

Original Research

COLD PRESSOR TEST IN NORMOTENSIVE AND GRADE – I ESSENTIAL HYPERTENSIVE PATIENTS

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ABSTRACT

Background: Hypertension is creating not only health problems but also economical burden on working population in India. Autonomic nervous system (ANS) via its sympathetic and parasympathetic limbs plays a crucial role in maintaining the blood pressure (BP). Generally hypertensive population reacts differently as compared to normotensive to various forms of the stress.**Aims and Objective:** Present study was carried out to assess the role of ANS, specifically sympathetic nervous system in cardiovascular hemodynamics in Grade-I essential hypertensive subjects compared to normotensive along with the gender variation.**Materials and Methods:** Study included 80 volunteers of age 35 to 50 years, 40 normotensive subjects (20 Male and 20 Female) forms control group and 40 diagnosed Grade–I essential hypertensive (20 Male and 20 Female) forms study group. Systolic and diastolic BP of participants was measured at rest, at 30 and 60 seconds intervals during cold pressor test and at 1 minute interval till BP returns to resting value or at least 5 mm of Hg less than resting systolic BP after the cold pressor test. Then difference between rise in systolic and diastolic BP and resting BP was calculated and compared between control and study group's males and females.**Statistical analysis:** Student's unpaired 't' test was applied and outcomes were presented as mean (SD). The 'p' value < 0.05 was considered as significant and < 0.001 as highly significant.**Results:** Study found highly significant rise in systolic and significant rise in diastolic BP of hypertensive male where as only significant rise in systolic BP of hypertensive females compared to normotensive

group. In females, the rise of diastolic BP was more but it was not statistically significant. Recovery towards basal level was also slow in hypertensive male and female subjects.

Conclusion: There is definite cardiovascular ANS dysfunction, specifically sympathetic in Grade-I essential hypertensive patients. More research work is needed to obtain precise relationship between ANS and hyper responsive response to stress in hypertensive patients as regulation of BP has multiple components.

Key words: Hypertensive, Normotensive, Autonomic Nervous System, Sympathetic Nervous System, Cold Pressor Test, Hyper responsive.

INTRODUCTION:-

Increased systemic arterial blood pressure (BP) or hypertension is one of the common non communicable diseases which clinicians come across. In systemic analysis of global disease burden in 2010, hypertension was considered as one of the leading risk factors. ^[1]In developing country like India, it's time to effectively address hypertension as a most common non communicable disease to prevent annual income loss of working adult population of families. ^[2]Systemic review and meta-analysis of hypertension in 2014 had shown that about 33% urban and 25% rural Indians were hypertensive and of these, 25% rural and 42% urban Indians are aware of their hypertensive status. ^[3]Same study was also concluded that incorporation of multicomponent and multilevel approaches are needed for better management of BP among Indians, as the rates for awareness, treatment and control of BP among those on treatment were very low.

Oxford medical dictionary states that 'Essential hypertension' is high BP for which there is no clearly defined aetiology. While considering the physiological aspects of the essential hypertension four major strongly dependent causative elements viz. phylogenetically transferred predisposition, environmental factors, neurogenic excitatory influences and early structural adaptation of heart and blood vessels, were suggested. ^[4] Many studies in present decade had come up with various conclusions regarding the essential hypertension. In pathologically increased BP and established hypertension, combined alterations in cardiac, vascular, and renal functions were more common and often associated.

^[5]Reduced glomerular filtration rate, humoral or genetic disorders stimulating sodium reabsorption in distal nephron, or acquired mechanisms involving renal ischemia, oxidative stress and inflammation, or varying combinations of all these pathways alter the physiological balance between sodium retention and excretion in kidney causing hypertension. ^[6]

The human autonomic nervous system (ANS) through its sympathetic and parasympathetic divisions exerts a rapid and effective control on various internal functions including BP. Some of the factors affecting ANS are exposure to cold, emotional stress, exercise, rapid breathing, injury, pain, shock and fear. ^[7]Cardiovascular reactivity to stress has been hypothesized to be marker for subsequent neurogenic hypertension. ^[8]One of the suggested mechanisms of obesity-related hypertension includes increased sympathetic nervous system activity. ^[9] ^[10]Sympathetic activation had represented a hallmark of essential hypertensive state and adrenergic neural factors may participate at the development and progression of the hypertensive state leading to complications. ^[11] All these studies had shown the role of ANS and especially sympathetic nervous system in pathogenesis of essential hypertension.

