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Study of Cardiac Autonomic Activity using Heart Rate Variability in Normotensive Children of Hypertensive Patients

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Abstract

Introduction: Hypertension is an iceberg disease which is a risk factor for cardiovascular mortality. 45% of children with hypertensive parents have got a possibility of developing hypertension. HRV is a tool to identify autonomic dysfunction. *Materials and Methods:* 50 normotensive male cases with the parental history of hypertension and 50 age-matched healthy male controls were selected for the study. ECG was digitally recorded using BPL Cardiart 1087 ECG machine & Analog Digital Converter (NI-DAQ 7.5) and analyzed for SDNN, LF, HF, LF/HF ratio and E: I ratio. *Results & Conclusion:* SDNN, E: I ratio, HFnu were significantly reduced and LFnu & LF/HF ratio was significantly increased in cases. This indicated a reduced parasympathetic activity and increased sympathetic activity.

Keywords: Heart Rate Variability; Cardiac Autonomic Activity; Hypertension; Sympathetic Overactivity; Parasympathetic Withdrawal.

Introduction

Globally, hypertension (HTN) is an "iceberg" disease. It is one of the major risk factors for cardiovascular mortality which accounts for 31% of all deaths. Hypertension can lead to a variety of complications such as cardiac failure, stroke, and renal damage. Thus, research to identify potential risk factors causing HTN is of great importance.

Early identification of risk factors can be used to prevent HTN and complications of HTN by suitable lifestyle modifications [1]. Family studies have shown that the possibility of developing HTN in children of hypertensives is 45% [2]. Normotensive siblings with a parental history of hypertension are known to be characterized by altered cardiovascular morphology and reactivity. Although the reason for this has not yet been completely clarified, it has been suggested that an imbalance in the autonomic nervous system (ANS) might play an important role.

Sympathetic overactivity and parasympathetic withdrawal are seen in overt HTN. It is also known that all the children of hypertensives will not progress to overt hypertension. This study intends to evaluate the autonomic functions in the children of hypertensives so as to identify the risk factor for hypertension development. Dysregulation of the ANS has been implicated in the development of HTN [3]. There are several tests to determine the autonomic activity. Recently the most accepted tool is Heart Rate Variability (HRV) [4]. HRV is a noninvasive tool to quantitatively estimate cardiac autonomic activity and has been used to document decreased cardiac autonomic activity in HTN. If autonomic dysfunction can be detected before the occurrence of overt HTN, it might help in designing of a scheme for early detection of HTN. Early identification of autonomic dysfunction in an individual will provide an opportunity for implementation of lifestyle modifications, such as weight reduction, moderate-intensity aerobic exercise program, which may prevent or postpone the occurrence of HTN. This study is an effort to assess the cardiac autonomic activity using HRV in normotensive subjects with the parental history of HTN.

Methodology

This is a case-control study done on the student community of Sri Siddhartha University, Tumkur. The study period is of 1-year duration between July 2009 and June 2010. Among the students who had the family history of HTN, 50 males who met with our inclusion criteria were selected for the study.

Inclusion Criteria

1. Healthy normotensive children of hypertensives (either or both parents are hypertensives) in the age group between 18-25 years. The hypertensive status of the parents was based on the information given by the subjects.

Exclusion Criteria

1. Subjects with HTN
2. Subjects with cardio-respiratory diseases.
3. Subjects on drugs like antihypertensives (amlodipine, atenolol, etc), drugs affecting the autonomic nervous system like alpha blockers (phentolamine), beta-blockers (propranolol) and others which might have an effect on HRV.
4. Subjects with the parental history of diabetes mellitus.

Fifty (50) healthy subjects, matched for age and gender, without the family history of HTN were selected from the same student community. These formed the control group.

Informed written consent was taken from all the subjects prior to the investigation. The cases and the controls were examined for general physical health. Weight, height, waist circumference & hip circumference were measured using standard procedures. Body mass index (BMI) was calculated as

BMI = Weight (kilograms) / Height (Meters^2)

Waist/Hip ratio was calculated as WHR = Waist circumference (cms) / Hip circumference (cms).

Resting pulse rate was counted for one minute using the radial artery. Average of three pulse readings was taken as resting pulse rate. BP was measured on the left arm in a supine position using mercury column sphygmomanometer. An average of three readings was taken as BP.

Procedures were conducted in the presence of subject's attendant.

Measurement of Heart Rate Variability (HRV) parameters[4]

A patient was explained in detail about the ongoing procedure and ECG was digitally recorded using BPL Cardiart 1087 ECG machine & Analog Digital Converter (NI-DAQ 7.5). The patient was made to lie down on a couch for 10 minutes and allowed to relax. ECG was recorded in lead II only, as the requirement for the procedure was only peak detection for the determination of RR intervals. First, a 5 minutes ECG in supine position was recorded, with subject breathing normally. Then, a deep breathing ECG was recorded for 2 minutes. The subject was trained to breathe at a rate of 6 cycles/min under oral instructions with each cycle comprising of 5seconds of inhalation and 5seconds of exhalation. The ECG recordings were converted from analog format to digital format using the Analog Digital Converter and the data was stored in notepad which was subsequently analyzed using HRV soft version 1. 1 software.

