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RESEARCH ARTICLE

AN EVIDENCE BASED STUDY OF AUTONOMIC DYSFUNCTION IN CHILDREN WITH A FAMILY HISTORY OF HYPERTENSION

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ABSTRACT

Aim: The aim of the present study was to perform the set of standard autonomic function tests in children with a family history of hypertension and compare the results with children of normotensive parents.

Background: Hypertension is considered one of the highest causes of morbidity worldwide and it becomes one of the leading causes of death due to cardiovascular and renal failure. Hypertension can be especially hard to manage when combined with other disorders, such as diabetes or obesity. Most of the children with a family history of hypertension forms the risk factor for being hypertensive in future life.

Results: The study included 60 young and healthy children. Out of them, 30 children were selected based on their family history of hypertension while the remaining were the children of normotensive parents. The subjects were selected based on exclusion-inclusion criteria. All the children underwent for a set of autonomic function tests which are non-invasive, simple and comfortable. Results showed that children with a family history of hypertension have abnormal values on autonomicfunction testing, when compared with children of normotensive parents. The results were obtained using ANOVA and student't' –test, to study the significance of autonomic parameters.

Conclusion: This study stated that the children with family history of hypertension experienced mild to moderate autonomic fluctuations in early age which may make them more susceptible to hypertension in their future life.

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INTRODUCTION

The autonomic nervous system is a part of the peripheral nervous system and plays a central role in maintaining cardiovascular homeostasis. It does this by regulating the stroke volume, heart rate, peripheral resistance and water retention. Autonomic function testing is designed to determine the mechanisms involved in the regulation of blood pressure and heart rate and some other functions. During these tests, heart rate is measured using an electrocardiogram and blood pressure using a cuff around your arm. The autonomic nervous system and its sympathetic arm play important roles in the regulation of blood pressure. Many cardiovascular disease have been shown to be characterized by a marked increase in sympathetic drive to the heart and peripheral vascular resistance which forms the main reason for essential hypertension and other cardiovascular disorders like heart failure, circulatory failure etc.

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This study focuses on the sympathetic nervous system and its pathophysiological role in the development of hypertension and forms an important target for the therapeutic intervention. Hypertension is the chronic elevation of blood pressure and an important human health problem. The main cause of the disease remains unknown till now in most of the cases. One of the important causes of primary hypertension is genetic susceptibility. Parental history of hypertension have been regarded as important risk factors of cardiovascular disorders. Family members share genetic factors, activities, habits and attitude that can determine the health and their risk for disease. When members of a family pass traits from one generation to another through genes, that process is called heredity. Genetic factors likely to play some role in hypertension, cardiovascular diseases and other related conditions. However, it is also seems that people with a family history of high blood pressure share common environments and other potential factors that increase their risk. The risk for high blood pressure can increase even more when heredity combines with Unhealthy diet, alcohol consumption and smoking.

Various studies suggested that the risk of becoming hypertensive for an individual with a family history of hypertension has been estimated to be up to four times higher than average throughout the world. It was also reported by some studies that the excess activity of the sympathetic nervous system increases blood pressure and contributes to hypertension. In our studies it was found that children with a family history of hypertension showed hyperactivity of sympathetic nervous system. It has been found that children with a family history of hypertension presented some abnormal features like weight gain, raised blood pressure and increased Blood pressure response to sympathetic function tests like cold press or and isometric hand grip tests. The present study aims that the determination of presence of autonomic dysfunction is usually based on a variety of autonomic function tests. From the current study, we attempted to conduct both sympathetic and parasympathetic function tests in children with family history of hypertension and children of normotensive parents by measuring the blood pressure response to standing, blood pressure response to isometric handgrip, deep breathing test, valsalva ratio and cold press or test and signifying that an assessment of cardiac autonomic functions may be of prognostic value in such individuals.