It is generally recognized that hypertensive individuals show greater lability of BP under various forms of stress than do the normotensive persons, but to what extent this characteristics precedes the development of hypertension remains uncertain. ^[12] Therefore in present study, emphasis has been on the objective assessment of the functioning of ANS especially sympathetic system in relation with cardiovascular hemodynamics in Grade-I essential hypertensive patients in comparison with normotensive subjects along with the gender variation was done. For this purpose cold pressor test a type of stress, was carried out on Grade –I essential hypertensive patients and normotensive individuals to find out its effect on blood pressure.

MATERIALS AND METHODS:

The present study was conducted in Physiology department of one of the major public hospital of Mumbai. Study was approved by the institutional ethical committee and written informed

consent of participants was taken. Our study was case-control study consists of 80 volunteers of age 35 to 50 years. Out of 80 participants, 40 normotensive (20 Male and 20 Female) forms the control group and 40 Grade –I essential hypertensive (20 Male and 20 Female) forms the study group. Control group subjects were selected from clerical and teaching staff of our hospital were as study group subjects were from hypertensive clinic run by our hospital. Detail history taking along with the general and systemic examination of each participant was done so as to select them as control and study group subjects.

Inclusion criteria for Control group:

1. Blood pressure, systolic up to 120 mmHg and diastolic up to 80 mmHg.
2. Normal sinus rhythm detected by electrocardiogram (E.C.G.) tracing.
3. Physically healthy individual with absence of any cardiopulmonary symptom.

Inclusion criteria for Study group:

1. Recently diagnosed hypertensive patients by trained and experienced physicians. i.e. history of hypertension less than 6 months.
2. Blood pressure, systolic - 140 to 159 mmHg and diastolic - 90 to 99 mmHg. i.e. Grade I according to Joint National Committee-VI criteria ^[13]
3. Investigations done in our hospital and showing normal values (Sr. creatinine, Blood urea nitrogen, Blood sugar, Sr. electrolytes etc.) to rule out Essential hypertension.

Materials used:

1. Digital blood pressure monitor (OMRON T-3)
2. E.C.G. machine with its standard limb leads.
3. Cold pressor test apparatus with temperature scanner.

Participants were told to have light breakfast as a test was carried out in morning after making them familiar with the equipments. They were instructed to discontinue the test if they face any discomfort and report immediately. Fortunately all of the hypertensive subjects of our

study were on medications other than sympatholytics so instructed to take their medications as per instruction of physician.

Cold pressor test^[14]

Resting systolic and diastolic BP of all the subjects was recorded in left arm, sitting position. BP cuff was kept attached to left arm throughout the procedure. When temperature scanner shows the temperature of ice-water as 4-5°C, subjects were asked to immerse their right hand in ice-water up to wrist for one minute and then remove it. During hand immersion both systolic and diastolic BP were recorded at 30 seconds and 60 seconds intervals on left hand.

Our all subjects performed the test for one minute without much discomfort. Again systolic and diastolic BP were recorded (at one minute interval) till it returns to resting value or at least 5 mm of Hg less than resting systolic BP. The difference between rise in systolic and diastolic BP and resting BP was calculated. This difference was then compared between control and study group's males and females.

STATISTICAL ANALYSIS:

Data analysis was done by using SPSS version 16.0 (SPSS Inc, Chicago, USA) software. Student's unpaired t test was applied to compare rise of blood pressure in study groups. The outcome of analysis was presented as a mean (SD). The 'p' value of less than 0.05 (*p<0.05) was considered as significant and less than 0.001 (**p<0.001) as highly significant.

RESULTS:

Table No 1 shows the statistical analysis of rise in systolic and diastolic BP in mm of Hg during cold pressor test for male and female, hypertensive and normotensive group subjects.

