Research Article

Autonomic reactivity in normal healthy children of hypertensive's

Premaraja R[1*], Chandra S[2]

[1]P G Student, [2]Professor, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Kalitheerthal Kuppam, Puducherry – 605110, INDIA.
Email: premaraja_r@yahoo.com

Abstract

Objectives: Aim of the study was to compare the reactivity between the offspring of normotensive parents and hypertensive parents. Autonomic functions were compared during rest and during physical stress. **Study Design:** Study was done with 80 subjects divided into two groups of 40 each. Subjects were grouped by the presence of parental hypertension ≥5 years. Blood pressure of ≥140/90 mm of Hg was used for classification (WHO Classification). Blood pressure of ≤120/80 mm of Hg was used for normotensives. Subjects were all normotensive and were in the age group of 18-27 years. Autonomic functions and heart rate variability were recorded for the study and compared between both the groups. **Results:** The basal Systolic ($P<0.05$) and diastolic pressures ($P<0.05$) and pulse rate ($P<0.05$) were found to be elevated in the study group. Autonomic functions such as heart rate and blood pressure changes during standing ($P<0.05$), cold pressor test ($P<0.0001$) and Valsalva maneuver ($P<0.05$) significantly differed between the groups. Heart rate variability showed elevated LF/HF Ratio ($P<0.0001$) and SDNN and RMSSD were decreased in the study groups ($P<0.05$). **Conclusion:** Heart Rate Variability and autonomic functions testing showed significantly increased sympathetic tone and the decreased parasympathetic activity before the onset of hypertension in predisposed individuals. This was evidenced by abnormality in basal levels of autonomic functions in rest and during reactivity to the physical stress in the subjects.
Keywords: Autonomic functions Heart rate variability Children of hypertensive parents.

*Address for Correspondence:
Dr. Premaraja R., P G Student, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Kalitheerthal Kuppam, Puducherry – 605110, INDIA.
Email: premaraja_r@yahoo.com
Received Date: 22/08/2015 Accepted Date: 22/08/2015

Access this article online	
Quick Response Code:	Website: www.statperson.com
	DOI: ---

INTRODUCTION

Hypertension is a known risk factor[1] for cardiovascular disease mortality and morbidity. This along with other chronic diseases affects health of people globally.[2] Prevalence of hypertension in India and particularly south India is found to be increasing according to recent studies.[2,3] As of 2013 32.5% and 30.4% of men and women are affected by hypertension in India.[4] Early identification of hypertension is important to prevent the development of both the disease and its complications. Most of the cardio vascular disease related deaths (>80%) are occurring in low and medium income countries.[5] The immediate biological risk factors are hypertension, dyslipidaemia and diabetes.[5] In addition to these behavioural risk factors like diet, physical activity and tobacco. Globalization, social inequity, poverty, rural to urban migration, educational status and cultural norms are the causes which influence the behavioural changes There is inadequate funding and incentives to control the non-communicable diseases such as cardio vascular diseases.[6] This problem is worse in low and medium income countries and therefore the mortality due to non-communicable diseases is high. Availability of easy and affordable essential medicines is needed to prevent and treat cardio vascular disease.[19] There is poor availability of effective medicines in the low and medium income countries. The individual users have to purchase the medicines on their own from private sector and it puts a heavy financial burden both on society and individuals. In India health care costs accounts for about 40% of household income and an adult male is 20% more likely to have spent in account of cardiovascular disease.[8] Increasing the awareness and availability of medicine at affordable cost or distribution through public sector is the strategy now proposed following the example of treating HIV (Human Immunodeficiency Virus) Infection.[9] Hypertension is characterized by a sustained elevation of systemic blood pressure. Heart rate, stroke volume and peripheral vascular resistance are the factors influencing blood pressure which are controlled by the autonomic nervous system.[10] Autonomic nervous functions in turn depend up on gender and genetic factors.[10] Some studies show increased sympathetic and some show decreased parasympathetic tone contributing to development of hypertension.[11,12] This study was aimed to see the abnormal reactivity of the autonomic nervous system in both rest and physical stress such as change in posture, temperature and breathing in offspring of hypertensive parents. In this study analysis of heart rate variability is used to assess the sympathovagal balance in the development of hypertension.

