

Effect of cold stress on heart rate and blood pressure in healthy offspring with and without parental history of type2 diabetes mellitus

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Abstract

Introduction: The cold pressor test which is considered to be a sympatho-excitatory maneuver is a simple, noninvasive and validated test of sympathetic activation. The heart rate and blood pressure responses to CPT could be used as indicators of global sympathetic activation, and thus of cardiac status and autonomic function. Autonomic nervous system dysfunction at the subclinical level seems to be the predisposing condition that occurs far earlier before developing an overt diabetic condition.

Aims: To evaluate the cardiac autonomic status and its reactivity among healthy offspring with and without parental history of Type2 Diabetes Mellitus (T2DM). To Compare the autonomic reactivity by recording Heart Rate (HR) and Blood pressure during and after CPT between healthy offspring with and without parental history of T2DM.

Materials and Methods: This study consists of 40 healthy male subjects with family history of T2DM (cases) and 40 healthy male subjects without family history of T2DM (controls) in the age group of 18-25 years. HR and BP during and after CPT were compared between cases and controls.

Results: Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups. HR response to post CPT showed significant differences between two groups across all the time points. Controls showed higher HR than cases at all the time points. However, the reduction of HR with time was more gradual in controls. The graphical representation of SBP changes after CPT, shows fluctuation among cases before it reaches the stable value, whereas, in controls the decrease was at constant level. **Conclusion:** The results suggest there was altered autonomic reactivity to physical stress among the offspring with parental history of T2DM when compared to their counterparts and hence this points towards the fact that they are at a risk of developing future autonomic dysfunction and cardiovascular complications.

Keywords: Cold Pressor test (CPT), Type2 Diabetes Mellitus (T2DM), Heart Rate (HR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP).

Introduction

Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.¹ It has been shown that the prevalence of T2DM among offspring with one diabetic parent was 40%, which increases to 80 % if both parents are diabetic.² A breakthrough study was done in which a genetic locus was confirmed and four other novel loci were identified which accounts for substantial portion of risk of development of T2DM.³ Therefore, genetic inheritance plays an important role in the pathogenesis of T2DM, thereby, increasing the susceptibility to develop the disease among individuals with strong family history of DM.

Autonomic nervous system (ANS) dysfunction at the subclinical level seems to be the predisposing condition that occurs far earlier before developing an overt diabetic condition.^{4,5} There is a rich ANS supply to major organs of glucose metabolism which includes liver, pancreas and skeletal muscles.⁶⁻⁸ Therefore ANS changes and metabolic alterations are linked to each other. Impaired autonomic activity may trigger hyperglycemia in non diabetic individuals.⁹ Studies

have shown that autonomic dysfunction is often detected among the population even at the time of diagnosis of T2DM.⁵ This provides a hint that impaired autonomic activity might have developed even during normoglycemic stage.

Materials and Methods

This is a comparative study having total of 80 subjects – 40 Healthy male non diabetic subjects without parental history of T2DM, in the age group 18-25 were included in the control group. 40 Healthy male non diabetic subjects with at least one parent with T2DM, in the age group 18-25 were included in the study group.

Subjects were selected among the general population and from the campus of Sri Siddhartha Medical College and Research Hospital, Tumkur. Ethical clearance of the protocol was obtained from “Ethical committee for human research” of Sri Siddhartha Medical College and Research hospital, Tumkur. Protocol was briefed to the subject and the informed written consent was obtained from all the subjects.

Subjects with history of with Type I Diabetes Mellitus, those suffering from cardiac, respiratory, endocrine, metabolic, psychiatric and neurological diseases, those who are smokers or alcoholics or drug abusers, those on regular medications affecting cardiovascular and respiratory system, those undergoing any physical conditioning programme were excluded from the study.

