

Sympathetic hyperactivity in children of hypertensive parents

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KEY WORDS

Normotensive children
Autonomic reactivity
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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. **Purpose:** The main objective of the study was to observe the magnitude of alterations in autonomic reactivity following the standard autonomic function tests in normotensive male offsprings of both—hypertensive and normotensive parents. **Methods:** Fifty young and healthy male subjects between 19-24 yr of age got examined for autonomic reactivity. Twenty five of them were having family history of hypertension (study group) while the remaining were the children of normotensive parents (control group). Non invasive autonomic function tests as per Ewing's criteria were performed in all the subjects. **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 hand grip test were highly significant in study group as compared with control one. However, the vagally mediated tests, for heart rate responses, denoting parasympathetic functions were similar in both groups. **Conclusion:** It seems that there is increased sympathetic activity in children of hypertensive parents without parasympathetic modulation in early life. It may predispose them to hypertension in their later life.

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Introduction

Prehypertension and family history of hypertension are considered as important risk factors for the beginning of cardiovascular diseases.¹⁻³ 30% 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 offspring of hypertensive parents exhibit several abnormal characteristics like being overweight,⁵ 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 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.

Methods

Fifty healthy male subjects between 19–24 yr volunteered to participate in the present study. The participants were divided into two groups of twenty five each viz study group- with family history of hypertension (FH+) and control group- without any family history (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.

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 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 AM 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 on 4 channel Polyrite (Medicaid Ambala) by non invasive autonomic function tests as per Ewing's criteria.¹⁵⁻¹⁸

For assessing parasympathetic activity

- (i) L:S ratio: The subject were made to be comfortably on the couch for 10 min. they were then asked to stand up within 3 second. 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.
- (ii) 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 30s, 60s and 2 min after standing posture. Highest fall in SBP was taken as test response.
- (iii) Deep breathing test (E: I ratio): The subject in lying posture were asked to take slow and deep breathing at the rate of 6 breath 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.

- (iv) The 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 mm of Hg for 15 seconds. ECG was recorded. The ratio was calculated between the maximum R-R interval (after release of strain) to the minimum R-R interval (during strain).

For assessing sympathetic activity

- (i) BP response to static exercise (hand grip test (HGT)) was also measured. 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.
- (ii) 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 sec interval for two minutes after which the subject was asked to remove the hand from cold water. Maximum increase in DBP were recorded.

Statistical analysis—Data are expressed as Mean \pm SD. Inter group comparison 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 HR, systolic and diastolic blood pressures were found to be marginally higher ($p>0.05$) in the study group (Table 1). There was more and significant ($p<0.001$) rise in diastolic blood pressure following isometric hand grip at 1/3 of MVC and cold pressor tests in study group as compared with the control group indicating an attenuated sympathoadrenergic 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.

Discussion

Although the resting heart rate, systolic and diastolic blood pressures were found to be higher in subjects of study group

Table 1: Mean \pm SD of physical characteristics of control (FH–) and study (FH+) groups

Physical characteristics	Control group (n = 25)	Study group (n = 25)	P values
Age (yr)	20.96 \pm 1.76	21.00 \pm 1.68	0.90
Height (cm)	162.60 \pm 8.26	166.68 \pm 6.93	0.06
Weight (Kg)	57.16 \pm 9.73	57.96 \pm 9.11	0.76
BMI (Kg/m ²)	21.52 \pm 2.61	21.06 \pm 2.25	0.50
Resting Heart rate (beats/min)	84.38 \pm 4.95	87.11 \pm 5.11	0.06
Resting SBP (mm of Hg)	116.64 \pm 4.92	119.52 \pm 6.30	0.07
Resting DBP (mm of Hg)	78.64 \pm 5.02	80.40 \pm 4.69	0.20
Resting RR (breath/min)	14.01 \pm 3.26	13.68 \pm 4.61	0.77
QTc (msec)	398.77 \pm 24.05	398.18 \pm 25.62	0.93

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 values
Hand grip test (mm of Hg)	19.36 \pm 2.05	26.72 \pm 2.93	0.001*
Cold pressor test (mm of Hg)	12.24 \pm 1.56	18.24 \pm 1.56	0.001*

* $p<0.001$

Table 3: Mean \pm SD of Parasympathetic functions tests in control (FH–) and study (FH+) groups

Name of the test	Control group (n = 25)	Study group (n = 25)	P values
L:S (30:15)	1.15 \pm 0.05	1.17 \pm 0.04	0.12
Orthostatic hypotension (mm of Hg)	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

as compared with control group but this difference was statistically insignificant ($p > 0.05$) (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 group and normal BMI of all the subjects in the studied groups. Though some researchers claimed the above mentioned parameters to be significantly higher in children of hypertensive parents due to some hereditary influence. Julis *et al*⁹ had described the probable reason for such rise as hyperactive sympathetic nervous system (SNS) thereby causing higher basal responses. The mechanisms of increase SNS activity leading to hypertension are complex and involve alteration in baro and chemo reflexes at both central and peripheral levels.

Autonomic reactivity

Autonomic reactivity to stress has been hypothesized 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 standardized cold stimulus to skin while in latter, it was done by sustained isometric exercise at 1/3 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 al*⁹ suggested that subjects exhibiting greater and prolonged response to stress induced tests are more prone to develop hypertension. Therefore, these tests may be used as predictor of hypertension. All the subjects of both the groups had complete recovery within five minutes indicating competent autonomic nervous system.

Evaluation of parasympathetic system includes measurement of heart rate variation at rest and in response to deep respiration, valsalva ratio and postural changes. These tests primarily provide an index to cardiac vagal functions. The present study did not exhibit any changes in all these tests in study group (Table 3). Studies have shown that young normotensive with family history of hypertension exhibit altered vagal balance with decreased parasympathetic activity at cardiac level. It appears that modulation in para sympathetic nervous system activity does not occur in children of hypertensive parents.

Limitations

This work was done in a small sample size due to difficulty in recruiting subjects. 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 follow up of our subjects were also limited within our resources.

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 but there is possibility of development of hypertension in future. Regular monitoring of autonomic activity may prove to be a useful tool in predicting the future hypertensive.

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