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Idiopathic intracranial hypertension: Are there predictors for visual outcome or recurrences?

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ABSTRACT

Objective: To find out the predictors of final visual outcome and recurrences in idiopathic intracranial hypertension (IIH).

Patients and methods: Medical records of 75 patients with IIH were analyzed retrospectively. Gender, age of disease onset (AODO), body mass index (BMI), lumbar puncture opening pressure (LP-OP), visual acuity (VA) in logMAR, optical disc appearance (ODA), visual field (VF) mean deviation (MD), treatment results and recurrence rates were considered.

Results: Mean age at onset age was 32.4 years, BMI was 311 kg/m^2 and median LP-OP was 380 mm H2O.

All patients were treated with acetazolamide with a median dose of 1500 mg. The mean follow-up period was 44.8 months. AODO, BMI, LP-OP were not correlated with any of the examination parameters (VA, ODA, VF) at the first or last visit. The correlation between the VA and VF both at the first and last visit was not very powerful. VA of the last visit was fairly correlated with the VA of the first visit. However, the correlation between the last and first visit VF was very good. A very significant improvement in both VA and VF was recorded after treatment.

Recurrences were noted in 23%. Demographic and clinical features of the recurring and non-recurring patients were not significantly different in terms of AODO, BMI, LP-OP, VA, VF or ODA.

Conclusions: The patients with IIH respond to treatment with acetazolamide. First visit VF is the main determinant of the final visual outcome. Recurrences cannot be predicted by the demographic or clinical features at presentation.

1. Introduction

Idiopathic intracranial hypertension (IIH) is characterized by raised intracranial pressure without any identifiable pathology in the brain and with normal cerebrospinal fluid (CSF) composition. A typical patient of IIH is an obese woman of childbearing age [1]. The annual incidence of IIH in the Western World is about 0.9/100 000 persons and 3.3/100 000 in females 15–44 years of age [2,3]. When obesity is considered, the incidence is increased to 19/100 000 for women 20–44 years of age who are 20% or more over ideal weight [2]. About 9% of the diagnosed patients are male [4].

Headache is the most common symptom [1]. Papilledema, or optic disc swelling is the hallmark of the disease [5]. It may be asymmetric or uncommonly unilateral [6,7]. Choices of medical treatment are diuretics particularly acetazolamide or furosemide and encouragement of weight loss [1]. Acetazolamide improves visual outcome defined by perimetric mean deviation in IIH [8]. Topiramate, an antiepileptic drug, is another treatment opinion [9]. Surgical treatment becomes necessary when visual loss progresses despite medical management or occasionally when patients initially present with severe optic neuropathy [1]. Optic nerve sheath fenestration (ONSF) and CSF diversion procedures are effective [10,11]. Visual loss which is the only serious complication, may occur either early or late in the course of the disease [12].

The etiology of IIH is still unclear and needs to be investigated [5]. In this study we aimed to define the characteristics of patients with IIH admitted to the neuro-ophthalmology unit of our University Hospital. The demographic and clinical features of the patients and their effect on the final visual outcome and recurrences was tried to be determined.

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2. Materials and methods

We retrospectively reviewed the medical records of 75 patients meeting the diagnostic criteria for IIH [13] who were on follow-up between 2010 and 2017 at the Neuro-ophthalmology Unit of Ege University Medical School, Department of Neurology. Seventy-five patients were the ones whose adherence to visits and treatment were complete with all the visual function studies performed during a follow-up period of at least six months. The study was approved by the ethics committee of Ege University Medical School and was performed in accordance with the ethical standards outlined in the Declaration of Helsinki.

All patients had been reviewed by magnetic resonance imaging (MRI) of the brain including venography to exclude intracranial abnormalities and venous thrombosis and a lumbar puncture had been performed with a lumbar puncture opening pressure (LP-OP) ≥ 250 mm of water in the lateral decubitus position with normal composition.

