EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 1
339-342
Year: 2016

TO ASSESS AUTONOMIC ACTIVITY IN PATIENTS OF PRIMARY OPEN ANGLE GLAUCOMA (POAG) BY HEART RATE VARIABILITY (HRV) AND VALSALVA MANEUVER (VM) AND TO COMPARE WITH HEALTHY CONTROLS.

***Harminder Singh, Indu Khurana, C. S. Dhull.**

*Post Graduate Department of Physiology, Pt. BDS, PGIMS Rohtak-Haryana (India).
Sr. Prof Department of Physiology, Pt. BDS, PGIMS Rohtak-Haryana (India).
Sr. Prof Department of Ophthalmology, Pt. BDS, PGIMS Rohtak-Haryana (India).

***Author for Correspondence: Dr. Harminder Singh**
Post Graduate Department of Physiology,Pt. BDS, PGIMS Rohtak-Haryana (India).

Article Received on 18/11/2015 **Article Revised on 10/12/2015** **Article Accepted on 01/01/2016**

ABSTRACT
Introduction POAG is known as'silent thief of vision' as it is asymptomatic disease progressing to blindness without exhibiting warning signs till advanced phase. Circulatory damage can occur on eye due to autonomic imbalance. HRV shows beat to beat fluctuation in heart rate. VM is used to assay integrity and stability of cardiac autonomic function depending on heart rate responses associated with arterial pressure stabilizing baroreflex mechanism. Material and method- Study was conducted Physiology department in collaboration with Ophthalmology department, PGIMS Rohtak. Study sample comprised of 30 POAG patients (group I) and 30 controls (group II). Basal HRV was assessed. HRV was recorded during after VM. Observation and results- Basal HRV showed significant (p 0.026) increase in LF(nu) in group I. During VM significant increase in SDNN ($p < 0.05$) in group I was observed. During valsalva recovery significant (p 0.035) decrease in NN50 was observed in group I than group II. Significant increase in LF(nu) [p 0.05], LF/HF ratio (p 0.048) and decrease in HF (nu) [p 0.013] was observed in group I. Discussion- HRV is regulated by constant involvement of sympathetic and parasympathetic system. Frequency domain variables of basal HRV showed reduced vagal tone and sympathetic predominance to heart in POAG patients. Significant increase in SDNN in group I depicted sluggish autonomic response during stress. POAG cases showed blunted response during strain showing delayed response to stress. Significant decrease in NN50 suggested incomplete recovery after stress. Conclusion- Basal HRV suggested decreased vagal tone and relatively sympathetic overdrive in POAG patients. VM suggested autonomic imbalance and inefficient compensatory mechanism during stress. During recovery persistently high sympathetic tone may be due to altered autonomic activity in POAG patients.

KEYWORDS: *Primary Open Angle Glaucoma, Heart rate variability, valsalva maneuver, valsalva recovery.*

INTRODUCTION
Primary open angle glaucoma (POAG) is frequently known to be 'the silent thief of vision' as it is an asymptomatic disease progressing to blindness without exhibiting warning signs till the advanced phase. POAG is diagnosed by the presence of "classical triad"; characterstic pattern of visual field defects, morphological changes of optic disc (cupping) and rise in intraocular pressure (IOP) (≥21 mm Hg).[1] Autonomic Nervous System (ANS) affects both heart rate and blood pressure, therefore adverse effects especially circulatory damage can occurs on eye due to autonomic imbalance. High sympathetic activity may lead to reduced ocular blood flow by constricting the microvasculature which provides nourishment to the optic nerve head (ONH). Heart rate variability (HRV) which is a non invasive procedure, shows beat to beat fluctuation in heart rate, depicting the effect of ANS on SA nodal activity and also detects symaptho-vagal imbalance. Heart rate at any point of time or intervals between consecutive normal complexes is determined in time domain analysis of HRV. Statistical indices in time domain are: SDNN (standard deviation of NN, so-called normal-to-normal intervals) which encloses long and short-term variability, RMSDD (square root of the mean squared differences of successive NN intervals) explains short-term variation and depicts parasympathetic action and pNN50 (proportion of differences in consecutive NN intervals that are longer than 50 ms) and its importance is equivalent to RMSDD. Spectral components in frequency domain analysis are: LF (low-frequency) component regulated by sympathetic and

parasympathetic nervous system and related with baroreceptor activity, HF (high-frequency) component regulated by parasympathetic activity and related with respiratory and blood pressure changes.[2] LF/HF ratio depicts absolute and relative variations between sympathetic and parasympathetic components of ANS therefore, autonomic modulation helps in characterizing sympatho-vagal balance on heart.[3] Valsalva-Weber maneuver is coupled with expiratory straining, carried out against a closed glottis and is used to assay the integrity and stability of cardiac autonomic function depending on heart rate responses associated with the arterial pressure stabilizing baroreflex mechanism. Valsalva ratio is employed as an index of baroreflex-mediated bradycardia and is calculated as the ratio of the maximum heart rate at the time of expiration and the minimum heart rate in first 20 s after expiratory strain. Normal Valsalva ratio is > 1:20. Valsalva ratio is < 1:20 in autonomic neuropathy. Valsalva ratio shows parasympathetic activity, whereas variations in blood pressure are a measure of sympathetic action.[4]