METHODS

This study was undertaken by me on behalf of Department of Physiology, Narayana Medical College. The approval of Medical ethics committee of Narayana Medical College, Nellore was taken for this "An Evidence based Study of Autonomic dysfunction in Children with a family history of Hypertension". Subjects were physiotherapy, lab technology, medical and dental students selected from Narayana medical college aged between 18 – 25 years, who volunteered to take part in the study. The procedure was explained and written consent was obtained from the subjects. All the subjects underwent a detailed clinical examination before being included in the study as per the study protocol. The subject selection was based on the predetermined exclusion-inclusion criteria. Sixty healthy volunteers aged between 18–25 years were participated in the present study. The participants were distributed into two groups. Study group includes children with family history of hypertension and control group includes children of normotensive parents. All participants completed a questionnaire regarding family history of hypertension.The family history was taken by having each participantselect "yes," "no," or "uncertain" in a table of questions onthe presence of hypertension in the grandfather,grandmother, father, mother, siblings, and children. Positivefamily history of hypertension was defined ashaving at least one member in the group including the father,mother and siblings with hypertension.

Inclusion and exclusion criteria

Normotensive children including males and females aged 18-25 years with normal body mass index (BMI: 19-25 Kg/m^2) were included in the present work. All the subjects were thoroughly examined clinically to rule out any illness which might impact the autonomic activity.

- No history of Cardiovascular and Respiratory system disorders
- No history of Smoking
- No history of Diabetes mellitus
- No history of any acute infectious diseases
- No history of any chronic diseases
- No history of metabolic disorder

Subjects with acute illness, on hypertensive medication and having known metabolic disorder were excluded. Cardiovascular Autonomic function tests were carried out in the morning in the department between 10 AM to 12 Pm after 2 hours of light breakfast, after intimate testing procedures with the subjects. The Autonomic function tests which were performed to assess the cardiovascular sympathetic functional status:

I. Cold Pressor test (cold pressure test): Subject was instructed regarding the test. Blood pressure was recorded under basal conditions. Cold water was taken in a container. Subject was asked to submerge one of his upper limbs in cold water for 60 seconds. Blood pressure was recorded at the end of 60 seconds of submersion of the limb. Submersion of the limb in ice cold water increases systolic blood pressure by about 10-20 mm of Hg and diastolic blood pressure by about 10 mm of Hg.

II. Hand Grip Test: In the hand grip test, there is a rise in heart rate and blood pressure. The blood pressure rise is due to increased sympathetic activity and heart rate rise is due to decreased parasympathetic activity. Subject was made to lie down in semi recumbent position. ECG electrodes were connected for lead II recording of ECG and sphygmomanometer for blood pressure measurement. Basal heart rate and blood pressure were recorded. Subject was asked to maintain a pressure of 30% of the maximum activity in the hand grip dynamometer for about 5 minutes. Heart rate and change in SBP, DBP were recorded.

III. Blood pressure response to standing: Patient is again allowed to assume a supine position, and a recording of blood pressure is done in the supine position. Patient is then asked to stand up and blood pressure is recorded at 0 and 1 minute intervals. The Autonomic function tests which were performed to assess the cardiovascular parasympathetic functional status:

I. Deep breathing test: This test is used to assess the parasympathetic activity. Subject was instructed to maintain deep breathing at a rate of six breaths per minute and was made to lie down comfortably in supine position with head elevated to 30^0. ECG electrodes were connected for recording Lead II ECG. While subject was breathing deeply at a rate of 6 breaths per minute (allowing 5 seconds each for inspiration and expiration) maximum and minimum heart rates were recorded with each respiratory cycle. Expiration to inspiration ratio was determined by using the formula.

II. Valsalva Manoeuver: The valsalva ratio is a measure of parasympathetic and sympathetic functions. Subject was made to lie down in a semi recumbent or sitting position. Nostrils were closed manually.

Mouth piece was put into the mouth of the subject and the Mercury manometer was connected to the mouth piece. ECG machine was switched on for continuous recording. Subject was asked to exhale forcefully into the mercury manometer and asked to maintain the expiratory pressure at 40 mm of Hg for 10 – 15 seconds. ECG changes were recorded throughout the procedure, 30 seconds before and after the procedure. Valsalva ratio were calculated by using the formula.

III. Heart rate response to standing: On changing the posture from supine to standing heart rate increases immediately by 10-20 beats per minute. This response is detected by recording ECG in supine and standing postures. Subject was made to lie down in supine posture. ECG electrodes were connected from the subject to the cardiowin system. Subject was asked to relax completely for a minimum period of 10 minutes. Basal heart rate was recorded by using cardiowin system. Subject was asked to stand up immediately and change in heart rate is noted from the monitoring screen of cardiowin. Heart rate response to standing was determined by using the formula heart rate in standing position – heart rate in supine position.

