Effect of isometric handgrip test on heart rate variability in primary open angle glaucoma

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Abstract

Introduction: Open angle glaucoma is a chronic, slowly progressive optic neuropathy characterised by progressive visual field loss. At systemic level; hypertension, hypotension leading to reduced ocular blood flow (OBF), vasospasm, oxidative stress and cardiovascular disease history are associated with glaucoma. Various studies suggest a relation between Open angle glaucoma (OAG) and autonomic dysfunction, yet the exact mechanism is still unclear. Heart rate variability (HRV) and a provocative cardiac stress test can provide an easy, non-invasive and indirect assessment of the autonomic control of the heart.

Material and Method: The present study consists of 20 patients with Primary Open angle Glaucoma (group II) and 20 age & sex matched healthy controls (group I). Frequency domain analysis of HRV at rest and during Handgrip testing was analysed.

Results: On immediate release of handgrip patients with POAG depicted a significant raised Low frequency variables LF (nu) (73.39± 4.04), ($p < 0.000$) and LF/HF ratio (2.79±0.17), ($p < 0.000$). On the other hand there is a step decrease in high frequency variable HF (nu) (32.04±1.83) in group II ($p = 0.002$).The decrease in HF (nu) (38.40±8.07), ($p < 0.000$) with high LF/HF (1.55±0.28), ($p<0.000$) in group II remained significant during recovery period.

Conclusion: The study thus concluded sympathetic overdrive in response to stress and low parasympathetic activity during recovery period suggestive of impaired autonomic activity in Primary Open angle Glaucoma.

Keywords: Stress Test, Autonomic Dysfunction, Primary Open Angle Glaucoma, Auto Regulation, Heart Rate Variability.

Introduction

Open angle glaucoma (OAG) is a chronic, slowly progressive optic neuropathy characterised by progressive visual field loss. Broadly OAG is classified into high tension glaucoma (intraocular pressure > 21mmHg) and low or normal tension glaucoma (intraocular pressure ranges between 10 – 21 mmHg). As far as the clinical picture and features of glaucomatous optic neuropathy are concerned, the causes of the primary insults which trigger the cascade of events leading up to its development are less clear and thus forms the current topic of research in the field of glaucoma. Few studies suggested neuronal regulatory mechanisms to play a key a role in the regulation of choroidal blood flow. Therefore, abnormalities such as vasospastic syndrome and autonomic dysfunctions have been implicated to play a role in the development of glaucoma.[(1-3)]

Factors more traditionally associated with OAG; such as elevated IOP, have been firmly established as part of the pathogenetic process yet there are still a number of studies which describe subtle but important differences in both the structural and functional optic nerve head changes, as well as the vascular risk in glaucoma. At the ocular level the regulation of blood flow has been identified as a multi-factorial and complex process, dependant on both ocular perfusion pressure (OPP) and vascular resistance which are further influenced by autonomic nervous system (ANS) and systemic factors like hormones. The high irregularity of sinus rhythm is evident when heart rate (HR) is examined beat by beat termed Heart rate variability (HRV). The R-R interval variations during resting condition represents a fine tuning of beat to beat control mechanism, whereas HRV reflects modulating effects of the ANS on the intrinsic firing rate of the cardiac pacemaker cells, i.e. it reflects fluctuations rather than absolute levels of sympathetic and parasympathetic impulses. The actual balance of sympathetic and parasympathetic is constantly changing in attempt to achieve optimum activity.[(4-6)]

The modulating effects of neural mechanism on heart can be inferred with the help of analysis of HRV. Heart rate variability can be quantified in time and frequency domains. Frequency domain analysis involves spectral analysis of the ECG in order to evaluate the predominance of the sympathetic and parasympathetic divisions of the ANS and their effects on HR. High frequency (HF) component is caused by vagal tone during respiratory cycle. Low frequency (LF) component usually originates in the vasomotor part (sympathetic component). Sympatho-vagal balance of ANS function can be assessed through the evaluation of the LF/HF ratio. Sustained handgrip testing infers autonomic activity through changes in HR, mean arterial pressure (MAP), and vascular resistance. Recently sustained handgrip has become an important cardiac stress test. The autonomic effector mechanisms by which circulatory response to isometric exercise occur remain unclear.[(7-10)]

Material and Methods

An approval is taken from the Institutional Ethics Committee to conduct the study on human subjects. At the beginning of the procedure, the whole procedure was explained in detail to each subject in his/her own language and a written consent was taken. The present study consists of 20 patients with Primary Open angle Glaucoma (group II) and 20 age & sex matched healthy controls (group I) aged between 45 – 60 yrs.