MATERIALS AND METHODS

The study was conducted in the subjects selected from students, staff and patients attending the hospital of Sri Manakula Vinayagar Educational Trust, Pondicherry. Study was conducted in 80 subjects divided into case and control groups of 40 each. Study protocol was explained to the subjects and informed and written consent was taken before the study. Previous study data was used for calculating number of subjects needed for the study.[13-16] Study group (cases) Offspring of Hypertensive parents with parental hypertension (Blood pressure ≥140/90 mm of Hg - WHO Classification[17]) Control group (controls) – Offspring of Normotensive parents (Blood Pressure ≤ 120/80 mm of Hg)

Inclusion Criteria

Age from 18 – 27 years, Male, clinically normal subjects, Normotensive, Non-smoker, Non-alcoholic and Parental hypertension ≥5 year.

Exclusion Criteria

Individuals with existing cardiovascular, respiratory, renal or endocrine diseases, obese individuals (BMI ≥ 30), athletes, hypertensive subjects and subjects with history of any drug intake affecting autonomic functions.

Parameters

Resting pulse rate and blood pressure were recorded after 10 minutes of rest in lying posture. Blood pressure was taken in both right arm and left arm using mercury sphygmomanometer. Blood pressure response to standing was measured in left arm of the subject in supine position before and after 1 minute of standing. Blood pressure response to cold pressor test was recorded in the left arm while the right hand is immersed up to wrist for one minute in 2-4 degree Celsius water.[18] Electrocardiogram was recorded with RMS Polyrite in standard limb lead II for Heart rate response to standing and Valsalva maneuver. Minimum R-R interval around 15th beat and maximum R-R interval around 30th beat after standing from supine position was used for calculating 30-15 ratio. Heart rate response to Valsalva-Weber maneuver[19] - subject was asked to blow in the sphygmomanometer to raise the pressure to 40 mmHg and maintain it for 15 seconds and Valsalva ratio was calculated using the ECG recorded during procedure.

Heart rate variability

European task force recommendations were followed for recording and interpretation of data.[20] ECG in standard lead II configuration was recorded for 5 minutes in supine position after 15 minutes of rest in the same position. Data acquisition was done by using computerized ambulatory ECG system (Niviqure, Bangalore). 1024 samples per second rate were used for recording and analysis. Acquired data was used for processed in HRV analysis software, version 1.1, from Biomedical Signal Analysis Group, Finland. Time domain and Frequency domain analysis were used on the data. Fast Fourier Transformation was used for frequency domain analysis. Power (n.u) normalized units were used for frequency domain of LF, HF and LF/HF ratio. Mean RR, SDNN (Standard deviation of all normal R-R intervals), RMSSD (Square root of the mean squared differences of successive normal to normal intervals) and pNN50 (Percentage of differences between successive RR intervals that are greater than 50 msecs) were used for Time Domain analysis.

Statistical Analysis

Values were expressed as mean ± SD and Unpaired Student't' test was done using SPSS Version 17 for comparison between cases and control groups. P values less than 0.05 were taken as significant.

RESULTS

Resting pulse rate, systolic and diastolic pressures between cases and controls were significantly different with p value <0.05. Table: 1

Table 1: Resting Vital Parameters

Parameters	Cases	Controls	P value
Resting pulse rate/ minute	69.45±8.68	65.53±8.45	0.044
Resting Systolic Blood Pressure mm of Hg	117.25±9.5	111.25±6.41	0.001
Resting Diastolic Blood pressure mm of Hg	73.15±7.71	68.75±5.01	0.003

Blood pressure response to standing Both systolic and diastolic blood pressures showed a statistically significant difference between the cases and controls P<0.05. Table:2

