Original article:

Evaluation of Relationship Between Intraocular Pressure and Rate of Visual Field Progression in Glaucoma Patients at a Tertiary Care Hospital

M. Hima Bindu

Assistant Professor, Department of Ophthalmology, Shadan Institute of Medical Sciences Teaching Hospital & Research Centre, Hyderabad, Andhra Pradesh, India.

Corresponding Author: Dr. M. Hima Bindu, Assistant Professor, Department of Ophthalmology, Shadan Institute of Medical Sciences Teaching Hospital & Research Centre, Hyderabad, Andhra Pradesh, India.

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ABSTRACT

Background: The major cause reported for the development of irreversible blindness is glaucoma. It is most commonly affecting the optic nerve and results in death or impairment of retinal ganglion cells. Therefore, the present study aims to evaluate the association between IOP and visual field progression associated with a wide spectrum of damage and effectively managed with recent therapeutic modalities.

Materials and Methods: A total of 550 eyes from 337 patients affected with primary glaucoma who had >5 HVF examinations. Of these, 380 eyes of 252 patients had IOP recordings available at all VF visits and were considered for the study. The association between these factors and ROP was first assessed using univariate regression methods. Factors associated with ROP with a P value of less than 0.1 on univariate analyses were evaluated using a multivariate model.

Results: Factors that were related with ROP with a P value of less than 0.1 were age, MD at presentation, glaucoma surgery during follow-up and the frequency of anti-glaucoma medications at the last follow-up.

Conclusion: Long-term fluctuation of IOP was observed to be the most important IOP parameter which is related with increased ROP of glaucomatous VF loss patients in our study. This association is likely due to the confounding effect for enhanced therapy in eyes which are suspected to be progressing the visual field.

Key words: Intraocular Pressure, Visual Field, IOP Fluctuation.

INTRODUCTION

One of the most leading aetiologies that has been documented behind the reasons for the development of irreversible blindness is glaucoma1 which is identified as an acquired disease of the optic nerve and is frequently characterized by the death or impairment of retinal ganglion cells. The prime importance in the management for glaucoma is directly focussed on lowering the intraocular pressure (IOP), as this is proven to be the modifiable risk factor which is related with the lowering the progression of glaucoma.2 Additionally, glaucomatous damage observed to be focal in the earlier stages and is often affecting the central field.3 The same authors had earlier reported that baseline damage to the 12 central-most points of the 24-2 visual field

(VF) is related with future faster rates of global field progression.4 And the central damage is basically measured with standard automated perimetry5 and optical coherence tomography6 has been directly related to worsen the vision-related quality of life as gauged by the National Eye Institute Visual Function Questionnaire (NEIVF). Hence, it is of utmost importance to study not only the predictive value of central field damage related with future progression but also better to understand the role of IOP in preventing further loss in this important region for daily activities. Reduction of baseline IOP and decreased fluctuation of IOP has been related with the decreased glaucoma progression in various other studies that has been reported earlier.7-10 This association between the various parameters was primarily explored in the Advanced Glaucoma Intervention Study-7 (AGIS-7)8 which researched that the relationship between consistent lowering of IOP and VF progression longitudinally. Patients who were at or below a set level of IOP at all of the visits did not have significant overall VF progression.8 Moreover, IOP was observed to be an important predictor of VF improvement in the Collaborative Initial Glaucoma Treatment Study. This report has found that lowering mean IOP, lowering minimum IOP and lowering the sustained levels of IOP were related with an improvement in VF of ≥3 dB.9

Therefore, the present study aims to evaluate the association between IOP and VF progression associated with a wide spectrum of damage and effectively managed with recent therapeutic modalities. Additionally, we seek to understand the relationship between IOP and the central 10 degrees of the VF. On observation, the macula contains 30% of all retinal ganglion cells11 and was hypothesized that the progression of the central VF (associated with macular function) will equally respond differently to higher IOP than the peripheral VF.

