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STUDY OF EVALUATION OF SILENT MYOCARDIAL ISCHEMIA IN TYPE 2 DIABETES MILLETUS BY EXERECISE STRESS TEST

KEYWORDS

treadmill test, Silent myocardial ischemia, diabetes mellitus type 2, exercise stress test.

Dr Tanuj Mehta

Senior Resident, Department of Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research Mullana, Ambala, Haryana India.

Dr Vijay Kumar.

Assistant Professor, Department of Cardiology, Maharishi Markandeshwar Institute of Medical Sciences and Research Mullana, Ambala, Haryana India.

Dr Sunita Gupta

Professor, Department of Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research Mullana, Ambala, Haryana India.

Dr Jasmeen Chahal

Resident, Department of Medicine, Maharishi Markandeshwar Institute of Medical Sciences and Research Mullana, Ambala, Haryana India.

ABSTRACT

Introduction Silent myocardial ischemia and infarction is recognized as a common occurrence in diabetic individuals with Coronary Artery Disease (CAD), even in those without autonomic neuropathy2. There are multiple means by which silent myocardial ischemia can be documented but exercise treadmill test and ambulatory ECG monitoring are most important and useful methods. Despite the many recent advances in technology related to diagnosis and treatment of cardiovascular disease, the exercise test remains an important diagnostic modality. Its many applications, widespread availability and high yield of clinically useful information continue to make it an important screening tool for more expensive and invasive procedure3. AIM: To study the prevalence of myocardial ischemia based on ECG changes on exercise stress test. METHODS: Fifty cases of type 2 Diabetes milletus with no clinical evidence of coronary artery disease with normal resting ECG (Electrocardiogram) were subjected to exercise stress test using Bruce protocol. Test was terminated according to "Criteria of termination of stress test." Test was considered as positive when horizontal or downslopping ST segment depression of 1 mm or more occurring at 80 mili seconds after J point during exercise which persisted for more than 2 minutes in recovery, hypotensive response during stress test i.e. systolic blood pressure drop of 20 mm of Hg or more after an initial rise but without a fall below resting level or systolic blood pressure drop below the standing rest value , ST segment depression, which appears shortly after exercise during recovery period were also taken as positive response. RESULTS: In this study prevalence of silent myocardial ischemia was in 28% of patients. TMT was positive in 14 patients (28%) and was negative in 36 patients (72%). Present study showed that silent myocardial ischemia increases with duration of DM. TMT was positive in 3/25 (12%), 3/13 (23.1%), 5/8 (62.5%) and 3/4 (75%) patient with duration of diabetes ≤5, 6 to 10, 1 to 15, and 16-20 years respectively. Mean duration of DM in TMT positive patients was 11.6 yrs whereas in TMT negative patients was 5.9 yrs. The characteristics of patients with treadmill positive and negative groups were compared and it was seen that the two groups varied significantly ($p<0.05$) with respect to their duration of diabetes, average triglycerides levels, HbA1C levels and exercise performance. CONCLUSION We conclude that the prevalence of silent myocardial ischaemia is more common in diabetics and it increases with duration of type 2 diabetes mellitus. Hypertriglyceridemia and poor glycemic control (HbA1c levels) are strong clinical predictors of silent myocardial ischaemia. There are multiple means by which silent MI can be documented but exercise treadmill test is most important and useful method. Early screening of patients with type 2 diabetes mellitus for evidence of silent myocardial ischaemia may prevent catastrophic cardiac events.

INTRODUCTION

Diabetics have an increased prevalence of atherosclerosis and coronary heart disease and experience higher morbidity and mortality after acute coronary syndrome and Myocardial Infarction (MI) than non diabetics. Involvement of cardiovascular system in diabetes can occur as coronary atherosclerosis, diabetic cardiomyopathy, cardiac autonomic neuropathy, preclinical heart disease.

The American Heart Association (AHA) has designated Diabetes Mellitus (DM) as a major risk factor for cardiovascular disease (same category as smoking, hypertension and hyperlipidemia). Type II diabetes patient without a prior MI have a similar risk for coronary artery related events as non diabetic individuals who have had a prior MI. It has been called Coronary Heart Disease (CHD) risk equivalent1.

Silent myocardial ischemia and infarction is recognized as a common occurrence in diabetic individuals with Coronary Artery Disease (CAD), even in those without autonomic neuropathy2.

There are multiple means by which silent MI can be documented but exercise treadmill test and ambulatory ECG monitoring are most important and useful methods. Despite the many recent advances in technology related to diagnosis and treatment of cardiovascular disease, the exercise test remains an important diagnostic modality. Its many applications, widespread availability and high yield of clinically useful information continue to make it an important screening tool for more expensive and invasive procedure[3].