The parameters taken into consideration were gender, age of disease onset (AODO), body mass index (BMI), LP-OP, visual acuity (VA) in logMAR, optical disc appearance (ODA) (optic disc photography graded from 0 to 3 as follows: Frisén Grade 0 was classified as Grade 0; Frisén Grades 1, 2 as Grade 1; Frisén Grade 3 as Grade 2 and Frisén Grades 4, 5 as Grade 3) [14], visual field (VF) (Humphrey automated perimetry, central 30-2 threshold SITA Fast program) mean deviation (MD), treatment results and recurrence rates. The results of the first visit were compared with the results of the sixth month which was regarded as the last visit. VA, ODA and VF were the major outcomes. The worst-affected eye of each patient was chosen for the statistical analyses.

Data about recurrences in patients with longer follow-up periods was also studied. Appearance of symptoms and signs of raised intracranial pressure after discontinuation of treatment for at least a month was accepted as recurrence.

2.1. Statistical analysis

IBM SPSS Statistics 23.0 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) Regarding numerical data conforming normal distribution, arithmetic mean, standard deviation, and 95% confidence intervals (CIs) were used. Data not showing normal distribution were evaluated with non-parametric tests. Wilcoxon test was used to compare the results of the first visit with the last and Spearman's correlation analysis was used to find out if there is a correlation between the BMI, LP-OP and first and last visit examination findings. Multiple regression (by checking their assumptions and stepwise method) analysis was performed to find the effect of BMI, LP-OP and clinical findings on the final visual outcome. Mann-Whitney test was used to compare the demographic and clinical features of the recurring and non-recurring patients.

All the test was performed at a = 0.05 level of significance ($p < 0.05$).

3. Results

Of the 75 patients 72 were women and 3 were men. Demographic and clinical characteristics of patients are presented in Table 1.

Sixty-one (81.3%) of our patients were overweight (BMI ≥ 25 kg/m²), and 38 (623%) of these were obese (BMI ≥ 30 kg/m²). Seven obese patients were morbid obese (BMI ≥ 40 kg/m²). All male patients were overweight and one was obese.

All patients were treated with acetazolamide with a median dose of 1500 mg (min: 500, max: 4000 mg/d). Eight patients (11%) used furosemide additionally with a median dose of 40 mg (min: 40, max: 120) and five patients (7%) topiramate with a median dose of 100 mg (min:50, max:150).

Due to rapid and progressive loss of vision, ONSF was performed in 4 female patients (bilateral in three and unilateral in one).

Table 1
Demographic and clinical characteristics of the patients.

	Number of patients	Mean	SD	Minimum	Maximum
Age at onset (years)	75	32.4	10.4	18	60
Weight (kg)	75	80.95	17.0	47	130
Height (cm)	75	161.6	7.2	145	182
BMI (kg/m²)	75	31.1	6.8	19.5	53.3
LP-OP (mm H20)	75	398.9	118.9	250	742
Follow-up period (months)	75	44.8	29.4	6	160

Median VA, ODA and VF-MD for the worst eye at the first and last visit are presented in Table 2.

VA in the first and last visit is given in Fig. 1 and VF-MD in Fig. 2.

The correlation analysis showed that AODO, BMI, LP-OP were not correlated with any of the examination parameters (VA, ODA, VF-MD) at the first or last visit (p > 0.05). ODA of the first visit was also not correlated with the VA (p: 0.25) or VF-MD (p: 0.50) of the first visit. The last visit ODA was fairly correlated with the last visit VA (p: 0.015, r: −0.28) and VF-MD (p:0.001, r: −0.465) indicating that resolving papilledema can be associated with the recovery of the VA and the VF-MD.