TABLE 1: Comparison of rise in systolic and diastolic BP in mm of Hg during cold pressor test in males and females

	M A L E (n = 2 0)		F E M A L E (n = 2 0)	
	S y s t o l i c (Mean \pm SD)	D i a s t o l i c (Mean \pm SD)	S y s t o l i c (Mean \pm SD)	D i a s t o l i c (Mean \pm SD)
Hypertensive group (n=40)	18.1 \pm 6.88	12.6 \pm 7.81	18.5 \pm 9.8	11.5 \pm 4.7
Normotensive group (n=40)	11.8 \pm 1.05	8.4 \pm 5.52	12.2 \pm 5.79	10.8 \pm 3.79
' p ' v a l u e	< 0.001 **	< 0.05 *	< 0.05 *	> 0.05

p < 0.05 – Significant ; p < 0.001 – Highly Significant; p > 0.05 – Non Significant

Study found a highly significant rise in systolic and significant rise in diastolic BP of hypertensive male where as only significant rise in systolic BP of hypertensive females after cold pressor test. Compared to normotensive group in females, the rise of diastolic BP is more but it was not statistically significant. So our study suggest that Grade I essential hypertensive subjects were significantly hyper responsive to rise in systolic BP in both the gender and as far as rise in diastolic BP was concern, only males were significantly hyper responsive to cold pressor test.

Chart No 1 and 2 shows the comparison of mean values for rise in systolic and diastolic BP in mm of Hg during cold pressor test in hypertensive and normotensive group subjects for males and females respectively.

CHART 1: Comparison of rise in systolic and diastolic BP in mm of Hg during cold pressor test in Males

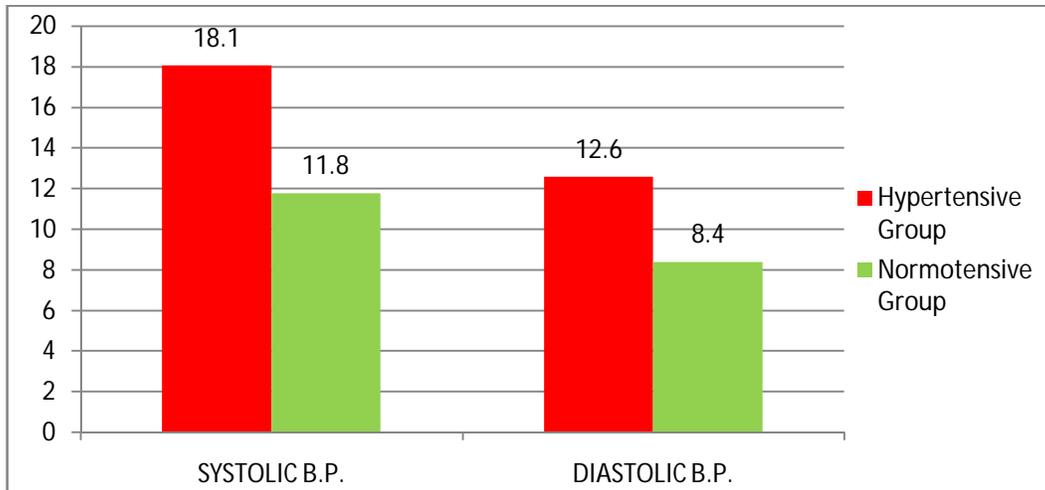
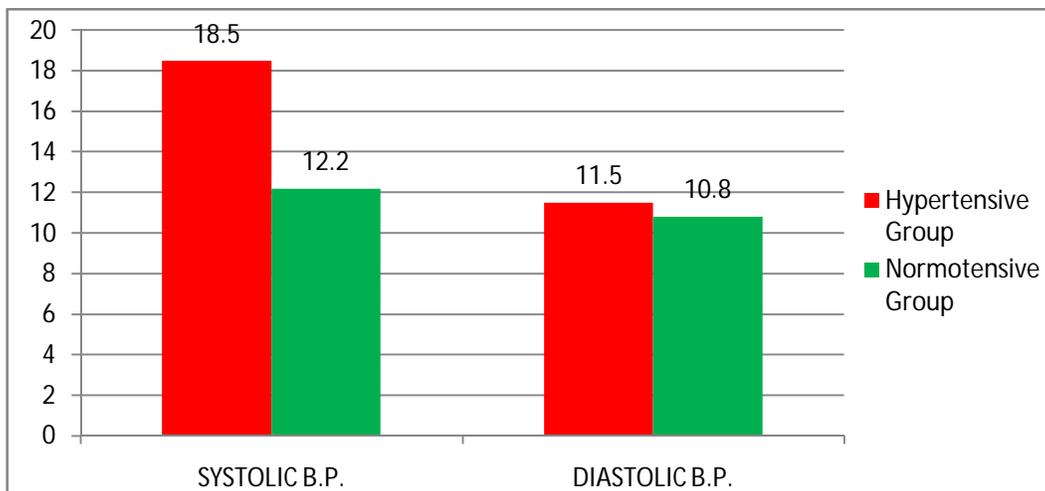


