

## EFFECTS OF COLD PRESSOR TEST ON BLOOD PRESSURE AND HEART RATE VARIABILITY IN THE WARDS OF HYPERTENSIVE PARENTS

Sheila R Pai<sup>1</sup>, Amrutha Mary<sup>2</sup>, Rekha D Kini<sup>1\*</sup> and Bhagyalakshmi K.<sup>1</sup>

<sup>1</sup>Department of Physiology, Kasturba Medical College, Manipal University, Bejai, Mangalore, Karnataka, India.

<sup>2</sup>Department of Physiology, Pushpagiri Institute of Medical Sciences & Research center, Tiruvalla, Kerala, India.

### ABSTRACT

Heart rate variability (HRV) is a topic of great interest because of its medical implications. Decreased HRV is associated with numerous conditions and has been used in risk stratifications for certain diseases. This study examines the effect of cold pressure stress on blood pressure and heart rate variability in the wards of hypertensive parents. The study included 67 subjects, 30 with parental history of hypertension and 37 with had normotensive parents. Subjects were divided into two groups; Control group (wards of normotensive parents) and Study group (wards of hypertensive parents). The height, weight and body Mass Index were noted. Cold pressor test was done. Blood pressure (BP) was measured and electro cardio gram (ECG) was recorded during normal breathing, deep breathing and cold pressor test. HRV analysis was done by time domain method. The data obtained was analyzed using student's t-test and by Mann-Whitney U-test and  $P < 0.05$  was considered significant. Cold pressure stress showed a significant increase in systolic Blood Pressure and Diastolic Blood Pressure (DBP) in study group with respect to control group ( $p < 0.01$ ). In the time domain analysis, mean value of RMSSD of study group was lower ( $p < 0.05$ ) than control group after the cold pressor test. The study thus concluded that wards of hypertensive parents showed an increase in the blood pressure and decrease in HRV to cold pressor test. Hence the result of current study represents the reduced parasympathetic activity that is present in the group with parental history of hypertension during cold pressor test.

**Keywords:** HRV, Cold pressor test, BP.

### INTRODUCTION

Hypertension is an important worldwide public-health challenge because of its high frequency and concomitant risks of cardiovascular and kidney disease<sup>1,2</sup>. It has been identified as the leading risk factor for mortality, and is ranked third as a cause of disability-adjusted life-years<sup>3</sup>. It is commonly asymptomatic, readily detectable, easily treatable and often leads to lethal complications if left untreated<sup>4</sup>. The identification of variant (allelic)

genes that contribute to the development of hypertension is complicated by the fact that the 2 phenotypes that determine BP, cardiac output and total peripheral resistance, are controlled by intermediary phenotypes, including the autonomic nervous system<sup>5</sup>.

The heart rate response to stress test is an important determinant of the healthy cardiovascular system<sup>6</sup>. Heart rate variability is the amount of heart rate fluctuations around the mean heart rate. The term heart rate variability

(HRV) conventionally describes the beat-to-beat fluctuations in the heart rate or the variations in consecutive RR interval. It is a valuable tool to investigate sympathetic and parasympathetic function of the Autonomic Nervous System<sup>7</sup>. Thus, HRV analyses the tonic baseline autonomic function. Time domain analysis measures the changes in heart rate over time or the intervals between successive normal cardiac cycles.

The cold pressor test which is considered to be a sympatho-excitatory maneuver is a simple, noninvasive and validated test of sympathetic activation<sup>8</sup>. The heart rate and blood pressure responses to cold pressor test could be used as indicators of global sympathetic activation, and thus, of cardiac status. As there is not much has been work done in Indian scenario to show whether the parental history of hypertension influence later development of the same, this work has been undertaken so that the cold pressor test could be employed as a mode of screening for cardiovascular risk in the wards of hypertensive parents, allowing for early intervention in order to prevent the associated morbidity and mortality.

#### **MATERIALS AND METHODS**

Present study was conducted after getting permission from the ethics committee. This study is a cross-sectional study. The first year medical students between the age group of 17-20 years (n=67) were the participants of the study. Subjects were included after counseling them about the nature and purpose of study. An informed consent was taken from the subjects for the same. A detailed relevant clinical history was obtained from them. This was followed by a brief general physical examination, examination of vital signs and a complete systemic examination. Healthy subjects who could follow instructions and who were non-smokers and non-alcoholics were included in the study. Those subjects with history of any respiratory, cardiovascular and neurological disorders, suffering from Diabetes Mellitus and known hypertensive were excluded from the study.