MATERIAL AND METHODS

The present prospective study was conducted in the department of Physiology in collaboration with Regional Institute of Ophthalmology (R.I.O), Pt. B. D. Sharma, PGIMS Rohtak. The study sample was comprised of two groups:

Group I- Thirty newly diagnosed patients with POAG.

Groups II-Thirty age and sex matched healthy controls.

Inclusion Criteria for group I (POAG)

- Intraocular pressure > 21 mm Hg without treatment.
- Optic disc changes suggestive of glaucomatous damage including one or more of these signs : neuroretinal rim notching , optic disc excavation, vertical or horizontal cup to disk (C/D) ratio >0.5 or C/D asymmetry between 2 eyes greater than 0.2, peripapillary splinter haemorrhages.
- Visual field outside normal limits on Humphery automated perimetry on three perimetry readings.
- All angles (360^0) open on gonioscopy.
- Pupil diameter ≥ 3mm without mydriatic or miotic drugs.

Inclusion criteria for group II (controls)

No suspicion of any form of glaucoma or any other eye disease.

Exclusion Criteria

- Patients with secondary causes of glaucoma, hazy media, optic neuritis, any disease involving the macula, retina, or visual pathway, high myopia (>6D), previous intraocular surgery and on drugs known to cause optic neuropathy.
- Diabetes mellitus patients.
- Hypertensives.
- Smokers.

After doing ophthalmological work up, the following autonomic function tests were carried out in the Physiology department.

- Basal heart rate variability (HRV) was assessed by *POWERLAB 26T POLYRITE D* system. The subject was asked to lie down on tilt table. Three disposable pre-gelled electrodes were attached to left arm, right arm and left leg for ECG recording to measure HRV
- HRV during Valsalva manoeuvre done by using Aneroid sphygmomanometer connected with a mouthpiece through a tube. The subjects were instructed to blow into mouthpiece to maintain 40 mm Hg pressure for 15 seconds. The subject was asked to release pressure. HRV was recorded during and after the procedure.

OBSERVATIONS

During basal HRV insignificant low values of time domain parameters of basal HRV were observed in group I as compared to group II. On comparison of frequency domain analysis of basal HRV (figure 1) showed significant (p 0.026) high values of LF(nu) in group I (64.41 ± 11.67) as compared to group II (56.48 ± 15.00) whereas HF (nu), HF (ms^2) and VLF (ms^2) showed low values in group I as 27.26 ± 9.86, 190.84 ± 236.68 and 976.35 ± 1736.70 respectively. Corresponding values of these parameters in group II were 29.79 ± 11.68, 213.89 ± 279.01 and 991.88 ± 1445.32. The value of LF/HF ratio was insignificantly higher in group I (2.89 ± 2.36) than in group II (2.66 ± 1.81). During Valsalva maneuver (table 1) significant increase in SDNN (52.04 ± 30.94, p< 0.05) in group I was observed as compared to group II (37.32 ± 24.64), whereas the values of RMSSD and NN50 were comparable in both the groups. Insignificant increase in LF (nu) and LF/HF ratio in group I as compared to group II and decreased HF (ms^2) was observed. During valsalva recovery time domain variables (figure 2) showed statistically significant (p 0.035) decrease in NN50 (7.20 ± 10.99) in group I as compared to group II (18.30±25.62).The values of RMSSD and SDNN also insignificantly decreased in group I. The frequency domain variables (table 2) showed a statistically significant increase in [LF(nu) 64.87 ± 13.88, p 0.05], LF/HF ratio (3.50 ± 2.93, p 0.048) and decrease in HF (nu) 25.04±9.65 p 0.013 in group I as compared to group II. Valsalva ratio was insignificantly lower in group I (1.19) as compared to group II (1.24).

Table.1 Time domain variables of HRV in group I and group II during Valsalva maneuver.

