

Original Research Article

## **Gender variations in cardiovascular responses to Cold Pressor Test in Normal subjects**

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**Abstract:** Abnormal Cold Pressor Response [CPT] is one of the important characteristic of autonomic dysfunction as well as future development of hypertension. Appropriate identification and intervention at early stages can prevent cardiovascular related morbidity and mortality. With this background we tried to identify if any abnormal response to Cold Pressor Test [CPT] in normal subjects. This test was carried on 60 healthy I MBBS 30 males and 30 females students aged between 19 – 25 years. Standard Mercury Sphygmomanometer was used to determine Blood pressure SBP and DBP. Heart Rates [HR] were recorded before and after the Cold Pressor Test [CPT]. The Cold Pressor Test [CPT] was performed following Hines–Brown’s method, with subjects immersing their left hand in 4°C water for 1 min and values were recorded in appropriate format. In males the Mean SBP was found to be  $118.96 \pm 5.86$  and in females the values were  $121.14 \pm 7.0$  before the start of the test. The mean values of SBP during CPT were  $129.41 \pm 6.04$  for males and  $135.5 \pm 4.14$  for females, the calculated p values were found to be  $< 0.05$  and were found to be significant. The mean value of DBP in males before test were  $83.86 \pm 8.02$  and females were  $84.53 \pm 6.51$  The mean values of DBP during CPT in males  $96.53 \pm 8.58$  and in female were  $95.9 \pm 7.29$ . Basal Heart Rate mean values in males were  $79.95 \pm 8.06$  and for females it was  $84.5 \pm 6.75$ . Maximum Heart Rates recorded during application of Cold Pressor Test [CPT] for males were  $110.05 \pm 10.9$  and for females it was  $118.86 \pm 15.5$  the calculated p values were significant. In the present study it was found that the response to CPT by both male and female varies. Whereas the females showed significant increase in SBP and heart Rate as compared to male counterparts. We also found that there were more numbers of hyperreactors to CPT in male as compared to females. This shows that CPT is a simple yet effective tool in monitoring vascular hyperreactivity and future development of hypertension in both genders.

**Keywords:** Blood Pressure, Cold Pressor Test [CPT], Heart Rate

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### **INTRODUCTION**

Cold Pressor Test [CPT] is widely used for testing autonomic functions. It has become a diagnostic test for autonomic related diseases like hypertension and other cardiovascular disorders. The Cold Pressor Test [CPT] originated by Hines and Brown [1] in 1936 is most widely used method. The idea of the test was to assess the function of sympathetic branches of cardiovascular system by observing Pressor response during immersion of one hand in cold water. CPT is thought to induce an  $\alpha$ -adrenergic response with vasoconstriction and an increased total peripheral resistance[2]. Individuals with more than 15 mmHg variations in Systolic or Diastolic Blood Pressure response were classified as hyper reactors to Cold Pressor Test[3,4]. It appears that the hyperreactors response is primarily caused by increased Heart rates

rather than an increase in cardiac contractility contractility [5,6]. It has been shown that cold pressor test represents wide spread neurogenic stimulation of multiple systems of Cardiovascular system. There are major cardiodynamic changes that occur due to stimulation which includes in addition to Pressor response, increased peripheral arterial resistance, increased cardiac output due to increased heart rate and increased pulmonary artery pressure[1]. Autonomic nervous system controls various visceral activities of body including blood pressure and heart rate. [7]. It is influenced by many factors like orthostatic stress, cold shower, body posture etc [8-10]. Previous studies on reactivity as a predictor of future hypertension have given conflicting results [11] but long term studies which studied reactivity for greater than 5 years have shown strong association between cardiovascular

hyperreactivity and future hypertension. [12-14]. The Heart Rate response to CPT is less well defined and is more variable on individual basis [15]. The Heart Rate was also not found to be homogenous during entire CPT. Contrary to vascular control the autonomic Heart Rate control needs to be precise during CPT. It was initially attributed to increased sympathetic involvement and decreased vagal out flow. However it is generally believed to be a combination of both. Although there are number of studies with CPT but there is very sparse data available regarding gender differences in response to CPT. With this background we tried to evaluate the Cold Pressor Test [CPT] response in both male and female normal subjects.

