.10.18

Patients diagnosed as IIH	
With lateral rectus palsy	7(20%)
Overweight	14 (41%)
Enlarged blind spot	7(20%)
Empty Sella on MRI	5(14.7%)
Transverse sinus effacement on MRI	3(8.8%)

Modified Dandy Criteria for IIH
Signs and symptoms related to an increase in intracranial pressure (headache, visual disturbances, papilledema)
No localized neurological symptoms (except for 6th nerve palsy) and normal CSF constituents
Absence of deformity, displacement, or obstruction of the ventricular system and otherwise normal neurodiagnostic studies, except for increased cerebrospinal fluid pressure
Patient is awake and alert
No other cause for increased intracranial pressure can be isolated

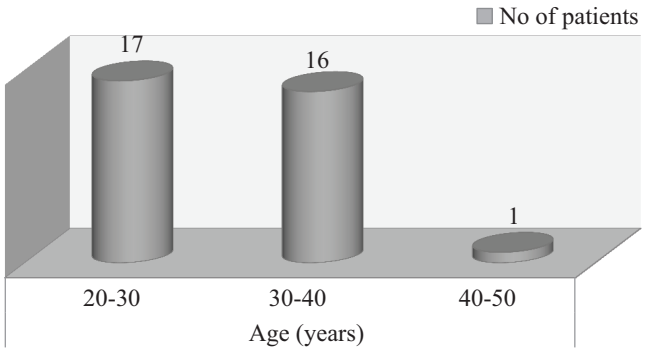

Figure-1: No of patients according to the age

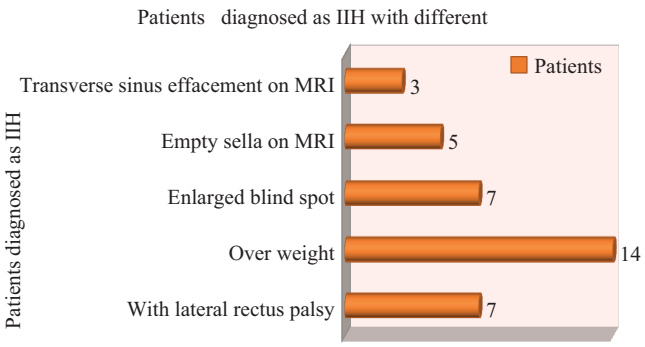

Figure-2: Patients diagnosed as IIH with different clinical entities

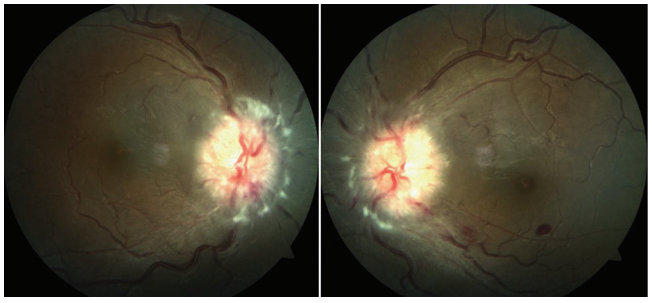

Figure-3: Fundus picture showing established papilledema (grade IV Frisen grade) in patient of IIH at the time of presentation

sella on MRI, 3 cases with mildly effaced of transverse sinus bilaterally without any evidence of thrombosis, all patients showing flattening of posterior sclera bilaterally at the optic disc, tortuosity of both nerves with prominent subarachnoid

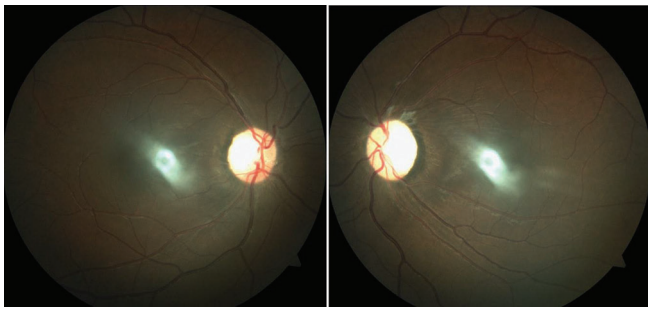

Figure-4: Fundus pictures at the end of 3 months follow up after medical management

spaces, all are between frisen 2-4 grades, all patients are started on oral acetazolamide 250 mg twice daily, all patients got resolved fundus changes and nerve palsy with the therapy within 3 months of follow up (figure-2,3,4).