Height was measured using a standard stadiometer with the subjects standing in erect posture. The readings were taken to the nearest 0.1 cm. Weight was measured using a calibrated weighing machine. Body Mass Index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. Subjects were divided in two groups; Control group (wards of

normotensive parents) and Study group (wards of hypertensive parents).

#### **Measurement of heart rate variability**

The following materials were included in the study: ECG appliances with jelly and electrodes, a digital data acquisition system. A high quality ECG recording was taken under standardized conditions to minimize artifacts. The ECG signal was first analogally recorded and then digitally converted. Analysis of heart rate variability was done by the time-domain method using Digital Data acquisition system HRV soft 1.1 VERSION, AIIMS, NEW DELHI. Recording was done in the evening hours, between 4.30 to 5.30 a.m. in a cool room, with temperatures around 20 to 28 degree Celsius. The room was darkened and kept free of any acoustic disturbances. The procedure was explained to the subjects. They were instructed to relax and breathe spontaneously at their own rate. After a resting period, the ECGs of the subjects were recorded in the supine position during normal breathing for a 5 minute period. This was followed by a two minute break. The next ECG recording was then taken during deep breathing for about one minute. The subjects were asked to inspire for the first 5 seconds from the count of 1 to 5 and expire the next 5seconds from the count of 5 to 1. This recording was taken for six such cycles, i.e. one minute.

#### **Cold Pressor test**

The cold pressor test was performed in the supine position, and the subject's right hand was immersed in cold water of 4 degree Celsius up to the wrist for one minute. Care was taken to ensure that the subject avoided any isometric contractions, breath holding or performance of Valsalva maneuver. HRV was continuously recorded during immersion. Data stored on the computer was analyzed after completion of the test. Blood pressure was also recorded after the test in supine position using sphygmomanometer by indirect method.

#### **Statistical Analysis of data**

Analysis of the data was done by using SPSS (Statistical Package for Social Sciences) version 11.5. Statistical tests included student's unpaired t test followed by Mann Whitney U test and  $P < 0.05$  was considered significant.

#### **RESULTS**

Subjects were of two group; control and study group. The Mean $\pm$ SD value of systolic blood

pressure after cold pressor test in control group was  $115.21 \pm 5.51$  and in study group was  $119.25 \pm 3.79$ . Cold pressor stress showed a significant increase in systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) in study group with respect to control group ( $p < 0.01$ ) (Table 1).

In the time domain analysis, the square root of the mean squared differences of successive NN intervals (RMSSD) in the study group was  $45.92 \pm 27.90$  and in control group was  $68.39 \pm 48.64$ . The results of the present study showed a significant decrease in HRV ( $p < 0.05$ ) in the study group compared to control group after the cold pressor test (Table 2).

## DISCUSSION

It is a well-known fact that the cold pressor test provokes a remarkable increase in sympathetic activity in humans mediated by central command and local metabolites, particularly adenosine<sup>9</sup>. Cold pressor test is often used to evaluate the sympathetic influence on circulation in humans. In the present study we assessed and compared the cardiac autonomic activities in wards of normotensive and hypertensive parents using a cold pressor test. The main finding of this study was that HRV were reduced in the wards of hypertensive parents when compared to those of normotensive parents. The result of the present study was in accordance with few previous studies<sup>10, 11, 12</sup>.

In the present study there was a significant increase in the SBP and DBP in study group compared to control group. Subjects with a positive history of familial hypertension are reported to have elevated blood pressure responsiveness to stress stimuli mediated by an over-activity of the sympathetic nervous system. Reports support the notion that individuals at high risk of hypertension may have an exaggerated stress-induced cardiovascular response at a younger age<sup>13</sup>. Studies have shown that patients with borderline hypertension shows an exaggerated response to cold pressor test<sup>14, 15</sup>.