**MATERIALS AND METHODS**

This cross sectional study was carried out at Mamata Medical College, Khammam. The study involved 60 healthy medical students males (n=30) and females (n=30) all the students were between the age group of 19-25 years. Only students who healthy normotensive and free from any clinical disorder and were not taking any medications. The details of the experiment protocol were explained to all the students and the informed consent was obtained. Every student was familiarized with the test. The ethical committee permission was obtained for the study. All the experiments were carried out in the physiology laboratory at an ambient room temperature of 25-28 degree Celsius.

After 5 minutes of rest the subjects were seated comfortably in a chair with back rest without crossing

of legs and arm well supported and at the level of heart. Resting blood pressure was measured in the upper right arm with a Standard mercury sphygmomanometer. Similarly a resting Heart Rate was recorded and tabulated appropriately as baseline readings. For the Cold Pressor Test [CPT] Hines and Brown method was used the left hand of the subject was immersed to just above the wrist in cold water at 4 degree Celsius for 1 minute blood pressure reading were recorded after immersion. The maximal changes in SBP and DBP from resting values during cold stimulus were defined as systolic response and diastolic response respectively. Subjects whose Systolic/Diastolic/ response exceeded 15 mm Hg were defined as Systolic /Diastolic hyperreactors. Similarly the maximum Heart Rate values were recorded during CPT.

**RESULTS**

All the 60 subjects males (n=30) and females (n=30) exhibited characteristic response to Cold Pressor Test [CPT]. The table 1 shows the SBP values recorded prior to the CPT. In males the Mean SBP was found to be  $118.96 \pm 5.86$  and in females the values were  $121.14 \pm 7.0$  and the calculated p values were  $>0.1$  and were not significant. As expected due to Cold Pressor Test [CPT] the values of Systolic Blood Pressure [SBP] increased in both male and females. The mean values of SBP during CPT were  $129.41 \pm 6.04$  for males and  $135.5 \pm 4.14$  for females, the calculated p values were found to be  $< 0.05$  and were found to be significant.

**Table 1: showing Mean SBP values recorded in males and females before and during CPT**

	Gender	Mean SBP in mmHg	Standard Deviation	p value	Result
Before the Test	Male	118.96	5.86	$> 0.1$	Not significant
	Female	121.14	7.00		
CPT	Male	129.41	6.04	$<0.05^*$	Significant
	Female	135.5	4.14		

The table 2 shows the mean values of Diastolic Blood Pressure DBP recorded in both males and females before and after application of CPT. The mean value of DBP in males before test were  $83.86 \pm 8.02$  and females were  $84.53 \pm 6.51$  and the calculated p values were  $>0.1$  and it was not significant. During the

application of CPT there will be an increase in DBP as expected due to immersion of hand in cold water which instantly causes vasoconstriction. The mean values of DBP during Cold Pressor Test [CPT] in males  $96.53 \pm 8.58$  and in female were  $95.9 \pm 7.29$  and the calculated p values were not significant.

**Table 2: showing Mean DBP values recorded in male and female before and during CPT**

	Gender	Mean DBP in mmHg	Standard Deviation	p value	Result
Before the Test	Male	83.86	8.02	$> 0.1$	Not significant
	Female	84.53	6.51		
CPT	Male	96.53	8.58	$> 0.1$	Not Significant
	Female	95.90	7.29		

Heart Rate recordings were done in each individual before the application of Cold Pressor Test

[CPT] and their mean values in males was  $79.95 \pm 8.06$  and for females it was  $84.5 \pm 6.75$  the calculated p

values were not significant. Maximum Heart Rates recorded during application of Cold Pressor Test [CPT] were noted and the mean values for males were 110.05 ± 10.9 and for females it was 118.86 ± 15.5 the

calculated p values were found to be significant. This indicates that the females had significantly increased heart rates during application of Cold Pressor Test [CPT] as shown in table 3.

