



Original Research Article

A Study to Evaluate the Involvement of Sympathetic Nervous System in the Medical Students Having Family History of Hypertension

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ABSTRACT

Context: Hypertension and familial incidence for hypertension have been associated with heightened cardiovascular reactivity. If a subject is diagnosed at this stage of sympathetic hyperactivity it could be possible to minimize, prevent or delay in the development of hypertension.

Objectives: The objective of the study is to evaluate the involvement of sympathetic nervous system in the students having family history of hypertension.

Methods: Various sympathetic function tests were done to assess the sympathetic activity in 110 students. In this study the cardiovascular responses to certain physiological stimuli were impaired in the students having family history of hypertension.

Results & Conclusion: The female group suggesting sympathetic function was involved more than the male group. Our test response conclude females are involved more than males, sympathetic function involved more in female and there is potential gender difference with definite predisposition of family history of hypertension.

Key words: Sympathetic nervous system, Cold Pressor test, Handgrip test.

INTRODUCTION

The term autonomic nervous system is to describe the system of nerves which regulates the function of all innervated tissues and organs throughout the vertebrate body except the striated muscle fibers that is innervations of the viscera, vasculature, glands and some other tissues. The autonomic nervous system handles monitoring and control of all internal functions such as blood pressure, blood flow, sweating, bowel and bladder. Dual innervations of the visceral organs by the

both branches of the autonomic nervous system permits precise control over an organs activity. The sympathetic nervous system dominates in emergency or stressful situation and promotes responses that prepare the body for strenuous physical activity. ⁽¹⁾ Autonomic over activity is known to precede overt hypertension and with intervention at this stage it could be possible to delay and minimize further evaluation in blood pressure. ⁽²⁾

All forms of progressive autonomic failures are insidious in their onset with mild

symptoms that may be concealed for years because of autonomic compensatory mechanisms as Cannon pointed that this system can respond to many and varied stresses from internal external environments in ways which conceal its dysfunction. Postural hypotension is one of the cardinal features of the autonomic failure. Patients may start with mild symptoms with vague weakness, postural dizziness or faintness which can be overlooked easily. ⁽³⁾

Hypertension status and an increased genetic risk for hypertension have been associated with heightened cardiovascular reactivity in which it is reported that individuals with hypertension, borderline hypertension are family history of hypertension showed heightened blood pressure response. Erin and Pickering found a significant of family history of hypertension on cardiovascular recovery using a more stringent definition of positive family history. Increased sympathetic activity has been implicated in the pathogenesis of hypertension and interest in the role of sympathetic nervous system has revived with the demonstration of the increased noradrenalin release and sympathetic over activity in early hypertension. ⁽⁴⁾

If a subject can be diagnosed at the stage of autonomic hyperactivity it could be possible to minimize further elevation in blood pressure. Since hypertension has a genetic basis and has a familial incidence detection of sympathetic over activity could identify individuals at risk. Intervention at this stage could lead to prevention or delay in the development of hypertension.

Aims and Objectives

1. To carry out standard sympathetic function tests in the students having family history of hypertension.
2. To assess significance of sympathetic function test in the same students.

MATERIALS AND METHODS

Study design: This is a prospective study with randomly selected sample. The sample size is one hundred and ten.

Study sample: The study subjects selected from the first year MBBS students, from 2010 batch, from Kakatiya Medical College, Warangal by considering the inclusion criteria. The study duration was from Jan. to June 2010 i.e. 6 months. They were divided into two groups.

* **A group** as cases comprises 25 males and 25 females with family history of hypertension.

* **B group** as control group comprises 25 males and 35 females with no family history of hypertension.

Inclusion criteria for selection

- In the age group of 17 to 21 years
- With no specific metabolic diseases or chronic diseases (elicited through history)
- Presently not on any treatment.
- Regular and normal menstrual cycles.
- With no history of premenstrual syndromes.
- Representing different strata of society.

Resting Heart Rate and Blood Pressure

ECG: The subjects and controls were monitored for the heart rate by Electrocardiographic tracing with Cardiart 108T-MK-VI which is a single channel, 12 lead cardiograph designed to record electrocardiogram in any location, and record 12 lead ECG.

Blood pressure: BP is record with the help of sphygmomanometer.

The BP and the heart rate were recorded at the beginning and then after continuous rest in supine position. The autonomic function tests were commenced when two consecutive heart rate and blood pressure readings taken five minutes apart were

identical. This meant that in all probability they had reached their basal values.

The sympathetic function tests done are thus based on cardiovascular reflexes and are reliable, reproducible, simple and non-invasive.

