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Original Article

Visual Field Changes in Idiopathic Intracranial Hypertension Treated with Oral Acetazolamide

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Abstract

***Background**: Idiopathic Intracranial Hypertension (IIH) is a disorder primarily among overweight women of childbearing age. Acetazolamide (AZM) is commonly used to treat IIH, but there is insufficient information regarding Visual Field (VF) changes in response to treatment with this drug. **Objective**: This study was designed to evaluate the visual field changes of patients with IIH treated with oral acetazolamide. **Materials and Methods**: A total of 30 patients with IIH treated with oral acetazolamide (500 mg twice daily) were followed up after 3 months and 6 months. Demographic features were recorded. Visual field analysis was done and papilledema was graded accordingly. Mean value of perimetric mean deviation of the follow-up periods were compared with that of baseline values. **Results**: The mean age of the study patients was 25.3±8.7 years with a female predominance (83.3%). Most common field defect was nasal or temporal field defects (46.67% in their right eye and 50.0% in their left eye). The mean of perimetric mean deviation (PMD) and papilledema of both eyes were reduced significantly over time. This study concluded that oral acetazolamide 500 mg twice daily is effective in reduction of symptoms/signs and improve perimetric mean deviation in visual filed among patients with idiopathic intracranial hypertension with minimum side effects. **Conclusion**: Changes in visual field parameter are important marker in diagnosis and monitoring of patients of IIH treated with oral acetazolamide.*

***Key words**: Acetazolamide (AZM); Idiopathic Intracranial Hypertension (IIH); Visual field (VF)*

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Introduction

Idiopathic intracranial hypertension (IIH) is the syndrome of elevated intracranial pressure (ICP) in the absence of space occupying or vascular lesions and without enlargement of the cerebral ventricles, for which no definite cause can be identified.[1] The reported incidence was approximately 0.9-1.7 per 100,000 in western societies, which may be as high as 14.88 per 100,000 in the obese population.[2,3] The pathophysiology underlying the raised intracranial pressure is still unclear. Patient present with altered visual function includes subjective blurred vision, visual field defects and binocular diplopia or may develop such visual disturbance if inadequately treated or remains untreated. Most common type of visual field

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defects in idiopathic intracranial hypertension (IIH) include an enlarging blind spot, loss of nasal or temporal visual field, or generalized visual field constriction.[4] Indications for starting medical treatment for patients with IIH are visual field changes and symptoms of elevated ICP.[5,6] The carbonic anhydrase inhibitor acetazolamide (AZM) is the drug most commonly used to treat idiopathic intracranial hypertension.[7] Management outcome is the measurement of visual function and papilledema grading, in which visual function consist of best corrected visual acuity (BCVA) and visual field (grading of field defects and perimetric mean deviations). Perimetry is the best diagnostic tool to follow up the patient during treatment.[8] Perimetric mean deviation (PMD) is one of the important variables of visual outcome.[7] It also helps escalation of dose of acetazolamide (AZM) as the PMD improves to equal to or better than -1 dB in each eye and signifies adequate improvement for dose adjustment.[9] This present study was designed to evaluate the visual field changes of patients with idiopathic intracranial hypertension treated with oral acetazolamide at a tertiary eye hospital in Bangladesh.

Materials and Methods

This prospective longitudinal interventional study was conducted at Department of Neuro-ophthalmology, National Institute of Ophthalmology and Hospital (NIO&H), Dhaka, Bangladesh from December 2019 to October 2021. The research protocol was approved by the ethical review committee of NIO&H. A total of thirty (30) patients with idiopathic intracranial hypertension (IIH) diagnosed by modified Dandy diagnostic criteria were enrolled for this study using purposive sampling technique.[8] All patients of idiopathic intra-cranial hypertension (IIH) selected for treatment with oral acetazolamide were included. Patients with co-existing intra-ocular disease, patients having history of ocular surgery and trauma in the previous six months, patients suffering from systemic immunological disease, pregnant patients and patients with age less than twelve years were excluded from this study. After selection informed written consent was obtained from each study participant. Detailed history was taken and ophthalmic and systemic examination was performed. All relevant investigations were done. Acetazolamide tablet 500 mg twice daily was prescribed in all the study subjects. Then they were advised to visual field analysis at baseline by Humphrey visual field analysis 24-2 testing pattern. HVFA follow up protocol was followed at month 3 and 6. Visual field changes were graded into grade-1 (normal), grade-2 (enlarged blind spot), grade-3 (nasal or temporal defect) and grade-4 (concentric constriction).[10] Perimetric mean deviation (PMD) was recorded at baseline and at follow up periods. Papilledema was graded accordingly. All the relevant data were recorded in a pre-designed data collection sheet, during baseline after 3 months and at 6 months of starting treatment. Mean values of the scores of mean deviations of the follow-up periods were compared with that of baseline values. Demographic variables and visual field changes of all study patients were recorded accordingly.