RESULTS

The collected data was expressed as Mean ±SD. These results were analyzed by ANOVA with SPSS version 17.0 using an unpaired‘t’ test. The results of the above tests were compared between Study group and control group

Table.1: Shows that there were no significant findings between anthropological variables like age and BMI.

Table 1. Anthropometric variables

Variables	Control group (n = 30)	Study group (n = 30)	P value
Age (yrs.)	18.96 ± 1.76	20.00 ± 1.68	0.91
Height (cm)	164.60 ± 8.26	166.68 ± 6.93	0.07
Weight (Kg)	57.16 ± 9.73	57.96 ± 9.11	0.74
BMI (Kg/m2	21.54 ± 2.61	21.96 ± 2.2	0.55

Table.2: Shows that the physiological findings like basal heart rate, SBP and DBP values were found to be higher in subjects of study group as compared with control group but this difference was statistically insignificant (p>0.05).

Table 2. Physiological Considerations

Variables	Control group (n = 30)	Study group (n = 30)	P value
Basal Heart rate BPM	84.28 ± 4.95	86.11 ± 5.11	0.05
Resting SBP (mm of Hg)	115.64 ± 4.92	119.52 ± 6.30	0.06
Resting DBP (mm of Hg)	76.64 ± 5.02	81.40 ± 4.69	0.23
Resting-RR (breath/min)	13.01 ± 3.26	14.68 ± 4.61	0.74

Table.3: Shows that all the parasympathetic autonomic function tests like heart rate response to standing i.e. 30:15 ratio, heart rate response to deep breathing i.e. E: I and valsalva ratios in the children of study group were almost similar to control group. These results were statistically not significant (p>0.05). It indicates that the parasympathetic reactivity tests are similar in both the groups.

Table 3. Statistical analysis of Parasympathetic function tests in Study group and control group

Variables	Control group (n = 30)	Study group (n = 30)	P value
Heart rate response to standing 30:15 Ratio	1.15 ± 0.05	1.17 ± 0.04	0.12
Valsalva ratio	1.25 ± 0.02	1.26 ± 0.04	0.26
Heart rate response to deep breathing E: I Ratio	1.25 ± 0.02	1.23 ± 0.05	0.07

Table.4: shows that all the sympathetic autonomic function tests like Blood pressure response to standing, Cold pressor test and Hand grip test shows marginally higher values in study group as compared with the control group. These findings were statistically significant (p< 0.001 and p< 0.05). It indicates that hyperactivity of sympathetic nervous system in children of study group.

Table 4. Statistical analysis of Sympathetic function tests in Study group and control group

Variables	Control group (n = 30)	Study group (n = 30)	P value
Isometric Handgrip SBP	14.85 ± 1.20	19.55 ± 0.86	<0.01**
Isometric Handgrip DBP	19.36 ± 2.05	26.72 ± 2.93	<0.001**
Cold Pressor Test SBP	8.2 ± 1.4	14.29 ± 1.6	<0.05
Cold Pressor Test DBP	12.24 ± 1.56	18.24 ± 1.56	<0.001**
Bp Response to standing SBP change	4.64 ± 1.38	6.60 ± 1.41	<0.001**
Bp Response to standing DBP change	2.20±0.43	5.43±0.66	<0.001**

