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Spectral Analysis of Short Term Heart Rate Variability in Healthy Volunteers: the Role of Gender

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Abstract- Clinical interest in HRV was sparked by the 1973 report of Wheeler and Watking, who first drew attention to cardiac vagal innervations as the mediation of HRV and its potential value as a clinical test of cardiovascular function HRV varies with age, gender, cardiac diseases, nutritional status with different drugs and in response to a number of other factors, such as diabetic autonomic neuropathy. In addition gender has a strong influence on mechanism on HRV. However the influence of gender and the underlying mechanisms has not yet been determined, till date no work has been conducted to understand the role of gender on HRV. This is a cross sectional study conducted in Jan – March 2010 with a sample size of 86 (43 male, 43 Female) was calculated based on the results of a study done on similar subjects. The temperature of the laboratory was kept between 25^o c - 28^o c and lights subdued. The subjects were asked to void urine before testing and made to sit in the lab comfortably to accustom to the new environment. ECG electrodes were connected for lead II. Baseline Heart Rate and Blood Pressure were recorded. Then at supine rest with the eyes closed and relaxed position, lead II ECG was acquired at the rate of 200 samples/second for 10minutes with the normal breath rate of 12 – 18/min using RMS Polyrite D hardware, INDIA, which is the data acquisition system. There was no significant difference in time domain measures of HRV in between male and females. But in frequency domain analysis Higher LF power, TP, LF/HF ratio and Lower LF values is seen in females.

Index Terms: HRV, gender, time domain measures, in frequency domain analysis, diabetic autonomic neuropathy

I. INTRODUCTION

The concept that sinus node pacemaker activity is under control of the autonomic nervous system has promoted the use of different measurements of sinus node cycle length to evaluate autonomic modulation of cardiovascular function. Among them, Heart Rate Variability (HRV) parameters and Baro Reflex Sensitivity (BRS) indexes are the most accepted well-known ones[3,4]. HRV has been a focus of interest in cardiovascular physiology for more than 150 years[1]. Clinical interest in HRV was sparked by the 1973 report of Wheeler and Watking, who first drew attention to cardiac vagal innervations as the mediation of HRV and its potential value as a clinical test of cardiovascular function[2].The resting autonomic control of the heart is regulated in the beat - to - beat fluctuations of the heart rate or the RR interval in the electrocardiogram (ECG). These variations in milliseconds of the duration of one cardiac cycle from the other is known as HRV and is traditionally expressed in statistical measures of time - domain analysis and as measures of spectral power under frequency – domain analysis. These measures are reproducible when obtained under resting conditions, implying constancy of the resting cardiac sympathetic and parasympathetic modulation[5]. Various studies have reported alterations in HRV parameters in disease conditions[6,7,13]. HRV analysis could be done by RR intervals, QT interval which is the part of RR interval in ECG. QT interval is a marker of sympatho - vagal balance[8]. QT interval is strongly influenced by autonomic conditions[9]. Female gender is an independent risk factor for cardiac events. Sex differences have been reported in human cardiac repolarization and the propensity for clinical arrhythmias[10]. HRV varies with age, gender, cardiac diseases, and nutritional status with different drugs and in response to a number of other factors, such as diabetic autonomic neuropathy. In addition gender has a strong influence on mechanism on HRV. However the influence of gender and the underlying mechanisms has not yet been determined, till date no work has been conducted to understand the role of gender on HRV.

II. MATERIAL AND METHODS

Participants:Subjects were enlisted from students and their relatives of our institution, who volunteered in response to the notice advertising for volunteers for the study. Healthy volunteers of both genders, aged 21-30 years with BMI of 19-25 kg/m^2 and physical activity levels of sedentary to moderate as per a questionnaire[11] were recruited to the study. All the subjects were non-smokers and were not on medications. Those already performing some form of yoga, breathing exercises and physical training were excluded from the study. Those with diabetes and cardiovascular diseases were also excluded from the study. All the female subjects had regular menstrual cycles of normal duration and none of them were on oral contraceptives. The study was prior reviewed and approved by Institute Ethics Committee of Meenakshi Medical College & Research IN statute, Kancheepuram, India. Each subject gave a written informed consent prior to recruitment into the study.

Experimental design: This is a cross sectional study conducted in Jan – March 2010 with a sample size of 86 (43 male, 43 Female) was calculated based on the results of a study done on similar subjects.

Study protocol:All experiments were performed at the Cardiac Autonomic Function research Laboratory in the department of physiology, Meenakshi Medical College & Research Institute. Base line heart rate, respiratory rate and Short – term HRV

indices in the morning following 20 min of supine rest, 2-4 hours after alight breakfast. The subjects were asked to refrain from heavy physical activity for 24 hours and from consumption of alcohol and caffeinated beverages for 12 hours prior to the measurements. The temperature of the laboratory was kept between 25^o c - 28^o c and lights subdued. The subjects were asked to void urine before testing and made to sit in the lab comfortably to accustom to the new environment. ECG electrodes were connected for lead II. Baseline Heart Rate and Blood Pressure were recorded. Then at supine rest with the eyes closed and relaxed position, lead II ECG was acquired at the rate of 200 samples/second for 10minutes with the normal breath rate of 12 – 18/min using RMS Polyrite D hardware, INDIA, which is the data acquisition system.