Experimental design: Cold Pressor Test

Subject instructed to immerse the hand till the wrist in cold water (1-4°C) for 2 minutes or until toleration whichever is earlier. Care was taken to ensure that the subject avoided any isometric contractions, breath holding or performance of Valsalva maneuver. HR, SBP and DBP using BPL cardiac monitor was obtained from the other arm at 30 seconds interval till subject

removed the hand or completion of two minutes. After removing the hand the HR was recorded at an interval of 30 seconds for 3 minutes.

Result

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, were used for the analysis of the data. Significance is assessed at 5 % level of significance.

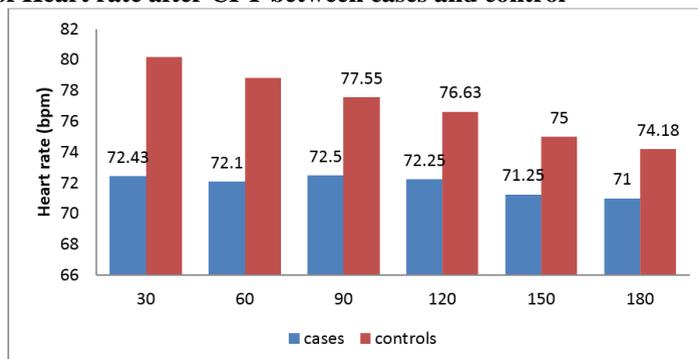
Table 1: Comparison of age and anthropometric measurements between cases and controls

Variables	Cases n=40	Controls n=40	P value
Age (years)	19.20±0.85	19.05±0.78	0.415
Height (cm)	1.71±0.07	1.70±0.05	0.594
Weight (kg)	61.10±8.29	61.18±7.14	0.966
BMI (kg/m ²)	20.88±2.61	21.06±2.07	0.739
Waist circumference (cm)	81.23±8.99	79.98±5.95	0.465
HIP circumference (cm)	94.58±8.89	93.20±5.44	0.407
W/H ratio	0.86±0.03	0.86±0.03	0.953
Wrist circumference (cm)	16.4±0.78	16.59±0.65	0.245

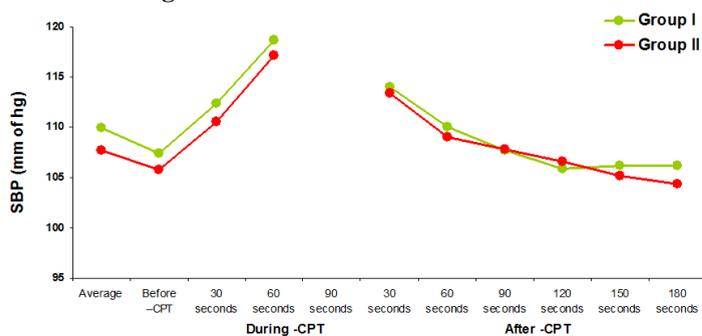
Table 2: Comparison of heart rate (bpm) during and after cold Pressor test (CPT) between cases and controls

Heart rate (bpm)	Cases (n=40)	Controls (n=40)	P value
Before -CPT	74.40±8.02	75.63±6.09	0.444
During -CPT			
30 seconds	78.70±7.33	80.93±6.69	0.160
60 seconds	81.35±8.44	83.35±7.67	0.271
After -CPT			
30 seconds	72.43±7.62	80.18±7.10	<0.001**
60 seconds	72.10±7.39	78.80±6.72	<0.001**
90 seconds	72.50±5.77	77.55±7.03	<0.001**
120 seconds	72.25±6.89	76.63±6.45	<0.001**
150 seconds	71.25±8.91	75.00±6.58	<0.001**
180 seconds	71.00±5.42	74.18±6.11	<0.001**

