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RESEARCH ARTICLE

A comparative study of effect of cold pressor test on heart rate between healthy offspring with and without parental history of Type 2 diabetes mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. There is an increased susceptibility to develop the disease among individuals with strong family history of DM. 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 and Objectives:** To evaluate the cardiac autonomic status and its reactivity among healthy offspring with and without parental history of Type 2 DM (T2DM). To compare the autonomic reactivity by recording heart rate (HR) during and after cold pressor test (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 during and after CPT was compared between cases and controls. **Results:** Student's *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. **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 toward the fact that they are at a risk of developing future autonomic dysfunction and cardiovascular complications.

KEY WORDS: Type 2 Diabetes Mellitus; Heart Rate; Cold Pressor Test

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both.[1] In India, the incidence and prevalence of Type 2 DM (T2DM) is growing rapidly, and therefore, its genetic inheritance too. 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 the 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.

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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.[4,5] 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 and 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 a history of Type 1 DM, 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, and those undergoing any physical conditioning program were excluded from the study.

Experimental Design: Cold Pressor Test (CPT)

Subject was instructed to immerse the hand till the wrist in cold water (1–4°C) for 2 min or up till toleration whichever is earlier. Care was taken to ensure that the subject avoided any isometric contractions, breath holding, or performance of Valsalva maneuver. Heart rate (HR) using BPL cardiac monitor was obtained from the other arm at 30 s interval till subject removed the hand or completion of 2 min. After removing the hand, the HR was recorded at an interval of 30 s for 3 min.

RESULTS

Student's *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's 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, and Stata 10.1, were used for the analysis of the data. Significance is assessed at 5% level of significance.

The mean and standard deviation 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 [Table 2]. Among parental history, paternal positive history predominates than maternal.

The comparison of HR before, during and after CPT, between cases and controls has been depicted in Table 3. The basal HR 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 HR during CPT was comparable between the two groups. At 30 s, HR was 78.70 ± 7.33 bpm and 80.93 ± 6.69 bpm ($P = 0.160$), and by 60 s, 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 increased in

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

BMI: Body mass index

Table 2: Distribution of parental history of T2DM among cases

Family history of T2DM	*n* (%)	
	Cases (*n*=40)	Controls (*n*=40)
Father		
No	24 (60.0)	40 (100.0)
Yes	16 (40.0)	0 (0.0)
Mother		
No	28 (70.0)	40 (100.0)
Yes	12 (30.0)	0 (0.0)

T2DM: Type 2 diabetes mellitus

Table 3: Comparison of HR (bpm) during and after CPT between cases and controls

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

HR: Heart rate, CPT: Cold pressor test. HR response to post CPT showed significant differences between two groups across all the time points. **Strongly significant (*P* value: $P \leq 0.01$).

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 [Graph 1]. However, the reduction of HR with time was more gradual in controls, whereas cases showed an abrupt reduction of HR at the 30 s which maintained later.

DISCUSSION

In the present study, the HR response to CPT was normal in both the groups. There was consistent increase in HR during 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 HR during 1st min after CPT. Hence, this information provides a greater insight into the way cardiac autonomic activity responds to a stressor.

Studies have shown variable response of HR 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. LeBlanc *et al*., 1975[10] and Shibahara *et al*., 1996,[11] observed HR elevation was found throughout CPT compared to baseline in normal subjects. The increase in HR is due to general sympathetic activation with no change or a decrease in vagal outflow. Sendowski *et al.,* 1997[12] and Cui *et al.,* 2002,[13] reported a marked increase in HR followed by slow decrease. However, there are a few studies evaluating the cardiac autonomic response and its reactivity among the healthy offspring of diabetics. Hence, in this study, we have attempted to do this and found that the autonomic status and its reactivity to physical stress are heightened in offspring with parental history of diabetes.

Besides, evaluating the cardiac autonomic status and its reactivity, the present study also shows the dynamics of physiological recovery to the stressor which may predict the development of diabetes and cardiovascular diseases in future. Limitation of the present study is small sample size. Studies with large sample size are needed to evaluate the cardiac autonomic status and its reactivity in off spring with parental history of diabetes.

Dysfunction in the ANS 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.[14,15] It has been postulated that offspring with parental history of T2DM is more likely to develop diabetes in future and longitudinal studies have proved this.

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. This as a whole signifies an altered autonomic reactivity to physical stress among the offspring with parental history of T2DM when compared to their counterparts, and hence, this points toward the fact that they are at a risk of developing future autonomic dysfunction and cardiovascular complications.

REFERENCES

1. Sahay BK. Diabetes Mellitus-Basic consideration. In: Shah SN, editor. API Text Book of Medicine. 8th ed. Mumbai (India): The Association of Physician of India; 2008. p. 1042-72.
2. Ramachandran A, Snehalatha C. Type 2 diabetes mellitus-the epidemic of the 21st century: The Indian scenario. Int J Diabetes Dev Countries 1999;19:158.
3. Sladek R, Rocheleau G, Rung J, Dina C, Shen L, Serre D, *et al.* A genome-wide association study identifies novel risk loci for Type 2 diabetes. Nature 2007;445:881-5.
4. Pfeifer MA, Weinberg CR, Cook DL, Reenan A, Halter JB, Ensinck JW, *et al.* Autonomic neural dysfunction in recently diagnosed diabetic subjects. Diabetes Care 1984;7:447-53.
5. Lehtinen JM, Uusitupa M, Siitonen O, Pyörälä K. Prevalence of neuropathy in newly diagnosed NIDDM and nondiabetic control subjects. Diabetes 1989;38:1307-13.
6. Nonogaki K. New insights into sympathetic regulation of glucose and fat metabolism. Diabetologia 2000;43:533-49.
7. Shimazu T. Innervation of the liver and glucoregulation: The role of the hypothalamus and autonomic nerves. Nutrition 1996;12:65-6.
8. Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities-the role of insulin

resistance and the sympathoadrenal system. N Engl J Med 1996;334:374-81.
9. Carnethon MR, Golden SH, Folsom AR, Haskell W, Liao D. Prospective investigation of autonomic nervous system function and the development of Type 2 diabetes: The atherosclerosis risk in communities study, 1987-1998. Circulation 2003;107:2190-5.
10. LeBlanc J, Dulac S, Cote J, Girard B. Autonomic nervous system and adaptation to cold in man. J Appl Physiol 1975;39:181-6.
11. Shibahara N, Matsuda H, Umeno K, Shimada Y, Itoh T, Terasawa K. The responses of skin blood flow mean arterial pressure and R-R interval induced by cold stimulation with cold wind and ice water. J Auton Nerv Syst 1996;61:109-15.
12. Sendowski I, Savourey G, Launay JC, Besnard Y, Cottet-Emard JM, Pequignot JM, *et al.* Sympathetic stimulation induced by hand cooling alters cold-induced vasodilatation in humans. Eur J Appl Physiol 2000;81:303-9.
13. Cui J, Wilson TE, Crandall CG. Baroreflex modulation of muscle sympathetic nerve activity during cold pressor test in humans. Am J Physiol Heart Circ Physiol 2002;282:H1717-23.
14. Frontoni S, Bracaglia D, Baroni A, Pellegrini F, Perna M, Cicconetti E, *et al*. Early autonomic dysfunction in glucose-tolerant but insulin-resistant offspring of Type 2 diabetic patients. Hypertension 2003;41:1223-7.
15. Carnethon MR, Jacobs DR, Sidney S, Liu K. Influence of autonomic nervous system dysfunction on the development of Type 2 diabetes. Diabetes Care 2003;26:3035-41.

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