

GLAUCOMA AND CONCOMITANT STATUS OF AUTONOMIC NERVOUS SYSTEM

RAMESH KUMAR AND VEENA M. AHUJA*

*Department of Physiology,
Maulana Azad Medical College,
Bahadur Shah Zafar Marg,
New Delhi - 110 002*

(Received on January 17, 1997)

Abstract : There is much clinical evidence to suggest that certain types of Glaucoma are related to activity of autonomic nervous system (ANS). Although some local changes have been documented but systemic association has not been established, so far. Hence, the present study was initiated and an attempt was made to bring out the association of systemic autonomic functions with glaucoma (especially Primary Closed Angle Glaucoma (PCAG)) if any. This study was carried out in the Department of Physiology, Maulana Azad Medical College in association with Glaucoma Clinic of Guru Nanak Eye Centre, New Delhi from June 1993 - August 94. ANS function tests were conducted using Polyrite-8-Medicare System. The subjects were confirmed cases of PCAG with $10P-22.1 \pm 4.4$ mmHg and possibility of autonomic neuropathy due to any other cause was ruled out. They were matched with normal subjects for their age, anthropometry and were compared for their sympathetic activity of ANS by Galvanic Skin Resistance (GSR); Cold Pressor Response (CPR); corrected QT interval (QTc) and T-wave amplitude (TWA) and for parasympathetic activity of ANS by Resting Heart Rate (RHR); Standing to Lying Ratio (SLR) and Valsalva Ratio and analysed statistically using standard 't' test. The results obtained in this study indicated increase in sympathetic activity in 61% of PCAG subjects and decreased parasympathetic activity in 80% of the PCAG subjects when compared with control group of subjects, suggesting association of autonomic neuropathy with PCAG.

Key words : autonomic nervous system intra ocular pressure
primary closed angle glaucoma

INTRODUCTION

The human internal environment is regulated in large measure by the autonomic nervous system (ANS) and its integrated activities with other systems. The concept of autonomic nervous system being involved

in the various systemic disorders was established in late nineteenth century (1). Unlike somatic neuropathy, autonomic neuropathy is characterised by rather late appearance of clinical symptoms whereas measurable abnormalities in autonomic nervous functions are often present before

*Corresponding Author

the appearance of clinical symptoms. Earlier tests of ANS functions were usually complex, difficult to interpret and lacking in control measurement (2, 3). Also the previous studies were concentrated more on the local autonomic activity of the eye. Further studies revealed new generation of tests (4, 5) with aims of confirming the presence of and severity of autonomic neuropathy in the body.

Increased autonomic activity is the major mechanism that produces PCAG in which pupil moves to dilate and produce shallow anterior chamber. Aqueous outflow is decreased by contraction of circular muscle fibers of ciliary muscle (6) while contraction of meridional fibers increases outflow (7). Also stimulation of sympathetic nerves produces increased Intra Ocular Pressure (IOP) (8) and cervical sympathectomy reduces the IOP (9). While the literature reveals the role of ANS in the pathogenesis of PCAG, the exact mechanism as well as the fact whether both sympathetic and parasympathetic division of ANS are involved or only one, is not clear. Also the studies showing extent of involvement are very few. The present study was undertaken to explore the subject further to provide a better insight to this problem.

METHODS

The present study of ANS functions in glaucoma was conducted in the Department of Physiology of Maulana Azad Medical College and associated Guru Nanak Eye Centre (GNEC), New Delhi from June, 93 to August, 94. Selection of subjects was done by random sampling from the Glaucoma

Clinic of GNEC. Any existing cause of autonomic neuropathy was noted to be ruled out. All the subjects were matched for their age and anthropometry. IOP of twenty normal individuals was 16.9 ± 7.6 mmHg and that of twenty diagnosed PCAG was 22.1 ± 4.37 mmHg with visual acuity often reduced to 6/60 or less.

History taking and medical examination was carried out for about half an hour during which the subject gets acclimatized to the environment. The nature of the test was explained to the subjects. All the tests were performed at the same time of the day (i.e. 1400 hrs-1600 hrs) in all the subjects and at a comfortable environmental temperature about $27 \pm 1^\circ\text{C}$ in the laboratory. Various tests used for the assessment of sympathetic and parasympathetic - activity are as follows :-

(1) Resting Heart Rate (RHR) was calculated from the EKG of standard limb lead II.

(2) Corrected QT Interval (QTc) - QTc standardizes the QT interval for rate from EKG (10).

(3) T-Wave Amplitude (TWA) was measured using a ruler in mm and then converted to mv as TWA (Height in mm) = 0.1 mv.

(4) Standing to Lying Ratio (SLR) - Each subject was asked to stand quietly and then lie down without help while an EKG was recorded continuously during this period. The results were expressed as a ratio of longest R-R interval during five beats before lying down to the shortest R-R interval during ten beats after lying down (11).

(5) Valsalva Ratio : Subject is asked to perform the valsalva maneuver for 15 sec by blowing air into the mouth-piece-attached to aneroid manometer and maintain a pressure of 40 mmHg for 15 sec. Three trials were performed at an interval of 5 min. Continuous EKG was recorded 1 min before to 1 min after the maneuver.

$$\text{Valsalva Ratio} = \frac{\text{max R - R interval after the strain}}{\text{shortest RR interval during strain}}$$

The maximum ratio of the three trials was taken for autonomic activity.

