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Study of Cardiac Autonomic Neuropathy and Its Association with Qtc Dispersion in Type-2 Diabetes Mellitus Patients Attending Rural Medical College

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Original Research Article

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Abstract: The prevalence of diabetes is on the rise, ranked seventh among leading cause of death. One of the major reasons for death among diabetes patient is cardiac autonomic neuropathy. Studies have found that QTc dispersion is an early predictor of cardiac autonomic neuropathy in diabetes, this study was designed to evaluate the association between cardiac autonomic neuropathy with QTc dispersion to improve our knowledge in this area. To evaluate the presence of cardiac autonomic neuropathy in Type 2 diabetes and to co relate autonomic dysfunction. Five standard cardio vascular response tests were carried out (i.e. Valsalva ratio, expiration inspiration ratio, immediate heart rate response to standing, fall in systolic pressure on standing and sustained hand grip test) to determine the severity of cardiac autonomic neuropathy by scoring system. QTc dispersion was determined by subtracting heart rate- corrected minimum QTc interval (QTc min) from maximum QT interval (QTc max) from standard electrocardiogram. Cardiac autonomic neuropathy was studied in 50 diabetic patients and was compared with 50 age and sex matched controls. 17 patients had evidence of cardiacautonomic neuropathy. The diabetics had statistically significant cardiac autonomic neuropathy compared to controls. QTc dispersion was prolonged in 9 patients out of 17 who had cardiac autonomic neuropathy. QTc dispersion was statistically significant in diabetes with cardiac autonomic neuropathy in comparison to those without cardiac autonomic neuropathy. This study has taken-up a large number of diabetic patients for the evaluation of cardiac autonomic dysfunction and for evaluation of relationship between cardiac autonomic neuropathy and QTc dispersion. The incidence of cardiac autonomic neuropathy in this study was 34%. Cardiovascular autonomic neuropathy is a common complication of diabetes mellitus. Prolonged QTc dispersion is common in patients with autonomic dysfunction due to diabetes. The QTc dispersion associated significantly with presence of cardiac autonomic neuropathy and may be simple and useful measure for detection of cardiac autonomic neuropathy.
Keywords: Diabetes mellitus; cardiovascular autonomic neuropathy; QTc dispersion.

INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder characterized by hyperglycemia, which arises as a result of insulin deficiency and / or insulin resistance. It is a disease known since ages, as early as 1500 B.C.

The prevalence of diabetes is on the rise, more alarmingly in the developing nations. Ranked seventh among leading cause of death, it has been rated third when all its fatal complications are taken into account. Although our knowledge of the disease is far from complete, advances in knowledge since the discovery of insulin has helped in understanding the natural history of diabetes mellitus in man.

Advances in the management of diabetes have reduced mortality enormously. Although the acute complications of diabetes such as ketoacidosis coma, hyperosmolar non-ketotic coma, and infections have been overcome, the long-term complication continues to pose a challenge to the management.

Amongst all the complication of diabetes mellitus, diabetic autonomic neuropathy is one of the most important challenging problems. Diabetic autonomic neuropathy can affect any organ of the body from gastrointestinal tract to skin, and its appearance pretends a marked increase in mortality risk of diabetic patients.

One of the earliest manifestations of diabetic autonomic neuropathy is denervation of cardiovascular system; hence assessment of cardiovascular reflexes affords a satisfactory evaluation. Cardiovascular dysfunction assumes maximum importance because it

leads to silent myocardial ischemia, intractable arrhythmias and sudden cardiac death.

An association between an abnormal QT interval and sudden cardiac death has been found in various diseases. Over the years several workers have studied the QT interval changes for detecting and assessing the severity of cardiac autonomic neuropathy. They have demonstrated that the QT interval prolongation as a test for cardiac autonomic neuropathy in diabetes. While some investigators have reported that the diabetics with cardiac autonomic neuropathy show QTc prolongation, some others have reported shortening of QT and QTc intervals. This study was designed to evaluate the association between cardiac autonomic neuropathy with QTc dispersion.

