ISSN : 0974 - 7427 Volume 9 Issue 5

BIOCHEMISTRY
An Indian Journal

Regular Paper

BCAIJ, 9(5), 2015 [169-173]

Relationship of fasting blood glucose and HbA1c with IOP in primary open angle glaucoma patients

N.R.Hazari[1]*, A.R.Hazari[2]

[1]Department of Biochemistry, Government medical college, Aurangabad, (INDIA)

[2]S.R.T.R Medical college and Hospital, Ambajogai, Maharashtra, (INDIA)

E-mail: nhazari60@gmail.com

ABSTRACT

Objective:-Primary open angle glaucoma (POAG) is a major cause of blindness in the world. Elevated intraocular pressure (IOP) is a major proven risk factor for glaucomatous optic neuropathy and has been shown to be associated with metabolic diseases, such as diabetes mellitus and hypertension. The aim of the present study was to evaluate the association of fasting blood glucose and HbA1c with IOP in POAG patients with and without diabetes mellitus.

Materials and Methods: - 40 patients of POAG with and without diabetes mellitus were included. Patients receiving IOP lowering treatment and other ocular diseases were excluded. Control group comprised of 45 age and sex matched individuals without glaucoma. Fasting blood glucose and HbA1c were estimated by using commercially available standard kits.

Results: - Fasting blood glucose (FBG) levels were found significantly higher in POAG patients with (115.33+7.42) and without (93.41+ 5.82) diabetes mellitus as compared to the control (90.27=11.76). HbA1c level was significantly increased in diabetic (9.75+/-1.64) and non diabetic (6.8+/-0.98) POAG patients than control (6.01+/-0.94). Mean IOP significantly raised with elevation of HbA1c levels in POAG patients. FBG (r=+0.51, r=+0.55 respectively) andHbA1c(r=+0.73, r=+0.71 respectively) levels were significantly correlated with IOP in POAG patients with and without diabetes mellitus.

Conclusion: - These findings indicate that FBG and HbA1c are associated with increased IOP in POAG patients with and without diabetes mellitus. We conclude that disturbances of glucose metabolism could play a role in glaucoma damage and pathogenesis and monitoring of HbA1c and fasting blood glucose with IOP in glaucoma patient is helpful to be made to assess the magnitude of damage.

KEYWORDS

POAG;
Fasting blood glucose;
HbA1c;
IOP.

INTRODUCTION

Glaucoma is a group of disorders that have in common a characteristic degeneration of the optic nerve associated with typical visual field defects and usually elevated intraocular pressure (IOP) if

Regular Paper

left untreated can cause absolute irreversible blindness. It is the second highest reason for blindness next to cataract. It is predicted that a number of glaucoma patients increase in India from 2010-2020(1).

There are different types of glaucoma, open angle glaucoma, angle closure glaucoma, secondary type and congenital one. Primary open angle glaucoma (POAG) is the most common autosomal dominant disease. Although the clinical picture of glaucoma is well described, the exact causative mechanism has not been elucidated. In addition to increased IOP which is established risk factor, many other risk factors have been described, such as age, race and family history(2). Among the identified risk factors, IOP is major and modifiable risk factor and lowering the IOP can reduce the risk of POAG (3-5). Many studies have shown that elevated IOP is clearly associated with several health problems, such as hypertension (6, 7), diabetes (8-11), elevated fasting blood glucose (12), insulin resistance (13), body mass index (14) and obesity(15).

A potential significance of carbohydrate intolerance in pathogenesis of POAG has been reported (16). The results of many studies indicate that high glucose levels lead to an excess accumulation of fibronectin in the trabecular meshwork through an overexpression of fibronectin leads to an increase in the aqueous overflow resistance (12, 17). A few studies (18-19) 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 increases with age in nondiabetic population and suggested that nonglycemic factors may contribute to the relationship of HbA1c with age (20). There is paucity of data with regard to these parameters in the pathogenesis of POAG in non diabetic and diabetic POAG patients.

The aim of the study was to find out the effect of fasting blood glucose and HbA1c levels in the pathogenesis of POAG in non diabetic and diabetic POAG patients.

