

Effect of chronic hyperglycemia on intraocular pressure in patients with diabetes mellitus

V S Hatolkar^{1*}, Yogita Phadke², N R Hazari³

{¹Professor, Department of Biochemistry} {²Assistant Professor, Department of Ophthalmology} MGM Medical College, Aurangabad, Maharashtra, INDIA.

³Associate Professor, Department of Biochemistry, Government Medical College, Aurangabad, Maharashtra, INDIA.

Email: veenashatolkar@gmail.com, yogietaa@gmail.com

Abstract

Introduction: Diabetes mellitus has emerged as a major cause of vision loss and visual disability, not only in the developed countries, but also in the developing countries. Diabetes has been found to be associated with elevated intraocular pressure (IOP) and has therefore been suggested as a possible risk factor for glaucoma, particularly primary open angle glaucoma (POAG). Diabetes is one of the risk factors for glaucoma. The purpose of the study was to investigate the effects of chronic hyperglycaemia on the intraocular pressure (IOP). **Materials and Methods:** We prospectively measured the IOP by Schiotz tonometry in 40 normal subjects (Group I) and in 60 subjects with type 2 diabetes (Group II). None of the subjects with diabetes had diabetic retinopathy, secondary glaucoma or a family history of glaucoma nor did they undergo any ocular or laser therapy. The glycosylated haemoglobin (HbA1c) levels of the subjects with diabetes were determined and based on that, they were classified into 3 subgroups as mild hyperglycemia with HbA1c levels of < 7%; moderate hyperglycemia with HbA1c levels of 7 to 8.0%; and severe hyperglycemia with HbA1c levels of > 8.0%. All the data were expressed as means \pm standard deviations. The statistical analysis was performed by the Student's t test. The correlation between HbA1c and IOP was statistically analyzed by Pearson's correlation coefficient. A p value of < 0.05 was considered to be significant. **Results:** We observed that the IOP values were higher in the subjects with diabetes (mean = 22.3 ± 4.18) than in the age and sex matched control groups. The mean IOP in the three groups were 16.43 ± 2.20 , 18.56 ± 3.36 mm Hg, and 20.18 ± 2.78 mm Hg respectively. The difference in the IOP between the mild and moderate, and moderate and severe groups was found to be statistically significant ($P = .001$). **Conclusion:** The intra-ocular pressure was increased in the subjects with diabetes as compared to the controls and especially those subjects with a poor glycaemic control were more prone to develop an increased intra-ocular pressure.

Keywords: Intra-ocular pressure, Glycosylated haemoglobin HbA1c, Glaucoma, Diabetes mellitus.

*Address for Correspondence:

Dr. V S Hatolkar, Professor, Department of Biochemistry, MGM Medical College, Aurangabad, Maharashtra, INDIA.

Email: veenashatolkar@gmail.com

Received Date: 02/11/2014 Accepted Date: 12/11/2014

Access this article online

Quick Response Code:



Website:

www.statperson.com

DOI:13 November 2014

INTRODUCTION

Glaucoma is a chronic, progressive optic neuropathy characterized by cupping of the optic disc, visual field defects and raised intra-ocular pressure.¹ Though IOP is only causal factor, it is the only modifiable factor that can prevent progression of glaucoma. Glaucoma is a leading cause of irreversible blindness worldwide.^{1,2} Diabetes mellitus is an important ocular risk factor. It has

established itself as a pandemic disease, projected to affect 438 million people by 2030 AD. In India, as of now, there are over 35 million people with diabetes, a number that is predicted to increase to around 80 million by 2030⁴. Diabetes has been found to be associated with elevated intraocular pressure (IOP)^{3,6} and has therefore been suggested as a possible risk factor for glaucoma, particularly primary open angle glaucoma (POAG). The average normal intra-ocular pressure is about 15mmHg, with a range from 12 to 20mmHg. A potential significance of carbohydrate intolerance in pathogenesis of POAG has been reported. The results of many studies indicate that high glucose levels lead to an excess accumulation of fibronectin in the trabecular meshwork which in turn leads to an increase in the aqueous outflow resistance. A few studies showed that HbA1c levels were associated with higher IOP in patients with diabetes and subjects with poor glycemic control were more prone to develop an increased IOP. Age is one of the risk factor of

POAG and HbA1c has been shown to increase with age in nondiabetic population and suggested that nonglycemic factors may contribute to the relationship of HbA1c with age⁵. Therefore, in this study, we tried to observe the intra-ocular pressure behaviour in patients with diabetes mellitus and to find whether there was a significant difference between the intra-ocular pressure values in the patients with diabetes and the control population and also to assess the effects of chronic hyperglycaemia on the intraocular pressure.