AIMS AND OBJECTIVES

To evaluate the presence of cardiac autonomic neuropathy in Type 2 diabetes and to co relate autonomic dysfunction.

METHODOLOGY

Five standard cardio vascular response tests were carried out (i.e. Valsalva ratio, expiration inspiration ratio, immediate heart rate response to standing, fall in systolic pressure on standing and sustained hand grip test) to determine the severity of cardiac autonomic neuropathy by scoring system. QTc dispersion was determined by subtracting heart rate-corrected minimum QTc interval (QTc min) from maximum QT interval (QTc max) from standard electrocardiogram.

RESULTS

Cardiac autonomic neuropathy was studied in 50 diabetic patients and was compared with 50 age and sex matched controls. 17 patients had evidence of cardiac autonomic neuropathy. The diabetics had statistically significant cardiac autonomic neuropathy compared to controls. QTc dispersion was prolonged in 9 patients out of 17 who had cardiac autonomic neuropathy. QTc dispersion was statistically significant in diabetes with cardiac autonomic neuropathy in comparison to those without cardiac autonomic neuropathy.

DISCUSSION

This study has taken-up a large number of diabetic patients for the evaluation of cardiac autonomic dysfunction and for evaluation of relationship between cardiac autonomic neuropathy and QTc dispersion. The incidence of cardiac autonomic neuropathy in this study was 34%. Pappachan *et al*. "Cardiac autonomic neuropathy in diabetes mellitus: prevalence, risk factors and utility of corrected QT interval in the ECG for its diagnosis" found that the prevalence of CAN was 60%. In the study done by D. Ziegler *et al*. on Prevalence of Cardiovascular Autonomic dysfunction at Various Stages of Diabetic Neuropathy the authors concluded that the overall prevalence of CAN in patients completing all parameters was 46.6%. The overall prevalence of cardiac autonomic neuropathy in diabetics is not precisely known. Depending upon the criteria used various authors have reported varying incidence of this complication. This is due to different populations in the studies and varying number of tests, which was used to elicit autonomic dysfunction. Prevalence of CAN, based on assessment of abnormal cardiovascular autonomic tests, is variable (5-90%)[1,2].

The QTc dispersion is a parameter that represents the spatial dispersion of repolarization and evaluates the heterogeneities of repolarization, and it is used as an indication of electrical instability and as a marker of arrhythmogenic risk. Several studies have found a significantly greater QTc dispersion in diabetics when compared with controls.

In this study, when comparing diabetics with controls, significant differences in QTc dispersion were observed. The QTc dispersion was significantly higher in diabetic patients when compared with controls. Others also have found a significantly higher QTc dispersion in diabetic patients when compared with controls, OB Familoni et al studied the relationship between QT intervals and cardiac autonomic neuropathy in Nigerian patients with Type 2 Diabetes Mellitus found that, the QT interval (QTc, QTd) were significantly longer in patients than controls. Cardoso Claudia et al studied clinical determinants of increased QT dispersion in patients with diabetes mellitus and opined that Diabetics had increased QT dispersion compared to controls. However, one study found no significant differences in QT dispersion between diabetics and controls. Michael Psallas et al, studied QT Dispersion: in a comparative study Between Diabetic and Non-Diabetic Individuals and its correlation with Cardiac Autonomic Neuropathy and concluded that QTd values do not differ between individuals with and without diabetes[3,4].

The results of the present study are in agreement with those of above studies which found significant differences in QTc dispersion between diabetics and controls.

In addition, the results of this study agree with those of above previous studies showing that QTc dispersion duration is greater in diabetics with CAN.