MATERIALS AND METHODS

This study is designed as a clinical based, retrospective study conducted in the Department of Ophthalmology, Shadan Institute of Medical Sciences Teaching Hospital & Research Centre, Hyderabad, Andhra Pradesh (India) in which all patients with primary open-angle (POAG) and primary angle-closure glaucoma (PACG) were comprised the study group. All the patients included had undergone Z5 HVF examinations prior to the study. For the study purpose, POAG was defined as the presence of an untreated IOP of more than 21 mm Hg, gonioscopy showed open anterior chamber angle, glaucomatous optic disc damage on clinical examination and corresponding VF defects. PACG was termed as the presence of an occludable angle on gonioscopy, glaucomatous optic disc damage and corresponding VF defects.

IOP was measured by Goldmann Applanation Tonometry and gonioscopy was undertaken using a Goldmann 2 mirror lens or a Sussmann 4 mirror gonioscope under standard conditions. VF defects were considered to be glaucomatous if at least 2 of the 3 Anderson's criteria was fulfilled. Optic disc examination and VF evaluation of all the patients were primarily conducted by a single physician. The following data were basically noticed from the medical records: age of the patient at presentation, sex, type of glaucoma, the presence of hypertension or diabetes, the number of VFs during the follow-up, the total duration of follow-up, and the total number of antiglaucoma medications at the last follow-up. Mean deviation (MD), pattern SD, and VFI values at all VF examinations were recorded. IOP measurements at all VF examination visits were recorded carefully. The association between these factors and ROP was first assessed using univariate regression methods. Factors associated with ROP with a P value of less than 0.1 on univariate analyses were evaluated using a multivariate model. A P value of less than 0.05 was considered statistically significant.

RESULTS

A total of 550 eyes from 337 patients affected with primary glaucoma who had >5 HVF examinations. Of these, 380 eyes of 252 patients had IOP recordings available at all VF visits and were considered for the study. As ROP estimation is reported to be confused in eyes with severe VF damage,12 84 eyes with an MD of worse than 20 dB at the time of presentation were basically excluded, leaving 296 eyes of 213 patients for the final analysis. The demographic and clinical features of these patients are tabulated in the table 1. The mean, peak and the fluctuation of IOP during the follow-up are also given in table 1.

Table 2 reveals factors that were related with ROP with a P value of less than 0.1 were age, MD at presentation, glaucoma surgery during follow-up and the frequency of anti-glaucoma medications at the last follow-up (in those where any glaucoma surgery has not performed during follow-up).

Table 3 observes the factors significantly associated primarily with ROP in the multivariate model were IOP fluctuation and MD at presentation. For every 1 mm Hg increase in IOP fluctuation, the ROP worsened by 0.34% per year. The coefficient associated with the interaction term, however, was not statistically significant (P = 0.07).

Table 1: Demographic and Clinical Features of Glaucoma Patients

Parameters	**Mean ± SD**	**Range**
Age (years)	53.8 ± 11.9	22 – 85
Sex	148:67	
Glaucoma type (POAG:PACG)	133:80	
Hypertension	65	
Diabetes		
Visual field parameters		
Mean deviation	8.3 ± 5.4	20.3 – 0.6
Pattern SD	6.1 ± 4.1	1.6 – 15.9
Visual field index	1.1 ± 0.9	41 – 98
Anticoagulant drugs	1.1 ± 0.8	0 – 4
Surgery		
Cataract extraction	25 (8.3%)	
Trabeculectomy	19 (6.3%)	
Combined cataract & glaucoma	39 (13%)	
Follow – up (years)	7.4 ± 2.2	5 – 17
Mean IOP (mm Hg)	16.1 ± 2.2	7.4 – 22.1
Peak IOP (mm Hg)	19.9 ± 3.7	11 – 37
IOP fluctuation (mm Hg)	2.9 ± 1.3	0.7 – 7.3

Table 2: Univariate Regression Showing Factors Associated with an Increased Rate of Progression of Visual Field Loss

Risk factor	Co-efficient	SE	P
Age	-0.04	0.02	0.08
Sex	-0.11	0.35	0.79
Glaucoma type	-0.02	0.29	0.97
Hypertension	-0.08	0.31	0.83
Diabetes	-0.46	0.38	0.25
MD at presentation	0.11	0.04	0.001
Glaucoma surgery	-0.72	0.44	0.09
Anticoagulant drugs	-0.33	0.21	0.11
Visual fields	0.07	0.07	0.27
Follow – up duration	0.08	0.04	0.16