DISCUSSION

In this study, all the patients had a headache as a presenting symptom compared with previous studies.[5,6] 14 out of 34 cases are overweight (30 kg/m^2), IIH has been associated with obesity, compared with previous studies[7,8]

In this study low doses of acetazolamide used in the treatment to avoid unusual side effects of acetazolamide compared with various studies[9,10]

Pseudo Tumor cerebri syndrome incorporates both the primary and secondary causes, IIH is a subset of a primary and secondary category that includes causes such as venous sinus thrombosis, drugs, and multiple medical conditions.[1,2] IIH (idiopathic intracranial hypertension) with peak presentation being between ages 20 and 40 years.[11] IIH is a disorder that affects women of reproductive age and overweight women, which has a strong association with obesity.[1,2] In this study, there is no difference in clinical features, including the occurrence of visual blurring, between normal BMI and overweight patients.

Epidemiology

Incidence of PTCS between 1 and 3/100000/year in the general population. When stratified for the female gender, reproductive age, and weight, the incidence rises by 12–28/100000/year.[11–12]

Pathophysiology

Raised ICP in IIH is a uniform characteristic, but the mechanism by which ICP is elevated in IIH is not clear with a different hypothesis. Raised ICP is associated with increased CSF production and decreased CSF absorption.

The choroid plexus is the primal site of CSF secretion, generating nearly two-thirds of the total CSF produced, rest of CSF produced from extrachoroidal sources, such as the ependyma and the blood-brain barrier.[13]

Extra ovarian estrogen high in CSF of obese women stimulates secretory cells of choroidal plexus to produce more CSF. Correlations between body mass index (BMI) and the risk of IIH have been demonstrated.[14] This was concluded in a prospective cohort study using a low-calorie meal replacement to induce weight reduction, generating

improvements in ICP and papilloedema, as well as symptomatic improvements in headache.[15]

Cytokines, and especially adipokines which are specifically produced by adipose tissue, have become a research focus. Significantly high levels of leptin, a product of the obese gene involved in weight homeostasis, found in the CSF of IIH patients.

Historically, CSF drains from the subarachnoid space through arachnoid granulations into the superior sagittal sinus. However, there is evidence of CSF drainage through the cranial nerves, and the cribriform plate into the lymphatics.

Increased CSF outflow resistance leading to compliance failure, even a small increase in CSF volume leads to a large rise in intracranial pressure.

Increased cerebral venous pressure reversing the normal gradient between the sinus and subarachnoid space or an increased in the resistance to flow of CSF across arachnoid villi.

Abnormality in the cerebral microvasculature is responsible for elevated cerebral blood volume, and that increases CSF pressure can be explained by only tissue swelling from an increase in total water content.

There is no ventricular enlargement in PTC; it has both defects in CSF absorption and increased cerebral volume associated with a non-compliant ventricular system that resists dilatation. The presence of cerebral edema could also account for the lack of ventriculomegaly.

IIH is also associated with orthostatic edema, is characterized by excessive sodium and or water retention in an upright posture. Pathogenesis due to vascular etiology and abnormal vasopressin regulation increased urinary excretion of vasopressin in patients with orthostatic edema. High levels of vasopressin are found in the CSF with PTC, the role of vasopressin in CSF is to regulate brain water content and it raises ICP by increasing transudation from central capillaries in the choroidal plexus epithelium and arachnoid villi.

High association of anxiety and depression in PTC, serotonin implicated in depression and anxiety is found in the highest concentration within the brain in the choroidal plexus, and serotonin receptors play a role in CSF production.