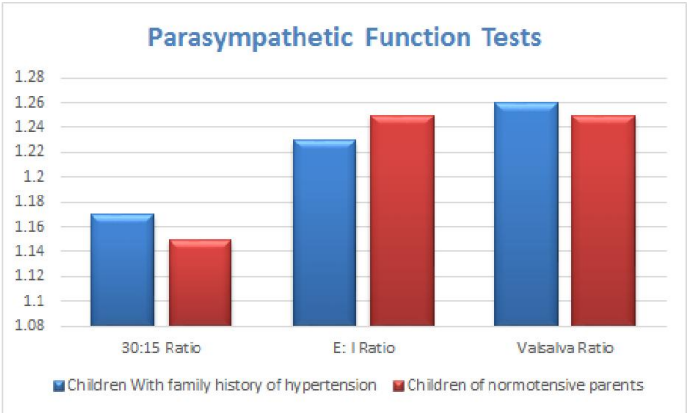

Figure 1. Parasympathetic Function tests

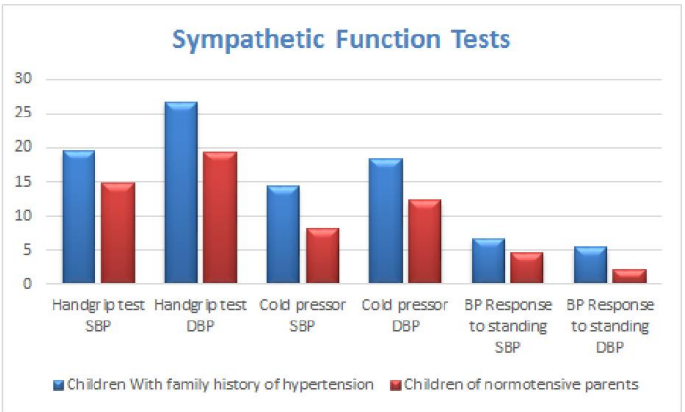

Figure 2. Sympathetic Function tests

DISCUSSION

In the present study, we demonstrated that young children with a family history of hypertension have increased risk of developing hypertension. Further, the blood pressure (BP) response to hyperactive sympathetic stimuli in young children can predict the future development of hypertension. In our study it was clear that children with family history of hypertension expressed statistically significant exaggerated cardiovascular and sympathetic reactivity when compared to children of normotensive parents. In our study it was seen that young normotensives with a positive family history of hypertension had higher blood pressure and also increased resting heart rate than young normotensives with a negative family history of hypertension. This increased blood pressure and heart rate observed in this study in the children of hypertensive parents indicated the importance of genetic influence on hypertension in children.

The results of the present study indicated that all the parasympathetic autonomic function tests like heart rate response to standing i.e. 30:15 ratio, heart rate response to deep breathing i.e. E: I and valsalva ratios in the children with a family history of hypertension were almost similar to control group. These results were statistically not significant ($p>0.05$). It indicates that the parasympathetic reactivity tests are similar in both the groups. These tests primarily provide an index to cardiac vagal functions. It was also indicated that sympathetic autonomic function tests cold press or test, isometric handgrip test, blood pressure response to standing have both prognostic and diagnostic importance to determine sympathetic reactivity. There was significant increase of blood pressure response to cold pressor test and isometric hand grip test in the test group which points towards sympathetic hyperactivity in children with a family history of hypertension. Blood pressure responds to standing values also slightly higher in test group when compared to control and these values also statistically significant.

The mechanisms of increased sympathetic nervous system activity in hypertension involve alterations in baroreflex and chemoreflex pathways at both peripheral and central levels. Persons with a family history of hypertension manifest augmented vasoconstrictor and sympathetic responses to laboratory stressors, such as cold pressor test and isometric handgrip test that may predispose them to hypertension. Exposure to stress increases sympathetic nervous system activity and this recurrent stress produces vasoconstriction leading to progressive increases in peripheral resistance and blood pressure. This study support the concept of inherited vascular reactivity as an indicator of sympathetic hyperactivity which forms the basis for the development of hypertension in the children with a family history of hypertension in their future life.

Conclusion

This study concluded that hyperactivity of sympathetic nervous system in children with a family history of hypertension increases the risk of hypertension in their future. The parasympathetic nervous systems remains unchanged in both test and control groups.

Initially children of study group may be normotensive but there is chance of development of hypertension in later life. Regular supervision of autonomic activity may prove to be a useful tool in predicting the future hypertension.Children belonging to hypertensive families should therefore, be targeted for primary prevention regular blood pressure monitoringalong with dietary and lifestyle modification. It is alsoimportant to screen these children toidentify markers to assist in prediction of development of essential hypertension in adulthood.

List of abbreviations

ECG – Electrocardiogram
SBP – Systolic blood pressure
DBP – Diastolic blood pressure
CPT – Cold pressor test
IGH – Isometric handgrip test

Competing interests

The Authors declare that they have no competing interests.

Authors Contributions

Dr. K.N. Maruthy have made substantial contributions to concept and study design. He has also done final approval of the work to be published. Dr. Sharan b.Singh was involved in acquisition of data, analysis and interpretation of data. Mr. Chiranjeevi Kumar Endukuru have done spell check, proof read, sequence alignment and statistical analysis. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. All authors read and approved the final manuscript.All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section.

Authors' information

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