

EVALUATION OF SYMPATHETIC DOMINANCE BY AUTONOMIC FUNCTION TESTS IN CHILDREN OF HYPERTENSIVE PARENTS

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ABSTRACT

BACKGROUND

Hypertension is a global problem. Positive family history of hypertension is one of the risk factors for being hypertensive in future life for their children. Hyperactive sympathetic nervous system is reported in children of hypertensive parents.

Aim- The main aim of the study was to observe the magnitude of alterations in autonomic reactivity in normotensive male offsprings of both hypertensive and normotensive parents.

MATERIALS AND METHODS

Fifty young and healthy male subjects between 19-24 years of age got examined for autonomic reactivity. Twenty-five of them were having positive family history (cases) while the remaining children were having negative family history (control group) of hypertension. Non-invasive autonomic function tests as per Ewing's criteria were performed in all the subjects and study group compared with cases.

RESULTS

The resting heart rate, systolic and diastolic blood pressures were not significantly raised in subjects of study group. The sympathetic function tests as assessed by rise in diastolic blood pressure following cold pressor test and handgrip test were highly significant in study group as compared with control one. However, parasympathetic functions were similar in both groups.

CONCLUSION

It seems that there is increased sympathetic activity in children of hypertensive parents which may predispose them to hypertension in their later life.

KEYWORDS

Hypertension, Cold Pressor Test, Hand Grip Test, Normotensive Parents.

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BACKGROUND

Prehypertension and family history of hypertension is considered as important risk factors for the beginning of cardiovascular diseases.¹⁻³ Thirty percent subjects of primary hypertension have genetic predisposition and some genes have been identified in some subjects.⁴ Hypertension is reported to be associated with sympathetic nervous system overactivity.^{5, 6} Normotensive subjects with family history of hypertension have greater sympathetic activity and also early parasympathetic attenuation.^{4,7,8} It has been observed that young normotensive offsprings of hypertensive parents exhibit several abnormal characteristics like being overweight, elevated basal blood pressure and produce exaggerated blood pressure response to exercise.⁹⁻¹¹ An assessment of cardiac autonomic functions may be of prognostic value in such individuals. The cardiac autonomic functions are based on the assumption that blood pressure responses are mediated through sympathetic nervous system

and heart rate response is vagally mediated.¹²⁻¹⁴ Prehypertension and family history of hypertension are the risk factors for hypertension and they might be considered as the beginning of cardiovascular disease. Also some studies provides evidence that cardiac autonomic functions play an important role in prehypertension and altered autonomic functions are already present in subjects with family history of hypertension. In the present study, the hypothesis that normotensive young male adults, with parental history of hypertension exhibit variations in cardiovascular autonomic functions compared to age and sex matched adults without family history of hypertension, is being tested and discussed.

Objectives

1. To assess the autonomic functions in medical students of hypertensive parents.
2. To compare the autonomic function tests of above group with medical students of normotensive parents.
3. To find out the hyper-reactors, irrespective of hypertensive or normotensive parents.

MATERIALS AND METHODS

Study Design

Descriptive Comparative Study.

The present work was designed and conducted in the Department of Physiology at LLRM Medical College, Meerut over a period of 12 months. Fifty healthy male subjects doing

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MBBS in the same college between 19-24 years volunteered to participate in the present study. On the basis of detailed family history, participants were divided into two groups of twenty-five each as study group- with family history of hypertension (FH+) and control group- without any family history of hypertension (FH-). Either or both parents of the subjects of study group presented with history of hypertension of varying degree and duration and were under antihypertensive therapy which was further confirmed by their medical prescriptions as well. Both the groups were assessed and compared for their autonomic function tests to find out hyper-reactors for those having higher risk for hypertension in future. Sample size of 50 participants was decided including both the groups due to lack of consent from most of the senior MBBS students.

Inclusion and Exclusion Criteria

Only healthy, normotensive, never smokers and with BMI between 18.5 - 24.9 kg/m² were included in the present work. Subjects not giving consent, with acute illness, on hypertensive medication and having known metabolic disorder were excluded. All the subjects were thoroughly examined clinically to rule out any illness which might impact the autonomic activity. Written informed consent was obtained from all subjects as per institutional ethical committee recommendations for human subjects. All the participants were called at the autonomic function laboratory of the department between 10 to 11 a.m. after 2 hours of light breakfast. They were allowed to rest in the laboratory at ambient room temperature (25°C–28°C) for fifteen minutes. The subjects were briefed in detail about the experimental procedure. Resting heart rate, respiratory rate, systolic and diastolic blood pressures and corrected QT interval (QTc) were measured in all subjects thrice and the mean of the three readings were recorded as the value for the measured physiological parameter. Autonomic activity in each subject was assessed by non-invasive autonomic function tests as per Ewing's criteria.¹⁵⁻¹⁸ The autonomic tests described below were performed during the afternoon with volunteers in a state of complete physical and mental rest. They are:

Parasympathetic Reactivity Tests

- Lying to standing test (30:15).
- Orthostatic Hypotension Test.
- Valsalva Ratio.
- Heart rate variation with deep breathing (E: I).

