Comparison of systemic autonomic functions in primary angle glaucoma and in normal subjects

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Abstract

The present study was conducted to assess the autonomic activity in 30 normal healthy [control] and 30 Primary Open Angle Glaucoma [POAG] subjects. The studies related to record the autonomic dysfunction in POAG was undertaken. The results showed that both the parameters used for sympathetic as well as parasympathetic activities were found to be statistically highly significant except in the case of resting heart rate. No changes were observed in the normal subjects. The changes in the parameters of autonomic function [i.e. Resting HR, T-wave amplitude, QTc, S/L ratio, Valsalva ratio and Cold Pressor Response] in the present study helped concluding that the autonomic involvement in POAG is present. POAG showed decrease in both the sympathetic and parasympathetic activity. Early detection and treatment of risk factors e.g. cardiovascular factors [systemic hypertension, hypotension], sympathetic and parasympathetic dysfunctions that affect optical circulation, aqueous production and innervations of ciliary body, muscles and processes is essential before irreversible changes set in and effect vision.

Keywords: POAG Primary Open Angle Glaucoma, Autonomic Function

Introduction

In the late 19th century, Langly J.N. established the concept of ANS being involved in the various systemic disorders e.g. diabetes, cerebral pathology etc.(1) The ANS is the part of the peripheral nervous system that acts as central systems functioning largely below the level of consciousness and control visceral functions. The preganglionic or 1st neuron will begin at the 'outflow' and will synapse at the post ganglionic or second neuron cell body. The post-ganglion neuron will then synapse at the target organ.(2) Recently a third subsystem of neurons that have been named 'nor adrenergic' and 'non cholinergic' neurons because they use nitrous oxide as neurotransmitter and found to be integral in autonomic function particularly in the gut and the lungs.(3) In everyday life, there is a sudden increment in blood pressure due to acute stress situation and during work are the result of general increase in sympathetic activity. They tend to cause over perfusion of the eye, resulting in break-down of the blood-aqueous and blood-retinal barriers. The sympathetic activity assists autoregulatory mechanism in maintaining the intraocular blood flow and volume constant.(4) The ocular hypertension refers to the intraocular pressure higher than normal [10mmHg-21mmHg] in the absence of optic nerve damage or visual field loss. Elevated IOP is the most important risk factor for glaucoma so these with ocular hypertension are frequently considered to have a greater chance of developing the condition. There is evidence that some glaucoma patients with normal IOP while sitting or standing may have elevated IOP enough to cause problems when they are lying down.(5) Glaucoma is an asymptomatic condition characterized by progressive field loss due to nerve damage from elevated intraocular tension. It is classified as primary and secondary glaucoma; the primary glaucoma is further classified as primary open angle and primary close angle glaucoma. Primary Open Angle Glaucoma [POAG] is a chronic, progressive multifactorial optic neuropathy which develops quite slowly and insidiously over many years which is a characteristic triad of symptoms- raised tension, typical field defects and cupping of disc. Early detection and treatment of risk factors e.g. cardiovascular factors [systemic hypertension, hypotension], sympathetic and parasympathetic dysfunctions affect optical circulation, aqueous production and innervations of ciliary body, muscles and processes. Ophthalmoscopy is helpful in detecting the pathological changes at early stage of disease so study is undertaken with similar objectives to provide a further insight to this disorder and to compare the autonomic functions of the POAG and normal subjects.

Materials and Methodology

Materials: This is a longitudinal study of systemic autonomic functions with 30 normal subjects and 30 primary open angle glaucoma patients. The study was conducted in the Department of Physiology, SMC Ghaziabad. The various autonomic function tests were performed in normal healthy subjects and glaucomatous patients.

Methodology: All the subjects studied were of both sex group i.e. males and females aged 30-60 years. The parameters recorded were height, weight and body surface area with the help of anthropometric scale, Avery-n-machine and Mc Kesson's nomogram

respectively. The tests involved in assessing the parasympathetic activity involves the resting heart rate using EKG calculated as

HR = 1 ÷ Max. R-R interval [in sec]

Standing to lying ratio [Postural Pressor Response] calculated as

S/L Ratio = Longest R-R interval during the 5 beats before lying down ÷ Shortest R-R interval during the 10 beats after

And Valsalva ratio was calculated by blowing against a mouthpiece attached to aneroid manometer and maintaining a pressure of 40mmHg for 15 sec using formulae

Valsalva ratio = Max. R-R interval after the strain ÷ Shortest R-R interval during strain

The tests to assess sympathetic activity involve the cold pressure response using the Le Blanc et al method. In this, the subject is asked to place his hand in the cold water which is a painful stimulus and therefore is used to study the autonomic response of different individuals. The last test conducted was T wave amplitude which was measured using a ruler in mm and was converted into the millivolts as the EKG sensitivity was set at V/cm i.e. T wave height of 1mm=0.1mV.