The VA at the first visit showed little correlation with the VF-MD at the first visit (p: 0,037, r: 0243). VA and VF-MD results of the last visit were fairly correlated with each other (p: 0.001, r: 0,368). VA of the last visit was fairly correlated with the VA of the first visit (p < 0.001, r: 0.489). On the other hand, the correlation between the last and first visit VF-MD was very good (p < 0.001 r: 0.751). Wilcoxon signed ranks test revealed a very significant improvement in both VA and VF-MD after treatment (p < 0.001) (confidence interval 95%).

Multiple regression analysis was also performed to find out if a predictive demographic or examination finding could be detected including BMI, LP-OP and ODA to decide the last visual outcome and it was seen that it was only the first visit VF-MD that could give information about the last VF-MD.

During the follow-up recurrence developed in 17 patients (23%).

Comparison of the demographic and clinical features of the recurring and non-recurring patients revealed that no significant difference was present in terms of AODO (p:0,568), BMI (p: 0,599), ODA (p:0,964), LP-OP (p: 0,778), VA (p: 0,973) or VF-MD (p:0,251) between groups at the first visit.

4. Discussion

The mean AODO in our study was 32.4 years (± 10.4). It was mainly similar with the previous population studies [5,15].

IIH is known to be associated with obesity. 62,3% of our patients were obese and males constituted 4% of the patient group. In accordance with the previously published studies [16–18] IIH is mainly seen in women who are obese and of childbearing age in Turkey.

AODO and BMI did not show any correlation with the first or the last examination findings including VA, VF-MD or ODA.

Visual disturbance has been reported as the most common symptom in IIH after headache [19]. Visual symptoms range from blurring of vision to progressive and, in some cases, rapid loss of VA or VF [20]. VA was affected in our 16 patients (21%) at the initial visit and was present in 7 (9 %9%) at the last visit.

VF loss has been reported at presentation and during follow-up in up to 82% to %92 of patients using Humphrey perimetry [15,21]. In our group VF loss was present in 69 of our 75 (92%) patients. VF assessment is known to be more sensitive in detecting minimal or mild visual deficit than other measurements of visual function [20].

All our patients were treated with acetazolamide, 11% used furosemide and 7% used topiramate additionally. A very significant

Table 2
Visual acuity, Optic disc appearance and Visual field changes over the follow-up period.

Worst eye	First visit			Last visit		
	median	minimum	maximum	median	minimum	maximum
Visual acuity (logMAR)	0.05	0	1.0	0.00	0	0.52
Optic disc appearance (grade)	1	0	3	1	0	3
Visual field (dB)	−7.6	−32.3	−0.4	−3.5	−29.5	0.5
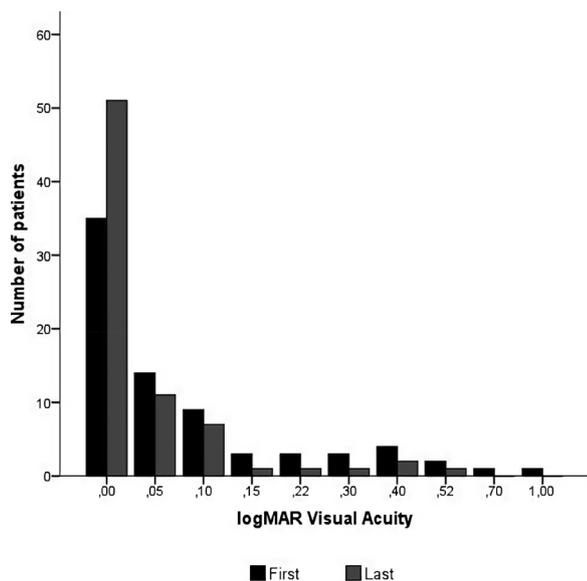
Fig. 1. Visual acuity (VA) in logMAR at the first and last visit.
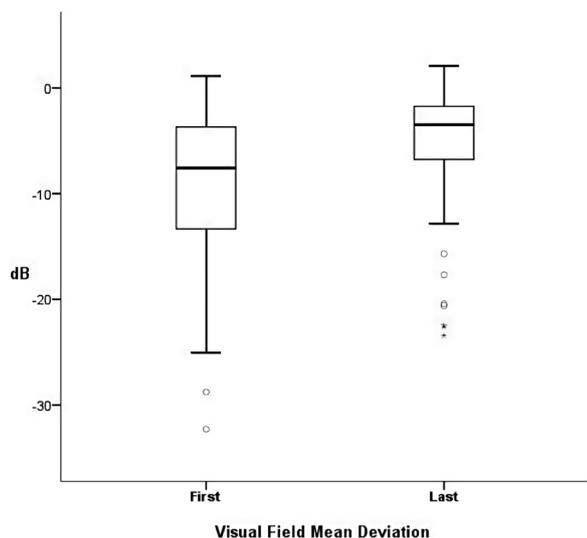
Fig. 2. Visual field (VF) mean deviation (MD) at the first and last visit.

