Original Article

Physiology

Intra-ocular Pressure in Subjects with Type 2 Diabetes Mellitus

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ABSTRACT

Background and objective: Open-angle glaucoma is estimated to afflict 66.8 million people worldwide and it is a leading cause of blindness [1]. Diabetes is one of the risk factors for glaucoma. The purpose of the study was to analyze the relationship between intraocular pressure and type 2 diabetes mellitus and to investigate the effects of chronic hyperglycaemia on the intraocular pressure (IOP).

Materials and Methods: We prospectively measured the IOP by Schiotz tonometry in 100 normal subjects (Group I) and in 150 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 divided into 3 subgroups as group IIa with HbA1c levels of < 7% (n = 62); group IIb with HbA1c levels of 7 to 8.0% (n = 48); and group IIc with HbA1c levels of > 8.0% (n = 40) 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 the 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 = 20.4 ± 3.44) than in the age and sex matched control groups. The mean IOP in the groups IIa, IIb and IIc were 17.32 ± 2.70 , 17.81 ± 2.76mm Hg, and 18.04 ± 2.58 mm Hg respectively. The difference in the IOP between the groups IIb and IIc 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.

Key Words: Intra-ocular pressure, Type 2 diabetes mellitus, Glaucoma

INTRODUCTION

The fluid pressure inside our eye is called as intra-ocular pressure (IOP). The average normal intra-ocular pressure is about 15mmHg, with a range from 12 to 20mmHg. The intraocular pressure is determined by the balance between the production of the aqueous humour (the clear fluid inside the eye) and the drainage of the aqueous humor, mainly through the trabecular meshwork which is located in the anterior chamber angle. An abnormally high IOP reading indicates that either the eye is producing too much fluid, or that it is not draining properly. Glaucoma is now considered as an abnormal physiology in the optic nerve head, that interacts with the level of intra-ocular pressure (IOP), with the degree and the rate of the damage depending on the IOP and presumably, on the degree of the abnormal physiology [2].

Diabetes mellitus is a group of metabolic diseases which is characterized by hyperglycaemia, resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycaemia in diabetes is associated with the long-term damage, dysfunction, and the failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels, causing severe systemic complications such as retinopathy, neuropathy and nephropathy [3]. 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 2030 [4]. Diabetes mellitus is an important ocular risk factor. It 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, besides its other ocular manifestations, also affects the intra-ocular pressure [5]. Numerous large population based studies have shown diabetes to be a risk factor for the development of open angle glaucoma (OAG) [6-11]. However, some studies have found no association between the same [12-14].

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 intra-ocular pressure.

MATERIALS AND METHODS

The present study included 150 subjects with diabetes, of the age range of 25-45 years, who attended the Out-Patients Department of Diabetology and Ophthalmology at SRM Medical College and Hospital, Kattankulathur, TamilNadu, India and 100 age and sex matched individuals without diabetes (control group). This research was approved by the institutional ethical committee of the SRM Medical College Hospital and Research Centre.

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. 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 haemoglobin, fasting and post prandial plasma glucose levels, glycated haemoglobin (HbA_{1C}) levels and the serum urea and creatinine levels and random urine examination for the microalbumin/creatinine ratio. 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 body mass index was calculated by using the formula, BMI = Weight in Kg/(Height in meters)^2. 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 erythrocyte [15].

The patients were prospectively divided into two groups. The group I consisted of the controls (n = 100) and the subjects with diabetes was considered as group II (n = 150). Group II was further divided into three sub groups according to the level of HbA1c into group IIa with HbA1c levels of < 7% (n = 48); group IIb with HbA1c 7 levels of 8.0% (n = 62); and group IIc with HbA1c levels of > 8.0% (n = 40). 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/Fig 1]. In the present study, the age range of the subjects was 25-45 years, with the mean age being 34.2 ± 6.116 years in group I and 35 ± 6.25 years in group II. Similarly, there was no significant difference in the means of other physical parameters like height, weight and body mass index in the groups I and group II. A significant increase in IOP was observed when group II (mean IOP = 20.4 ± 3.44) was compared with group I (mean IOP = 16 ± 2.91) and the p value was 0.001. When the IOP was related to the glycaemic status and compared between the subgroups, as in [Table/Fig-2], in group IIa, no significant difference in the IOP was observed. The IOP in the groups IIb (mean IOP = 20.98 ± 3.06) and IIc (mean IOP = 21.90±3.13) showed a significant increase (p = 0.001), with that in IIc being comparatively more than that in IIb.