Observations and Results

The present study consisted of thirty normal healthy subjects males / females, belonged to the age group of 45 + 15 years (i.e. 30 to 60 years age group) and their weight ranged from 130-175 lb and their body surface area 1.5-1.9 square meter (1.67 + 0.04 square) meters acting as a control group, and thirty subjects were cases of primary open angle glaucoma (POAG), matched for their age and anthropometry. The various autonomic function tests were carried out at a comfortable temperature of 27 ± 1^0C at the same time of the day between 2-4 P.M. and the data obtained from the observations and records were analyzed statistically to elicit important and significant results.

Test to Assess Sympathetic Activities

1. T-Wave Amplitude of Lead II EKG

Table 1 & Fig 1, show T wave amplitude of lead II of EKG (X) i in POAG group and the control group of subjects.

POAG = 0.161± 0.1535 mV

Control = 0.433± 0.1373 mV

Table 1: T- Wave Amplitude(mV) of lead 11 of EKG of Control and POAG

	POAG		Control		P
	Mean	S.D	Mean	S.D	value
'T' Wave Amplitude (mV)	0.161	0.1535	0.433	0.1373	0.00

P=Significant X-Arithmetic Mean S.D.-Slandered Deviation

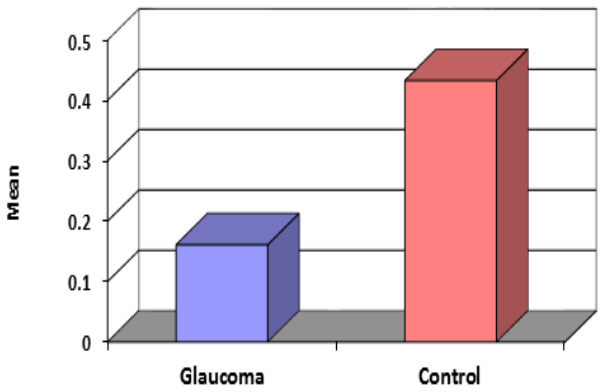

Fig. 1

2. Cold Presser Response (CPR)

Table 2 and Fig. 2 show systolic CPR in POAG group and control group of subjects.

POAG = 17.27± 3.463 mmHg

Control = 37.13 ±7.195 mmHg

Table 2A: Systolic CPR(mmHg)

	POAG		Control		P
	Mean	S.D	Mean	S.D	value
Systolic CPR(mmHg)	17.27	3.463	37.13	7.195	0.000

P=Significant X-Arithmetic Mean S.D.-Standard Deviation.

The Table 2A gives the comparison of mean and standard deviation of systolic CPR of group-1 POAG and group- 2 control subjects show there is statistically significant difference in systolic CPR of group 1POAG and group-2 control subjects.

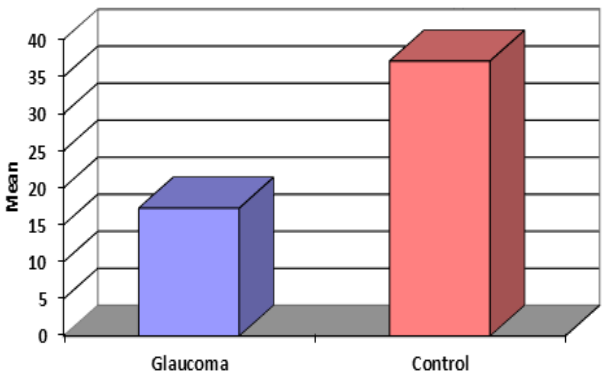

Fig. 2A

Table 2B and Fig. 2B show diastolic CPR in POAG group and control group of subjects

POAG = 14.27± 4.258 mmHg

Control = 22.57 ±5.157 mmHg

Table 2(B): Diastolic CPR(mmHg)

	POAG		Control		P value
	Mean	S.D	Mean	S.D	
Diastolic CPR(mmHg)	14.27	4.258	22.57	5.157	0.000

P=Significant X-Arithmetic Mean S.D.-Standard Deviation.

The Table 4.6B gives the comparison of mean and standard deviation of diastolic CPR of group-1 POAG and group- 2 control subjects show there is statistically significant difference in diastolic CPR of group 1POAG and group-2 control subjects.