Heart Rate Variability analysis: The recommendations of Task Force on HRV were followed, an RR series was extracted from ECG using maximum amplitude and sharpness of the peaks for R wave detection, these are RMS proprietary algorithms & validated with Fluke Biomedical, USA. After exclusion of artifacts and ectopics a stationary 256s RR series was chosen and analyzed with Finland v 1.1 software for HRV (Bio-signal analysis Group, Finland). Mean RR was measured in milliseconds. In the time domain, the standard deviation of normal to normal RR intervals (SDNN) was taken as an index of overall HRV. The RR series was resampled at 4HZ, its mean and trend removed, a Hann window applied and the 1024 data – point series transformed by Fast Fourier Transformation (FFT). Low Frequency (LF) and High Frequency (HF) spectral powers were determined by integrating the power spectrum between 0.04 - 0.15Hz and 0.15 – 0.4Hz respectively. The sum of LF and HF powers were also calculated. LF and HF powers were expressed in normalized units (nu).

Statistical analysis:The data were examined for normality. Wherever the data was not normally distributed, nonparametric test was used. Data expressed as Mean±SD. 2 tailed paired t - test for normally distributed data and Mann - whitney U - test for skewed data. The null hypothesis was rejected at $p<0.05$. Trial version of Graphpad InStat 3.0 and Microsoft Excel were used for analysis of data.

III. RESULTS

There were no significant differences in the age, BMI and Physical Index in between male and female subjects (Table – I) There were no significant difference in the basal systolic and diastolic blood pressure in between male and females.

Table I: General parameters

	Male n=43 Mean±SD	Female n=43 Mean±SD	P value
Age in years	19.7±1.9	20.8±2.4	0.08
BMI in kg/m^2	24.4±3.1	24.0±53.5	0.71
HR in b.p.m	68.6±10.4	79.9±11.01	0.05
SBP mmHg	106±8.9	103±7.0	0.15
DBP mmHg	69.8±7.8	65.7±7.2	0.06
PP mmHg	38.2±8.2	37.2±7.7	0.66

Data are the Mean+SD. P<0.05 compared with Male, Female.
BP=Blood Pressure SBP=Systolic Blood Pressure DBP=Diastolic Blood Pressure PP=Pulse Pressure.

There was no significant difference in time domain measures of HRV in between male and females. But in frequency domain analysis Higher LF power, TP, LF/HF ratio and Lower HF values is seen in females (Table - II)

Table II: Time and Frequency Domain measures of HRV

	Female (n=43) Mean±SD	Male (n=43) Mean±SD	P Value
Mean RR(ms)	748.47 ± 118.90	756.51 ± 113.89	0.5800
SDNN (ms)	18.987 ± 4.911	15.980 ± 4.477	0.0072
HR	82.032 ± 11.418	80.980 ± 11.036	0.5800
RMSSD (ms)	19.133 ± 5.947	18.333 ± 5.557	0.5141
NN50 (count)	6.333 ± 8.377	6.400 ± 10.186	0.4905
pNN50 (%)	1.827 ± 2.738	1.833 ± 3.086	0.4417
LF (nu)	57.173 ± 9.468	43.493 ± 13.531	< 0.0001##
HF (nu)	42.260 ± 8.795	55.980 ± 13.650	< 0.0001##
LF/HF	1.469 ± 0.5050	0.8943 ± 0.4630	< 0.0001##
TP (ms^2)	277.20 ± 108.15	206.77 ± 144.86	0.0048#

Highly significant##Extremely significant

IV. DISCUSSION

We compared short term HRV measures of male and female healthy volunteers. The outcome of this study was a significant low HF, high LF, TP and LF/HF ration in females.

It is well established that LF power reflects modulation of sympathetic tone with contribution from the parasympathetic tone, while HF power reflects the modulation of parasympathetic tone alone12. Significant higher LF/HF ratio of females indicates the presence of Sympathovagal imbalance. However, LF/HF ratio as assessed by spectral analysis of HRV is considerably reduced resulting in significant reduction in both LF and HF power. As remarkable decrease in total power of HRV is not an ideal indicator of Sympathovagal balance, especially when heart rate variability is considerably reduced resulting in significant reduction in both LF and HF may not be associated with proportionate alterations in LF and HF power, decreased HRV representing poor vagal modulation of cardiac activities could possibly manifest with decreased LF/HF ratio. Therefore, changes in LF/HF ratio should be corroborated with classical autonomic function tests such as heart rate and blood pressure response to orthostatic challenges, deep breathing and isometric handgrip. Thus, the present study reveals that a greater degree of vagal with drawl and relatively less increase in sympathetic drive contribute to the early development of Sympathovagal imbalances in females cannot be ascertained, it could be suggested that female sex hormones contributes to these autonomic dysfunctions.

V. CONCLUSION

There was significant difference in frequency domain analysis. Higher LF power, TP, LF/HF ratio and Lower HF values is seen in females.

VI. FUTURE DIRECTIONS

Future studies should include more accurate methods of assessment of cardiac autonomic activity such as plasma Catecholamine or metabolites of Catecholamine in urine like Vanillylamandelic acid (VMA), Metanephrine and Normetanephrine.

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