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Sympathovagal Imbalance in Newly Diagnosed Essential Hypertension

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Abstract: *Hypertension affects nearly one billion people worldwide and kills approximately nine million people every year. Greater sympathetic drive has been established in early stages of essential hypertension. Heart rate variability (HRV) analysis is a specific, sensitive and non invasive tool to evaluate cardiac autonomic functions. The study included a total of 73 participants in age group 29-48 years, of which 38 had newly diagnosed essential hypertension and 35 were healthy volunteers. NN interval time series was extracted from ECG records it by removing all non sinus beats and HRV analysis performed to obtain time domain & frequency domain measures. Results showed a significant fall in absolute values of time domain parameter RMSSD ($p<0.05$), NN50 ($p<0.05$) & highly significant fall ($p<0.01$) in pNN50 values in hypertensive subjects , thus indicating decreased parasympathetic activity in hypertension. In frequency domain measures the LFnu was significantly higher in hypertensive individuals ($p<0.05$) whereas HFnu showed significant decline in hypertensive subjects ($p<0.05$). Consequently the LF/HF ratio which is a sensitive indicator of sympathovagal balance showed a highly significant ($p<0.01$) rise in hypertensives. Thus, Sympathovagal imbalance was noted in hypertensives with overall balance in favor of sympathetic predominant activity which may contribute significantly to the target organ damage associated with the hypertension*.

Keywords: *hypertension, heart rate variability, symapthovagal imbalance*

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I. Introduction

Hypertension is a silent, invisible killer affecting nearly one billion people worldwide and killing approximately nine million people every year.[1] In India about 35.25% of people are having hypertension.[2] According to the 7th Joint National Committee (JNC-VII), the Hypertension is defined as persistently elevated blood pressure of, any one of the following, systolic blood pressure (SBP) more than or equal to 140 mm Hg or diastolic blood pressure (DBP) more than or equal to 90 mm Hg.[3] There is a considerable evidence to suggest that autonomic nervous system plays an important role in the regulation of blood pressure and consequent development of hypertension. Greater sympathetic drive has been established in early stages of essential hypertension suggesting that autonomic dysregulation may be the key to the etiology, progression as well as the subsequent end organ damage seen in hypertension.[4] Heart rate variability (HRV) analysis is a specific, sensitive and non invasive tool to evaluate cardiac autonomic functions. It describes the oscillations in the interval between consecutive heart beats (RR interval), as well as the oscillations between consecutive instantaneous heart rate.[5]

II. Material and methods

The present study was conducted in the Autonomic Function Lab of the Department of Physiology, LLRM medical college, Meerut (UP) with prior approval of institutional Ethical Committee**.** In this study, 38 newly diagnosed untreated non obese patients of either sex having essential hypertension were randomly selected from the Medicine OPD of SVBP Hospital, Meerut in the age group of 29-38 years along with 38 age and sex matched normotensive volunteers taken from healthy attendants of the patients as well as staff of institution for comparison**.**

The following subjects were excluded:-Subjects unwilling or not consenting to participate in study, Subjects having gross ECG abnormalities, Subjects having history of systemic diseases causing altered HRV like Diabetes mellitus, preexisting cardiac diseases , history of alcoholism, smokers and tobacco users as well as Subjects on drugs like steroids, anti-arrhythmic or antihypertensive medications. Before starting the procedure a detailed history was taken from all subjects and a written informed consent obtained. All participants were requested to refrain from eating 2 hours prior to recording, as well as to avoid heavy exercise and intake of alcoholic and caffeinated beverages from the previous night. On the test day, basic anthropometric data were taken. A baseline heart rate as well as blood pressure were also recorded in all the subjects as per updated American Heart Association guidelines [6].

Thereafter subjects were allowed rest for 10 minutes duration and then a short-term 5-minute, lead II ECG recording was obtained in lying posture at screen sweep speed of 200mm/s at a voltage of 10mm/mV using a four channel digitalized polygraph data acquisition system Physiopac - 4 (Medicaid systems and Neuro labs, Chandigarh) as per guidelines of international task force[5]. The recording thus obtained was then transferred for HRV Analysis. The HRV analysis was done using "HRV analysis software, version 1.1" developed by Biosignal analysis group, University of Kubios , Finland. The NN interval time series was extracted from ECG records it by removing all non sinus beats. The statistical methods were applied to obtain time domain measures. They included Mean HR, Mean RR, RMSSD (Square root of the mean of the sum of the squares of differences between adjacent NN intervals) ,NN50 count (the number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording) & pNN50(number of successive difference of intervals, which differ by more than 50 ms, as proportion of total beat cycles) [5,7].

The frequency domain analysis was also performed using the parametric i.e. Auto-regression (AR) model. It involves decomposition of the series of sequential RR intervals into a sum of sinusoidal functions of different amplitudes and frequencies thereby dividing entire spectrum into frequency bands. Low frequency band LF_{nu} (0.04 - 0.15 Hz, High frequency band HF_{nu} (0.15 - 0.4 Hz) LF/HF Ratio (the ratio between the power of Low Frequency and High Frequency bands) were obtained .[5,7]The data thus obtained was analyzed by Student`s unpaired t-test with a p value ≤ 0.05 considered to be significant.