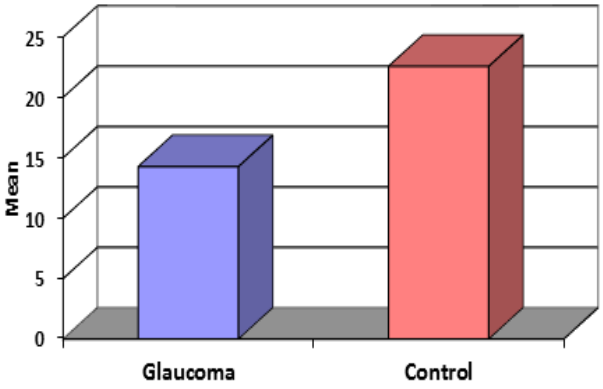

Fig. 2B

3. Corrected QT Interval (QT_C)

Table 3 & Fig. 3 shows corrected QT_C interval (QT_C) of lead II of EKG in POAG group of subjects and control group of subjects.

POAG = 0.468 ± 0.0774 s
Control = 2.362 ±0.3283 s

Table 3: Corrected QTc Interval(sec)

	POAG		Control		P value
	Mean	S.D	Mean	S.D	
Corrected QTc interval(sec)	0.468	0.0774	2.362	0.3283	0.00

P=Significant X-Arithmetic Mean. S.D.-Standard Deviation.

The Table 3 gives the comparison of mean and standard deviation of Corrected QT Interval of group-1 POAG and group- 2 control subjects show there is statistically significant difference in QTc of group 1POAG and group-2 control subjects.

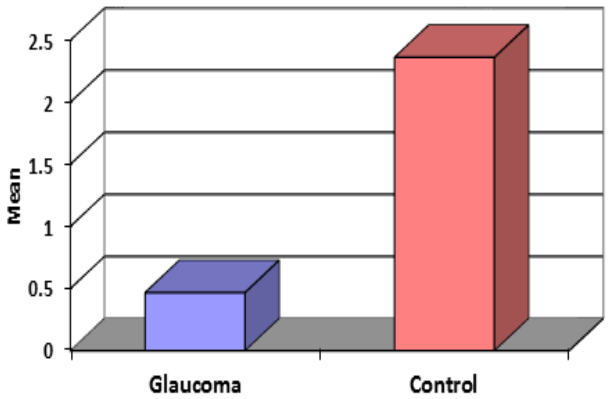

Fig. 3

Tests to Assess Parasympathetic Activity

a. Resting Heart Rate

Table 4 & Fig. 4 show Resting heart rate in POAG group as compared to the normal group of subjects.

POAG = 64.88 ± 4.048 bpm
Control = 69.22 ±14.024 bpm

Table 4: Resting Heart Rate(Beats/min)

	POAG		Control		P value
	Mean	S.D	Mean	S.D	
Resting heart rate(Beats/ min)	64.88	4.048	69.22	14.024	0.112

P=Non Significant X-Arithmetic Mean. S.D.-Standard Deviation.

The Table 4 gives the comparison of mean and standard deviation of resting heart rate of group-1 POAG and group- 2 control subjects show there is statistically non-significant difference in resting heart rate of group 1POAG and group-2 control subjects.

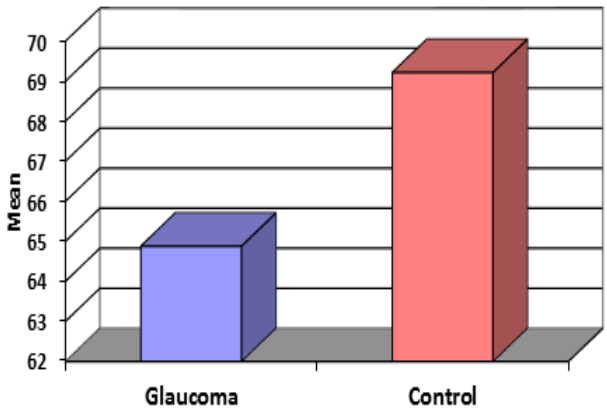

Fig. 4

b. Standing to Laying Ratio

Table 5 shows standing to lying ratio in POAG groups and normal group subjects.

POAG = 1.334 ± 0.1929
Control = 1.439 ±0.2134

Table 5: Standing to lying ratio

	Glaucoma		Control		P value
	Mean	S.D	Mean	S.D	
SL Ratio	1.334	0.1929	1.439	0.2134	0.0510

P=Significant X-Arithmetic Mean S.D.-Slandered Deviation.

The Table 5 gives the comparison of mean and standard deviation of Standing to lying ratio of group-1 POAG and group- 2 control subjects show there is statistically significant difference in resting heart rate of group 1POAG and group-2 control subjects.