Table 3: Multivariate Regression Model Showing the Factors Associated with an Increased Rate of Progression of Visual Field Loss

Risk factor	Co-efficient	SE	P
Age	-0.03	0.03	0.09
MD at presentation	0.09	0.04	0.003
Glaucoma surgery	-0.39	0.44	0.37
IOP fluctuation (mm Hg)	-0.38	0.17	0.03

DISCUSSION

Hip There are many studies that had evaluated the association between IOP parameters and VF progression The major question still persists is that to assess the relative importance of long-term IOP fluctuation and the level of IOP (mean and peak) during the follow-up as these are considered as the major risk factors for progression. There are couple of studies which have found that both the mean and the fluctuation of IOP as the risk factors for VF progression,13 data from popular randomized controlled studies (RCT) have observed contradictory results.14 The comparison of our study results with the result values observed from the previous studies is not direct since there are noticeable differences in the methods. Our results are in corroboration with the results obtained from Advanced Glaucoma Intervention Study data, which revealed that long-term IOP fluctuation was the most important risk factor which is associated with VF progression in the glaucomatous patients.15 Our results are also identical to that obtained from the Collaborative Initial Glaucoma Treatment Study, which found that IOP fluctuation and peak IOP has significantly predicted the progression of VF.14,15 The findings resulted in this current study were reported to be contradictory to the results revealed from early manifest glaucoma trial (EMGT) data in which they found the mean IOP to be the IOP parameter are basically related to progression.17 These contradictory results might be well detailed by the differences in the cohort between EMGT and in the present study. In EMGT where the randomized early glaucoma patients either had no treatment or undergone

treatment with argon laser trabeculoplasty and betaxolol.16 The mean IOP of EMGT patients was reported to be slightly above 20 mm Hg with little long-term IOP fluctuation: within 0.5 mm Hg/y in 59% of patients and within 3 mm Hg/y in 92%. Also, no change in the management was occurred in the EMGT participants during the study period.17 Contradictorily, this present study was a clinic-based study with treatment that were customized to individual patients. The mean IOP observed in this study was little below 16 mm Hg. The median change in IOP over the follow-up was 0.25 mm Hg/y. Patients in our study showed larger IOP fluctuations with 31% of eyes having an IOP fluctuation of >3 mm Hg. Patients in this study had undergone a change in the treatment depending on their clinical situation, which is meant to be the "real-life scenario." These may be the possible reasons why the ROP was related with IOP fluctuation but not with the level of IOP in this study.

The results obtained in this study should not be viewed as eliminating the importance of the level of IOP in glaucoma progression. The results of our study are commonly applicable for a clinic-based situation where the treatment is customized to each patient after taking into account about their entire clinical and demographic information. Our results reiterate the relative importance of IOP fluctuation over the level of IOP in this real-life situation. All the IOP parameters that had been evaluated in this study were significantly corroborated with each other, with the peak IOP revealing the greatest correlation with both mean IOP and IOP fluctuations. Similar findings have been reported by earlier studies.18,19 This basically shows that although each IOP parameter provides some specific information regarding the IOP in a patient, it is practically not feasible to trace out the effect of one totally from the other parameter.

Greater IOP fluctuations that were seen in this study was observed in those eyes that underwent glaucoma surgery or stepping up of medical therapy during the follow-up period. This is a real possibility that this could happen in a real-life scenario too and the enhancement of the clinical situation by improving the therapy is very likely to be seen in the eyes which are suspected of progression. In order to attribute for the confounding effect of management on IOP fluctuations, a study by Bengtsson and Heigl20 skeletonised the data up to the date of any IOP-lowering intervention. In this study also we evaluated the risk factors for the progression separately in eyes that underwent no surgical intervention for glaucoma and still found IOP fluctuation to be significantly related with progression. Therefore, the confounding effect of a change in therapy on the relation between IOP fluctuation and ROP needs to be taken into account.

CONCLUSION

To conclude the present study, long-term fluctuation of IOP was observed to be the most important IOP parameter which is related with increased ROP of glaucomatous VF loss patients in our study. This association is likely due to the confounding effect for enhanced therapy in eyes which are suspected to be progressing the visual field.

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