MATERIAL AND METHODS

The present study included 40 subjects with Diabetes mellitus of the age range of 50-80 years, who attended the Out-Patients Department of Ophthalmology and 40 age and sex matched individuals without diabetes (control group). This research was approved by the institutional ethical committee. Informed consent was taken from the volunteers for this study. Subjects with systemic hypertension, a family history of glaucoma, a habit of smoking, alcoholism, pregnancy, refractive errors, ocular infection or inflammation or the usage of ocular drugs within the previous three months, a history of ocular surgery, the usage of any medications that would affect the IOP, a history of cardiac diseases and a history of endocrinal diseases or any other major medical problems were excluded from the study in the control group. A detailed medical history was collected from all the participants and they underwent a thorough physical examination, screening laboratory tests and screening eye examinations. The screening laboratory tests included the estimation of fasting blood glucose levels, glycated haemoglobin (HbA1C) levels and the urine examination. The screening eye examinations included the assessment of visual acuity, tonometry, slit-lamp examination, and dilated fundus examination. The blood pressure was measured with the subjects in a sitting posture. The intra-ocular pressure was measured by using a Schiotz tonometer. None of the patients with diabetes had proliferative diabetic retinopathy or secondary glaucoma, none had undergone laser treatment, and none had a history of glaucoma treatment. All the patients had an open angle. The concentration of HbA1c which was formed through the non-enzymatic attachment of glucose

to haemoglobin, was commonly considered to reflect the integrated mean glucose levels over the previous 8–12 weeks, the time period being dictated by the 120 day lifespan of the erythrocyte¹¹. The patients were prospectively divided into two groups. The group I consisted of the controls (n=40) and the subjects with diabetes was considered as group II (n=60). Group II was further divided into three sub groups according to the level of HbA1c into mild hyperglycemia with HbA1c levels of <6.5% (n = 18); moderate hyperglycemia with HbA1c levels of 6.5-8.0% (n=22); and severe hyperglycemia with HbA1c levels of >8.0% (n=20). After an overnight fast, blood samples were collected in fluoride and EDTA bulb from patients and controls for determination of blood glucose and HbA1c. Blood glucose was estimated by GOD-POD method using kit of Bayer diagnostics, Baroda (GUJARAT) and HbA1c was estimated by chromatographic spectrometric ion exchange method using kit of Biosystems SA, Barcelona (Spain). All the data were expressed as means + standard deviations. The statistical analysis was performed by the Student 's t-test. The correlation between HbA1c and IOP was analyzed by using the Pearson's correlation coefficient. A p value of <0.05 was considered to be significant.

RESULTS

The physical characteristics of the group I (control) and the group II (subjects with diabetes) are shown in (Table 1). In the present study, the age range of the subjects was 50-80 years, with the mean age being 57.3 ± 10.4 years in group I and 61.2 ± 10.8 years in group II. A significant increase in IOP was observed when group II (mean IOP = 19.36 ± 2.92) was compared with group I (mean IOP = 16.18 ± 1.60) and the p value was 0.001. (Table 1). When the IOP was related to the glycaemic status and compared between the subgroups, as in (Table 2), in patients with mild hyperglycemia, no significant difference in the IOP was observed. The IOP in patients with moderate hyperglycemia (mean IOP = 18.56 ± 3.36) and severe hyperglycemia (mean IOP = 20.24 ± 2.78) showed a significant increase ($p < 0.001$), with that in severe hyperglycemia being comparatively more than that in moderate hyperglycemia.

Table 1: Physical characteristics of Group I and Group II

Characteristic	Control	Diabetes	p value
No. of cases	40	60	
Age in years	57.3 ± 10.4	61.2 ± 10.8	
Gender	22/18	36/24	
HbA1c	6 ± 0.1	7.32 ± 1.12	0.001
IOP	16.18 ± 1.60	19.36 ± 2.92	<0.005

Table 2: Patients with Diabetes grouped according to HbA1c Level

Characteristic	Mild (HbA1c \leq 6.5%)	Moderate (HbA1c 6.5% – 8.0%)	Severe (HbA1c \geq 8.0%)	p value
No. of patients	n = 18	n = 22	n = 20	
Gender (M/ F)	11/7	13/9	12/8	NS
Mean age (yrs)	57.3 \pm 10.1	61.2 \pm 10.6	58.6 \pm 10.7	
Mean HbA1c (%)	6.09 \pm 0.71	7.10 \pm 0.82	8.29 \pm 1.68	<0.001
Mean IOPmmHg	16.43 \pm 2.20	18.56 \pm 3.36	20 \pm 2.78	<0.001