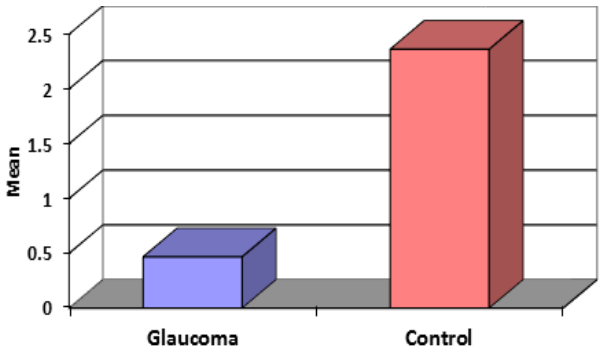

Fig. 5

c. Valsalva Ratio

Table 6 shows Valsalva ratio in POAG groups and the normal group of subjects

POAG = 1.463± 0.2359

Control = 1.889±0.4721

Table 6: Valsalva ratio

	POAG		Control		P value
	Mean	S.D	Mean	S.D	
Valsalva Ratio	1.463	0.2359	1.889	0.4721	0.0001

P=Significant X-Arithmetic Mean S.D.-Slandered Deviation.

The Table 6 gives the comparison of mean and standard deviation of Valsalva ratio of group-1 POAG and group- 2 control subjects show there is statistically significant difference in resting heart rate of group 1POAG and group-2 control subjects.

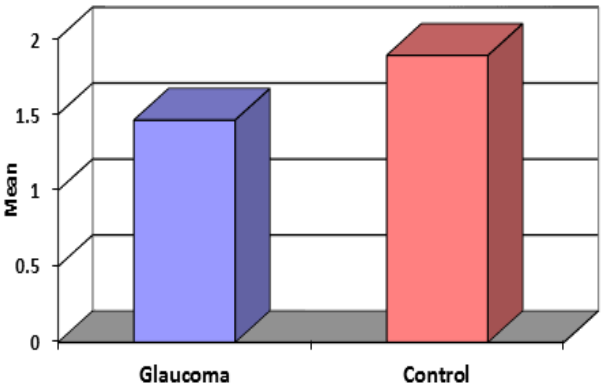

Fig. 6

Discussion

The results of present study showed that the parameters used for the sympathetic as well as parasympathetic activities were found to be statistically highly significant except in the case of resting heart rate. The Cold Pressor Response [CPR], being a sensitive indicator of sympathetic activity confirms the decrease in the sympathetic activity in the present study. The study done by Le Blance et al[7] in which he demonstrated that under any condition which causes stress of either physical or physiological origin, there is activation of sympathetic nervous system noted. Gherghel et al[8] performed a modified CPR and found a differing BP and ocular blood flow response in patients with POAG suggestive systemic autonomic failure and ocular vascular dysregulation. The T-wave amplitude confirms the decrease in the sympathetic activity. According to Furedy and Hoselgrave[9] T wave amplitude is a measure of the sympathetic activity of the heart. Its amplitude is affected by certain factors like R-R interval- *Tachycardia tends to decrease the voltage of the t-wave;*[10] Hypokalemia- *Hypokalemia causes decrease in T wave amplitude*[11] and Hyperkalemia- *Hyperkalemia causes increase in T wave amplitude*.[12] The results disclosed that the mean QTc is shortened in POAG group when compared with the control group. In another study done by Merdler et al[13] showed that QTc interval change is associated with autonomic imbalance. During evaluation of cardiovascular autonomic function tests in normal subjects, Chu-TS[14] demonstrated that alteration of QTc was associated with autonomic imbalance. The study resulted in a statistically non-significant decrease in the parasympathetic activity in case of resting heart rate. Leon Shaver[15] demonstrated that heart rate is decreased by vagal activity and increased by sympathetic activity. Under normal resting conditions, reduction in vagal activity or its blocking with atropine causes tachycardia. In a study done by Doina Gherghel and Sarah Louis Hosking[16] in which they studied the abnormal systemic and ocular vascular response to temperature provocation in POAG patients. The study of Valsalva ratio revealed that POAG patients showed

that the significant fall in parasympathetic activity when compared with control subjects. According to Bennet,[17] Valsalva ratio is classified under the parasympathetic function test, as evident by blockage of heart rate response which can be abolished by atropine but it was observed that the outcomes of valsalva maneuver is dependent on both parasympathetic and sympathetic innervations as the cardio-acceleration produce during the straining phase of maneuver is a sympathetic function.

Summary and Conclusion

The present study was conducted to assess the autonomic activity in 30 normal healthy [control] and 30 Primary Open Angle Glaucoma [POAG] subjects. The studies related to record the autonomic dysfunction in POAG was undertaken. The results showed that both the parameters used for sympathetic as well as parasympathetic activities were found to be statistically highly significant except in the case of resting heart rate. No changes were observed in the normal subjects. The changes in the parameters of autonomic function [i.e. Resting HR, T-wave amplitude, QTc, S/L ratio, Valsalva ratio and Cold Pressor Response] in the present study helped concluding that the autonomic involvement in POAG is present. POAG showed decrease in both the sympathetic and parasympathetic activity.

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