**Table 3: showing Mean Heart Rate values recorded in male and female before and during CPT**

	Gender	Mean Heart Rate/ BPM	Standard Deviation	p value	Result
Before the Test	Male	79.95	8.06	> 0.1	Not significant
	Female	84.5	6.75		
CPT	Male	110.05	10.9	<0.05*	Significant
	Female	118.86	15.5		

In this study it was found that 9 persons 6 males and 3 females were having variations in Blood pressure readings greater than 15mmHg and they were classified as hyper reactors. They were also having slightly significantly higher variations in heart rates as compared to other individuals.

**DISCUSSION**

Cold Pressor Test CPT which measures the response of blood pressure to application of cold externally has been used as a standard test for characterization of sympathetic function and is used to predict the subsequent risk of hypertension in normotensive persons. [10, 16,17] Several studies have shown that exaggerated cold pressor responses to possible future development of hypertension with advancement of age. [4, 18] This test thus allows us to identify subjects with future risk for development of hypertension. In such individuals possible close monitoring and modification of life styles can delay or stop the future development of hypertension and its adverse effects. CPT is based on the assumption that the normal human subject sympathetic stimulation by cold would cause constant degree of elevation of blood pressure (± 10 mmHg). Thus the cold pressor test is basically an indicator of vasoconstrictor response and elevation of DBP is more subtle to cold stress as compared to SBP. [19] Rise in heart rate is also an integral part of cold pressor response. Immersion of hand in water causes increase in sympathetic activity and which in turn increases the heart rate. Therefore the physiological reactions on application of Cold Pressor Test are increase in SBP and DBP and increase in heart rate, rise in vascular resistance and increase in muscular sympathetic activity which are mediated by stimulation of autonomic neural pathways [20] Some investigators have found that the pain sensation on immersion to cold water contributes to greater increase in blood pressure in hyperreactors and cardiac responses in hyperreactors depend on the heart rate rather than contractility suggesting that parasympathetic withdrawal may contribute to exaggerated cardiovascular responses to hyperreactors. [5] Gender variations in CPT have not been clearly reported so far. It is generally assumed that

both male and female response to CTP almost comparable. However it was not found to be true. In the present study we compared the results of CPT in relation to Gender and found that SBP variations between two groups during CPT were significant. Females have shown significantly higher elevations of the SBP as compared to male subjects. The probable underlying mechanism could be due difference in pain threshold and pain reactivity between two individuals, which in turn could lead to increase in heart rate and SBP. Our results were similar to study done by RD Srivastav et al; [21] who found that there was greater responsiveness to CPT in females as compared to males. They found both SBP and DBP raise in females was more than males a finding that is similar to our finding. They also found that DBP rise was more than SBP in males in the present study we also noted a similar observation however our findings were not significant. One of the probable reasons for this variation could be due to the presence of more estrogen in females which has vascular protective actions especially in young females.

In a similar study by Kilguor RD et al [22] on normotensive male and female found that both genders experienced similar increase in pressor response and additionally in males the pressor response remained elevated where as in females it declined progressively. In one study by Mclean JK et al [23] found that gender differences in response to CPT were significant in SBP and DBP but no gender differences were found in relation to heart Rates which is contrary to our study where we found significant differences in heart rate variability in both sexes which was significant. It may be attributed to several reasons including the pain threshold, psychogenic, environmental and other genetic factors.

**CONCLUSION**

Within the limitations of the present study it was found that the response to CPT by both male and female varies. Whereas the females showed significant increase in SBP and heart Rates as compared to male counterparts. This could be due to fact that young

females have estrogen which as vascular protective actions by its hypocholesterolaemic effects and also by increased production NO and decreased production of Endothelin. We also found that there were more numbers of hyperreactors to CPT in male as compared to females. This shows that CPT is a simple yet effective tool in monitoring vascular hyperactivity and future development of hypertension in both genders.

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