(6) Galvanic Skin Resistance (GSR) : GSR was performed by using Polyrith-8-medicare machine Electrodes were applied over three fingers supplied with constant current of 5 micro ampere to GSR-DC. The level of skin resistance was calculated from pen deflection measuring 1 mv equal to 10 kohm of resistance change. Greater the GSR lower this skin resistance (12) hence lower sympathetic activity.

(7) Cold Pressor Response (CPR) : performed at the end because of slight unpleasantness associated with the test. Blood Pressure of the subject was recorded under resting conditions. The subject was

then asked to immerse his hand in a jug of water with temperature maintained at 7-10°C throughout the test. B.P. readings were made from the other arm at 30 sec intervals for a period of two min. The maximum increase in systolic and diastolic B.P. was determined and results recorded.

For each variable group of autonomic function tests performed in the study-mean and standard deviation of results were calculated and intergroup relationship was assessed for statistical significance by standard 't' test.

RESULTS

As shown in Table I, sympathetic ANS functions show increasing trend in PCAG group when compared with normal subjects. GSR and CPR showed significant variation ($P < 0.05$) whereas TWA and QTc showed small variations. GSR is decreased in 90% PCAG subject with statistical relationship being highly significant ($P < 0.001$). CPR both systolic and diastolic are increased in 62.5% PCAG subject with statistical significance established in only diastolic CPR ($P < 0.05$). Although increase in TWA and QTc is seen

TABLE I : Showing sympathetic activity in normal (N) : PCAG.

	N	Mean value \pm S.D. PCAG	P - value N vs PCAG
GSR (kohm)	63.45 \pm 9.59	45.66 \pm 10.79	<0.001 (HS)
CPR-systolic (mmHg)	36.70 \pm 7.71	37.2 \pm 7.98	>0.05 (NS)
Diastolic	20.75 \pm 5.84	23.55 \pm 6.66	<0.05 (S)
TWA (mv)	0.31 \pm 0.10	0.32 \pm 0.15	>0.05 (NS)
QTc (mv)	0.46 \pm 0.07	0.47 \pm 0.05	>0.05 (NS)

TABLE II : Showing parasympathetic activity in normal (N) : PCAG.

	N	Mean value \pm S.D. PCAG	P value N vs PCAG
Valsalva Ratio	1.89 \pm 0.47	1.27 \pm 0.15	< 0.001 (HS)
SLR	1.42 \pm 0.20	1.20 \pm 0.19	< 0.05 (S)
RHR (bpm)	68.50 \pm 14.01	74.18 \pm 17.35	> 0.05 (NS)

HS = Highly significant

S = Significant

NS = Non-significant

in 40% and 50% PCAG subjects respectively but statistical significance could not be established ($P > 0.05$).

Table II showed decrease in parasympathetic functions in PCAG. SLR and Valsalva ratio showed significant variation ($P < 0.05$) whereas RHR showed small non-significant variation ($P > 0.05$). SLR is decreased in 95% PCAG subjects which is also statistically significant ($P < 0.05$).

DISCUSSION

It is well known that the IOP is influenced by both divisions of ANS viz sympathetic and parasympathetic. There is anatomic basis for neurohumoral control of IOP as well which can be seen from the rich innervation of trabecular network (13,14). Role of sympathetic system may be involved in regulation of IOP as this control mechanism becomes defective in glaucomatous eyes. Autonomic neuropathy can also be associated with PCAG (15,16).

The present study showed increase in sympathetic activity in PCAG group in individuals. Decreased GSR and increased

CPR indicates increased sympathetic activity (12, 17). Increase in IOP is also associated with increase in both systolic and diastolic blood pressure (18). Also blood pressure is positively associated with increase in sympathetic activity (13,14). This increase in sympathetic activity in PCAG group of individuals may cause contraction of smooth muscle of orbit leading to increasing in IOP which could lead to development of PCAG. This increased activity could be because of denervation hypersensitivity during development of autonomic neuropathy. Autonomic denervation of eye in diabetes may be associated with alteration of Anterior chamber of eye causing glaucoma development (19). Autonomic denervation hypersensitivity may also cause development of PCAG (8). Indirect evidence in support comes from various studies when surgical sympathectomy leads to fall in IOP (9). Significant fall in SLR and Valsalva ratio that have been noted in the present study suggest decreased parasympathetic activity in PCAG group of subjects. This decreased parasympathetic tone could lead to pupillary dilatation and obstruction of aqueous flow with increase in IOP causing glaucomatous changes in the eye. Studies showing decrease in SLR have been noted

in autonomic neuropathy of diabetes (11, 20, 21) and also decrease in Valsalva ratio (4) are indicative of decreased parasympathetic function (4, 21). Although confusing reports regarding the association of increased IOP and autonomic dysfunction are revealed by the literature (19, 22). The present study is suggestive of both the sympathetic and parasympathetic dysfunction leading to prevalence of autonomic neuropathy in PCAG. However, further work is essential to get more definitive answer to the fact that PCAG is a complication of autonomic

neuropathy or PCAG leads to autonomic neuropathy.

CONCLUSION

The present study is suggestive of association of autonomic neuropathy with PCAG by showing increased sympathetic and decreased parasympathetic activity in PCAG group of subjects. However, to establish more accurate association between autonomic function and PCAG, further work is required.

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