

CLINICAL STUDY

Idiopathic intracranial hypertension: a retrospective clinical study

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Abstract: *Background:* Idiopathic intracranial hypertension is a disorder characterized by an increased intracranial pressure, without deformity and obstruction of the ventricular system. There is a predilection of occurrence in obese women of childbearing age. The pathogenesis of idiopathic intracranial hypertension is likely related to abnormalities in the balance between production and drainage of cerebrospinal fluid. Diagnosis is made by excluding the known causes of elevated intracranial pressure.

Objective: To evaluate the features, possible causes, treatment, and incidence of idiopathic intracranial hypertension as seen in patients attending our Department of Neurology.

Methods: We retrospectively analysed a group of patients diagnosed with idiopathic intracranial hypertension in our Department of Neurology during a twenty-year period (1989 to 2008).

Results: In six patients we confirmed the diagnosis of idiopathic intracranial hypertension during this period. Five of them were females and one was male, the average age of the patients was 32.30 years (22 to 52). The calculated incidence of idiopathic intracranial hypertension in our group was 0.15 per 100,000 persons. Out of these six persons there were four cases diagnosed in the last five years, changing the calculated incidence to 0.4 per 100,000 persons in this period. The average body mass index in our patients was 26.33 kg/m² (20.1 to 31.38).

Conclusion: We suppose that the increased incidence of idiopathic intracranial hypertension in our patients in the last five years has been associated with an advance in diagnostics. With literary data, half of our patients were obese or overweighted, but all of them underwent also hormonal treatment, some had iron deficiency and one of them was pregnant (*Tab. 3, Fig. 1, Ref. 17*). Full Text in free PDF www.bmj.sk.

Key words: idiopathic intracranial hypertension, incidence, treatment.

Idiopathic intracranial hypertension (IIH) is a disorder of unknown cause, occurring in women of the childbearing age. It is characterized by an increased intracranial pressure (ICP) with its associated signs and symptoms in patients without localizing neurological findings except for the sixth nerve palsy (1). Furthermore, there is a normal cerebrospinal fluid content (sometimes low proteins levels can be found), and normal contrast-enhanced computerised tomography (CT) or magnetic resonance imaging (MRI) (2, 3). Although the hallmark of IIH is the raised ICP, the underlying aetiology of IIH is not known. An elevated ICP is likely related to abnormalities in the balance between production and drainage of cerebrospinal fluid (CSF). Many medical conditions and medications are associated with IIH. But the studies of this conditions are mostly uncontrolled and retrospective and this has led to erroneous conclusions. For example, pregnancy, irregular menstruation and oral contraceptive use are reported as associations (4, 5, 6). In case-controlled studies, no significant associations are found between IIH and multivita-

min, oral contraceptive or antibiotic use (5, 6). A case-controlled study has found a strong association between IIH and obesity and weight gain during 12 months before diagnosis (6). The symptoms are headaches, pulse synchronous tinnitus and transient visual obscuration. The signs are papilledema, visual loss and the sixth nerve palsy. IIH has to be diagnosed according to the modified Dandy's criteria (7), which include signs and symptoms of an increased intracranial pressure, normal neurological examination (except for the sixth nerve palsy) in an alert and awake patient, absence of ventriculomegaly or intracranial space-occupying lesions on neuroimaging studies (sometimes small cortical veins and superior sagittal, straight, transverse, and sigmoid sinuses, flattening of the posterior sclera, vertical tortuosity and elongation of the orbital optic nerves, distension of the perioptic subarachnoid space, and a partially empty sella can be found), and an increased opening pressure on lumbar puncture with normal cerebrospinal fluid composition (8).

Subjects and methods

In our study we intended to analyse cases of IIH, which were diagnosed in the years 1989–2008 in our Department of Neurology. The diagnosis was confirmed in six patients from the total number of 19 200 inpatients in this period. The analysis of these cases was retrospective, non-controlled. Every patient underwent

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a complete neurological examination, complete ophthalmologic examination (including fundoscopy, perimetry, visual acuity, pupillary response), neuroimaging studies (CT or MRI, and in four cases also magnetic resonance angiography), lumbar puncture, routine blood tests, thyroid function test, clotting studies, herpetic virus, and Lyme disease in CSF. None of the persons were on vitamin A supplements. Patients were defined as obese if their body mass index (BMI) was more than 30 kg/m², overweight was defined as BMI of 25 to 30 kg/m².

Results

Diagnosis of ITH was confirmed in six patients (five women and one man). Tables 1–3 displays the patients' data. The mean age was 32.30 years (22 to 52). The calculated incidence of ITH in our population was 0.15 per 100,000 persons. Four cases were diagnosed in the last five years with the calculated incidence of 0.4 per 100,000 persons. The average BMI was 26.33 kg/m² (20.10 to 31.38 kg/m²). Two persons were over 30 kg/m² (30.10 and 31.38 kg/m²) and one was overweight (29.40 kg/m²). One patient was pregnant and used a thyroid replacement therapy due to hypothyreosis, one overweight patient used a concomitant thyroid replacement therapy due to hypothyreosis, too. Two patients used hormonal therapy of menstrual irregularities, in one of them associated with iron deficiency anaemia. All patients were symptomatic, all patients complained of headache, five of them felt

nausea and eventually vomited, three of diplopia, two of transient visual obscuration, and one of tinnitus. Three patients had the sixth nerve palsy and the other three patients were without localized neurological findings.