The cold pressor test (CPT) is known to trigger in healthy subjects a vascular sympathetic activation and an increase in blood pressure. Hence the findings in our study can be attributed to an enhanced sympathetic activity with either an increase or a decrease in the vagal activity in the wards of hypertensive parents compared to the normal group. Consulting with the previous studies we can say that this may be an early indicator of their vulnerability to hypertension

and those with the family history of hypertension can take precautionary methods like life style modification at the earlier age itself.

**Table 1: Effect of cold pressor test on blood pressure**

Group	Systolic blood pressure	Diastolic Blood Pressure
Control	$115.21 \pm 5.51$	$70.89 \pm 5.65$
Study	$119.25 \pm 3.79^{**}$	$76.50 \pm 8.12^{**}$

Values are expressed as Mean  $\pm$  SD. \*\* $P < 0.01$  study group compared with control group.

**Table 2: Effect of cold pressor test on hrv by time domain method**

Group	RMSSD (Mean $\pm$ SD)
Control	$68.39 \pm 48.64$
Study	$45.92 \pm 27.90^*$

Values are expressed as Mean  $\pm$  SD. \* $P < 0.05$  study group compared with control group. Number of subjects in study group is 30 and control group is 37.

## REFERENCES

1. He J, Whelton PK. Epidemiology and prevention of hypertension. Med Clin North Am. 1997; 81(5):1077-97.
2. Whelton PK. Epidemiology of hypertension. Lancet. 1994; 344: 101-6.
3. Ezzati M, Lopez AD, Rodgers A, Vander HS and Murray CJ. Selected major risk factors and global and regional burden of disease. Lancet. 2002; 360:1347-60.
4. Gaziano T.A, Gaziano J.M. Epidemiology of cardiovascular diseases. In: Longo D.L, Fauci A.S, Kasper D.L, Hauser S.L, Jameson J.L, Loscalzo J, eds. Harrison's Principles of Internal Medicine. 18<sup>th</sup> Edition. New York: McGraw-Hill; 2011.
5. Williams RR, Hunt SC, Hopkins PN, Hasstedt SJ, Wu LL, Lalouel JM. Tabulations and expectations regarding the genetics of human hypertension. Kidney Int. 1994; 45(44):57-64.
6. Lauer MS, Francis GS, Okin PM, Pashkow FJ, Snader CE, Marwick TH. Impaired chronotropic response to exercise stress testing as a predictor of mortality. JAMA. 1999; 281:524-9.
7. Conny MA, Ravenswaaij V, Louis AA, Hopman CWJ, Stoeltinga BAG, Van Geijn HP et al. Heart rate variability. Ann Intern Med. 1993; 118:436-47.
8. Lafleche AB, Pannier BM, Lalous B, Safar ME. Arterial response during cold pressor test in border-line hypertension. Am J Physiol. 1998; 275: H409-H415.

9. Pasini, Capecchi, Colafigli, Randisi. Systemic adenosine increase during cold pressor test is dependent on sympathetic activation. *Clin Exp Pharmacol Physiol*. 1999; 26:774-778.
10. Verma V, Singh SK, Ghosh S. Identification of susceptibility to hypertension by the cold pressor test. *Indian J Physiol Pharmacol*. 2005;49(1):119-2011.
11. Kelsey RM, Patterson SM, Barnard M, Alpert BS. Consistency of haemodynamic response to cold stress in adolescents. *Hypertension*. 2000;36:1013.
12. Ashwini S, Lingaraj J, Vinitha S, Nachal A. Blood pressure response in children of hypertensive and normotensive parents to cold pressor test. *Indian J Physiol Pharmacol*. 2004;48(5):165.
13. Mathews KA, Woodall KL, Allen MT. Cardiovascular reactivity to stress predicts future blood pressure status. *Hypertension*. 1993;22:479-485.
14. Letizia, C., S. Cerci, A. De Ciocchis, C. D'Ambrosio, L. Scuro, and D. Scavo. Plasma endothelin-1 levels in normotensive and borderline hypertensive subjects during a standard cold pressor test. *J. Hum. Hypertens*. 1995; 9: 903-907.
15. Matsukawa, T., E. Gotoh, S. Uneda, E. Miyajima, H. Shionoiri, O. Tochikubo, and M. Ishii. Augmented sympathetic nerve activity in response to stress in young borderline hypertensive men. *Acta Physiol Scand*. 1991; 141: 157-165.