Instruments used

- ECG machine (BPL Cardiart 1087/MK-V) was used to acquire the analog ECG signal from the subject.
- Analog to digital converter (National Instruments NI-DAQ 7.5 USBD 6008) was used as the hardware, which converted the analog to digital signal and processed it to the computer with the help of the NI-DAQ software.
- HRV soft (version 1.1) was used to detect the peak to peak intervals and to analyze HRV parameters.

Parameters used [4]

The following are the parameters recorded in each group-

The analysis of HRV was considered under two headings – Time Domain analysis & Frequency Domain analysis. All the various parameters of HRV like Standard deviation of Normal to Normal intervals (SDNN), Low-frequency power (LF), High-frequency power {HF), LF/HF ratio, LF normalized units (LFnu) and HF normalized units (HFnu) were deduced using resting ECG recording. Expiratory: Inspiratory ratio (E: I ratio) was deduced using the deep breathing ECG recording. The analysis of the data was done by the principal investigator. Random cross verifications of data analyses were done by co-investigator.

Statistical Software

The Statistical software namely SPSS 15.0 was used for the analysis of the data and Microsoft Excel has been used to generate graphs & tables. The data was analyzed for descriptive statistics like numerical data expressed as mean±standard deviation and non-numeric data expressed as percentages. Inferential statistics like Chi-square test was used to calculate significance. p value <0.05 was considered significant.

Results

This study included 100 subjects of which 50 were cases and 50 were age- and gender-matched controls.

The physical parameters of the cases and controls were matched. There were no significant differences in the systolic and diastolic blood pressures between the groups (Table 1).

The ECG recordings were analyzed for HRV parameters using HRVsoft. SDNN was significantly reduced in the cases (81.32±37.98) compared to the controls (48.56±26.05) (Table 2).

E: I ratio was significantly less in the cases (1.65±0.22) in comparison to the controls (1.42±0.25) (Table 2).

HFnu was significantly less whereas LFnu was significantly more in the cases compared to the controls (Table 3).

There was a significant increase in the LF/HF ratio in the study group in comparison with the control group. (Table 3).

Table 1: Comparison of basic characteristics between controls and cases

	Group	N	Group Statistics Mean	Std. Deviation	T
Age(Yrs)	Controls	50	19.2800	1.51240	1.732
	Cases	50	18.8000	1.24540	p=0.086
Height (cms)	Controls	50	168.7400	13.28619	0.351
	Cases	50	167.9400	9.09678	p=0.726
Weight (cms)	Controls	50	65.4000	11.64965	2.003
	Cases	50	60.9500	10.54255	p=0.048
Waist-hip Ratio (WHR)	Controls	50	0.8510	0.04367	1.498
	Cases	50	0.8346	0.06393	p=0.136
Heart Rate (beats per minute)	Controls	50	78.1600	6.91747	1.074
	Cases	50	79.5800	6.29250	p=0.286
SBP (mm/Hg)	Controls	50	115.2800	5.85205	0.225
	Cases	50	115.5600	6.59363	p=0.283
DBP (mm/Hg)	Controls	50	76.6000	6.93115	0.116
	Cases	50	76.7600	6.91511	p=0.908

Results are presented as Mean ±SD
p<0.001 –Significant

Table 2: Comparison of Time Domain parameters between controls and cases

	Group	N	Mean	Std. Deviation	T
SDNN(ms)	Controls	50	81.32	37.98	5.029
	Cases	50	48.56	26.05	P<0.001
E:I	Controls	50	1.65	0.22	4.854
	Cases	50	1.42	0.25	p<0.001

Results are presented as Mean ±SD
p<0.001 –Significant

Table 3: Comparison of Frequency Domain parameters between controls and cases

	Group	N	Mean	Std. Deviation	t
LF(nu)	Controls	50	39.54	12.03	8.231
	Cases	50	63.58	16.79	p<0.001
HF(nu)	Controls	50	60.41	11.77	8.280
	Cases	50	36.40	16.78	p<0.001
LF/HF	Controls	50	0.76	0.62	6.25
	Cases	49	2.50	1.87	p<0.001

Results are presented as Mean ±SD
p<0.001 –Significant

Discussion

This study intended to evaluate the autonomic function in children of hypertensives. Because of a paucity of female subjects, who didn't voluntarily get recruited for the study, only male subjects were recruited. 50 cases and 50 age, gender, BMI, and WHR matched controls were recruited from the same student community.