III. Results

The study included a total of 73 participants in age group 29-48 years, of which 38 had newly diagnosed essential hypertension and 35 were normal healthy volunteers. The table 1 exhibits that there was a significant fall in absolute values of time domain parameter RMSSD ($p<0.05$) and NN50 and along with a highly significant fall ($p<0.01$) in pNN50 values in hypertensive subjects as compared to the controls i.e., when hypertensives were compared with control group, a significant decrease existed not only in RMSSD values but also in NN50 ($p<0.05$) and pNN50 ($p<0.01$) as well, thus indicating decreased parasympathetic activity in hypertension. Table 2 depicts that in frequency domain measures the LFnu values indicating the sympathetic activity increases significantly in hypertensive individuals ($p<0.05$) when compared to normotensives. The values of HFnu similarly declined significantly in hypertensive subjects ($p<0.05$) indicating a significant decline in parasympathetic activity. Consequently the LF/HF ratio which is a sensitive indicator of sympathovagal balance shows a highly significant ($p<0.01$) rise in hypertensives.

Table 1: Comparison Of Time Domain Measures Control Vs Hypertensive

Parameters	Control (n= 35) Mean ± SD	Hypertensive (n=38) Mean ± SD	p-value
MEAN RR (s)	0.78 ± 0.11	0.73 ± 0.13	0.08
MEAN HR (beats/min)	81.61 ± 10.19	84.13 ± 10.17	0.29
RMSSD (ms)	24.25 ± 12.18	17.89 ± 13.14	0.035*
NN50 (count)	8.62 ± 7.19	5.65± 5.68	0.05*
pNN50 (%)	6.97 ± 4.87	4.27 ± 3.47	0.008**

*p value ≤0.05 significant **p value ≤0.01 highly significant

Table 2: Comparison Of Frequency Domain Measures Control Vs Hypertensives

Parameters	Control (n= 35) Mean ± SD	Hypertensive (n=38) Mean ± SD	p-value
LF nu	67.36 ± 14.32	74.51 ± 18.41	0.025*
HF nu	22.30 ± 15.4	15.43 ± 12.58	0.03*
LF/HF ratio	4.62 ± 3.15	9.19 ± 8.68	0.005**

*p value ≤0.05 significant **p value ≤0.01 highly significant

IV. Discussion

Mancia et al (2014) reviewed role of autonomic nervous system in hypertension and found evidence of an attenuation of autonomic cardiovascular control in essential hypertension. It was noted that adrenergic overdrive is a major component of this autonomic dysregulation. This adrenergic activation has an early appearance in the course of the disease and becomes more pronounced with the increasing severity of the hypertensive state. The evidence showed that adrenergic mechanisms also participate in the development of target-organ damage, which is frequently detectable in patients with hypertension.[8]

Vanderlei et al (2009) concluded that HRV is a measure that can be used to assess the ANS modulation under physiological conditions such as wakefulness and sleep conditions, different body positions, physical training and also pathological conditions. Changes in the HRV patterns provide a sensible and advanced indicator of health involvements. Higher HRV is a signal of good adaptation and characterizes a healthy person with efficient autonomic mechanisms, while lower HRV is frequently an indicator of abnormal and insufficient adaptation of ANS [9]

The findings in our study are similar to Viratnen et al (2003) who compared 191 newly diagnosed untreated hypertensive men and women, 35–54 years of age with a random population sample of 105 normotensive men and women. It was observed that time domain measures of heart rate variability RMSSD, SDNN were reduced significantly in hypertensive subjects ($p<0.01$) as compared with normotensive controls [10]. Desilva et al (2004) also reported a significant decrease in RMSSD and pNN50 values ($p<0.05$) on comparing the HRV parameters in hypertensives without LVH to the individuals with normal values of blood pressure [11]. Natrajan et al (2011) also found that LFnu values of hypertensives were significantly increased compared to the normotensives and HFnu in hypertensives was significantly decreased compared to the normotensives. The LF/HF ratio was also found to be significantly high in the hypertensive group ($p<0.001$) [12]

Our results also parallel these studies with a decreased parasympathetic activity, as indicated by RMSSD and NN50, found in hypertensive subjects. The frequency domain measures in this study also indicate that there is indeed a sympathetic predominance associated with the higher values of blood pressure. A decline in parasympathetic activity was also seen along with the increased sympathetic activity thereby further re-establishing a sympathetic predominant output in hypertension.

V. Conclusion

The middle aged subjects with essential hypertension showed decreased parasympathetic activity on the time domain measures of HRV. A significant fall in the parasympathetic activity was noted on frequency domain measures also in these individuals. The sympathetic activity as measured by frequency domain parameters was also found to be increased in the hypertensives. Therefore a Sympathovagal imbalance (SVI) was noted in the hypertensive individuals with the overall balance (LF/HF Ratio) in favor of sympathetic predominant activity. This SVI may be present even before the onset of end organ damage and rather contribute to the target organ damage associated with the hypertension. Thus HRV may be used as early indicator as well as for monitoring of disease progression in hypertensive individuals.

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