Parameter	Group I (Mean ± SD)	Group II (Mean ± SD)	p value
SDNN (ms)	52.04 ± 30.94	37.32 ± 24.64	***0.046**
RMSSD	23.84 ± 13.72	23.23 ± 21.98	0.898
NN 50	1.97 ± 4.02	1.77 ± 4.14	0.850

* statistical significance (p<0.05)

Table.2 Frequency domain variables of HRV in group I and group II during Valsalva recovery.

Parameter	Group I (mean ± SD)	Group II (mean ± SD)	p value
VLF(ms^2)	841.57 ± 1517.62	736.32 ± 926.98	0.747
LF(nu)	64.87 ± 13.88	52.27 ± 19.27	***0.005**
LF(ms^2)	284.71 ± 401.54	288.10 ± 294.81	0.970
HF(nu)	25.04 ± 9.65	33.11 ± 14.22	***0.013**
HF(ms^2)	280.10 ± 455.43	198.06 ± 258.24	0.444
LF/HF ratio	3.50 ± 2.93	2.21 ± 1.87	***0.048**

*statistical significance ($p<0.05$)

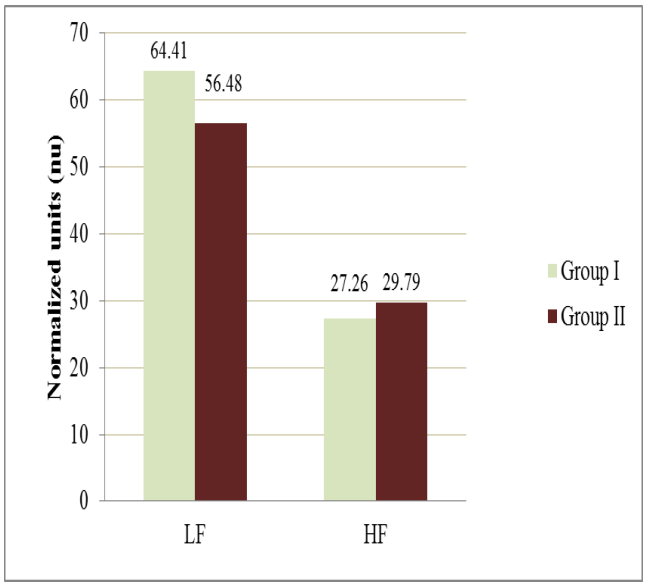

Figure 1. Comparison of frequency domain variables (LF and HF) of basal HRV in group I and II in normalized units.

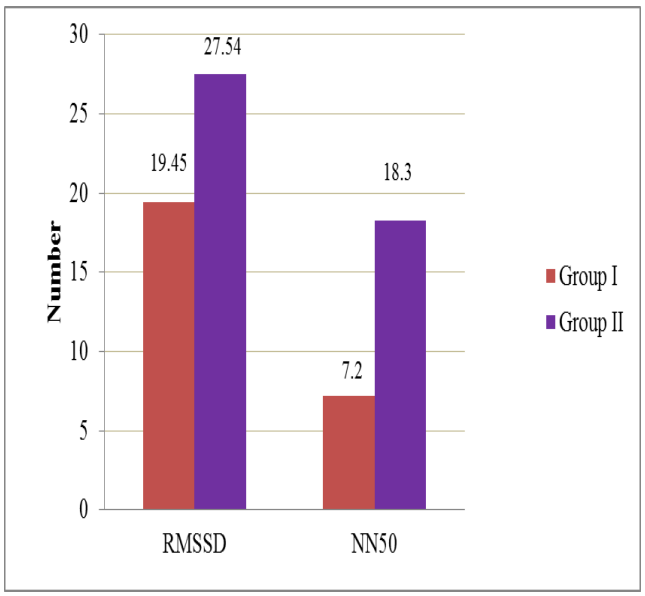

Figure 2. Comparison of Time domain variables (RMSSD and NN50) of group I and group II during valsalva recovery.

DISCUSSION

Heart rate variability is mainly regulated by constant involvement of both sympathetic and parasympathetic divisions of ANS. Time domain variable of basal HRV were insignificantly low in group I than in group II which is suggestive of low HRV. SDNN and RMSSD are qualitative markers of vagal activity. RMSSD and NN50 measure the short term variation in heart rate and thus are highly correlated. Low values of time domain variables observed in the present study document reduced parasympathetic tone in patients of POAG. A study by Menezes Jr et al in hypertensive individuals reported that on analysis of time domain variables, low value of SDNN, RMSSD and NN50 are indicative of reduced HRV, probably because of sympathetic hyperactivity.[5] Frequency domain variables of basal HRV of both groups showed significant high values of LF and LF/HF ratio in group I. All these parameters of HRV show reduced vagal tone and sympathetic predominance to the heart in POAG patients. Akselord and Appel ML had reported that LF factor is influenced by sympathetic as well as parasympathetic activity.[6,7] Malliani and associates have proposed that LF/HF ratio is better predictor of relative levels of sympathetic as well as parasympathetic activities as opposed to absolute values of either.[8] So, higher LF/HF ratio of basal HRV among group I in our study suggests higher degree of sympathetic tone and less parasympathetic tone. The findings suggest that there is a reduced parasympathetic tone. R Xavier et al studied the effect of Valsalva maneuver on short term HRV recording and found that there is an increased sympathetic activity during the strain (higher LF band) and an increased parasympathetic response after the strain period (higher HF band).[9]