Statistical analysis

All collected data were cross-checked and compiled. Statistical analysis was done by using window-based software statistical package for social science (SPSS) version 26.0. Categorical data were presented as frequency with percentage and continuous data were expressed as mean with standard deviation (SD). The statistics used in this study was descriptive statistics. Paired ‘t’ test was done for analysis of quantitative data and Chi-square test was performed for qualitative data. A p value <0.05 was considered as statistically significant.

Results

The present study was intended to evaluate the visual field of patient with idiopathic intracranial hypertension (IIH) treated with oral acetazolamide. Total 30 patients who fulfilled the selection criteria were treated with acetazolamide (500 mg twice daily) and followed up at 3 and 6 months. The mean age of the study patients was 25.3±8.7 years which ranged from 15-44 years. Most of the patients were in age group 15-20 years (26.7%) (Table I). Of them, 25 (83.3%) patients were female and 5 (16.7%) patients were male.

Table I: Age-based distribution of the study patients (N=30)

Age (years)	
Mean ± SD	25.3±8.7 years
Range	15–44 years

Age groups	Frequency	Percentage
15–20 years	8	26.7
20–25 years	6	20.0
25–30 years	6	20.0
30–35 years	4	13.3
>35 years	6	20.0

Grading of visual field defects revealed at baseline 1 (3.33%) patients had grade 1 (normal) visual fields (both eyes); nasal or temporal defect (Grade 3) was present among 14 (46.67%) patients in right eye and 15 (50.0%) patients in left eye. Enlarged blind defect (Grade 2) was present among 11 (36.67%) patients in right eye and 12 (40.0%) in left eye. Concentric constricted visual field (Grade 4) was present among 4 (13.33%) patients in right eye and 2 (6.67%) patients in left eye (Table II).

We observed the mean value of mean deviation in dB of both eyes by Humphrey visual field analyser (HVFA) (24-2) of the study subjects at different follow-up periods (taking absolute values). The baseline value of mean of perimetric mean deviation (PMD) in right eye was 4.86 dB. After treatment with acetazolamide, the PMD reduced to -2.93 dB and -2.28 dB at 3 months and 6 months respectively (Fig 1).

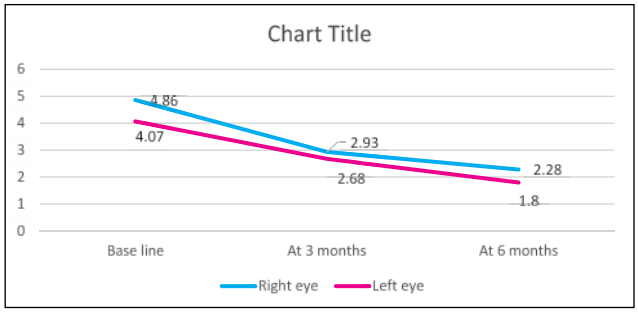

Fig 1. Line chart showing distribution of mean value of mean deviation in dB of right and left eyes of the study subjects by HVFA (24-2) of the study subjects at different follow-up periods (taking absolute values)

Similarly, the baseline value of the mean of perimetric mean deviation (PMD) at left eye was -4.07dB. After treatment with acetazolamide, the PMD reduced to -2.68dB and -1.38dB at 3 months and at 6 months respectively (Figure 1).

Table III shows the comparison of mean values of mean deviation from baseline with that of final follow-up (at 6 month). The baseline value of the mean of perimetric mean deviation (PMD) at right eye was -4.86±1.67dB and that was decreased (-2.28±1.51dB) significantly after treatment ($p<0.001$). In accordance, before treatment the mean of PMD at left eye was -4.07±2.06 dB and after treatment that was -2.38±1.94 dB, which also decreased significantly after treatment ($p<0.001$) (Table III).