The tests reflecting sympathetic function –

1) Orthostatic test: Immediate heart rate and blood pressure response to standing

Procedure:

Only the limb leads of the ECG machine were attached to the subject. The blood pressure cuff was tied to the right arm

and kept inflated and the sphygmomanometer was held at heart level. With this arrangement, the subject was asked to stand up from the supine position and was instructed to remain motionless for 2 minutes. The ECG was recorded from about 15 beats before to 40 beats after standing. The maximum R-R interval around 30th beat and minimum R- R interval around 15th beat were measured. The subjects BP were recorded when lying down quietly and again when the subject stands up.

Change in Blood pressure -

Interpretation of results:

Heart rate change		Fall in systolic blood pressure
Normal	30:15 > 1.04	< 10 mm of Hg
Borderline	30:15 = 1.01 - 1.03	11-29 mm of Hg
Abnormal	30:15 < 1.00	>30 mm of Hg

2) Hand Grip Test: Blood Pressure Response to Sustained Hand Grip

Procedure:

A sphygmomanometer cuff was rolled over and partially inflated with air up to 20mm Hg the subject was asked to use the maximum voluntary effort (maximum voluntary contraction-MVC) and squeeze the inflated cuff. The level to which the mercury column was elevated during the procedure was noted. Then, the subject was asked to maintain the hand grip at a level of 30% of the maximum effort for 5 minutes. The rise in diastolic blood pressure was measured. The test is a useful measure of autonomic damage and when abnormal, implies extensive damage to sympathetic efferent pathways.

Interpretation of results:

Increase in diastolic blood pressure	
Normal	>16 mm of Hg
Borderline	11-15mm of Hg
Abnormal	<10mm of Hg

3) Cold Pressor test: Blood Pressure Response to Cold

Procedure:

The cold pressor test was originally described by Hines and Brown in 1930. The subject was made to immerse one hand in iced water at 4⁰C for one minute. The blood pressure response was measured in the opposite arm.

Interpretation of results: A rise in diastolic blood pressure of more than 10mmHg is considered a normal response. If the blood pressure does not increase, the reflex arc is probably incomplete.

The following references values of Ewing and Clark were used to interpret the results of the tests:

Sr. No.	Autonomic function tests	Normal	Borderline	Abnormal
1.	Heart rate variation to deep breathing	>15 beats /min	11-14 beats /min	<10 beats /min
2.	Fall in systolic blood on standing	<10 mmHg	11-29 mmHg	>30 mmHg
3.	30:15 ratio on standing	>1.04	1.01-1.03	<1.00
4.	Rise in diastolic blood pressure to cold pressor test	>11 mmHg	-----	<10 mmHg
5.	Rise in diastolic blood pressure to sustained hand grip	>16 mmHg	11-15 mmHg	<10 mmHg

The results from each of these tests enable the severity of autonomic damage to be categorized:

1. Normal	All tests normal or one borderline
2. Early involvement	One of the three heart rate tests abnormal or two border line
3. Definite involvement	Two or more of the heart rate tests abnormal
4. Severe involvement	Two or more of the heart rate tests abnormal plus one or both of the blood pressure tests abnormal or both borderline
5. Atypical involvement	Any other combination of abnormal tests.

The use of a single cardiovascular reflex test to assess the autonomic function is misleading and should be avoided.

RESULTS AND OBSERVATIONS

Females: Heart rate			Males: Heart rate		
F- Test Two-sample for variances			F- Test Two-sample for variances		
Family history	A Sample	B Sample	Family history	A Sample	B Sample
Mean	80.32	78.62857	Mean	77.44	76.96
Variance	58.89	27.94	Variance	21.173	7.373
Observations	25	35	Observations	25	25
D.f.	24	34	D.f.	24	24
F	2.107		F	2.8716	
P(F<=f) one-tail	0.0226		P(F<=f) one-tail	0.0061	
F Critical one-tail	1.84		F Critical one-tail	1.983	
Inference: significant p value			Inference: significant p value		
Females: BP: SYSTOLIC			Males: BP: SYSTOLIC		
F- Test Two-sample for variances			F- Test Two-sample for variances		
Family history	A Sample	B Sample	Family history	A Sample	B Sample
Mean	112	111.14	Mean	117.76	113.44
Variance	116.66	139.83	Variance	118.44	94.173
Observations	25	35	Observations	25	25
Df	24	34	Df	24	24
F	0.834		F	1.2576	
P(F<=f) one-tail	0.3257		P(F<=f) one-tail	0.2893	
F Critical one-tail	0.5216		F Critical one-tail	1.983	
Inference: p-30% is not significant p value			Inference: p-20% is not significant p value		

Females: BP: DIASTOLIC			Males: BP: DIASTOLIC		
F- Test Two-sample for variances			F- Test Two-sample for variances		
Family history	A Sample	B Sample	Family history	A Sample	B Sample
Mean	66.96	66.74	Mean	75.52	77.36
Variance	58.7	66.6	Variance	47.09	50.24
Observations	25	35	Observations	25	25
Df	24	34	Df	24	24
F	0.8813		F	0.93736	
P(F<=f) one-tail	0.3786		P(F<=f) one-tail	0.4377	
F Critical one-tail	0.5216		F Critical one-tail	0.504	
Inference: p-37% is not significant p value			Inference: p-43% is not significant p value		

1. **Basal Heart Rate**- In group A & B, basal heart rate was statistically significant. In females p value is 0.02 & in male p value is 0.006 (As shown in table 1).