Inclusion Criteria: For group II (POAG) include intraocular pressure (IOP) >21 mm Hg without treatment, disc changes with peri-papillary splinter haemorrhages, cup to disk ratio more than 0.5, defective visual field, deep anterior chamber and all angles (360^0) open on gonioscopy.

Exclusion Criteria: Any macular or retinal diseases, refractive errors (high myopia > 6 dioptre), previous intraocular surgery or secondary causes of glaucoma, chronic illness like diabetes mellitus and hypertension.

The test on each subject consisted of a thorough opthalmological examination in glaucoma clinic followed by autonomic function tests.

After the subject was asked to lie down, three disposable pre-gelled electrodes were attached on left arm, right arm and left leg. ECG recording was taken for 5 minutes and frequency domain analysis were analysed by POWERLAB 26T POLYRITE D system. (Sampling rate**:** 256 Hz. Filters used: For HRV high filter -99 Hz, low filter -0.1Hz. Screen speed was 30 mm/sec.)

Maximal voluntary contraction (MVC) was noted by asking the patient to take a full grip on the handgrip dynamometer. Then he/she was supposed to maintain a tension of 30% of MVC for 2 minutes. On immediate release of handgrip after 2 minutes and then after 5minutes (recovery period) ECG was recorded and analysed for HRV respectively.

Observations

The study showed no significant difference in the variables of Basal HRV (Table 1). However on provocation in the form of stress (handgrip test) LF component has shown a significant rise in contrast to HF component which is low in group II (Table 2 and Fig. 1&2).

During the recovery period of handgrip the values of LF component [LF(nu)p<0.000 and LF (ms2) p =0.01] in group II remained significantly raised and the values of high frequency (HF nu) has been low significantly in group II as compared to control group (p<0.000) thus resulting in a significant high value of LF/HF ratio in group II (p<0.000) both during handgrip and recovery phase of handgrip testing (Table 3 and Fig. 3 & 4).

Increased LF component or high LF/HF ratio suggested sympathetic hyperactivity and also delayed recovery due to impaired sympatho-vagal balance in POAG (II).

Frequency domain parameters

Table 1: Basal HRV in group I and group II

Parameter	Group I Mean±SD	Group II Mean±SD	p-value
LF (nu)	42.75±2.78	44.72±6.41	0.11
LF (ms2)	421.90±126.9	403.09±67.39	0.41
HF(nu)	44.96±3.89	46.99±4.71	0.16
HF(ms2)	445.97±130.65	427.13±70.07	0.41
LF/HF	0.98±0.08	0.95±0.13	0.19

Table 2: Handgrip testing in group I and group II

Parameter	Group I Mean±SD	Group II Mean±SD	p-value
LF (nu)	52.13±2.97	73.39±4.04	<0.000***
LF (ms2)	524.84±96.5	550.10±32.72	0.05*
HF (nu)	37.15±8.40	32.04±1.83	0.002**
HF (ms2)	371.59±101.33	197.17±21.56	0.002**
LF/HF	1.47±0.29	2.79±0.17	<0.000***

*** Very high significant (p<0.000)
** High significant (p<0.001)

Table 3: During handgrip recovery period in group I and group II

Parameter	Group I Mean±SD	Group II Mean±SD	p-value
LF(nu)	45.05±3.31	57.8±4.94	<0.000***
LF (ms2)	440.39±100.71	352.29±33.76	0.01**
HF(nu)	45.67±6.65	38.4±8.07	<0.000***

HF (ms2)	445.22±105.55	237.41±65.93	<0.000***
LF/HF	0.99±0.12	1.55±0.28	<0.000***

*p<0.05 significant
**p<0.001 highly significant
***p<0.000 highly significant

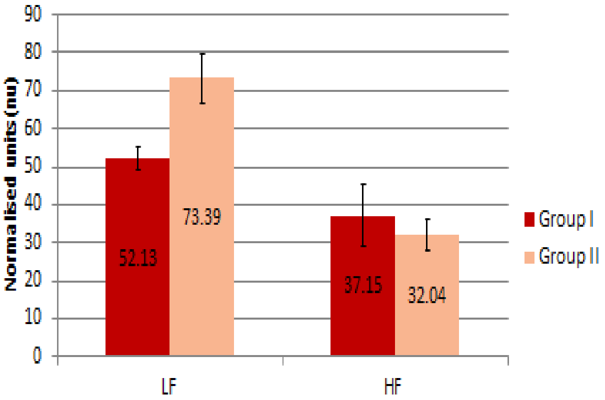

Fig. 1: Comparison of immediate effect of handgrip on frequency domain variables LF & HF (nu)

