

## ALTERED CARDIOVASCULAR REACTIVITY IN CHILDREN OF HYPERTENSIVE PARENTS

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### ABSTRACT

**Background:** Hypertension is a burning health problem worldwide. It has familial disposition. Stress factor increases risk of essential hypertension especially in offsprings of hypertensive parents. Cardiovascular autonomic reactivity is one of the indicators for prediction of hypertension in future life.

**Aims and Objectives:** To compare cardiovascular reactivity in normotensive offsprings of hypertensive parents and normotensive parents.

**Material and Methods:** Study included 100 medical students both male and female between ages 18 to 30 years. During assessment, weight, height, resting heart rate, resting SBP and resting DBP was measured. Change in DBP in isometric handgrip test and cold pressor test, were recorded by automated blood pressure monitor (Omron SEM-1 model, 6607551LF) and Hand-grip dynamometer. Subjects were divided into group I and II and each group contained 50 students with and without history of familial hypertension respectively.

**Statistical analysis:** Student's unpaired t test was applied for statistical analysis. The outcomes were presented as a mean (SD) and 'p' value of less than 0.05 was considered as significant. Statistical analysis was done using Graph pad Instat 3.0 and SPSS-IS software. Mann-Whitney test used to compare the autonomic function tests.

**Result and Conclusion:** There was statistically significant (p value < 0.0005) rise in DBP in both isometric handgrip test and cold pressor test showing sympathetic over reactivity especially in young normotensive subjects with hypertensive parents, significant results obtained. The offsprings of hypertensive parents who show higher cardiovascular reactivity, to a stressor given by cold pressor test and isometric handgrip test, is due to sympathetic over reactivity in early life. Purpose of this study is to help in framing guidelines for preventing cardiovascular risk in future for the individuals with hypertensive parents.

**Key Words** – Cardiovascular reactivity, Hypertensive, Normotensive, Isometric handgrip test, Cold pressor test

### INTRODUCTION

In this era of hectic time and a competitive life style, people are subjected to stress in day to day life. These stresses produce wide spread autonomic variations in our physiology. One such

stressful condition is hypertension where there is autonomic imbalance. Children of two normotensive parents had 3% possibilities of developing hypertension whereas this possibility is 45% in children if both hypertensive parents.<sup>(1)</sup>

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Autonomic abnormality in the form of increase in sympathetic tone has been demonstrated in young normotensive children of hypertensive parents. <sup>(2)</sup> Hypertension is reported to be associated with sympathetic nervous system over activity. <sup>(3)</sup> It has been observed that young normotensive children of hypertensive parents exhibit several abnormal characteristics like being overweight, <sup>(4)</sup> elevated basal blood pressure and produce exaggerated blood pressure response to exercise. <sup>(5-7)</sup> 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 mediated through parasympathetic nervous system. <sup>(8-10)</sup> There is altered cardiovascular autonomic reactivity among such adults.

Thus assessment of autonomic function tests in offspring of hypertensive and normotensive parents will help in framing guidelines for preventing cardiovascular risk in future.

## MATERIAL AND METHODS

The present study was conducted in the department of physiology, at Seth G.S Medical College and KEM hospital in Mumbai. The study group comprised of 100 young healthy students in the age group of 18- 30 yrs. Group I (study group) - Medical students with hypertensive first degree relatives; Group II (control group) - Medical students with normotensive first degree relatives. Ethical clearance for the study protocol was obtained from institutional ethical committee. Subject's detail clinical history and examination were carried out. Informed written consent was taken from all subjects in the study. Subjects with history of cardiac disease, diabetes mellitus, acute illnesses like respiratory tract infection, gastroenteritis, chronic renal, thyroid, adrenal diseases of any duration, Influences of any medication were excluded from this study.

