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RESEARCH ARTICLE

A case-control study of cardiovascular parasympathetic function tests in offsprings of type 2 diabetes mellitus parents

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ABSTRACT

Background: Type 2 diabetes mellitus (DM) has a strong genetic component. Individuals of a parent with type 2 DM have an increased (40%) risk of diabetes. If both parents have type 2 DM, the risk approaches to 70%. Thus, this study was designed to evaluate cardiovascular parasympathetic functions in offsprings of type 2 diabetic parents. **Aims and Objectives:** Study was done to compare and observe the degree of changes (if any) in the cardiovascular parasympathetic function tests in the offsprings of diabetic parents (cases) with offsprings of non-diabetic parents (controls) and provides timely lifestyle modifications to prevent the development of diabetes and its complications. **Materials and Methods:** The cardiovascular parasympathetic function tests were carried out in 50 healthy offsprings of type 2 diabetic parents (study group) and 50 healthy offsprings of non-diabetic parents (control group) in the age range of 18-25 years randomly selected medical and para-medical students. Statistical analysis was done by unpaired Student's *t*-test. **Results:** Study shows decrease in all the three parasympathetic function tests (heart rate variability in response to deep breathing, heart rate variation in response to standing, and valsalva maneuver) in offsprings of type 2 diabetic parents (cases) as compared to non-diabetic parents (controls). However, the results were not statistically significant. **Conclusion:** Our observations indicate that genetic factors in the form of altered genes could pass from diabetic parents to their offsprings and could manifest as altered response in parasympathetic function tests in healthy offsprings of diabetic parents even before the offsprings developing diabetes.

KEY WORDS: Parasympathetic Function Tests; Offsprings of Type 2 Diabetes Mellitus; Autonomic Neuropathy

INTRODUCTION

Various studies show that type 2 diabetes mellitus (DM) is found to have a strong genetic component. The concordance of type 2 diabetes in mono-zygotic twins is ~70% compared with 20-30% in dizygotic twins.[1] The lifetime risk of developing the disease is ~40% in offspring of one parent with type 2 diabetes, greater if the mother is affected and approaching 70% if both parents have diabetes.[2] Individuals with DM may develop signs of autonomic dysfunction.[3] The possibility of early alterations in neural cardiovascular regulation in healthy offsprings of diabetic patients has been addressed recently.[4-7] As studies show, there are chances of offsprings of such diabetic parents to be affected by this sub-autonomia, and this can be detected by the cardiovascular parasympathetic function tests. Thus, Ewing et al.[8] suggested utilization of a standard battery of parasympathetic function tests including heart rate variability in response to deep breathing, HR variation in response to standing, and valsalva maneuver. As seen through meticulous search, there is much less research work done on

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the assessment of parasympathetic function tests on offsprings of diabetic parents; particularly at regional level especially in northern parts of India. With this perspective, this study was designed to assess the cardiovascular parasympathetic function tests and provides timely lifestyle modifications to prevent the development of diabetes and its complications.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology, Muzaffarnagar Medical College, Muzaffarnagar, following the approval of the Institutional Ethical Committee. For the study, 100 medical and para-medical students of Muzaffarnagar Medical College, Muzaffarnagar, within the age group of 18-25 years were taken to assess their cardiovascular parasympathetic functions. They were classified into cases and controls. The results were statistically analyzed by applying Student's *t*-test by Statistical Product and Service Solution (SPSS) 17 software.

Inclusion Criteria

A total 50 healthy medical and para-medical students who were offspring of diabetic parents within the age group of 18-25 years were taken as cases. Age- and sex-matched 50 healthy medical and para-medical students who were offsprings of non-diabetic parents were taken as controls.

Exclusion Criteria

Exclusion criteria were subjects not willing to give consent for the study; subjects with history of DM, hypertension, cardiovascular diseases, thyroid abnormality, giddiness on standing, syncopal spells, asthma, and chest disease; subjects receiving drugs that are known to interfere with cardiovascular parasympathetic functions; subjects with history of smoking, alcohol intake and/or tobacco consumption in any form.

Parasympathetic function tests were performed in each subject according to a standard protocol by Ewing and Clarke.[9] Instruments used were sphygmomanometer, stethoscope, valsalva apparatus, and electrocardiogram (ECG) machine (VESTA 302i[RMS]).

The test was performed under thermoneutral conditions and at the same time of day (12-1 pm) in all the subjects. After explaining the procedure of test, written consent was taken from all the subjects. Before going for cardiovascular parasympathetic function tests, age (years), height (cm), weight (kg), resting blood pressure, heart rate, and respiratory rate were recorded. A battery of non-invasive cardiovascular parasympathetic function tests was performed in each subject. The parasympathetic function tests were as follows: Deep breathing test (DBT), lying to standing ratio (L/S ratio), and valsalva ratio.

Parasympathetic Function Tests

DBT

The subject was instructed about the test. It was explained that the breathing should be smooth, slow, and deep. For 6 cycles/min, the inspiration was done for 5 s and expiration for 5 s. Hand signal was given to maintain the rate and timing of the breathing while the ECG was recorded continuously. After taking the baseline recording of ECG for 30 s, the DBT was started, and recording of ECG was continued for throughout the test. The results were recorded as expiration to inspiration ratio (E:I ratio), which was the ratio of the longest R-R interval during expiration to the shortest R-R interval during inspiration. A value of 1.20 or higher was taken as normal.[10]

L/S test

The test was performed after 10 min of supine rest. Each subject was asked to lie down. Then, the subject was asked to stand immediately without help while ECG was recorded continuously for 1 min. The ECG was recorded for 30 s to get the baseline value and then during standing position for 1 min. The 30:15 ratio was calculated by taking ratio of the longest R-R interval at beat 30 and the shortest R-R interval at beat 15 after standing. The value of 1.00 for 30:15 ratio was taken as normal, and value of <1.00 was considered as abnormal.