CHART 2: Comparison of rise in systolic and diastolic BP in mm of Hg during cold pressor test in Females



DISCUSSION:-

Present study was undertaken to evaluate role of sympathetic nervous system, a component of ANS during acute circulatory cold stress in Grade-I essential hypertensive patients as compared to normotensive subjects. Our study initiated on hypothesis that sustained high BP in hypertensive patients is basically due to deranged cardiovascular autonomic function which in turn leads to several physiological and biochemical changes, thus creating a vicious cycle of

interrelated chain reaction which finally puts seal of “permanency”.^[15] Sympathetic nervous system an important part of ANS plays a crucial role for the regulation of blood pressure^[16, 17] so blood pressure can be used as parameter for assessing functioning of sympathetic nervous system.

Hypertensive patients have increased basal sympathetic activity and sympathetic hyperactivity in response to mental stress.^[18] Change in BP was also more in hypertensive to various forms of stress compared to normotensive.^[12] As far as cold stress is concerned, it had been shown that cold air might exert continuous impacts on systolic BP and other cardiovascular diseases risk factors in rats.^[19] So there might be relation between various forms of the stresses, sympathetic nervous system and their responses in the hypertensive patients. In present study the form of stress that we have used was cold pressor test (CPT) as this test was found to be useful technique to measure sympathetic function in humans and also useful to define the cardiac and systemic hemodynamic under cold exposure.^[20]

In our study there was significantly rise in systolic BP in hypertensive patients of both gender. Whereas diastolic BP rise was statistically significant in male hypertensive over normotensive male group. The pattern of rise of BP was within 30 seconds reaching its peak at around 60 seconds and the basal BP was achieved within two minutes in normotensive subjects, whereas a prolonged pressor response was displayed in hypertensive patients. There was no gender variation in response to test was found.

Research had classified the persons as responders when there was increased in their systolic BP by at least 16 mm of Hg or diastolic BP by at least 12 mm of Hg.^[21] In our study hypertensive male group were among the responders. These findings were in keeping with studies of Douglas L and Wood et al.^[22] While investigating pathophysiological response to CPT, it had been seen that there was a predominant rise in total peripheral resistance and also higher level of plasma nor epinephrine.^[22, 23] Hyper responsiveness may represent one pathogenic mechanism in the development of essential hypertension, be a marker of central defect in the autonomic control of cardiovascular system or reflect early changes in arterial compliance of

future hypertensive individuals.^[24, 25] Hyperactivity was a manifestation of wide spread basic membrane transport disorder that disturbs cellular cation homeostasis.^[26]

One finding of our study was that rise in diastolic BP in hypertensive females was more but not significant. This thought to be unexpected finding is difficult to explain. But it had been suggested that the physiological "strategy" used to regulate blood pressure in young women was fundamentally different from that in young men^[27] and might be the cause of our finding. While our study we have not analyse other factors such as age, body mass index etc. and also the role of parasympathetic system but this information possess some questions for future autonomic function research. Other limitation of the present study was in its design. This was a small group study which was carried out in single institute. A larger sample size from multiple institutes and a longitudinal study will definitely be of a great value in predicting the role of ANS and regulation of blood pressure.

CONCLUSION:-

Present study is based on premise that there is difference in autonomic responses to various forms of stresses in hypertensive and normotensive subjects specifically the sympathetic nervous system response. Based on results of this study, there is significant rise in systolic BP of both the genders after cold stress in first 60 seconds. There is gender difference for rise in diastolic BP as significant rise is seen only in male subjects. After cessation of cold stimuli the recovery of BP towards basal value is also slow in hypertensive patients without gender difference. Causes for these differences are difficult to explain as regulation of BP has multiple components but there is possible role of increased levels of nor epinephrine and peripheral resistance along with hyper responsiveness of cardiovascular system producing the defective sympathetic nervous system response. So our study conclude that there is definite cardiovascular sympathetic and autonomic dysfunction in grade-I essential hypertensive patients as compared to normotensive subjects so hyper responsive to cold pressor test.

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