### Study procedure –

The apparatus used were, Automated Blood

Pressure Monitor (OMRON HEALTH CARE CO.LTD, SEM-1 model, 6607551LF) for recording blood pressure having cuff size of Omron was 121 mm (width) × 446 mm (length), Hand-grip dynamometer (Manufactured by ANAND agencies): for isometric hand grip test, Ice cube box and cotton towel: for cold pressor test.

### 1) Hand grip test:

In this test, sustained muscle contraction is measured by a handgrip dynamometer, which causes a rise in systolic and diastolic blood pressure and heart rate. The dynamometer was first squeezed to isometric maximum, and then held at 30% maximum for 5 min if possible, at least 3 minutes is considered as adequate. Blood pressure was measured in the other hand three times before and at one-minute intervals during handgrip. The result was expressed as the difference between the highest diastolic blood pressure during handgrip exercise and the mean of the three diastolic blood-pressure readings before handgrip began.

### 2) Cold pressor test

After recording the baseline BP, subject is instructed about the test. They are instructed to indicate to the investigator, if there is any discomfort while performing the test. Cold water of 1°C is prepared. The subject immerses the hand in water up to the wrist for 1 min. Once removed, hand is covered by towel.

Rise in diastolic blood pressure = Highest DBP during test – baseline DBP

Normal values = Increased in DBP  $\geq$  10 mm Hg.

## STATISTICAL ANALYSIS

Data was entered in Microsoft Excel (2010). The mean and standard deviation was calculated for all the parameters. Statistical analysis was done using

Graph pad Instat 3.0 and Statistical Package for Social Sciences (SPSS-IS) software. Mann Whitney test is used to compare the autonomic function tests in students with hypertensive and normotensive parents. The p value of less than 0.05 was considered as statistically significant.

## RESULTS

Table no. 1: Statistical analysis of physical characteristics of Group I and group II students

| Physical characteristics       | Group I<br>Mean $\pm$ SD | Group II<br>Mean $\pm$ SD | P value   |
|--------------------------------|--------------------------|---------------------------|-----------|
| Age (Years)                    | 22.1 $\pm$ 2.29          | 24.48 $\pm$ 3.51          | 0.0009*   |
| Weight (kg)                    | 55.62 $\pm$ 8.71         | 56.22 $\pm$ 8.55          | 0.7459    |
| Height (cm)                    | 164 $\pm$ 4.66           | 164 $\pm$ 4.66            | 0.0102*   |
| BMI (kg/m <sup>2</sup> )       | 21.27 $\pm$ 2.49         | 20.90 $\pm$ 3.17          | 0.4734    |
| Resting heart rate (beats/min) | 80.980 $\pm$ 5.24        | 86.40 $\pm$ 6.08          | < 0.0004* |
| Resting systolic BP (mmHg)     | 117.26 $\pm$ 3.43        | 118.20 $\pm$ 2.65         | 0.9972    |
| Resting diastolic BP (mmHg)    | 76.92 $\pm$ 3.43         | 78.32 $\pm$ 2.36          | 0.0324*   |

\* p value < 0.05 was considered as significant

Table no 2: Comparison between changes in diastolic BP in isometric handgrip test among students with hypertensive (Gr I) and normotensive parents (Gr II)

| Isometric Handgrip Test | Change in diastolic blood pressure (mm of Hg) (Mean $\pm$ SD) | P value  |
|-------------------------|---|----------|
| Group I (n = 50)        | 21.64 $\pm$ 3.34  | 0.0012*  |
| Group II (n=50)         | 19.96 $\pm$ 1.873   | <0.0001* |

\* p value < 0.05 was considered as significant

Table no. 3: Comparison between change in diastolic BP in cold pressor test among students with hypertensive (Gr I) and normotensive parents (Gr II)

| Cold Pressor Test | Change in diastolic blood pressure (mm of Hg) (Mean $\pm$ SD) | P value |
|-------------------|---|---------|
| Group I (n = 50)  | 17.90 $\pm$ 1.474   | 0.0001* |
| Group II (n=50)   | 13.80 $\pm$ 1.629   | 0.0009* |

\* p value < 0.05 was considered as significant

**Table No 1** depict the comparison of physical parameters between study group and control group. Both the groups were homogeneous when weight and BMI were considered as difference was not statistically significant. But difference was

statistically significant for age and height. Unexpectedly resting heart rate, resting systolic and diastolic BP readings were lower in study group, but difference was not statistically significantly for resting systolic BP.