A fundus examination was performed on all eyes. Optic disc swelling was noted in ten eyes, atrophy was noted in two eyes. All patients suffered from visual field defect, three of them had scotomas, one of them with bilateral constriction, and three of them had only enlarged blind spots. All patients underwent a lumbar puncture with the opening pressures higher than 25 cmH₂O with a normal cerebrospinal fluid composition in four patients, low proteins were present in two patients.

MRI of brain was performed in five patients, magnetic resonance angiography (MRA) in four patients, and a contrast-enhanced CT in one patient. They demonstrated a normal finding except for one patient, in whom the aplasia sinus transversus on the right was revealed.

Five patients were treated with fluid and sodium restriction and low-fat diet. One patient was treated also with intravenous steroids (dexamethason), one with oral steroids and osmotherapy, and one with acetazolamide (750 mg/day) and osmotherapy. After this treatment, the symptoms and visual field improved in this group. In the other group of patients, one was treated with acetazolamide (1000 mg/day) and oral steroids, two were treated with acetazolamide (750 mg/day) and osmotherapy without improvement.

Tab. 1. Demographics, risk factors and symptoms in patients with idiopathic intracranial hypertension.

Case	Age	Gender	BMI	Associated factors	Symptoms
1	27	Female	30.1	Hypothyreosis, pregnancy	Headache, nausea, vomiting
2	29	Female	29.4	Hypothyreosis, overweight	Headache, nausea, vomiting, diplopia
3	22	Female	24	Dysmenorrhea	Headache, nausea, vomiting, diplopia, tinnitus
4	39	Female	23	Iron deficiency anaemia, dysmenorrhea	Headache, nausea, vomiting, transient visual obscuration
5	52	Female	20.1	-	Headache, deterioration of visual acuity
6	25	Male	31.38	Obesity	Headache, nausea, vomiting, diplopia, transient visual obscuration

Abbreviations: BMI – body mass index

Tab. 2. Examination findings in patients with idiopathic intracranial hypertension.

Case	Signs	Visual fields	Papilledema	CSF opening pressure >25 cmH ₂ O	Neuroimaging studies CT/ MRI/ MRA
1	Normal	Sco	Yes	Yes	Normal
2	Sixth nerve palsy	Sco	Yes	Yes	Aplasia sinus transverses
3	Sixth nerve palsy	EBS, Sco	Yes	Yes	Normal
4	Normal	EBS	Yes	Yes	Normal
5	Normal	Bilateral constriction	Atrophy	Yes	Normal
6	Sixth nerve palsy	EBS	Yes	Yes	Normal

Abbreviations: BMI – body mass index, EBS – enlarged blind spot, Sco – scotoma, CSF – cerebrospinal fluid, CT – computed tomography, MRI – magnetic resonance imaging, MRA – magnetic resonance angiography

Tab. 3. Treatment and outcome in patients with idiopathic intracranial hypertension.

Case	Treatment				Visual field outcome
	Diet	Acetazolamide	Corticosteroids	Osmotherapy	
1	No	No	Yes	No	Normal
2	Yes	No	Yes	Yes	Normal
3	Yes	Yes	No	Yes	EBS
4	Yes	Yes	No	Yes	Normal
5	Yes	Yes	Yes	No	Bilateral constriction
6	Yes	Yes	No	Yes	EBS

Abbreviations: EBS – enlarged blind spot, Sco – scotoma

Discussion

IIH is a disorder occurring in obese women of childbearing years. The annual incidence of IIH is usually given about 0.9 per 100,000 persons and 3.5 per 100,000 in females 15 to 45 years of age (9). In obese women aged 20 to 44 years, the incidence is 19 per 100 000 (9). With the current epidemic of obesity in developed countries, these figures likely underestimate the real incidence (10). The mean age at the time of diagnosis is about 30 years.

The underlying pathogenic mechanism of IIH is still not known. The elevated ICP is likely to relate to abnormalities in the balance between production and drainage of cerebrospinal

fluid, increased CSF secretion (11), increased cerebral volume (12), increased CSF outflow resistance due dysfunction of the absorptive mechanism of the arachnoid granulations or the extracranial lymphatics (13) or increased cerebral venous pressure (14, 15).