Valsalva ratio

In this test, subject was made to perform valsalva manoeuvre in sitting posture for 15 s by blowing against closed glottis through a mouthpiece attached to manometer and maintained an expiratory pressure of 40 mm of Hg for 15 s. A small air leak in the system is useful to prevent the closure of glottis during the manoeuvre. At the end of 15 s, the pressure is released. Care was taken to prevent deep breathing before and after the manoeuvre. A continuous ECG was recorded for 15 s before the maneuver to get the baseline value and then during the maneuver (strain period, 15 s) and for 15 s after release of pressure. The valsalva ratio was calculated as the ratio of the longest R-R interval after manoeuvre to the shortest R-R interval during manoeuvre. Value >1.21 was taken as normal, and value <1.21 was considered as abnormal.

$$\text{Valsalva ratio} = \frac{\text{Maximum RR interval after strain}}{\text{Shortest RR interval during strain}}$$

Statistical Analysis

The results were presented in mean ± standard deviation (Table 1). The unpaired *t*-test was used to compare the study parameters between cases and controls. The $P < 0.05$ was considered significant. All the analyses were carried out using SPSS software 17 version.

RESULTS

In this study, we assessed the parasympathetic functions in offsprings of diabetic parents and compared their parasympathetic status with that of age- and sex-matched healthy offsprings of non-diabetic parents. The results of parasympathetic function tests in cases compared with the controls are summarized in Table 1. The study shows a decrease in all the three parasympathetic function tests (heart rate variability in response to deep breathing, heart rate variation in response to standing, and valsalva maneuver) in offsprings of type 2 diabetic parents (cases) as compared to non-diabetic parents (controls). However, the results were not statistically significant.

Table 1 depicts the comparison of parasympathetic function tests between cases and controls. It is evident from the mean values that there is a decrease in all the three parasympathetic function tests: DBT, LS ratio, and valsalva ratio among the cases as compared to controls although changes are not statistically significant ($P > 0.05$) between cases and controls.

DISCUSSON

In this study, we assessed the parasympathetic functions in offsprings of diabetic parents and compared their parasympathetic status with that of age- and sex-matched healthy offsprings of non-diabetic parents (Table 1). It is evident from the mean values that there is decrease in all the three parasympathetic function tests: DBT, LS Ratio, and valsalva ratio among the cases as compared to controls, although the changes are not statistically significant ($P > 0.05$) between cases and controls. It depicts decreased parasympathetic tone in offsprings of diabetic parents which is in concordance with findings of other authors. Tuppad et al.[2] observed an insignificant decrease in all the three parasympathetic function tests similar to our study as both studies have a small sample size. Foss et al.[11] observed subjects with parental type 2 diabetes had significantly lower heart rate variation in all three bedside tests ($P < 0.01$) than subjects without parental diabetes. The difference in results could be due to large sample size in this study as compared to our study. Findings of the study could be explained as follows: Variation of heart rate with respiration is primarily mediated by the vagal innervations of the heart. The output from the neurons of respiratory center influences the gain of the afferent and efferent outputs at the nucleus tractus solitarius. Heart rate variation is regulated by pulmonary stretch receptors, cardiac mechanoreceptors, and baroreceptors. In diabetics, due to the impairment of parasympathetic system the E:I ratio decreases. Heart rate response to immediate standing causes reflex tachycardia followed by bradycardia. This response is mediated by vagal and baroreflex mechanism. In diabetics with parasympathetic neuropathy, there is abnormal response due to damage to the reflex pathways mediating the response. This study also showed that valsalva ratio is lower in cases than normal persons, so this reflects decreased parasympathetic function due to decreased vagal tone.

Table 1: Comparison of parasympathetic function tests between cases and controls

Parasympathetic function tests	Cases (n=50) Mean±SD	Control (n=50) Mean±SD	P value
DBT	1.61±0.44	1.76±0.90	0.30
LS ratio	1.24±0.28	1.84±0.52	0.42
Valsalva ratio	1.84±0.52	1.92±0.79	0.57

DBT: Deep breathing test, LS ratio: Lying to standing ratio, SD: Standard deviation. *Significant $P<0.05$, Standard values DBT≥1.20, LS ratio=1, Valsalva ratio>1.21

Strength of the Study

Our study shows altered response in parasympathetic function tests in healthy offsprings of diabetic parents even before the offsprings develop diabetes. So, we can use these autonomic function tests as a screening test for diabetes in healthy offsprings of diabetic parents.

Limitations of the Study

A long-term study, including a greater number of subjects along with a wider age group range, is recommended for further assessment.

CONCLUSION

In this study, we conclude that genetic factors in the form of altered genes may pass from diabetic parents to their offsprings and could manifest as an altered response in parasympathetic function tests in healthy offsprings of diabetic parents even before the offsprings developing diabetes. Thus, genetic influence, insulin insensitivity, stress, and sedentary lifestyle are responsible for such altered response to parasympathetic function tests. The inheritance of genetic factors is a non-modifiable risk factor, but the behavior and lifestyle come under modifiable risk factors, and thus development of diabetes in high-risk group can be prevented by following measures:

- Screening programs should be effectively implemented among high-risk groups
- Weight reduction
- Relaxation exercises including yoga and meditation
- Adopt problem-solving skills to avoid stress
- Involvement in hobbies such as listening to music, painting, and dancing
- Positive thinking
- Organizing work/activities in daily life.[10]

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