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Original research article: Study of correlation of glycemic status with indicators of myocardial oxygen usage

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Abstract
Background: Patients with diabetes mellitus are at increased risk for myocardial infarction (MI) and diabetes is considered a coronary risk equivalent by the National Cholesterol Education Program. Poor glycemic control in diabetic patients and stress hyperglycemia in nondiabetic patients is associated with worse outcomes after acute MI but it is not fully understood as to whether strict glycemic control during AMI hospitalizations improves outcomes.
Objective: The objective of the study is to investigate the correlation between poor glycemic control determined by glycosylated haemoglobin (A1C) and myocardial oxygen demand.
Methodology: This Prospective study consist of total 180 participants of age group 35-45 year and they were divided in to 3 group, based on their blood sugar level and blood pressure level. Group 1 consist of 60 healthy control, Group 2 consist of 60 prediabetic patients and group 3 consist of 60 newly diagnosed diabetes mellitus patients. Glycemic status (Fasting blood sugar and (HbA1C) is determined by per American Diabetic Association 2011 (ADA) criteria. The haemodynamic determinants of myocardial oxygen demand measured were heart rate (HR), systolic blood pressure (SBP) and rate pressure product (RPP).
Result: The mean concentration of fasting blood sugar and HbA1C was found to be high in prediabetes and diabetes group as compared to control group. The systolic & diastolic blood pressure in healthy control, prediabetes, and diabetes was 114/74, 126/84 and 132/86 respectively. The resting HR was significantly higher in patients with T2DM (93±3 bpm; p=<0.0001) in comparison with controls and prediabetics. The RPP was estimated to be significantly higher in T2DM (12276±895) compared to prediabetics and controls. Positive correlation was found between resting HR and RPP with FBS levels in prediabetic and T2DM patients. Similar positive correlation was established between resting HR and RPP with A1C values.
Conclusion: Diabetic autonomic neuropathy is a common and serious complication of diabetes. It is present in a quarter of patients with type 1 and one-third of patients with type 2 diabetes. In addition, prediabetes has been identified as risk factors for overt diabetes and cardiovascular disease so at least regular checking of resting heart rate and blood pressure might be useful for early detection of autonomic neuropathy. The public health measures, such as healthful diet, exercising regularly, controlling weight, and clinic-based diabetes screening for the early detection of hyperglycemia may be effective in lowering diabetes risk and diabetes-related complications in the general population.

Keywords: resting heart rate (HR), rate pressure product (RPP), systolic blood pressure (SBP)

Introduction

Diabetes mellitus is associated with a 2 to 4 fold increase of the risk for cardiovascular disease [1, 2]. 75 to 80% of the deaths in patients with diabetes mellitus are conditioned by a thrombotic event5 This increased risk is the main factor underlying the excess mortality and reduced life expectancy of people with type 2 diabetes; the life expectancy of people with type 2 diabetes at the age of 40 is reduced by an estimated 8 years in comparison with individuals without diabetes [3].

The prognosis is poorer in patients with diabetes mellitus type 2 that suffers a myocardial infarction compared with people without diabetes mellitus. In patients with acute myocardial infarction the underlying mechanism in the increase of mortality associated to glucose levels are poor understood. In a study by Nicolau JC and cols, with 52 patients with acute myocardial infarction with ST segment elevation and hyperglycemia, in the first 24 hours compared radionuclide ventriculography at day 4 and six months, finding that basal glucose level like independent and powerful predictor of left ventricular growth after an acute myocardial infarction [4].