The cardiac autonomic activity can be assessed by several methods like Valsalva maneuver, deep breathing test, handgrip test, cold pressor test, lying down to standing test, etc. But HRV has evolved as a specific and sensitive noninvasive tool to evaluate cardiac autonomic activity, which expresses the total amount of variation of both instantaneous heart rate and RR intervals. HRV indicates the extent of neuronal damage to an autonomic nervous system [4].

The SDNN values reveal the alterations in the autonomic tone that are predominantly vagally mediated [4-8]. In this study, the SDNN values were significantly reduced in children of hypertensives thus suggesting the reduction in the resting parasympathetic activity. The E/I values also reveal the contribution of the parasympathetic component in altering the heart rate during respiratory cycles [4-8]. In this study the values of E/I ratio were also significantly reduced in children of hypertensives thus further supporting the above finding of reduced parasympathetic activity [9].

The LF nu values are considered as a measure of sympathetic activity [4,5-8]. In this study, the LF nu values were significantly increased in children of hypertensives thus suggesting the presence of elevated cardiac sympathetic activity in them. This correlates with the results of the study done by Stolarz K et al. [10].

The HF nu values are considered as a measure of parasympathetic activity [4,5-8]. In this study the HF nu values were significantly reduced in children of hypertensives, which further adds on to the earlier finding of decreased cardiac parasympathetic activity [11].

The LF/HF values reveal the global sympathovagal balance [4-8]. In this study the LF/HF values were significantly higher in children of hypertensives when compared to children of normotensives thus suggesting the alteration in the sympathovagal balance towards the sympathetic component. This is in corroboration with the recent report that exaggeration of increased sympathetic activity facilitates the onset of hypertension in prehypertensives [12].

The fact that the offspring of hypertensive parents were still normotensives indicates that the observed changes in cardiovascular responsiveness occur at an early stage. They are probably of genetic origin and could play a role in the pathogenesis of hypertension. Indeed, a hyper-reactivity of the SNS has long been suspected in the development of hypertension, but most studies have yielded inconsistent results [13].

Emily B, Schroeder et al. [3], have investigated the temporal sequence linking hypertension and HRV. According to them, individuals with HTN had decreased HRV at baseline, and this association was present across the full blood pressure range.

The Framingham heart study showed that the presence of reduced LF in men is a risk factor for developing hypertension [14].

Sevre K et al. [15] showed that in hypertensive subjects there was decreased HRV compared to controls using 2-hour Holter ECG recordings. Virtanen R et al. [16] have studied the relations between HRV, HTN, lifestyle factors and renin-angiotensin-aldosterone system According to this study, all absolute measures of HRV were reduced in hypertension.

HTN is a major cause for morbidity and mortality in developed and developing countries.

Development of HTN is dependent on a number of environmental and dietary factors. There is strong evidence to suggest that HTN runs in families. The manifestation of HTN is likely to be affected by dietary and environmental factors to varying extent. An insight into the heritability, the contribution from father and mother to the expression of HTN will give ample opportunities to modify the other factors in order to prevent or postpone the onset of hypertension.

Syed Faraz Kazim et al. have studied the relationship between blood pressure levels and BMI between children of hypertensive and normotensive parents. Children of hypertensive parents had a significantly higher mean systolic, diastolic blood pressure and BMI [17]. Based on the observation, they have concluded that there is a strong genetic basis for essential hypertension and significant inheritability [18,19]. Asymptomatic children of hypertensive parents are reported to develop essential hypertension during the first two decades of life [20] Jens Tank et al., based on a study on the normal twins, have concluded that baroreflex sensitivity is strongly influenced by genetic factors. Identification of gene influencing baroreceptor sensitivity will provide an important clue for a comprehensive understanding of cardiovascular regulation and pathogenesis of cardiovascular disease [21].

Thus the study shows the presence of reduced parasympathetic activity & reactivity in children of hypertensives. In addition, this study also showed an elevated level of resting sympathetic activity in children of hypertensives. Thus, it showed a definite shift in the sympathovagal balance towards the sympathetic component.

The autonomic nervous system plays a crucial role in blood pressure and heart rate control and may thus be an important pathophysiological factor in the development of hypertension [22]. An early detection of risk of developing HTN can be used to institute prevention strategies, to decrease associated morbidity and mortality.

Our study has a shortfall of not having female subjects. It has also not accounted for the effect of the history of hypertension in single parent and both parents on autonomic functions.

Summary

This is a case-control study of 50 normotensive male children of hypertensives and 50 normotensive healthy age-matched males. The heart rate variabilities of these groups were analyzed using HRV soft. The cases were found to have increased sympathetic activity and reduced parasympathetic activity. This increases the risk for developing hypertension in later life. A further study including female subjects and a long-term follow-up is needed.

Conclusion

From our study, it can be concluded that there are increased sympathetic activity and a parasympathetic withdrawal in children hypertensives. This can act as a risk factor for the development of hypertension in later life. These children have to undergo lifestyle modification to reduce the risk of developing hypertension.

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