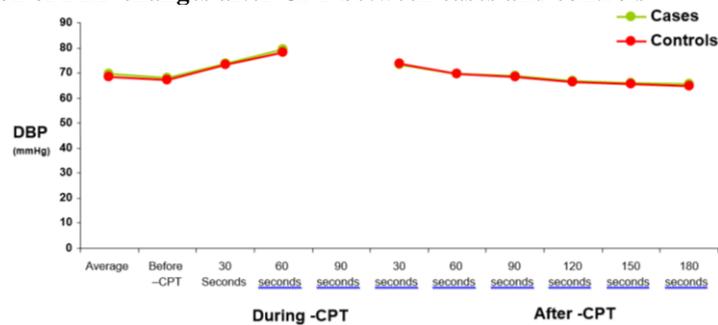
** Strongly significant (P value: P≤0.01)

Graph 1: Comparison of Heart rate after CPT between cases and control**Table 3: Comparison of SBP (mm of Hg) during and after CPT between cases and controls**

SBP (mm of Hg)	Cases (n=40)	Controls (n=40)	P value
Before -CPT	107.38±7.95	105.78±7.02	0.343
During -CPT			
30 seconds	112.35±9.12	110.55±7.64	0.342
60 seconds	118.63±8.41	117.18±7.61	0.421
90 seconds	-	-	-
After -CPT			
30 seconds	113.98±7.56	113.35±7.93	0.719
60 seconds	110.08±7.61	109±7.68	0.531
90 seconds	107.7±6.73	107.85±7.39	0.925
120 seconds	105.85±6.69	106.6±7.17	0.630
150 seconds	106.15±6.78	105.2±6.53	0.525
180 seconds	106.15±7.05	104.4±6.44	0.250

Graph 2: Representation of SBP changes after CPT between cases and controls**Table 4: Comparison of DBP (mm of Hg) during and after CPT between cases and controls**

DBP (mm of Hg)	Cases (n=40)	Controls (n=40)	P value
Before -CPT	67.83±7.91	67.08±6.20	0.638
During -CPT			
30 seconds	73.78±6.76	73.20±6.34	0.696
60 seconds	79.48±9.05	78.15±8.76	0.508
90 seconds	-	-	-
After -CPT			
30 seconds	73.23±7.17	73.58±7.24	0.829
60 seconds	69.58±7.73	69.83±7.41	0.883
90 seconds	68.65±7.74	68.38±7.36	0.871
120 seconds	66.83±7.35	66.55±6.48	0.860
150 seconds	66.1±6.72	65.55±6.22	0.705
180 seconds	65.63±6.75	64.73±5.73	0.522

Graph 3: Representation of DBP changes after CPT between cases and controls

The mean and standard deviation (SD) of age, anthropometric variables and their comparison between cases and controls are depicted in Table 1. Both the groups were comparable for age and anthropometric measurements. Diabetic family history among cases showed that about 40% had paternal and 30 % had maternal. Among parental history, paternal positive history predominates than maternal.

The comparison of heart rate before, during and after Cold Pressor test, between cases and controls has been depicted in Table 2. The basal heart rate before beginning of CPT was comparable between the two groups (Cases = 74.40 ± 8.02 bpm, Controls = 75.63 ± 6.09 bpm, $P = 0.444$). The heart rate during CPT was comparable between the two groups. At 30 sec HR was 78.70 ± 7.33 bpm and 80.93 ± 6.69 bpm ($P = 0.160$) and by 60 sec it reached 81.35 ± 8.44 bpm and 83.35 ± 7.67 bpm ($P = 0.271$) in cases and controls. The normal response to CPT is increase in HR by 7-12 beats/min. In the study both cases and controls showed difference of about 7 beats/min and 8 beats/min respectively, which is a normal response. However, HR response to post CPT showed significant differences between two groups across all the time points. Controls showed higher HR than cases at all the time points in Graph.1. However, the reduction of HR with time was more gradual in controls. Whereas, cases showed an abrupt reduction of heart rate at the 30 sec which maintained later.