**Table No 2 and 3** depict the comparison of change in diastolic BP during isometric handgrip test and cold pressor test respectively in study group and control group. Difference in diastolic BP in isometric handgrip test of group I was statistically significant as compared to group II; with p value <0.005. Rise in diastolic blood pressure in cold pressor test, of group I was statistically significant as compared to group II (p value < 0.0001)

## DISCUSSION

Hypertension runs in families. Hyper-responsiveness to stress is mediated by an over-activity of the sympathetic nervous system. These stresses produce wide spread autonomic variation in our physiology. Studies have shown that stress factor is one of the trigger factors for prediction of hypertension. <sup>(2)</sup> Subjects at high risk of future hypertension are either the persons belonging to hypertensive family or having high resting heart rate or ephemeral increase in arterial hypertension. <sup>(11)</sup> So the present study was undertaken to evaluate the role of autonomic nervous system during acute circulatory stress in children of hypertensive and normotensive parents.

The present study was initiated on the hypothesis of genetic predisposition for hypertension, children with hypertensive parents showed deranged cardiovascular autonomic function which in turn leads to several physiological and biochemical changes, thus creating a vicious cycle of interrelated chain reactions which finally puts seal "permanency". <sup>(12)</sup> Cold pressor test and isometric handgrip test were the tests, largely related to sympathetic efferents. So, these tests were used as circulatory stresses to induce hemodynamic changes. Blood pressure and heart rate were used as parameters for the autonomic nervous system functioning, both the sympathetic and parasympathetic limb.

It has been opined that those with parental history of hypertension; their children show high resting DBP, probably due to hyperactive sympathetic nervous system.<sup>(13)</sup> Normotensive young adults with family history of hypertension have exaggerated cardiovascular reactivity which is due to peripheral vasoconstriction mediated by adrenergic receptors of sympathetic nervous system.<sup>(12)</sup>

#### **Isometric handgrip test:-**

All the subjects could maintain 30 percent maximum voluntary contraction throughout five minutes without any clinical symptoms. It has been suggested that 30 percent maximum voluntary contraction was quiet safe protocol,<sup>(14)</sup> and the same was observed during our test. In our study  $\Delta$  DBP of group I was found statistically significant as compared to group II in isometric handgrip test. Rise in BP during test could be genetically correlated with hypersensitivity to circulating catecholamine.<sup>(15)</sup> This predominant rise in diastolic BP is due to increase in after load which is produced because of compression of blood vessel underneath the contracting muscle.<sup>(16)</sup> Subjects exhibiting greater and prolonged response to stress induced tests are more prone to develop hypertension.<sup>(11)</sup>

In isometric handgrip test, there is peripheral vasoconstriction mediated by adrenergic receptors of sympathetic nervous system. 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 due to a hypothalamus mediated reflex releasing norepinephrine at vascular smooth muscle cells, further accentuated by concomitant release of endothelin-1.<sup>(2)</sup>

#### **Cold pressor test :-**

All the subjects could continue the test for one minute without much of discomfort. The rise in diastolic BP was statistically significant in children of hypertensive parents over the normotensive parents. The pattern of rise of BP was within 30 seconds reaching its peak and at around 60 seconds the basal blood pressure was achieved within two

minutes in subjects of normotensive parents, whereas a prolonged pressor response was displayed in children of hypertensive parents.

