To study autonomic variability in offsprings of hypertensive parents in Lucknow using cold pressor test

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Abstract
Introduction: Hypertension runs in family, and familial hypertension is one of the most important risk factor for children to become hypertensive in future life. Teenagers comprise very special group that have hypertensive first degree relatives, these should be very closely monitored. Autonomic derangement in the form of increased sympathetic tone has been seen in young offsprings with a history of hypertension in their parents. Sympathetic nervous system over-activity is reported in hypertension. If we can detect early proneness to hypertension, it may help an individual to lead a healthy life by changing his/her lifestyle and daily activities.

Objective: To study sympathetic autonomic variability in offsprings of hypertensive parents.

Materials and Methods: This is a cross sectional study. In this study 52 healthy young subjects (26 study group i.e., offsprings of hypertensive parents and 26 control group i.e., offsprings of non-hypertensive parents) age: 18-25 years both male and female were chosen. The blood pressure of the participants was recorded using an electronic blood pressure instrument (Citizen 432). The participants were asked to immerse their right hand in ice cold water (4 degree Celsius) for 1 minute. At the completion of one minute, blood pressure was measured. Five minutes after the test, the blood pressure was noted again (recovery). Body mass index was also noted of each individual.

Results: It is evident from the results that in both study group and controls, a rise in systolic blood pressure occurred as a result of stress induced by cold test but in study group the diastolic blood pressure showed a significant increase whereas in controls it showed no change after stress induced by cold test.

In both the study group and controls, the systolic component returned to the baseline value after a duration of 5 minutes of stress (recovery), whereas the diastolic component of controls returned to the baseline value and even below baseline but the diastolic component of study group did not returned to baseline after 5 minutes and even remained elevated.

When Body Mass Index (BMI) of both the groups (study and control) was compared it was seen that predisposed subjects i.e., the study group subjects showed a significant elevated BMI when compared to non predisposed individuals i.e., controls.

Keywords: Hypertension, Autonomic, Cold pressor test, Body mass index.

Introduction
As per World Health Organization, increased blood pressure is one of the important causes of premature deaths around the world.¹ 20.6% of men (Indian) and 20.9% of women (Indian) were suffering from high blood pressure (hypertension) in 2005 and the rates are expected to go up to 22.9 and 23.6 by 2025 (approx. 5 million).¹

It is well established fact that increased blood pressure increases one’s risk for coronary artery disease, stroke, and cardiovascular events.²

Pre-hypertension, these patients succumb to sudden coronary death, myocardial infarction and stroke more easily as evident by Framingham Heart Study.³ Environmental and genetic factors play an important role in the causation of high blood pressure (hypertension).³

Family history is an important non-modifiable risk factor for hypertension, demonstrating associations of blood pressure among siblings and between parents and children’s.⁴

Compared to the offsprings of two normotensive parents, blood pressure is higher in the offsprings of one normotensive and one hypertensive parent, and the highest in the offsprings of two hypertensive parents.⁵

Hypertension is an “iceberg” disease. It became evident in the early 1970s that only about half of the hypertensive subjects in the general population of most developed countries were aware of the condition, only about half of those aware of the problem were being treated, and only about half of those treated were considered adequately treated.⁶

Hypertension is reported to be associated with sympathetic nervous system over activity. Autonomic imbalance in the form of raised sympathetic tone has been shown in offspring’s of high blood pressure parents. Young normotensive offspring’s of hypertensive parents exhibit abnormal characteristics like being overweight and elevated basal blood pressure.⁷

If we can detect proneness of a subject to hypertension in early ages, he/she can lead a healthy life by altering his/her few daily habits and activities e.g., avoidance of alcoholic beverages, smoking, intake of extra fatty foods and inculcation of the practice of yoga, moderate exercise (aerobic), mental relaxation techniques etc. in daily lifestyle.

This, idea motivated me to have my work planned on this topic.

A lot of previous work has shown that sympathetic nervous system may play a important role in the causation of hypertension (essential). Individuals that are at increased risk of being hypertensive in future – e.g., those with a history of hypertension in family, showed increased
response of blood pressure to stress stimuli caused by an increase response of sympathetic nervous system.⁸

Sympathetic system leads to increase in blood pressure when it is stimulated by stress and the blood pressure returns to normal or near normal level when the stress is withdrawn, this happens within a short period of time. Subjects with weak autonomic activity show high reactivity to stress and slow rate of recovery once the stress is removed. These individuals are at increased risk for becoming hypertensive in early age in their future. A lot of work done in the past also support the fact that even in the absence of hypertension and its development during stress could be considered a positive predictive marker for the future development of early onset of hypertension, and can be a tool for identifying individuals at high risk having apparently normal blood pressure at present. These individuals should be regularly followed up.⁸

In our study, the young adults with normal blood pressure and with family history of hypertension show variations in autonomic functions when compared to age and sex matched subjects without family history of hypertension, is being tested and discussed.