Table 2: Blood pressure response to standing

Parameters (Blood Pressure in mm of Hg)	Cases	Controls	P value
Lying down Systolic	117.25±9.50	111.25±6.41	0.001
1 min after standing systolic	113.50±10.01	108.05±6.60	0.005
Lying down diastolic	73.15±7.71	68.75±5.01	0.003
1 min after standing diastolic	83.10±7.30	78.15±7.90	0.005

Blood pressure response to cold pressor test. Blood pressure changes were statistically very different with P value <0.0001 between the control and case groups in cold pressor test. Table: 3

Table 3: Cold pressor test

Parameters (Blood Pressure in mm of Hg)	Cases	Controls	P value
Before immersion systolic	118.00±11.01	109.10±7.49	<0.0001
1 min after immersion systolic	128.05±12.64	118.70±10.90	0.001
Before immersion diastolic	76.35±7.05	70.45±6.78	<0.0001
1 min after immersion diastolic	85.30±7.78	78.55±6.34	<0.0001

Heart rate response to standing In heart rate response to standing only 30/15 ratio was statistically significant between the case and control groups P<0.05. Table: 4

Table 4: Heart rate response to standing

Parameters	Cases	Controls	P value
Maximum R-R interval at 30th beat in seconds	0.75±0.135	0.71±0.100	0.098
Minimum R-R interval at 15th beat in seconds	0.53±0.055	0.54±0.096	0.405
30/15 ratio	1.433±0.203	1.335±0.212	0.038

Heart rate response to Valsalva-Weber maneuver In Valsalva maneuver only Valsalva ratio during the maneuver was statistically significant P<0.05. Table: 5

Table 5: Heart rate response during Valsalva maneuver

Parameters	Cases	Controls	P value
RR interval in seconds after Valsalva maneuver	0.692±0.106	0.719±0.103	0.258
RR interval in seconds during Valsalva maneuver	0.443±0.087	0.424±0.049	0.184
Valsalva Ratio	1.586±0.253	1.716±0.288	0.036

Heart rate variability

Results were tabulated as Frequency domain and Time domain analysis. All of them were statistically different between cases and controls P<0.05. Table: 6 and Table: 97.

Table 6: Frequency Domain analysis

Parameters	Cases	Controls	P value
LF normalized unit	57.58±7.05	41.31±7.42	<0.0001
HF normalized unit	41.87±7.57	58.04±8.42	<0.0001
LF/HF Ratio	1.43±0.51	0.76±0.21	<0.0001

Table 7: Time Domain analysis

Parameters	Cases	Controls	P value
Mean RR (sec)	0.882±0.12	0.935±0.11	0.045
SDNN (sec)	0.036±0.014	0.503±0.019	0.001
RMSSD (msec)	33.53±16.45	55.85±24.67	<0.0001
pNN50	12.93±13.75	32.09±19.82	<0.0001

DISCUSSION

Around 26% of the world adult population was suffering from hypertension according to a study by Kearney *et al*, published in Lancet 2005.[21] This was projected to increase up to 29% of the population by 2025. Which in other words around 1.5 billion people will be having hypertension by 2025.[21] Hypertension was associated with number of risk factors such as smoking, diet, body weight, sedentary lifestyle, age, sex, sodium intake, vitamin D intake[22], potassium intake and family history of hypertension.[23] Gene and gender, race all were associated with hypertension.[24] Interaction between gender and genetic causes are not understood fully. Estrogens related genes were also found to be involved in regulation of blood pressure seems to be one of the causes of gender related hypertension.[25] Chromosomes 6 and 7 were found to be associated with hypertension.[26] Single Nucleotide Polymorphisms were found in 3 regions in chromosomes 6 and 7. All those could be causes genetic association in hypertension. Autonomic nervous system is responsible for maintaining the homeostasis of perfusion to the organs. Both the major divisions of autonomic nervous system namely sympathetic and parasympathetic are involved in maintaining the homeostasis. Sympatho-Vagal imbalance was involved with many cardiovascular diseases. Sympatho-Vagal imbalance causes stimulation of cardiac myocyte growth and vascular remodeling. This elevates vascular resistance and changes myocardial thickness.[27] Thus Sympatho-Vagal imbalance was involved in pathology of both hypertension and cardiovascular diseases.