Similar findings are in keeping with the study- cold pressor test as a predictor of hypertension of **Douglas LW et al**<sup>(17)</sup>. They have explained that early hyper reactivity was related to future hypertension in enough subjects to suggest that abnormal response to external cold stimulus may be useful as an indicator of future hypertension.

Investigated pathophysiologic response to cold pressor test has shown that the children of hypertensive and normotensive parents respond to cold pressor stimulus with a predominant rise in total peripheral resistance and also there was a higher level of plasma norepinephrine.<sup>(1)</sup> In research studies it has been found that the hyperresponsiveness may represent one pathogenic mechanism in development of essential hypertension, be a marker of central defect in the autonomic control of the cardiovascular system or reflect early changes in arterial compliance of future hypertensive individuals.<sup>(18)</sup> Hyperreactivity is a manifestation of wide spread basic membrane transport disorder that disrupts cellular cation homeostasis.<sup>(19)</sup>

Cardio-vascular reactivity to stress may have a pathological role in neurogenic hypertension. Sympathetic nervous system might play a pivotal role in the pathogenesis of essential hypertension.<sup>(20)</sup> There is a shift in cardiac autonomic regulation towards sympathetic activation in response to real life stresses. The sympathetic noradrenergic fibers are vasoconstrictor in function. The noradrenergic post ganglionic sympathetic nerves also contain neuropeptide Y, a vasoconstrictor. Vasoconstrictor discharge is associated with increased arteriolar constriction and a rise of blood pressure.<sup>(21)</sup> Impulses in nor-adrenergic sympathetic nerves cause an increase in heart rate and force of cardiac contraction.

The present study reveals that not only the incidence of prehypertension is more prevalent in children of hypertensive parents, but also they have

greater risk of cardiovascular dysfunctions linked to their increased degree of sympathetic reactivity. The present report is the first of its kind to assess the cardiovascular reactivity in young children of hypertensive parents. It reveals the impact of parental hypertension on their offsprings and importance of sympathovagal inhibition in the possible causation of prehypertension in these young genetically susceptible individuals.

Therefore in spite of limitation of less sample size and some unexpected findings in study, present study emphasizes the necessity to improve vagal tone and lower sympathetic tone in young children of hypertensive parents. Sympathetic nervous system hyperactivity develops in children of hypertensive parents whereas the parasympathetic nervous system remains unaltered. Though the subjects of study group may be normotensive initially, there is a possibility of development of hypertension in future. On the basis of present study the children of hypertensive parents may be advocated to change or bring modification in their lifestyles so that hypertension can be prevented or delayed at later stages of life. Regular practices of slow breathing exercises have been reported to improve autonomic functions.<sup>(22)</sup>

## CONCLUSION

Our results suggest that vasoconstrictor and cardiac acceleratory responses to autonomic stress test are subnormal in young adults with hypertensive parents as compared to that of adults with normotensive parents.

Further this study gives an indication that the persons, who showed greater and specially prolonged responsiveness to DBP due to sympathetic stimulation through Isometric Handgrip Test and Cold Pressure Test may be prone to develop hypertension in their future life.

The offsprings of hypertensive parent who show higher cardiovascular reactivity to a stressor given by cold pressor test and isometric handgrip test is due to sympathetic over reactivity without modulation of parasympathetic system in early life. On the basis of present study the offsprings of hypertensive parents may be advocated to change or bring modification in their lifestyle, so that

hypertension at a later stage of life can be delayed or prevented.

An individual with proneness to hypertension may live a healthy life by altering his lifestyle. Therefore, if a person can be informed that he may suffer from hypertension well ahead the hypertension sets in, it will be obviously beneficial. Regular monitoring of autonomic activity may prove to be a useful tool in predicting the future hypertension.