The systolic and diastolic blood pressure response to CPT is given in Table 3 and Table 4 respectively. Normally during CPT the SBP increases by 10-20 mm of Hg and DBP increases by 8-10 mm of Hg. The SBP during CPT was comparable between the two groups. At 30 sec SBP was 112.35 ± 9.12 mm of Hg and 110.55 ± 7.64 mm of Hg ($P = 0.342$) and by 60 sec it reached 118.63 ± 8.41 mm of Hg and 117.18 ± 7.61 mm of Hg ($P = 0.421$) in cases and controls. The DBP during CPT was comparable between the two groups. At 30 sec DBP was 73.78 ± 6.76 mm of Hg and 73.20 ± 6.34 mm of Hg ($P = 0.696$) and by 60 sec it reached 79.48 ± 9.05 mm of Hg and 78.15 ± 8.76 mm of Hg ($P = 0.508$) in cases and controls. But, the post CPT changes in either of blood pressure did not demonstrate any significant differences. However, the graphical

representation of SBP changes after CPT (Graph 2) shows fluctuation among cases before it reaches the stable value, whereas, in controls the decrease was at constant level. Even though the absolute values were not much significant the dynamics of physiological response among cases give an insight to cardiovascular regulation among offspring of T2DM. The graphical representation of DBP changes after CPT is shown in Graph 3.

Discussion

The hypothesis is that autonomic status and its reactivity to physical stress is heightened and sustained in offspring with parental history of diabetes. The present study intends to evaluate the autonomic status and its reactivity among healthy offspring with parental history of diabetes and compare the same with age and gender matched offspring without parental history of diabetes. Here we have attempted to assess the changes in the cardiac autonomic activity and its reactivity to cold stress among the healthy offspring of diabetics; which if present may act as warning bells of future diabetes, among healthy offspring with parental history of T2DM.

Dysfunction in the autonomic nervous system activity is associated with increased risk of developing diabetes in future and therefore it may serve as a predicting factor in early detection of diabetes risk among the population.^[10,11] The reactivity hypothesis has suggested that exaggerated response and the dynamics of physiological recovery to the stressor may predict the development of cardiovascular diseases in future and any deviation from the normal recovery could be the earliest subclinical sign. Autonomic reactivity to a challenge like that of cold offers a greater scope to evaluate and assess the capability of autonomic system to regulate and maintain homeostasis.¹²⁻¹⁴

The cold pressor response is an indicator of sympathetic activity after cold stress. The cold Pressor test (CPT) triggers in healthy subjects a vascular sympathetic activation and increase in blood pressure. This may be due to an increased CO during the initial period of the test with little increase in muscle sympathetic nerve activity; while an increase in this

activity elevates peripheral resistances in the later period.¹⁵

Studies have shown variable response of HR and BP during CPT among healthy adults. There can be an initial rise and consistent increase in HR or HR may rise initially and reduce subsequently. This variation in response is attributed to interplay between cardiac sympathetic and parasympathetic innervations. In the present study subjects of both groups showed an increase in HR in CPT which infers that there was an increase in cardiac sympathetic activation. However, the interesting observation was the HR response during recovery after CPT. The controls demonstrated attenuation of HR which was gradual and at a constant rate whereas in offspring of diabetics there was abrupt reduction of heart rate during first minute after CPT. So this information provides a greater insight the way cardiac autonomic activity responds to a stressor. Whereas, such a response of blood pressure was not observed among cases. Both SBP and DBP after CPT recovered in the same phase in both the groups. So in the present study even though heart rate response to recovery after CPT was within normal limits but the projector of response seems to be more acute, abrupt and deviated among cases as compared to controls.

Conclusion

In the present study the HR response to CPT was comparable, but after CPT the recovery of HR was smooth and gradual in the controls, whereas it was abrupt in cases and was maintained thereafter and the graphical representation of SBP changes after CPT shows fluctuation among cases before it reaches the stable value, whereas, in controls the decrease was at constant level. This as a whole signifies altered autonomic reactivity to physical stress among the offspring with parental history of T2DM when compared to their counterparts and hence this points towards the fact that they are at a risk of developing future autonomic dysfunction and cardiovascular complications.

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