Kumhar MR *et al*. studied Cardiac autonomic neuropathy and its correlation with QTc dispersion in type 2 diabetes and opined that severity of cardiac autonomic neuropathy strongly correlated with QTc dispersion. Study done Michio Shimabukuro et al studied Increased QT dispersion and cardiac adrenergic dysinnervation in diabetic patients with autonomic neuropathy and concluded that diabetic patients with

autonomic neuropathy showed an increase in QTc dispersion correlated with cardiac adrenergic dysinnervation. Few other studies concentrated on assessing ECG changes and cardiac dysinnervation among diabetic patients found an increase in QTc dispersion correlating with cardiac adrenergic dysinnervation[5].

In the present study, it was observed that as the CAN score increased QTc dispersion also increased.

The findings presented here are in accordance with those of earlier studies in this regard. In contrast, the present study disagrees with the findings of one a study done by Psallas M *et al*. studied QT dispersion: and its association with microalbuminuria in diabetes and concluded that no significant differences were found in QTd between patients with and without CAN. CAN is not associated with QTd interval in both types of diabetes.

The present study as with the studies mentioned above has found that CAN is Positively correlated with the QTc dispersion, thereby implying that there is a need for earlier and regular evaluation of autonomic nervous system in Type 2 DM to prevent further cardiac complication[6].

The present study showed that as the duration of DM increased there was increase in incidence of CAN but this was not statistically significant.

The results of this study showed that with increasing levels of HbA1c there was increase in QTc dispersion but this was not statistically significant.

Diabetics with prolonged QTc dispersion are at higher risk for arrhythmias due to imbalance between the sympathetic and parasympathetic limbs of autonomic nervous system. Diabetic patient develop vagal denervation frequently and early in their disease and therefore may lose the protective influence on adrenergically mediated arrhythmias [7].

The result of this study reveals a significant co relation between cardiac autonomic neuropathy and prolonged QTc dispersion was found. QTc dispersion prolongation may arise from imbalance in sympathetic innervations of the diabetic myocardium, and this imbalance may increase the risk of ventricular arrhythmia [8].

The clinical importance of cardiac autonomic neuropathy lies not only in its recognition, but also in realization that some of the deaths may be avoidable .It is therefore possible that apart from being marker for cardiac autonomic neuropathy, QTc dispersion prolongation is also a marker for sudden death in diabetic cardiac autonomic neuropathy [9].

This study is not without limitations. A larger sample would certainly increase the statistical power of the study, and probably some differences would therefore become more expressive. Moreover, manual measurements of intervals without the support of any technology that could ensure a more precise measurement may also be an aspect to be taken into account. The accuracy and reproducibility of measurements of repolarization parameters were limited by difficulties in identifying the end of the T wave in some cases. One other problem encountered was the lack of a consensus on the values of several normal electrocardiographic parameters.

Despite some methodological limitations, this study clearly demonstrated a relationship between diabetes and changes in a set of electrophysiological parameters that indicate a prolonged and more heterogeneous repolarization in these patients, when compared with healthy subjects. This fact may be involved in the greater vulnerability of these patients to cardiac arrhythmias.

Therefore, the assessment of these new markers for arrhythmogenic risk may be important for better risk stratification of diabetic patients, a conclusion that needs confirmation in larger prospective studies.

QT abnormalities predict cardiac death in several medical conditions including diabetes. Increased QTc dispersion is probably more predictive of ventricular arrhythmia and mortality than QT prolongation. Standardization of assessment of QTcdispersion is necessary, although some consider that the measure itself is an artefact. QT interval is affected by cardiac ischemia and autonomic neuropathy but the influence of hyperglycemia is uncertain. Increased QTc dispersion could be used as a cost effective marker to identify diabetic patients at high risk of cardiovascular morbidity and mortality.

CONCLUSION

Cardiovascular autonomic neuropathy is a common complication of diabetes mellitus. Prolonged QTc dispersion is common in patients with autonomic dysfunction due to diabetes. The QTc dispersion correlates significantly with presence of CAN and may be simple and useful measure for detection of CAN. QTc dispersion is easily measured from resting ECG and does not involve active participation or performance by the patient and hence can be used as a parameter to assess cardiac autonomic neuropathy.

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