**Aim and Objective**

To study sympathetic autonomic variability in offsprings’ of hypertensive parents.

**Materials and Methods**

This is a cross sectional study conducted in the Department of Physiology, Era’s Lucknow Medical College and Hospital, Lucknow from July 2017 till December 2017. In this study 52 healthy young subjects, who were not accustomed to take regular exercise, led a sedentary lifestyle, although had a normal blood pressure (n = 52; 26 study group i.e., offsprings of hypertensive parents and 26 control group i.e., offsprings of non-hypertensive parents) were chosen randomly from para-clinical courses of Era’s Medical College as volunteers to participate in the study.

**Inclusion Criteria**

1. Study Group: 18-25 year young healthy individuals of hypertensive parents.
2. Controls: year young healthy individuals of non-hypertensive parents.
3. Subjects with proper consent.

**Exclusion Criteria: 18-25 Subjects with**

1. Major/chronic disorder (Asthma, Tuberculosis, and seizure disorders)
2. Smokers/alcoholic
3. On any drugs/medications
4. And those not providing consent.

**Method**

All the subjects fulfilling the inclusion criteria and not falling into the domain of exclusion criteria were invited to enroll in the study till the sample size requirements were fulfilled. The protocol of study was explained to all the subjects and a written informed consent was obtained. Ethical clearance was taken through proper channel. The participants were asked about their history of FAMILIAL hypertension, existing worries/anxieties. The blood pressure of the participants was recorded using a electronic blood pressure instrument (CITIZEN-CH-432). Systolic pressure and diastolic blood pressure was measured. Blood pressure was measured between 10:00 – 11:00 AM after 2 hours of light breakfast and 5 minutes of rest.

**Cold Pressor Test Protocol**

First the baseline blood pressure was recorded from one arm, and then the subjects were instructed about the test. They were also instructed to indicate to the instructor if they were unable to keep their hand in cold water for 1 minute.

The cold water of 4 degree C was prepared. (At Postgraduate Laboratory of Era’s Lucknow Medical College). The subject was made to immerse his one hand (the hand without blood pressure cuff) up to the wrist in cold water for 1 minute. After the hand was removed from the water, it was covered by a towel.

**Recording**

First the resting BP was recorded then the, blood pressure was measured from the other arm (the arm not exposed to cold water) at 1 minute and at 5 minutes interval. Changes in blood pressure were recorded.

**Body Mass Index**

Weight of the subjects were measured in kilograms using electronic weighing scale of department of Physiology (Omron digital ultra slim) and height was recorded in centimeters using departments Stadiometer, using standard scale.

BMI was calculated using the formula:

\[
\text{BMI}= \frac{\text{Weight}}{\text{Square of the Body Height}}
\]

Weight= in kilograms.

Height= in meters.

**Results**

| Table 1: Comparing mean values of both study group and controls at rest and at various time intervals after the Cold Pressor test | Study group | Control | t value | p value |
|---|---|---|---|---|
| MEAN±SD | MEAN±SD | | |
| **Baseline SBP** | 117.5±6.28 | 112.61±6.38 | 2.78 | 0.008* |
| **Baseline DBP** | 73.27±5.31 | 75.88±4.46 | -2.06 | 0.044* |
| **SBP at 1 min of cold test** | 124.73±5.45 | 121.11±5.71 | 3.22 | 0.029* |
| **DBP at 1 min of cold test** | 77.5±2.48 | 75.73±3.14 | 2.25 | 0.037* |
| **SBP recovery after 5 minute of cold test** | 116.38±6.78 | 112.34±6.81 | 2.14 | 0.047* |
| **DBP recovery after 5 minute of cold test** | 75.76±5.53 | 72.53±5.92 | 2.03 | 0.045* |
Table 2: Compares mean body mass indices of study group and controls

| BMI in kg/meter square | Study group (26) | Control (26) | t value | P value |
|------------------------|------------------|--------------|---------|---------|
| MEAN ±SD               | 28.38 ±1.74      | 26.99 ±1.49  | 4.16    | < 0.001*|

Table 1 shows and compares baseline values (i.e., the values before the start of test), values after 1 minute of cold test and values after 5 minutes of cold test of both systolic and diastolic component of blood pressure of both study group and controls.