Cardio vascular reactivity

Cardio vascular reactivity is defined as the pattern of individual's hemodynamic responses to behavioral or psychological stressors.[28] It was established to have a predictive role in development of essential hypertension and other cardio vascular diseases.[28] **Resting Blood Pressure:** Offspring of hypertensive parents are found to be having higher systolic and diastolic blood pressure levels in this present study. The elevation of basal blood pressure itself is risk factor for essential hypertension and other cardio vascular diseases.[29-32] The present study also showed a significant increase in heart rate in the offspring of hypertensive parents. **Autonomic function tests:**[33] Autonomic function tests were used widely in clinical trials and tests such as blood pressure responses to dynamic exercise or stress can be risk marker for essential hypertension or cardio vascular disease as established by several studies.[34] **Blood pressure response to standing:** Both diastolic and systolic blood pressures were elevated compared to controls in cases when recorded after 1 minute after standing. This showed an elevated sympathetic tone in the study group. The results were statistically significant. **Cold pressor test:** Cold pressor test was established as a predictive tool in development of hypertension by various studies.[35,36] In the present study the results showed statistically significant increase in the sympathetic tone in the cases compared to controls. **Heart rate response to standing:** The 30:15 ratios is an index of cardio vagal function. The ratio was elevated in cases compared to controls, which was statistically significant. **Heart rate response to Valsalva maneuver:** This is also a method for cardio vagal function. The Valsalva ratio was significantly different between the cases and controls. The ratio was decreased in cases compared to control group showing a decreased cardio vagal function in the group studied. **Heart rate variability** One of the most established tests for assessing the autonomic function.[17]

Frequency Domain Analysis

LF_{nu} (Low Frequency spectrum of heart rate variability in normalized units) indicates the sympathetic activity.[20,37] In the present study LF_{nu} was very significantly increased in the study population compared to the control population showing increased sympathetic activity. The P value is <0.0001.HFnu (High Frequency spectrum of heart rate variability in normalized units) is an indicator of parasympathetic activity.[20,37] In the present study the HF_{nu} was very much reduced in cases compared to controls. And the data was highly significant (P<0.0001). This showed a reduced parasympathetic activity in the study population.LF/HF ratio indicates the sympatho-vagal balance.[20,37] This ratio was very significantly increased in the study population compared to control population (P<0.0001). This showed an increase in sympathetic tone and decrease in the parasympathetic activity in the study group.

Time Domain Analysis

SDNN (standard deviation of Normal-Normal interval) is used to measure the overall Heart Rate Variability and RMSSD (the square root of mean squared distances between two successive NN intervals) is used to measure the short term components of Heart Rate Variability.[20] pNN50 (Percentage of differences between successive RR intervals that are greater than 50 msecs) estimates high frequency variations of heart rate.[20] The mean RR difference is significantly decreased in the study population. That was followed by significant reduction of overall Heart Rate Variability in the study population indicated by reduction in the SDNN component. RMSSD and pNN50 were also very significantly reduced in the study population (P<0.0001). Normally vagal tone or parasympathetic influence is the dominant force regulating the heart rate[35]. The vagal and sympathetic components of autonomic nervous control constantly interact to control the heart. Under stress or exercise there will be reduction in vagal component. Likewise there was a circadian component showing higher LF during day and higher HF during night.[39,40] In this study the reduction in overall Heart rate variability showed the involvement of sympathetic system by increased sympathetic tone or a reduction in vagal tone early in the subjects before the development of hypertension. Pharmacological treatment or therapy for decreasing weight, calorie restriction and exercise improves the autonomic function and reduces the blood pressure and insulin resistance.[41] this correlates with the present study. Thus autonomic reactivity can be used as a predictive tool for development of hypertension.

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Source of Support: None Declared
Conflict of Interest: None Declared