2. **Basal Blood Pressure**- In group A & B, basal systolic & diastolic blood pressure

were statistically not significant. In females p is 30% & 20% respectively & in males p is 37% & 43% respectively (As depicted in table 2).

3. **Orthostatic test**- In both A&B groups, the test was statistically very much significant.

The p value in females is 0.00001% & in males is 0.009% (As shown in table 3).

4. **Cold pressor test-** In group A & B, increase in diastolic blood pressure was statistically significant. P value in females is 0.04% & that of in males is 0.1% (As observed in table 4).

5. **Sustained Handgrip test-** Sustained handgrip increases diastolic pressure, was statistically significant in females than in males. P value in females is 1% & in males is 48% (As mentioned in table 5)

Table 3: Orthostatic test						
	mm Hg	Female A group	Female B group	Male A group	Male B group	
Normal	10	12	35	19	25	
Border line	30	13	0	6	0	
Abnormal	More	0	0	0	0	
Females: Orthostatic decrease in systolic BP			Males: Orthostatic decrease in systolic BP			
F- Test Two-sample for variances			F- Test Two-sample for variances			
Family history	A Sample	B Sample		Family history	A Sample	B Sample
Mean	12.56	4.25		Mean	9.36	6.24
Variance	78.5	8.31		Variance	27.9	7.44
Observations	25	35		Observations	25	25
Df	24	34		Df	24	24
F	9.44			F	3.7	
P(F<=f) one-tail	4.65			P(F<=f) one-tail	0.00096	
F Critical one-tail	1.84			F Critical one-tail	1.9	
Inference: significant p value			Inference: significant p value			

Table 4: Cold Pressor test						
	mm Hg	Female A group	Female B group	Male A group	Male B group	
Normal	10	0	0	0	0	
Abnormal	More	25	35	25	25	
Females: Cold pressor increase in diastolic BP			Males: Cold pressor increase in diastolic BP			
F- Test Two-sample for variances			F- Test Two-sample for variances			
Family history	A Sample	B Sample		Family history	A Sample	B Sample
Mean	13.04	1.082		Mean	16.56	16.96
Variance	12.04	0.0017		Variance	13.84	5.3733
Observations	25	35		Observations	25	25
Df	24	34		Df	24	24
F	0.3448			F	2.5756	
P(F<=f) one-tail	0.0041			P(F<=f) one-tail	0.01212	
F Critical one-tail	0.5216			F Critical one-tail	1.9837	
Inference: significant p 0.04% value			Inference: significant p 1% value			

Table 5: Sustained hand grip						
	mm Hg	Female A group	Female B group	Male A group	Male B group	
Abnormal	10	3	1	0	0	
Border line	15	5	4	5	2	
Normal	More	17	30	20	23	
Females: Sustained hand grip increase in diastolic BP			Males: Sustained hand grip increase in diastolic BP			
F- Test Two-sample for variances			F- Test Two-sample for variances			
Family history	A Sample	B Sample		Family history	A Sample	B Sample
Mean	15.2	16.62		Mean	16.56	17.36
Variance	14	4.6521		Variance	4.5066	4.5733
Observations	25	35		Observations	25	25
Df	24	34		Df	24	24
F	3.0093			F	0.9854	
P(F<=f) one-tail	0.0016			P(F<=f) one-tail	0.4858	
F Critical one-tail	1.8427			F Critical one-tail	0.504	
Inference: significant p 1 % value			Inference: significant p-48 % value not significant			

DISCUSSION

Cardiovascular autonomic reflexes in humans are essential for the maintenance of arterial BP during the orthostatic stress, and for preventing wide fluctuations of arterial BP in response to stress, exercise and other adaptive responses.

This study indicates that the cardiovascular responses to certain physiological stimuli were impaired in the students having family history of hypertension called "A group" compared with family history of non hypertensive controls called "B group" and further divided in to male and female groups.