Table II: Distribution of study patients based on grading of visual field defects (N=30)

Grading of visual field defects	Right eye	Left eye
Grade 1 (normal)	1 (3.3%)	1 (3.3%)
Grade 2 (enlarged blind defect)	11 (36.67%)	12 (40.0%)
Grade 3 (nasal or temporal defect)	14 (46.67%)	15 (50.0%)
Grade 4 (concentric constricted)	4 (13.33%)	2 (6.67%)

Table III: Comparison of mean values of mean deviation of baseline with that of final follow-up

Eye examined	Baseline	At final follow-up	p values
Right eye	-4.86±1.67	-2.28±1.51	<0.001[s]
Left eye	-4.07±2.06	-2.38±1.94	<0.001[s]

p value obtained by paired t test, s= significant

Discussion

Idiopathic intracranial hypertension (IIH) is characterized by increased intracranial pressure of unknown cause, occurring most commonly in obese women of childbearing age.[9] The carbonic anhydrase inhibitor acetazolamide (AZM) is the drug most commonly used to treat idiopathic intracranial hypertension[7]. Other diuretics, such as frusemide, are sometimes used if acetazolamide is poorly tolerated.[6,10] The mechanism of action of acetazolamide is multi-factorial. Acetazolamide has been found to reduce CSF production in humans by 6-50%.[8,11] It has been thought to work by inhibition of carbonic anhydrase that causes a reduction in transport of sodium ions across choroid plexus epithelium.[9] Also, it changes the taste of foods and causes carbonated beverages to taste metallic aiding the patient in weight loss.[6,9] Additionally, some patients experience nausea, further helping them to lose weight.[6,9] Acetazolamide is usually started at a dose of 0.5–1 g/day and can be gradually increased until clinical improvement is seen or a dose of 3–4 g/day is reached, unless the patient develops intolerable side effects.[6,11] Although the safety and tolerability of acetazolamide dosing at 1 g/day has been documented, there is uncertainty regarding the safety and tolerability of acetazolamide beyond 1 g/day due to the lack of high-level clinical evidence.[12] This present study was designed to evaluate the visual field changes of patient with idiopathic intracranial hypertension (IIH) treated with oral acetazolamide. A total of 30 patients of idiopathic intracranial hypertension, who were treated with acetazolamide (500 mg twice daily), were followed to assess the reduction of intracranial pressure (ICP), symptoms, signs and visual field changes.

In this study, the mean age of the study patients was 25.3±8.7 years which ranged from 15 years to 44 years. A retrospective study of Hatem et al[8] among Danish population found the mean age at diagnosis 29.5 years. Another multicentred trial of Smith and Friedman[7] also observed that the average age was 29 years . These findings were consistent with the present study. It was documented that, the incidence of IIH is highest among young overweight women which is also found in this study.[5,7]

In this study, out of 30 patients nasal or temporal defect was present in 46.67% in their right eye and 50.0% patients in their left eye, enlarged blind defect (Grade 2) was present among 11 (36.67%) patients in right eye and 12 (40.0%) in left eye and concentric constricted visual field was also present among 13.33% patients in their right eye and 10.0% patients in their left eye. Common field defects in IIH were enlarged blind spots, arcuate defects, nasal step and global constriction of the visual fields.[2] Enlarged blind spot was the most common perimetric findings.[9] In this study, the baseline value of perimetric mean deviation (PMD) in right eye was -4.86 dB. After treatment with acetazolamide, the PMD reduced to -2.93 dB and -2.28 dB at 3 months and 6 months respectively. Similarly, the baseline value of perimetric mean deviation (PMD) in left eye was -4.07 dB. After treatment with acetazolamide, the PMD reduced to -2.68 dB and -2.38 dB at 3 months and 6 months respectively. The mean reduction of PMD was observed at 3rd month. The PMD of both eyes reduced significantly at 6 months follow up periods. Mean changes of PMD in right eye was 2.59dB and fellow eye was 1.69dB over six months follow up. In a previous study it was found that mean improvement of mean deviation in study eye was 1.43 dB and 0.87dB in fellow eye.[5] NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee reported that mean improvement was significantly greater in the acetazolamide group than the placebo group at 6 months.[13] It was reported that perimetric mean deviation (PMD) significantly improved after treatment of IIH with acetazolamide from -7dB to -2dB.[14] Majority of the patients of the present study had initial PMD>-2.27 dB. Therefore, the improvement of PMD of this present study was consistent with related previous studies.[12,14] Changes in visual field parameter are important marker in diagnosis and monitoring of treated patients of IIH with oral acetazolamide. A significant PMD reduction occurs after treatment with oral acetazolamide mostly at 3 months.

To assess visual field changes while treating with oral acetazolamide and effect on visual field changes in different dose of acetazolamide in the treatment of IIH, a multicentre, large-scale study with long term

follow up is recommended.

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