## REFERENCES

- 1) Gupta L, Dondiya D, Panchal V, Jain D, Goyal B, Cardiovascular responses to autonomic stressors in young adults belonging to hypertensive family. *Integrative Journal of Medicine and Pharmacological Science* 2014; 04(06): 19-25
- 2) Pal GK, Pal P, Nanda N, Lalitha V, Dutta TK and Adithan C. Sympathovagal imbalance in prehypertensives offspring of two parents versus one parent hypertensive. *Indian journal of hypertension* 2011; 10: 1-8
- 3) Rathi P, Agarwal V and Ajay Kumar. Sympathetic hyperactivity in children of hypertensive parents. *Journal of annals of neurosciences* 2013; 20: 4-6
- 4) Leon DF and Shaver AJ. Reflex heart rate control in man. *American heart J* 1970; 80: 729-39
- 5) Julius S, Schark MA. Prediction of hypertension. *Ann NyAcad Sci* 1978; 304: 38-42
- 6) Julius S. Autonomic nervous system dysregulation in human hypertension. *Am J Cardiol* 1991; 67(10): 38-78
- 7) Matthews CF, Pate RR, Ward DS, Jackson KL, Ward DS, Macera CA et al. Exaggerated blood pressure response to dynamic exercise and risk of future hypertension. *Journal Clinical Epidemiology* 1998; 51:

- 29–35
- 8) Bristow JD, Honour AJS, Smyth HS, Pickering GW and Peter S. Diminished baroreceptor sensitivity in high blood pressure. *Circulation* 1969; 39: 1176–87
  - 9) Muralikrishnan K, Balasubramaniam K, Rao B. Heart rate variability in normotensive subjects with family history of hypertension. *IJPP* 2011; 55(30): 253–61
  - 10) Sowmaya R, Maruthy KN, Gupta R. Cardiovascular autonomic responses to whole body isometric exercise in normotensive healthy young adult males with parental history of hypertension. *IJPP* 2009; 54(1): 37–44
  - 11) Pramanik T, Regmi P, Shrestha P. Detection of Individuals prone to develop hypertension in their future life. *Nepal Med Col. J* 2008; 10(1): 35-37
  - 12) Ikhlas MJ, Noriah MN. Family history of hypertension is associated with exaggerated cardiovascular reactivity to mental, but not to physical test. *Medicine Journal of Indonesia* 2010; 17(2): 118–23
  - 13) Steve J. Autonomic Nervous System Dysregulation in Human Hypertension. *Am J Cardiol.* 1991 Apr 22; 67(10): 3B-7B.
  - 14) Clarke RS, Hellon RF and Lind AR. The duration of sustained contraction of the human forearm at different muscle temperature. *Journal of Physiology* 1958; 143: 454-59
  - 15) Charles Marks. Surgical management of systemic hypertension. Future publishing co. New York 1981
  - 16) Fixler DJ, Laird P, Bradne R. Response of hypertensive adolescent to dynamic and isometric exercise test. *Pediatric journal* 1979; 64(5): 579-583
  - 17) Douglas LW, Sheldon GS, Lila E. Cold Pressor test as predictor of hypertension. *Journal of hypertension* 1984; 6: 301-306
  - 18) Mathews KA, Weiss TM, Dembruski TM. Handbook of stress reactivity and Cardiovascular disease. New York, John and Sans Inc 1986; 3(1): 1-82
  - 19) Bjorn Folkow. Physiological aspect of primary hypertension. *Physio. review* 1982; 62(2): 342-504
  - 20) Selvamenthy W, Shridharan K, Ray US, Tiwary RS. A new physiological approach to control essential hypertension. *Indian journal of physiology and pharmacology* 1998; 42(2): 205-213
  - 21) Levy MN. The cardiovascular system. In: Berne RM, Levy MN, editor. *Physiology.* 4th ed. St. Louis: Mosby; 1998, p.394.
  - 22) Pal GK, Velkumary S, Madanmohan. Effect of short-term practice of breathing exercises on autonomic functions in normal human volunteers. *Indian J Med Res.* 2004; 120(2): 115-21.

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