Valsalva maneuver (VM) is mainly for assessment of parasympathetic activity. During VM baroreceptors respond to blood pressure changes occurring due to increased in intrathoracic pressure. Valsalva ratio is an index for baroreflex mediated bradycardia. PK Jones et al in their study emphasized the role of valsalva ratio in identifying parasympathetic dysfunction as a cause of syncope in many clinical disorders.[9] The table 1 showed significant increase in SDNN ($p<0.05$) in group I as compared to group II. This further depicts sluggish autonomic response during period of stress. Insignificantly increased values of LF (nu) and LF/HF ratio and decreased HF (nu) in group I as compared to group II reflects the presence of inefficient compensatory mechanisms during period of stress and hence disturbed autonomic activity in cases of POAG.

In the present study it was observed that cases of POAG showed a blunted response during the strain period (decreased LF). This concludes that there is delayed response to stress in these patients. Thayer JF et al reviewed the evidence of vagal function as a cardiovascular risk factor and concluded that decreased vagal function precedes the development of a number of risk factors, both modifiable and non – modifiable.[10]

RW Shields in his review concluded that HRV with deep breathing is a reliable and sensitive clinical test for early detection of cardiovagal dysfunction in a wide range of autonomic disorders.[11]

Insignificantly decreased value of SDNN and RMSSD and a significant decrease in NN50 variables suggest that there is a reduced parasympathetic tone and a relative sympathetic overdrive in patients of POAG as compared to controls after the cessation of stress. This was suggestive of incomplete recovery after the period of stress.

CONCLUSION

Basal HRV showed low values of SDNN and high value of LF/HF ratio indicated reduced HRV, suggested decrease in vagal tone and relatively high overdrive of sympathetic activity in patient with POAG. Increased value of time domain variables and raised value of LF/HF during VM suggests autonomic imbalance and inefficient compensatory mechanism during stress. During the recovery period there is persistently high sympathetic tone, which did not touch the baseline values, may be due to altered autonomic activity in POAG patients.

REFERENCES

1. Khaw PT, Cordeiro MF. Towards better treatment of glaucoma. BMJ, 2000; 320: 1619-20.
2. Vanderlei LC, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Basic notions of heart rate variability and its clinical application. Rev Bras Cir Cardiovasc, 2009; 24(2): 205-17.
3. Patel SA, Verma A, Raval R. Profile of primary open angle glaucoma patients.Int J BAP, 2014; 3(1): 85-90.
4. Zygmunt A, Stanczyk J. Methods of evaluation of autonomic nervous system.Arch Med Sci., 2010; 6(1): 11-8.
5. Menezes Jr AS, Moreira HG, Daher MT.Analysis of variability of heart rate in hypertensive patients before and after treatment with angiotensin converting enzyme inhibitors of angiotensin II. Arq Bras Cardiol, 2004; 83(2): 165-8.
6. Askelord S, Gordon D, Ubel FA, Shannon DC, Barger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat to beat cardiovascular control. Science, 1981; 213: 220-2.
7. Appel ML, Berger RD, Saul JP, Smith JM, Cohen RJ. Beat to beat variability in cardiovascular variables: noise or music? J Am Coll Cardiol, 1989; 14: 1139-48.
8. Malliani A. Cardiovascular sympathetic afferent fibres.Rev Physiol Biochem Pharmacol, 1982; 94: 11-74.
9. Xavier R, Laranjo S, Ducla-SE, Andrade A, Boto JP, Santos-BM, Ducla-Soares JL, Carvalho LS, Rocha I. The Valsalva maneuver revisited by wavelets. Rev Port Cardiol., 2008; 27(4): 435-41.
10. Thayer JF, Lane RD. The role of vagal function in the risk for cardiovascular disease and mortality. Biol Psychol., 2007; 74(2): 224-42.
11. Sheilds RW Jr. Heart rate variability with deep breathing as a clinical test of cardiovagal function. Cleve Clin J Med., 2009; 76: S 37-40.