MATERIAL AND METHODS

The current study was carried out on 70 selected subjects attending the out patient clinics of ophthalmology department in S.R.T.R Medical College and Hospital Ambajogai, Maharashtra, India, from July2011-May2012 The study was conducted as per ethical guidance. The subjects were divided into two groups:

Group I. Subjects with POAG

The included 40 subjects, aged between 50-80 years, of POAG exhibiting acquired characteristic glaucomatous optic nerve damage and/or retinal nerve fiber layer changes and visual field defect. All patients have open anterior chamber angle and IOP>22mmHg without treatment. No patients had undergone previous ocular surgery.

Group II. Control subjects

Forty five normal healthy subjects were having IOP<22mmHg, normal optic disc clinical findings and normal visual field and no family history of POAG included.

At the clinic a detailed history was obtained including a history of hypertension, diabetes mellitus and systemic vascular diseases. In all individuals a complete ophthalmologic history was taken and full ophthalmologic examination was carried out including, visual acuity, slit lamp examination, applanation tonometry, gonioscopy, examination of fundus and visual field.

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).

Statistical analysis

The results were expressed as means±SD. The levels of significance was calculated by applying unpaired student't' test. A one way analysis of variance (ANOVA) across the different groups was carried out. Pearson correlation was used for the correlations of different parameters. Statistical significance was set at p d" 0.05.

RESULTS

Clinical parameters of the study are shown in TABLE 1. POAG patients were of age 61.20±10.80 (ranged 50-80) years. Total number of POAG patients was 40, out of which 14 patients had history of diabetes mellitus, 11 patients had history of hypertension. The two groups were well controlled in terms of age, sex, smoking habits. Mean IOP and cup/disc ratio were significantly elevated in patients with POAG compared to control group. Blood pressure was significantly high in POAG than control. Urine sugar was nil.

Fasting blood glucose (FBG), postprandial blood glucose and HbA1c levels were significantly higher as compared to control in POAG patients. Serum uric acid level was significantly low in POAG patients TABLE-2.

The mean age of nondiabetic POAG patients was 63.33±11.14 (ranged 55-80) years which was more than diabetic patients (57.08±9.94, ranged 50- 72) years and control group (57.30±10.42, ranged 50-80). Fasting blood glucose, HbA1c, IOP and C.D.ratio were significantly high in both diabetic and non diabetic POAG patients as compared to controls TABLE-3.

A positive correlation was seen in fasting blood glucose level, HbA1c and IOP in both diabetic and non diabetic POAG patients. But highly significant correlation was found between HbA1c and IOP in both diabetic and non diabetic POAG patients TABLE 4.

DISCUSSION

Primary open angle glaucoma is a major cause of blindness. It has been suggested that metabolic diseases may play a role in the evolution of the disease. Clinical parameters of the study population

TABLE 1 : Clinical parameters of the study subjects

Parameters	Control	POAG	'p' value
No. of cases	45	40	
Age(years)	57.30±10.42	61.20±10.80 (50-80)	NS
Gender(M/F)	26/14	17/13	
Smoking(n)	12	13	
Diabetes mellitus(n)	4 (10%)	17 (42.5%)	
Systemic hypertension(n)	7 (17.5%)	12 (30%)	
Systolic B.P. (mmHg)	117.33±8.18	122.74±9.54	<0.05
Diastolic B.P. (mmHg)	76.93±3.50	81.13±6.08	<0.005
IOP(mmHg)	16.48±1.15	28.32±3.15	<0.005
C.D. ratio	0.28±0.03	0. 64±0.15	<0.005
Urine Sugar	Nil	Nil	

Mean±S.D.

TABLE 2 : Biochemical parameters in control and POAG patients

Parameters	Control (n=45)	POAG (n=40)	'p' value
Fasting blood glucose (mg/dl)	90.27±11.76	104.38±12.96	<0.001
Postprandial blood glucose (mg/dl)	122.01±11.32	206.25±66.84	<0.001
HbA1c (%)	6.09±0.71	8.29±2.00	<0.001
Serum uric acid(mg/dl)	5.25±0.94	4.43±1.43	<0.05

Mean±S.D.