improvement in both VA and VF was revealed in our group with treatment (p < 0.001). Acetazolamide therapy for IIH has been reported to be associated with improvement in visual field, LP−OP and papilledema in adults with mild visual field loss [22].

ONSF was performed in 4 patients (bilateral in three and unilateral in one). ONSF provides an effective surgical treatment for patients in whom medical therapy fails. Unilateral ONSF significantly decreases the grade of papilledema in both operated and non-operated eyes and bilateral ONSF may not always be necessary [10]. We had seven patients with low VA at the last visit. Four of them were patients with ONSF. In one no improvement in VA could be achieved after surgery, in

three prominent improvement was noted.

In our group there was a positive but not a powerful correlation between the VA andof the first visit (p = 0,037, r: 0,243) and the last visit (p = 0.001, r: 0,368). The correlation between the VA of the last and the first visit was fair (p < 0.001, r: 0.489). On the other hand, the last visit VF-MD was highly correlated with the VF-MD of the first visit (p < 0.001 r: 0.751) and by multiple regression analysis we identified that the first visit VF was the indicator of the final visual outcome in IIH. These results are concordant with three previous studies dealing with the predictors of visual outcome in IIH [16,18,23]. On the other hand, high grade papilledema which has been reported as a risk factor for treatment failure in a previous study [24] was not the case in our group. Initial ODA was not correlated with the initial or final VA or VF-MD. Similarly LP-OP, reported to be associated with the visual outcome in another study [18] was not associated with the initial or final VA or VF-MD in our group.

During the follow-up period recurrences developed in 23% of our patients. The disease may recur and perhaps, may require lifelong follow-up. Comparison of the demographic and clinical features of the recurring and non-recurring patients revealed that no significant difference was present in terms of AODO, BMI, LP-OP, VA, ODA or VF-MD at the first visit that could help us to know which patients could show recurrences from the very beginning (p > 0,05).

The main limitation of this study is the retrospective collection of the data from the medical records. Subjective nature of papilledema grading is another limitation which we tried to overcome by asking the same experienced reader (NC) to assess the ODA. Automated perimetry providing quantitative data is also a subjective measure influenced by physical and behavioral factors. At least the same VF programe had been used for all the patients of this study. The efficacy of weight loss was also not taken into consideration.

5. Conclusion

The patients with IIH respond well to treatment with acetazolamide with a median dose of 1500 mg/d. ONSF must be considered in patients with deterioration of vision despite medical therapy. We do not now the effect of weight loss as the BMI at the sixth month visit was not recorded in most of the subjects. We suggest that the first visit VF findings determine prognosis and the final visual outcome. Patients who have VF defects at presentation should be closely monitored and appropriate treatment should be chosen. Recurrences were noted in 23% of the patients. We couldn't find distinguishing demographic or clinical features at presentation that could predict recurrences. Therefore, it seems necessary for all the patients to be on follow-up for long periods.

Ethics

The present study was approved by the Ethics Committee of Ege University Medical School (ref number: 58153)

Conflict of interest

None of the authors have any conflict of interest.

Acknowledgement

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