Many medical conditions and medications are associated with IIH. A case-controlled study has found a strong association between IIH and obesity and weight gain during 12 months before the diagnosis (6) and no significant associations between IIH and multivitamin, oral contraceptive or antibiotic use (5, 6). Addison disease, corticosteroid withdrawal, hypoparathyroidism, menstrual irregularities, pregnancy, sarcoidosis, systemic lupus

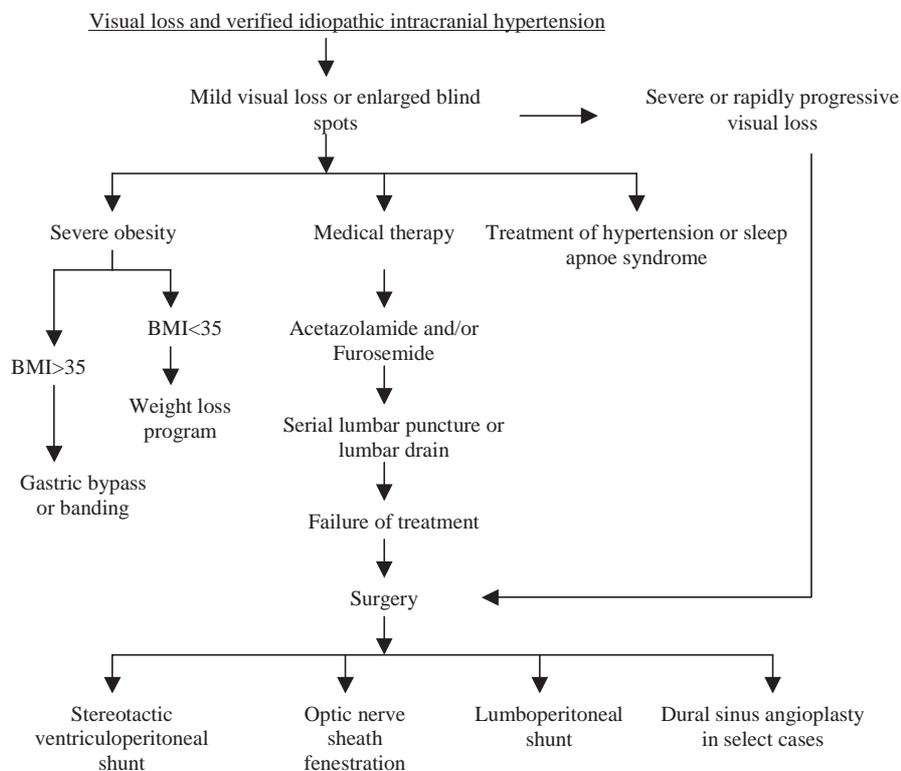


Fig. 1. Treatments for idiopathic intracranial hypertension – modified according Atkinson (17).

erythematous, iron deficiency anaemia, some medications as anabolic steroids, thyroid replacement therapy, amiodarone, phenytoin, lithium carbonate are mentioned in literature as possible causes of IIH. The fact that most studies following on these conditions are uncontrolled and retrospective, is the reason why many questions in this fields remain unanswered (16).

The treatment of IIH can be both medical and surgical. It is aimed at lowering the intracranial pressure and affecting symptoms directly. Unfortunately, there have not been any controlled clinical trials on IIH. One of the possible algorithms of treatment is illustrated in Figure 1 (17). Any presumed inciting factors (like tetracycline or excessive vitamin A) should be eliminated. Symptomatic patients with no visual field loss can be reasonably managed with close observation, a low-salt diet, and encouragement to loss weight. Patients with visual loss can be treated medically or surgically. Medical treatment includes acetazolamide, topiramate, furosemide, and corticosteroids. Serial lumbar puncture, or lumbar drain placement, can be useful medical strategies. Surgical treatment includes optic nerve sheath fenestration, shunting procedures such as lumboperitoneal shunts, stereotactic ventriculoperitoneal shunts, and dural sinus angioplasty in selected cases (16).

In conclusion, the increased calculated incidence of IIH in our patients in the last five years is explainable by a higher knowledge about the IIH and use of new advanced technology, which helps us to detect more cases of IIH compared to the period before. The incidence of IIH is in our patients still lower in the last five years in comparison with literature data. Also, in our patients, only two had BMI higher than 30 kg/m², one was overweighted and half of them were normal-weighted. We hypothesize that few aspects of this problem have to be discussed. Fewer patients might be diagnosed and treated in our population compared to other countries. Our population might not be so obese like it is in other countries. The majority of statistical data on the incidence of the IIH come from the United States of America, where the incidence of obesity is the highest in the world. In our population, there might be a lower incidence of obesity associated with a lower incidence of IIH. Comparative data, which might elucidate the incidence of these relations, does not exist yet. Another aspect is a possible association of IIH in our patients with hormonal changes and treatment, which were very often present: taking contraceptives, thyroid replacement therapy, treatment of menstrual irregularities and pregnancy. Iron deficiency anaemia was rare (only one person).

Clearly, the small number of subjects in this work precludes the ability to generate definitive conclusions. Further prospective controlled and multicenter studies might help us to better understand the aetiopathogenesis of IIH and to progress in therapeutic approaches.

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