HbA1c could be considered a good marker of glycated proteins and its assay has been used as a measure of glycemic control in several landmark trials. Moreover, a recent report found that elevated HbA1c levels are also predictive for cardiovascular disease and mortality in patients without diabetes mellitus, regardless of fasting glucose levels, indicating that long-term glycometabolic derangement in the sub-diabetic range also poses a risk for cardiovascular disease [5]. HbA1c levels of more than 7% are associated with a significant increase in the risk of cardiac events and deaths. [6]

Heart rate is a major determinant of myocardial oxygen consumption and energy utilization [7]. furthermore, an increase in heart rate reduces the diastolic coronary perfusion time. Therefore, increase in heart rate may trigger is chaemic events. Systolic hypertension is known to increase myocardial oxygen demand [8]. Hyperglycemia showed independent association with heightened rate pressure product. These haemodynamic derangements may contribute to undesirable adverse cardiovascular events in T2DM patients. [3] Present study aimed to examine the association of Fasting blood sugar

level and HbA1c with determinants of myocardial oxygen usage.

Material and Method

This prospective study was conducted at department pf physiology in association with medicine department at pacific medical college and hospital (PMCH), Udaipur, Rajasthan, India from Dec 2017 to April 2018.

A total of 400 adults who visited PMCH in the age range of 35-45 years were screened. On the basis of ADA 2011 criteria [9] subjects were classified. Among them 180 Partcipants selected based on blood sugar and BP level.

History of prior anti-hypertensive and anti-diabetic drugs use were excluded from the study.

Study participants were divided into three groups; Controls (group 1) (n=60) defined as normoglycemics and normotensives (SBP<120Hg, DBP<80 mm Hg); Prediabetics (group 2) (n=60) defined as FPG 100-125 mg/dl or A1c 5.7-6.4% and SBP <140 mm Hg and/or DBP < 90 mm Hg and T2DM (group 3) (n=60) defined as FPG ≥126 mg/dl; A1c≥6.5 gm% Baseline clinical characteristics, anthropometric measurements and biochemical data were recorded as per the standard procedures. Subjects underwent clinical examination under standardized conditions. Resting heart rate was recorded after 5 min rest in supine position by using Electrocardiograph (ECG) machine.

Brachial artery blood pressure (first and fifth Korotkoff Sounds) of right arm was measured three times consecutively with 15 minutes interval on seated participants after they had rested for 5 minutes, with the use of a standardized mercury Sphygmomanometer (Diamond).The mean of the last two of these measurements was used for estimation of blood pressure.

Rate pressure product (Robinson Index is calculated as a product of systolic blood pressure and heart rate (RPP=SBPxHR) and expressed in mm Hg. bpm [10, 11]

Estimation of Fasting blood glucose (FBS) was done by GOD POD method in semi auto analyzer of central laboratory of our institute by using Transasia kit.

(Normal blood sugar: <100 mg/dl, Prediabetic: 100-125 Mg/dl, diabeteic: >126 mg/dl)

Statistical analysis

Statistical analysis was done by using graph pad prizam software. correlations between variables were evaluated by Pearson's correlation.

Result

As depicted in table1 baseline characteristics are distributed differently in three study groups (p<0.001), which is indeed a prerequirement for study.

Table 1: showing various physiological parameters of study group

Parameters	Group 1(n=60)	Group 2(n=60)	Group 3(n=60)	P- value
Age(yr)	39.5±4.5	38.9±3.9	40.1±2.5	>0.01(NS)
HR (bpm)	73±2.0	82±4.0	93±3.0	<0.01(S)
BMI (kg/m2)	21.9±1.3	26.5±2.2	29.2±3.2	<0.01(S)
SBP (mm Hg)	114±5	126±4	132±5	<0.01(S)
DBP (mm Hg)	74±4	84±5	86±2	<0.01(S)
RPP(SBPxHR)	8322±535	10332±705	12276±895	<0.01(S)

Table 2: showing biochemical parameter of study group

Parameter	Group 1(n=60)	Group 2(n=60)	Group 3(n=60)
FBS(mg/dl)	82±4	114±4	153±6
A1c (%)	4.5±0.5	6.1±0.4	7.8±0.2

Table 3: Correlation of metabolic indicators of oxygen usage with glycemic status

	Group 1(n=60)	Group 2(n=60)	Group 3(n=60)
FBS vs SBP	0.65	0.94	0.94
HbA1c vs SBP	0.08	0.94	0.92
FBS vs DBP	0.52	0.92	0.94
HbA1c vs DBP	0.12	0.94	0.95
FBS vs HR	0.72	0.96	0.97
HbA1c vs HR	0.16	0.95	0.96
FBS vs RPP	0.72	0.96	0.96
HbA1c vs RPP	0.12	0.92	0.95

This study does establish a very strong correlation among variables of glycemic status (FPG and A1C) and variables of myocardial oxygen usage (resting HR, SBP, RPP) in prediabetics and T2DM patients compared to normoglycemic participants [Table 3].