Regular Paper

TABLE 3 : Biochemical and ophthalmic parameters in Non diabetic and Diabetic POAG patients

	Control	Non diabetic poag	Diabetic POAG	'P' Value
No. of cases	45	23	17	
Age(Yrs)	57.30±10.42	63.33±11.14	57.08±9.94	NS
Fasting blood glucose (mg/dl)	90.27±11.76 (70-114)	99.92±5.86 (90-127)	115.69±7.42 (100-130)	<0.0001
HbA1c (%)	6.09±0.71 (4 -7.4)	6.8±0.98 (4.7-7.9)	9.75±1.64 (8.5-13.1)	<0.0001
IOP(mmHg)	16.48±1.15	27.43±2.01	29.88±2.72	<0.005
C.D.Ratio	0.28±0.03	0.58±0.15	0.69±0.16	<0.05

Data are Means ± S.D.

TABLE 4 : Correlation between fasting blood glucose and HbA1c with IOP in Diabetic POAG and nondiabetic POAG patients

	Fasting blood glucose/IOP 'r' value	HbA1c/IOP 'r' value
Diabetic POAG (n=14)	+0.51	+0.73
'p' value	<0.05	<0.001
Non diabetic POAG (n=15)	+0.55	+0.71
'p' value	<0.05	<0.001

were shown in TABLE 1 Age has been identified as one of the major risk factor of glaucoma. In the present study the mean age of the POAG patients was 61.20±10.80 years (ranged 50-80 years). The means IOP was significantly elevated in POAG patients. Mean C.D. ratio was greater than 0.5 and most of the studied POAG patients had C.D.ratio between the ranges of 0.6-0.9.

Fasting blood glucose and HbA1c levels were significantly high in POAG patients than control group. These findings were in agreement with Elisaf et al (16). Many previous studies (8-11) have reported the associations of diabetes, fasting blood glucose and POAG.A number of explanations have been proposed for the association between disturbances of carbohydrate metabolism and POAG.

The elevated blood glucose level in diabetes may induce as osmotic gradient and attract fluid into the intraocular space, resulting in elevated IOP (10). Furthermore, 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 excessive accumulation of this in trabecular meshwork and accelerate the depletion of trabecular meshwork cells, a characteristic feature of the outflow system of POAG (13,17) Recent basic studies shown that diabetes not only affects vascular tissues but also comprises neuronal and glial functions and metabolism in the retina, which ultimately gives rise to apoptotic death of retinal neurons including RGCs. The impaired metabolism of neurons and glia by diabetes may render RGCs susceptible to additional stresses to POAG such as elevated IOP (11).

In the present study, 42.5 % POAG patients had known history of type –II diabetes mellitus. When we excluded diabetic POAG patients, non diabetic POAG patients (57.5%) had significantly increased levels of fasting blood glucose and HbA1c than control. In the current study, 30% patients of nondiabetic POAG were hypertensive and age of nondiabetic POAG patients were more as compared to diabetic POAG patients. Glycemia is recognized to change with age and the prevalence of diabetes and impaired glucose homeostasis (impaired fasting blood glucose, impaired glucose tolerance and HbA1c) is increased among older individuals (20).

There is increasing evidence that glucose intolerance and insulin resistance play key role in the pathogenesis of hypertension. Abnormalities in glu-

cose utilization are estimated to exist in 25% of general elderly population and in up to 80% of persons with essential hypertension (21-22) and it has been reported that insulin resistance might contribute to elevation of IOP in diabetes, obesity and hypertension (13). The results of current study clearly reveal disturbances of carbohydrate metabolism in older POAG patient. Insulin resistance or glucose intolerance may involve in the elevation of IOP & glaucomatous damaging process of POAG patients. These findings indicate that FBG and HbA1c might play role in progression of POAG and monitoring of HbA1c and fasting blood glucose with IOP in glaucoma patient is helpful to be made to assess the magnitude of damage.

Conûict of Interest: None to declare

REFERENCES

[1] H.A.Quigly, A.T.Broman; The number of people with glaucoma worldwide in 2010 to 2020.Br J.Ophthalmol., **90**, 262-67 **(2006)**.

[2] R.Shitole, R.Tandon; The Glaucoma, Parsons' diseases of the eye, 9th Edition, Butterworth-Heinemann Publication, 299-319 **(2003)**.