Sympathetic Reactivity Tests

- Blood pressure changes to sustained hand grip test.
- Blood pressure changes to cold pressor test.

Blood pressure and heart rate was recorded at the beginning and then after continuous rest in supine position, the autonomic function tests were commenced when three consecutive reading taken five minutes apart were identical. This meant that in all probability they had reached their basal values.

For Assessing Parasympathetic Activity

L: S Ratio

The subjects were made to lie down comfortably on the couch for 10 min. They were then asked to stand up within 3

seconds. The ECG was recorded continuously. The L:S ratio (30:15) was calculated as the ratio between the R-R interval at beat 30th and 15th of ECG after attaining standing posture.

Orthostatic Hypotension

After 10 minutes of supine rest, the subjects were asked to attain standing posture within 3 seconds. BP was recorded in lying and at 30 seconds, 60 seconds and 2 minutes after standing posture. Highest fall in SBP was taken as test response.

Deep Breathing Test (E: I Ratio)

The subjects in lying posture were asked to take slow and deep breathing at the rate of 6 breaths per min. ECG was recorded continuously. The ratio was calculated from longest R-R interval during expiration divided by shortest R-R interval during inspiration average over 6 cycles.

Valsalva Ratio

The subjects remained seated and asked to exhale into a mouthpiece connected to a mercury manometer and to maintain the expiratory pressure at 40 mmHg for 15 seconds. ECG was recorded. The ratio was calculated between the maximum R-R intervals (after release of strain) to the minimum R-R interval (during strain).

For Assessing Sympathetic Activity

Hand Grip Test (HGT)

The resting BP of the subject was taken in sitting posture. Then the subject was asked to apply pressure on hand grip dynamometer at 30% of maximum voluntary contraction (MVC) for 1 minute. BP was simultaneously recorded from non-exercising arm.

The procedure was repeated thrice with sufficient interval in between. The average increase in DBP was noted as the test response.

Cold Pressor Test (CPT)

After taking the resting BP, the subject was asked to immerse his hand in cold water (temperature maintained between 5°–9°C). BP measurement from other arm was done at 30-second interval for two minutes after which the subject was asked to remove the hand from cold water. Maximum increase in DBP was recorded as a test response.

Statistical Analysis

Data are expressed as Mean ± SD. Intergroup comparisons were done by using Student's unpaired 't' test. Differences in the means were considered statistically significant when the two tailed p value is <0.05.

RESULTS

There were no significant differences between age, BMI and other physical indices between two groups. All the physical characteristics of subjects of control as well as study group were statistically matched (p >0.05). However, the resting heart rate, systolic and diastolic blood pressures were found to be marginally higher (p>0.05) in the study group (Table 1). There was higher and significant (p <0.001) rise in diastolic blood pressure following isometric hand grip test at 1/3 of MVC and cold pressor tests in study group as compared with

the control group indicating an attenuated sympatho-adrenergic system in subjects of study group (Table 2).

Table 3 shows that heart rate responses as exhibited by L: S, E: I and Valsalva ratios in the subjects of study group were almost similar to control ones ($p > 0.05$). Also the maximum fall in systolic blood pressure on standing (OHT) was comparable with the study group subjects (Table 3). It indicates that the parasympathetic reactivity tests are similar in both the groups.

Physical Characteristics	Control Group (n = 25)	Study Group (n = 25)
Age (years)	20.96 $\pm$ 1.76	21.00 $\pm$ 1.68
Height (cm)	162.60 $\pm$ 8.26	166.68 $\pm$ 6.93
Weight (kg)	57.16 $\pm$ 9.73	57.96 $\pm$ 9.11
BMI (Kg/m ²)	21.52 $\pm$ 2.61	21.06 $\pm$ 2.25
Resting Heart Rate (beats/min.)	84.38 $\pm$ 4.95	87.11 $\pm$ 5.11
Resting SBP (mmHg)	116.64 $\pm$ 4.92	119.52 $\pm$ 6.30
Resting DBP (mmHg)	78.64 $\pm$ 5.02	80.40 $\pm$ 4.69
Resting RR (breaths/min.)	14.01 $\pm$ 3.26	13.68 $\pm$ 4.61
QTc (msec)	398.77 $\pm$ 24.05	398.18 $\pm$ 25.62
Table 1. Mean $\pm$ SD of Physical Characteristics of Control (FH-) and Study (FH+) Groups		