DISCUSSION

Primary open angle glaucoma is a major cause of blindness⁵. It has been suggested that metabolic diseases, especially diabetes may play a role in the evolution of the disease. In the present study the mean age of the diabetic patients was 61.2 \pm 10.8. The mean IOP was significantly elevated in diabetic patients. Many previous studies have reported the association of diabetes and POAG. A no. of explanations have been proposed for the association between disturbances of carbohydrate metabolism and POAG. The elevated blood glucose level in diabetes may induce an osmotic gradient and attract fluid into the intraocular space, resulting in elevated IOP¹⁰. Furthermore in in vitro study it has been reported that a high glucose level in aqueous humor of patients with diabetes may trigger excess fibronectin synthesis and lead to its excessive accumulation in trabecular meshwork and accelerate the depletion of trabecular meshwork cells¹³. Recent basic studies have shown that diabetes not only affects vascular tissues but also neuronal and glial functions and metabolism in the retina. This may render apoptotic death of retinal neurons including RGCs which is an additional stress in case of POAG¹¹. Considering the deterioration of neuronal cell death in the condition of diabetes, a 1.0 mm Hg difference of IOP could be clinically relevant in our patient population. Our results confirmed our hypothesis that patients with diabetes with chronic hyperglycemia have far higher IOP. Our findings support the report that the prevalence of glaucoma in patients with diabetes is higher than in patients without diabetes. We conclude that abnormalities of glucose metabolism could play a role in glaucoma damage and pathogenesis. Long-term follow-up of the cohort to establish whether these patients with higher IOP and higher HbA1c levels are more likely to develop open-angle glaucoma is needed to demonstrate the clinical importance of our findings.

CONCLUSION

The results of our study showed that chronic hyperglycemia was associated with higher IOP in patients with diabetes. Since the prevalence of glaucoma is increased in subjects with diabetes, it is advisable to

measure IOP routinely at regular intervals in diabetic patients to detect the development of ocular hypertension at an early stage. Also good glycemic control helps in better control of IOP in diabetic patients. For this a long term study is required in large number of diabetics and POAG pts.

REFERENCES

1. Ramanjit Sihota, Parson's diseases of the Eye. 19th Edition. Glaucoma Pg :299 to 306
2. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol. 2006; 90(3): 262–6
3. Mitchell P, Smith W, Chey T, Healey PR. Open-angle glaucoma and diabetes: the Blue Mountains Eye Study, Australia. Ophthalmology 1997; 104:712-18.
4. Wild S, Roglic G, Green A, Sicree R, King H. The global prevalence of diabetes: estimates for the year 2000 and projections for the year 2030. Diabetes Care. 2004; 27(5):1047-53.
5. Arora VK, Prasad VN. Intra-ocular pressure and diabetes-A correlative study. Indian J Ophthalmol 1989; 37:10-12.
6. Ivan Goldberg. Primary Open Angle Glaucoma. The Medical Journal of Australia, 2002;177(10):535-536.
7. Katz J, Sommer A. The risk factors for primary open angle glaucoma. Am J Prev Med. 1988; 4:110 -14.
8. Ramkrishnan R. Glaucoma in a rural population of South India. The Arvind Comprehensive Eye Survey Ophthalmology. 2003; 110:1484-1490.
9. Wise LA, Rosenberg L, Radin RG, Mattox C, Yang EB, Palmer JR, *et al.*, A prospective study of diabetes, lifestyle factors, and glaucoma among African-American women. Ann Epidemiol. 2011; 21(6):430-39.
10. Bourne RRA, Prevalence of glaucoma in Thailand: A population based survey in Rom klao district, Bangkok. Br.J.Ophthalmol. 2003; 87:1069-1074.
11. Chopra V, Varma R, Francis B A., Wu J, Torres M, Stanley P. Azen Los Angeles Latino Eye Study Group, Type 2 Diabetes Mellitus and the Risk of Open-angle Glaucoma The Los Angeles Latino Eye Study, Ophthalmology 2008;115:227-32.
12. L.M. Weih. Association of demographic, Familial, Medical and Ocular factors with intra-ocular pressure. Arch. Ophthalmol 2001; 119(6):875-880.
13. Leske MC, Connell AM, Wu SY, *et al.* Risk factors for open-angle glaucoma: the Barbados Eye study. Arch Ophthalmol 1995; 113: 918-24.

Source of Support: None Declared
Conflict of Interest: None Declared