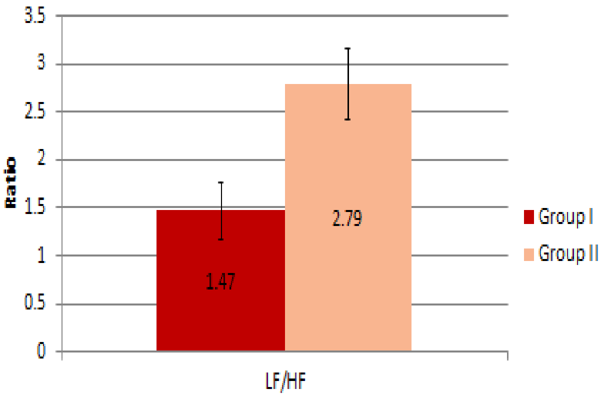

Fig. 2: Comparison of immediate effect of handgrip on LF/HF ratio

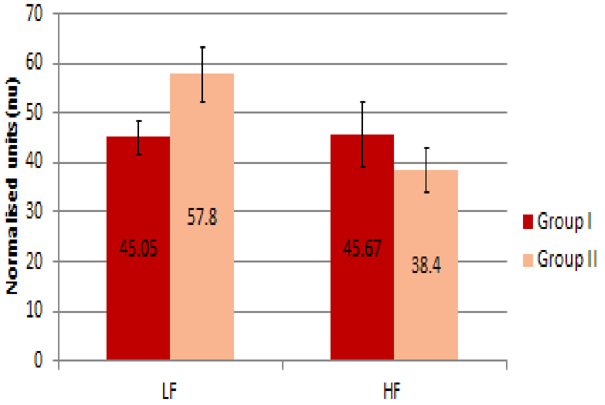

Fig. 3: Comparison of frequency domain variables LF & HF (nu) during handgrip recovery phase

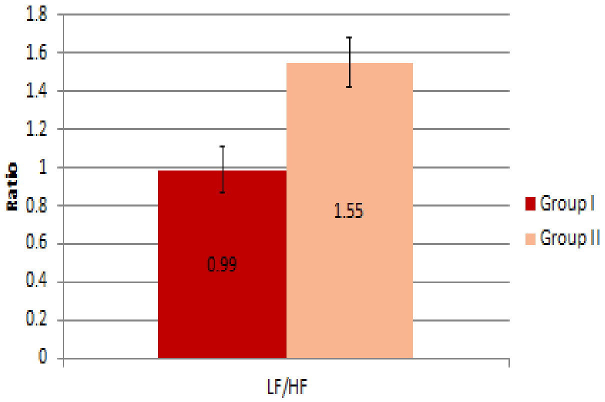

Fig. 4: Comparison of LF/HF ratio during handgrip recovery phase

Discussion

Highly significant increased values of Low frequency variable [LF (nu) {73.39± 4.04), (p < 0.000)] in POAG (group II) and low values of high frequency variable [HF(nu){ 32.04±1.83), (p = 0.002] in group II are in accordance with the study conducted by Askelord (1981) and Apple ML (1989). The findings of a significant rise in LF/HF ratio in group II with p value <0.000 during stress are consistent with the study by Mallani and associates. According to Mallani LF/HF ratio could indicate the balance between sympathetic and parasympathetic influences in body more accurately than LF and HF components individually.[10-12]

During handgrip testing HRV analysis in glaucoma patients suggested increased HRV due to greater withdrawal of parasympathetic activity. Significantly high values of frequency domain (LF and LF/HF) variables of HRV during recovery phase of HGT, suggested delayed recovery response from stress, which further indicated sympatho-vagal imbalance in glaucoma patients.

Significant increased values in LF (nu) {57.8 ± 4.94}, p<0.000} in group II as compared to group I (45.05 ± 3.31), decreased values in HF (nu) in group II [(38.40±8.07), (p < 0.000) as compared to group I (45.67 ± 6.65) and high values of LF/HF ratio in group II (p=0.001) suggested that there is incomplete recovery from stress during HGT in glaucoma patients. These findings were consistent with the study by Khurana RK and Gasser p et al.[13,14]

Conclusion

The present study was carried with the aim to compare the effect of handgrip (stress) test on autonomic activity, if any, in primary open angle glaucoma (POAG) with healthy controls. The results and discussion of HRV analysis during provocative tests concluded that autonomic imbalance was present in glaucoma patients.

Future prospects: The available literature has provided evidences that HRV provides indirect indices of autonomic modulation, which are very sensitive and reproducible. Yet these patients (POAG) are to be followed up to find out that the comparable findings in the early stage remain consistent as the disease progresses or become less consistent.

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