[3] A.Sommer, J.M.Tielsch, J.Kartz et al., Relationship between intraocular pressure and primary open angle glaucoma among white & black Americans, The Baltimore Eye Survey, Arch Opthalmol, **109**, 1090-1095 **(1991)**.

[4] M.C.Leske, A.M.Conneli, S.Y.Wu et al., Risk factors for open angle glaucoma. The Barbodos Eye Study, Arch Opthalmol, **113**, 918-924 **(1995)**.

[5] I.Goldberg; Relationship between intraocular pressure and preservation of visual field in glaucoma, Surv.Opthalmol., **48**, 53-57 **(2003)**.

[6] I.Bonomi, G.archini, M.Marraffa et al., Vascular risk factors for primary open angle glaucoma, The Egna-Neumarkt Study, Opthalmology, **107**, 1287-1293 **(2000)**.

[7] I.Dielemans, J.R.Vingerling, D.Algra et al., Primary open angle glaucoma, intraocular pressure and sysremic blood pressure in the general elderly population. Opthalmology, **102**, 54-60 **(1995)**.

[8] P.Mitchell, W.Smith, T.Chey et al.; Open angle glaucoma and diabetes, The Blue Mountains Eye Study, Australia. Opthalmology., **104**, 712-718 **(1997)**.

[9] I.Dielemans, P.T.deJong, R.Stolk et al,; Primary open angle glaucoma, intraocular pressure and diabetes mellitus in the general elderly population, The Rotterdam Study, Opthalmology, **103**, 1271-1275 **(1996)**.

[10] B.Baker; Diabetes mellitus and Primary open angle glaucoma, Am J.Opthalmol., **70**, 1-16 **(1971)**.

[11] M.Nakamura, A.Kanamori, A.Negi; Diabetes mellitus as a risk factor for glaucomatous optic neuropathy, Opthalmologica. **219**, 1-10 **(2005)**.

[12] T.Sato, S.Roy; Effect of high glucose on fibronectin expression and cell proliferation in trabecular meshwork cells.Invest Opthalmol Vis Sci., **43**, 170-175 **(2002)**.

[13] W.Sang, L.Sangyeoup, P.Cheolyoung, J.K.Dong; Elevated intraocular pressure is associated with insulin resistance and metabolic syndrome, Diabetes Metab.Res.Rev., **21**: 434-440 **(2005)**.

[14] S.Pai, S.Pai, A.Pai C.Ramasamy, R.Kini; A correlative study of BMI and IOP in diabetic and nondiabetic south Indian population, Thai.J.Physiol.Sci., **21**, 74-78 **(2008)**.

[15] K.Mori, F.Ando, H.Nomura, Y.Sato, H.Shimokata; Relationship between intraocular pressure and obesity in Japan, Int.J.Epidemol., **29**, 661-666 **(2000)**.

[16] M.Elisaf, G.Kitoes, E.Bairaktari, R.Kalaitzidis et al.; Metabolic abnormalities in patients with primary open angle glaucoma, Acta Opthalmol.Scand., **79**, 129-132 **(2001)**.

[17] S.Roy, E.Cagliero, M.Lorenz; Fibronectin overexpression in retinal microvessels of patients with diabetes, Invest Opthalmol Vis.Sci., **37**, 258-266 **(1996)**.

[18] T.Oshitari, N.Fujimoto, K.Hanawa, E.Adachi-Usami; Effect of chronic hyperglycemia on intraocular pressure in patients with diabetes, Am.J.opthalmol., **143**, 363-365 **(2007)**.

[19] S.A.Lakshmi, H.Petricia, A.Saravanan, C.Ramchandran; Intraocular pressure in subjects with type-2 diabetes mellitus, J.Clin.Diag.Res.,(serial online), **5**, 1336-1338 **(2011)**.

[20] L.Pani, L.Korenda, J.Meigs, C.Driver et al,; Effect of aging on A1C levels in individuals without diabetes, Diabetes care, **31**, 1991-1996 **(2008)**.

[21] E.Ferrannini, E.Buzzigolia; Insulin resistance in essential hyper tension, N.Engl.J.Med., **313**, 350-357 **(1987)**.

[22] G.M.Raven; Insulin resistance, hyperinsulinemia and hypertriglyceridemic in the etiology and clinical course of hypertension, Am.J.Med., **2A**, 75-95 **(1991)**.