As we can see from the table 1, Study group having predisposing factors of hypertension, a rise in systolic blood pressure occurred (after stress precipitated by cold exposure) after 1 minute (124.73) that returned below the baseline value (117.5) after 5 minutes (116.38).

1. In controls without predisposing factors of hypertension there was rise in systolic blood pressure too after 1 minute (121.11) of stress by cold test, that returned to the baseline value (112.6) after 5 minutes (112.34).

2. In study group a rise in diastolic blood pressure occurred (after stress precipitated by cold exposure) after 1 minute (77.5) that did not return to the baseline value (73.07) after 5 minutes (75.76) and even remain elevated.

3. In controls there was no rise in diastolic blood pressure after 1 minute (75.73) of stress by cold test, that remained near to the baseline value (75.88) after 5 minutes and even below baseline (112.34).

Table 1 also compares the MEAN ± SD values of both systolic and diastolic blood pressure at various intervals and the baseline values.

When mean baseline value of systolic blood pressure in study group was compared to controls, the relation was significantly correlated (p<0.01), also on comparing the diastolic baseline values the relation was significant too (p=0.04).

But, when we compared the systolic blood pressure values of both study group and controls after 1 minute of cold test the p value came out to be 0.240 that was not significantly correlated and when the diastolic values of both study group and controls were compared after 1 minute of post test the correlation was found to be significant. (p=0.029).

Again, when we analyzed the recovery components after 5 minutes, it was seen that after 5 minutes of cold test both the systolic and diastolic component of blood pressure of both the study group and control was significantly correlated (p=0.037) systolic, (p=0.047) diastolic.

Table 2 compares the body mass indices of both study group (28.38±1.74) and control (26.99 ±1.49) that is the mean ±sd values. The comparison was statistically significant i.e. p < 0.001.

Fig. 1: To compare diastolic blood pressure of study group before and after the autonomic test
Discussion
Fibers that are sympathetic noradrenergic are vasoconstrictors in nature. The Post-ganglionic (noradrenergic) sympathetic nerves have neuropeptide-Y, which is also a vasoconstrictor. When there is vasoconstriction, there is an increase in arteriolar constriction and a decrease in blood pressure. Stress stimulates sympathetic system, that leads to an increase in blood pressure, the blood pressure returns to normal level (or near to normal) after the stress is withdrawn, this occurs in a short time period. The individuals with weak autonomic function, when stimulated by stress show high cardio-vascular reaction to stress and slow rate of recovery once the stress is withdrawn. These individuals are at high risk to suffer from hypertension in their further life.

Work done in past also support the fact that even in the absence of hypertension and its development during stress could be considered a positive marker for the future development of early onset of hypertension in individuals, and this can be used as a tool for selecting individuals at high risk having near normal blood pressure at present. These individuals should be very closely followed up.

Sympathetic system is stimulated by cold pressor test.
It is clear from results, that both controls and study group showed a rise in systolic blood pressure as a result of stress precipitated by cold test, this is in accordance with study done by T Pramanik et al in 2008, and M T Sherpa et al 2012, they also showed a rise in systolic blood pressure after stress test.

The diastolic blood pressure was increased in study group but remained unchanged in controls after stress mediated by cold test, this observation contradicted with that seen by T Pramanik et al in 2008, in which there was a rise in diastolic blood pressure in both study group and controls.

In both study group and controls the systolic blood pressure came to the base line value after 5 minutes i.e., recovery blood pressure, whereas in controls the diastolic blood pressure came to the base line value after 5 minutes, but in study group it failed to reach the baseline after 5 minutes and even remain elevated, this finding was in accordance with findings of T Pramanik et al in 2008.

When BMI of both the groups (study group and control) were compared it was seen that predisposed subjects i.e., the study group showed a significant elevated BMI in comparison to non predisposed individuals i.e., controls.

Conclusion
So, by the help of this study we conclude that young subjects who showed greater and prolonged responsiveness to blood pressure (diastolic), after stimulation of sympathetic system by stress (cold test) [i.e., those subjects whose diastolic blood pressure not returned to the base value after 5 minutes.] are at high risk for becoming early hypertensive in future.

Conflict of Interest: None.

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