Name of the Test	Control Group (n = 25)	Study Group (n = 25)	P value
Hand Grip Test (mmHg)	19.36 $\pm$ 2.05	26.72 $\pm$ 2.93	0.001
Cold Pressor Test (mmHg)	12.24 $\pm$ 1.56	18.24 $\pm$ 1.56	0.001
Table 2. Mean $\pm$ SD of Rise in Diastolic Blood Pressure during Sympathetic Functions Tests in Control (FH-) and Study (FH+) Groups			

Name of the Test	Control Group (n = 25)	Study Group (n = 25)	P value
L:S (30:15)	1.15 $\pm$ 0.05	1.17 $\pm$ 0.04	0.12
Orthostatic Hypotension (mmHg)	6.64 $\pm$ 1.38	6.60 $\pm$ 1.41	0.91
Deep Breathing Test (E:I)	1.25 $\pm$ 0.02	1.23 $\pm$ 0.05	0.07
Valsalva Ratio	1.25 $\pm$ 0.02	1.26 $\pm$ 0.04	0.26
Table 3. Mean $\pm$ SD of Parasympathetic Function Tests in Control (FH-) and Study (FH+) Groups			

DISCUSSION

Although the resting heart rate, systolic and diastolic blood pressures were found to be higher in subjects of study group as compared with control group, this difference was statistically insignificant ($p > 0.05$) as shown by Table 1. This shows that both the groups are normotensive at rest. It was not concordant with Krishnan et al and could be due to younger age of subjects and normal BMI of all the subjects in the studied group. Some researchers claimed that the abovementioned parameters to be significantly higher in children of hypertensive parents due to some hereditary

influences. Julis et al had described the probable reason for such rise in BP responses due to hyperactive sympathetic nervous system (SNS) thereby causing higher basal responses. The mechanisms of increased SNS activity leading to hypertension are complex and involve alteration in baroreceptor and chemoreceptor reflexes at both central and peripheral levels.

Autonomic reactivity to stress has been hypothesised to be a marker of subsequent neurogenic hypertension. CPT and HGT are of prognostic importance to determine sympathetic reactivity. In the former, the assessment is done by applying standardised cold stimulus to skin while in latter, it was done by sustained isometric exercise at 1/3rd of MVC. Both tests cause peripheral vasoconstriction mediated by adrenergic receptors of SNS. In the present study, there was significant increase in diastolic blood pressure ($p < 0.001$) following both the test in study group in comparison to control group (Table 2). The results support the concept of inherited vascular reactivity as an indicator of sympathetic hyperactivity which is more or less a predictor of hypertension. The possible reason may be hypothalamus mediated reflex releasing NE at vascular smooth muscle cells, further accentuated by concomitant release of endothelin 1. Pramanik et al¹⁹ suggested that subjects exhibiting greater and prolonged response to stress induced by tests are more prone to develop hypertension. Therefore, these tests may be used as predictors of hypertension. All the subjects of both the groups had complete recovery within five minutes indicating competent autonomic nervous system. Evaluation of parasympathetic nervous system provides an index to cardio-vagal functions. The present study did not exhibit any changes in all these tests in study group (Table 3). It appears that modulation in parasympathetic nervous system activity does not occur in children of hypertensive parents.

CONCLUSION

It may be concluded that sympathetic nervous system hyperactivity develops in children of hypertensive parents whereas the PNS remains unaltered. Though the subjects of study group may be normotensive initially, there is possibility of development of hypertension in future. Hyper-reactors who have positive family history were more vulnerable to future hypertension due to their sympathetic overactivity. Regular monitoring of autonomic activity may prove to be a useful tool in predicting the future hypertensive cases. It also appears that genetic and environmental factors might be responsible for essential hypertension in families.

Limitations

This work was done as a purpose of thesis for MD in a small sample size due to difficulty in recruiting subjects. These limitations in sample size were due to lack of consent from most of the senior MBBS students who already passed out from Physiology. We performed the present work in male subjects only and cannot comment on the autonomic reactivity in normotensive daughters of hypertensive parents. Moreover, we were not having the facilities of HRV analysis in our laboratory which could be a better choice to measure the autonomic balance. Future followup of our subjects were also limited within our resources.

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