Basal Heart Rate and Blood Pressure

In this test the comparison between the A groups and B groups for the basal heart rate reports were statistically significant, for females p is 0.02 and for males p is 0.006 suggesting the samples belongs to different populations. My results correlated with some studies who proposed that variation in heart rate at rest is mediated by the combined effects of cardiac, vagal and sympathetic nerves acting on the sinoatrial node. ⁽⁵⁾

Basal Blood Pressure

In this test the comparison between the **A group** and **B group** for the basal systolic and diastolic reports were statistically not significant in females (the p is 30% and 20% respectively) and in males (the p is 37% and 43% respectively). It was reported that the arterial baroreflexes exert buffering influence on the magnitude of centrally induced variations of arterial pressure during day and night. They act by reducing arterial BP oscillations and their activity is manifested by beat-to beat variations of the HR opposite in direction to the changes in arterial BP if the arterial baroreflex is acting normally. There are small arterial BP oscillations and a large HR oscillation occurs in patients with baroreflex failure. It was reported that

mechanoreceptors in the atria and ventricles innervated by vagal afferents exert tonic inhibitory influence on sympathetic outflow and AVP release. These reports are correlated with our reports.

The tests reflecting sympathetic function -

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1. Orthostatic decrease in Systolic BP

In the test the comparison between the A groups and B groups for the orthostatic decrease in systolic B.P reports were statistically very much significant the P value for females is 0.00001 % and for males it is 0.009 % these reports are corresponding with the responds to postural change was similar in men and woman. ⁽⁶⁾

Bannister roger autonomic failure reported that the processing of standing up involves the integration of number of cardiovascular reflexes. There is pooling of blood in the legs with a consequent fall in BP. It was suggested that the response of the blood pressure to change in body position has been used in epidemiological studies as a measure of cardiovascular reactivity. ⁽⁷⁾ It was reported that a 10 mm Hg or grater increase in diastolic BP from supine to standing position significantly modified the effect of seated systolic BP. ⁽⁸⁾ These reports are corresponding with our results. Other studies reported a gender difference in the blood pressure response to standing which was not found in our study.

2. Sustained Handgrip

In this test comparison between the A groups and B groups for sustained handgrip increase diastolic pressure test reports were statistically significant in females the P is 1% and males the P is 48% which is not significant. During the isometric work test B.P reaction to sustained hand grip is measured. The mechanism involves the exercise reflex that withdraws parasympathetic activity and increase sympathetic tone. Normally the diastolic B.P rise is more than 15 mmHg. These responses

are greater in males than females. Some results show that the baroreflex response is modified by Sustained handgrip. ⁽⁸⁾ Cold pressor test and sustained handgrip tests were done, in both tests; there is significantly increased heart rate and blood pressure. These reports are correlating with our reports.

3. Cold Pressor increase in Diastolic BP

The comparison between the A groups and B groups for coldpressor increase in diastolic BP test reports were statistically significant in females the estimated P is 0.04% and males the P is 0.1%. It is found that systolic and diastolic blood pressure was heritable. ⁽⁷⁾ Coldpressor test measures the effect of stress on inherited vascular reactivity. Previous studies showed an average BP value to be higher in hyper reactors than in normo reactors. Some studies showed rise during cold pressor response. ⁽⁹⁾

Cold pressor response is mediated by efferent in the sympathetic nervous system and is considered a good index of sympathetic activity. ⁽¹⁰⁾ It is reported that the rise of systolic BP and diastolic BP during cold pressor test were also higher in hyper reactors as compared to normoreactors of all age groups. ⁽¹¹⁾ The rise of systolic BP and diastolic BP during cold pressor test was significantly higher in controls than in normoreactors in the two female groups. The study suggests that identification of hyper reactors in population gives a better indication of potential hypertensives of future than the children of hypertensives. These reports are corresponding with our reports. ⁽¹²⁾

SUMMARY & CONCLUSION

Before beginning of the study we had taken the null hypothesis, according to this hypothesis in our study we should not be anticipating any altered response in the students having family history of

hypertension compared to normal control group but after evolution of results some of the subjects proved against null hypothesis. In this study the cardiovascular responses to certain physiological stimuli were impaired in the students having family history of hypertension.

The tests reflecting sympathetic function:

1. Blood pressure response to standing (fall in systolic blood pressure) was significant.
 2. Blood pressure response to sustained handgrip (increase in diastolic blood pressure) was significant.
 3. Blood pressure response to cold pressor test (increase in diastolic blood pressure) was significant.
- Suggesting sympathetic function was involved more.

The tests reflecting sympathetic function:

1. Blood pressure response to standing (fall in systolic blood pressure) was significant.
 2. Blood pressure response to sustained handgrip (increase in diastolic blood pressure) was not significant.
 3. Blood pressure response to cold pressor test (increase in diastolic blood pressure) was not significant.
- Suggesting function not much involvement.

Our study concludes that -

- Females are involved more than males.
- Sympathetic function was involved more in females due to emotional component.
- There is potential gender difference.
- There is definite predisposition of family history of hypertension.

Looking the results probably the life style changes, genetic, familial and environmental factors surfacing itself more so for the A group (with family history of hypertension) in early ages.

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