Variables	Group I Control (n=100)	Group II Diabetes (n=150)	P value
Age (years)	34.2 ± 6.116	35 ± 6.25	t = 0.957 p = 0.340
Height (m)	1.66 ± 0.11	1.67 ± 0.13	t =1.821 p = 0.072
Weight (Kg)	65.4 ± 8.8	64.4 ± 11.5	t =1.82 p =0.07
Body mass index (BMI)	23.52 ± 3.2	23.8 ± 3.37	t = 0.100 p = 0.9204
Intraocular pressure (IOP)	16 ± 2.91	20.4 ± 3.44	t = 7.61 p = 0.001

[Table/Fig-1]: Physical Characteristics of Group I and Group II

Subgroups	Mean HbA1c%	Mean IOP	p value	r value
Group IIa (n = 62)	6.00 ± 0.698	17.32 ± 2.70	0.975	0.004
Group IIb (n = 48)	7.42 ± 0.32	20.98 ± 3.06	0.001	0.82
Group IIc (n = 40)	9.17 ± 0.40	21.90 ± 3.13	0.001	0.88

[Table/Fig-2]: Correlation between Glycated Haemoglobin and Intraocular Pressure in Subgroups

The correlative analysis showed a statistically significant association between the increased HbA1c and the IOP in the subjects with diabetes (r = 0.82 and 0.88 respectively in the subgroups IIb and IIc)

DISCUSSION

Diabetes is a risk factor for glaucoma, which is the second leading cause for blindness [5]. However, it has not yet been clearly established as to how diabetes affects the intra-ocular pressure. Our results showed that the subjects with diabetes, with no previous history of ocular hypertension, had a significantly higher mean IOP (20.4 ± 3.44 mm Hg) than the normal control group (16 ± 2.91 mm Hg), which was matched for age, sex and body mass index. These findings are consistent with the conclusions of other investigators [16,17].

Our results also confirmed the hypothesis that the subjects with diabetes, with chronic hyperglycaemia (indicated by elevated HbA1c levels), have far higher IOP than the subjects with newly diagnosed diabetes (comparatively lower HbA1C levels), as shown in [Table/Fig 2].

The relationship between elevated intra-ocular pressure, diabetes, glycated haemoglobin (HbA1c), and insulin resistance has been well documented in several studies [12, 18-20].

Davies et al [21] have reported that the glucose levels in the aqueous humor of patients with diabetes were significantly higher (3.2 mM vs. 7.8 mM) as compared to the glucose levels in persons without diabetes. Although the reason for the increased incidence of open-angle glaucoma in persons with diabetes has not been elucidated, it is likely that the diabetes associated changes in the trabecular extra-cellular matrix may contribute to a decreased aqueous outflow. A high glucose level induces fibronectin overexpression in the trabecular meshwork cells and may contribute to excess fibronectin accumulation in the trabecular meshwork. High glucose–induced fibronectin upregulation may be a common biochemical link that on the one hand, contributes to the development of thickened vascular basement membranes in diabetic microangiopathy and on the other hand, alters the structural content, compromises resiliency, reduces cellularity, blocks the aqueous outflow in the trabecular meshwork and leads to the development of POAG in persons with diabetes [22]. Diabetes is known to cause microvascular damage and it may affect the vascular auto regulation of the retina and the optic nerve. The development of glaucomatous optic nerve damage, based on the visual field loss and/or the optic disc findings, is more likely to be associated with high intraocular pressure [13]. Besides an increased intra-ocular pressure (IOP), a disturbed microcirculation at the level of the optic nerve head, as well as a

primary neurodegenerative component, are thought to contribute to glaucomatous optic neuropathy [23]. In addition to altering the vascular tissues, diabetes mellitus brings about a compromise on the glial and neuronal functions and the metabolism in the retina, which can make the retinal neurons including the retinal ganglion cells, more susceptible to glaucomatous damage [24]. Furthermore, diabetes mellitus increases the susceptibility of the retinal ganglion cells to additional stresses which relate to OAG, such as elevated IOP [25]. It seems reasonable to consider that a poor glycaemic control in subjects with diabetes mellitus, with a prolonged insult to the retina, would be associated with a higher risk of OAG.

CONCLUSION

The intra-ocular pressure was increased in subjects with diabetes as compared to the controls and especially those subjects with a poor glycaemic control were more prone to develop increased intra-ocular pressure.

Since the prevalence of glaucoma is increased in subjects with diabetes, our observations of increased IOP in a group of patients who were taken from a diabetic OP, would suggest that the IOP of subjects with diabetes should be measured routinely at regular intervals to detect the development of ocular hypertension at an early stage. Thus, diabetes is a modifiable risk factor for open angle glaucoma. Interestingly, in our study, those with higher HbA1C values had an even higher intra ocular pressure. This suggests that an improved blood sugar control may indeed aid in better intra-ocular pressure control. This study may require further investigations in a large number of subjects.

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