Discussion

Type 2 diabetes mellitus (T2DM) is a public health concern [12]. T2DM is increasingly frequent in the world in association with the increase of sedentary behaviours, unhealthy diet, obesity and metabolic syndrome [13-17]. The number of people with T2DM is predicted to double within the next three decades.

Diabetic autonomic neuropathy is a frequent cause of morbidity and mortality among diabetic individuals [18-22] and is characterized by widespread neurological degeneration affecting the small nerve fibers of the parasympathetic and sympathetic branches of the autonomic nervous system. Autonomic nervous system abnormalities may occur quite early in the course of diabetes, followed by a continued gradual decline [23]. Early detection of subclinical autonomic dysfunction in diabetic individuals is important for risk stratification and subsequent management, possibly including pharmacologic and lifestyle interventions [24].

Elevated heart rate (HR) is a risk factor for cardiovascular morbidity and mortality in healthy people as well as in

patients with cardiac diseases is supported by numerous epidemiological association studies [25, 26]. Elevated HR is frequently associated with high blood pressure (BP) and metabolic disturbances and increases the risk of new onset hypertension and diabetes. In the present study resting HR was found higher in T2DM patients as compared to healthy normoglycemic controls. No resting tachycardia was found (Table 1). The pathogenetic connection between HR and cardiovascular disease has been discussed in several reports [27-28].

A resting heart rate is generally considered as a surrogate marker for autonomic activity, and increased sympathetic nerve system activity induces both acute and chronic insulin resistance [29-30]. Several mechanisms have been proposed by which sympathetic activation may lead to higher diabetes risk. One of the most important mechanisms might be that sympathetic activation causes vasoconstriction and decreases skeletal muscle blood flow, resulting in the impairment of glucose uptake into the skeletal muscle [31-32]. Additionally, sympathetic activation has been associated with many diabetes-related risk factors, including reduced insulin sensitivity, high BP, obesity, subclinical inflammation and the metabolic syndrome.

An important observation in present study was that SBP was found in prehypertensive range in prediabetics and newly diagnosed T2DM patients. Elevated SBP also increases myocardial oxygen demand and together with elevated heart rate would tend to increase future cardiovascular risk. The elevated RPP is an important indicator of heightened oxygen demand. The higher values of HR, SBP and RPP in prediabetic group indicates increased myocardial oxygen usage much before the beginning of T2DM.

Glycated haemoglobin has been used to monitor glycaemic control in diabetics for more than two decades. It helps clinicians and their patients to stratify the treatment strategy and avoid long-term complications. In the present study fasting blood glucose (mg/dl) and A1C levels were positively correlated with resting heart rate and rate pressure product.

Park S *et al* studied the effect of A1C in non-diabetic population as a better predictor of cardiovascular disease and coronary heart disease related mortality than fasting or post prandial glucose levels [33]. Poor glycemic control in patients with T2DM as evidenced by their A1C values (>7%) makes them more vulnerable to future cardiovascular complications.

Conclusion

Diabetic autonomic neuropathy is a common and serious complication of diabetes. It is present in a quarter of patients with type 1 and one-third of patients with type 2 diabetes. In addition, prediabetes has been identified as risk factors for overt diabetes and cardiovascular disease so at least regular checking of resting heart rate and blood pressure might be useful for early detection of autonomic neuropathy. The public health measures, such as healthful diet, exercising regularly, controlling weight, and clinic-based diabetes screening for the early detection of hyperglycemia may be effective in lowering diabetes risk and diabetes-related complications in the general population.

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