Sinclair et al. also suggested that the role of 11β-hydroxysteroid dehydrogenase type 1, an enzyme regulating CSF production through the glucocorticoid signaling pathway.[16] An increase of the water channel aquaporin 1 in choroid plexus is also suggested to promote the raise of intracranial pressure. In patients with IIH, following medical therapy with a low-calorie diet, ICP decrease in correlation with a reduction in 11B-HSD1 activity.[16] 11B-HSD1 is also dysregulated in obesity, and the metabolic syndrome and consequently, specific inhibitors are being developed as novel therapies.

Clinical features

Headache is the common presenting symptom of IIH, which is bilateral, frontal, or retroocular. Features consistent with migraine, including unilateral throbbing pain, nausea, vomiting, and photophobia is also reported.[17]

Ophthalmic-related symptoms include diplopia and transient visual obscurations.[18] Diplopia occurs in one-third to two-thirds of patients with IIH at presentation. Diplopia tends to be binocular and horizontal, as a consequence of abducens nerve palsy and can resolve with normalization of ICP.

Transient visual obscurations (TVO) are characterized by transient visual loss and are usually related to postural changes or straining.TVO is thought to be the result of disc edema causing transient ischemia at the optic nerve head. In a hospital-based series reported bilateral blindness in up to 10%.[19]

Pulsatile tinnitus is common which may be unilateral or bilateral.[19] Other associated symptoms include back pain, neck pain, and radicular pain, mood disturbance and, impairments in memory and concentration.

Management

The two approaches in the management of IIH are to preserve visual function and to reduce long-term headache disability. Early diagnosis, medical management with acetazolamide, and dietary therapy will improve subjective symptoms and objective signs. Accepted medical interventions range from dietary therapy to medical management and surgical treatment (in non-responding and extreme cases).

Pharmacotherapy

Acetazolamide

Acetazolamide is the mainstay of medical management in IIH. It is a potent inhibitor of carbonic anhydrase enzyme, and it impedes the activity at the choroid plexus reducing CSF secretion, which in turn decreases papilledema grade, Improves visual field function and preventing vision loss due to optic atrophy by decreasing CSF pressure.

Adverse effects of acetazolamide fatigue, nausea, diarrhea, vomiting, and paraesthesia, altered taste sensations were significantly higher in some cases.

Other drugs like, topiramate, diuretics such as furosemide, are used in IIH when acetazolamide is not tolerated. Octreotide is a somatostatin analogue. Somatostatin receptors are expressed in choroid plexus and arachnoid villi, therefore, octreotide may be related to CSF production and absorption.[20] Octreotide is given subcutaneously 0.3 mg per day, and the dose gradually increased to 1mg per day for 6 to 8 months showed improvement in IIH symptoms, which was an ongoing study.

Treatment of headache

Headache is the most common feature presented in IIH and leads to significant morbidity.[21] Short-term painkillers may be helpful in the first few weeks following diagnosis. These could include non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol.

Non-medical interventions

If medical therapy fails, is not tolerated, or there is fulminant IIH, more aggressive measures should be considered like:

- Lumbar puncture
- Optic nerve sheath fenestration
- CSF diversion surgery
- Transverse sinus stenting

Follow up[22]

1. visual acuity
2. pupil examination
3. formal visual field assessment
4. Dilated fundal examination to grade the papilloedema.
5. BMI calculation.
6. Improvement in symptoms (headache, nausea, vomiting, transient loss of vision, pulsatile tinnitus)
7. Improvement in lateral rectus palsy

CONCLUSION

In our study all patients were female, of which 41% were obese with papilloedema ranging from early to marked (established) papilloedema, all patients responded well with minimal effective dose acetazolamide and showed symptomatic relief, improvement in papilloedema and lateral rectus palsy and no cases have gone to severe stage. In this study administration of low doses of acetazolamide 250mg, twice daily for a duration of 3 months and there are no signs of recurrence after cessation of acetazolamide and in the further follow-up.

Acetazolamide plays an important role in cases of IIH for its best outcome. Early diagnosis and early treatment with acetazolamide give a good outcome in all cases of Idiopathic intracranial hypertension.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 31-08-2019; **Accepted:** 23-09-2019; **Published:** 18-10-2019