The myocardial ischemia or infarction may be associated with mild symptoms or may be totally silent. In the Framingham study group 25% of the myocardial infarctions were unrecognized. Silent infarctions are more common in diabetes (39%) when compared to non diabetics (22%). Similarly during treadmill exercise test, angina is absent during ischemic episodes (painless ST depression) almost twice in diabetics than in non-diabetics (75% Vs 35%) and is due to severe

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autonomic neuropathy. The delay in time from the onset of ST depression to angina may be twice as long to patients with diabetes than in patients without diabetes and correlates with the extent of autonomic nervous dysfunction.[4]

Prevalence of silent myocardial infarction and ischaemia is more in diabetics. In diabetes mellitus, there is greater prevalence of painless sudden death particularly during sleep. Silent myocardial ischaemia is evident during treadmill and thallium stress tests. Incidence of painless ST depression is twice in diabetics (75%) versus non diabetics (35%)5. So the present study planned to find out the prevalence of silent myocardial ischemia in diabetes mellitus.

METHODS AND MATERIALS The study was conducted at M.M Institute of Medical Sciences and Research Mullana, Ambala, Haryana India. Fifty Type 2 diabetic patients were taken as per American diabetes association guidelines.

Inclusion Criteria:
- All patients of Type 2 diabetes mellitus.
- Absence of any symptoms suggestive of coronary artery disease.
- Resting ECG normal.

Exclusion Criteria:
Any patient with contraindication to stress testing.
- Resting ECG abnormal or suggestive of established ischemia.
- Patients taking Digitalis and Beta-blockers.

Patients were called for TMT on scheduled date and time. All selected patients for study were subjected to a standardized maximal exercise test on a treadmill using Bruce protocol.6
The informed consent was obtained from each and every patient.

The following points related to stress test were explained to each patient in detail :
- The entire procedure of the stress test was explained.
- A demonstration of walking on the treadmill was given to each patient.
- The patients were asked to report immediately in case of chest pain, any discomfort, giddiness, breathlessness or fatigue.
- The patients were told not to stop abruptly while walking on treadmill.

Technique of treadmill test
A standard 12 lead electrocardiogram was taken following which a torso ECG was obtained in the supine position and in the sitting or standing position. Blood pressure was recorded in both positions and the patient was instructed on how to perform the test. Standard multistage maximal exercise test was done on a motorised treadmill according to Bruce protocol.7 The heart rate, blood pressure and electrocardiograms were recorded at the end of each stage of exercise, immediately before and after stopping the exercise and for each minute for at least 5 to 10 minutes in the recovery phase. Exercise test was terminated in all patients following the achievement of target heart rate or an abnormal ischemic response. This was defined as development of 0. 10 mV (1 mm) of J point depression measured from the PQ junction, with a relatively flat ST segment slope (<lmV/sec), depressed ≥ 0.10 mV 60 to 80 msec after the J point in three consecutive beats with a stable baseline. Exercise test was also terminated if patient developed dysponea, fatigue or chest pain. The data obtained was subjected to appropriate statistical analysis for assuring the results of the study.

The test was terminated, according to "Criteria for termination of stress test".[7]

Following responses were considered positive8:
1. Horizontal or down slopping ST segment depression of 1 mm or more occurring at 80 mili seconds after J point, during exercise which persisted for more than 2 minutes in recovery.
2. Hypotensive response during stress test i.e. systolic blood pressure drop of 20 mm of Hg or more after an initial rise but without a fall below resting level or systolic blood pressure drop below the standing rest value.
3. ST segment depression, which appears shortly after exercise during recovery period were also taken as positive response.

RESULTS In our study the age range of patients was 34-69 years with a mean of 49.9 years and standard deviation (SD) was 9.2 years. Most of the patients belonged to the age group 40-60 years.

Out of 50 cases, 40 were males and 10 were females. The ratio of males to female was 4:1
This study showed that TMT was positive in 14(28%) and was negative in 36(72%) patients. Out of 14 positive cases 11 were males and 4 were females. Statistically there was no significant difference in SMI in male and female patients (p=0.87).

Among the 14 patients, who had positive stress test, 3(21%) patients were having horizontal ST-depression, 10(71%) were having downward sloping ST- depression and 1(7%) patient had appearance of ST- depression during recovery.

Present study showed that silent myocardial ischemia increases with duration of DM. TMT was positive in 3/25 (12%), 3/13 (23.1%), 5/8 (62.5%) and 3/4 (75%) patient with duration of diabetes ≤5, 6 to 10, 1 to 15, and 16-20 years respectively. Mean duration of DM in TMT positive patients was 11.6 yrs whereas in TMT negative patients was 5.9 yrs.

Present study showed Out of 14 patients with positive TMT results, 11(78.5%) patients were having HbA1c levels in the poor control range(10-12) where as number of subjects with negative TMT result in this range was only 3(8%) out of 36. Mean HbA1C of TMT positive patients was 9.7 whereas in TMT negative patients was 8.

Table 1 shows comparison of lipid profile in TMT test positive and negative patients. It was found that there was a statistically significant difference in TMT positive cases and TMT negative cases with reference to triglycerides levels (p=0.01). Average triglycerides levels in TMT positive and negative cases was 152.7 and 121.1 mg% respectively.

Table 2 shows the mean exercise duration of patient with negative TMT test was 624.3 sec. which was significantly higher than the mean exercise duration of patients with positive TMT results i.e. 521.9 sec. Another significant finding in this table is that only one patient out of 14 patients with positive TMT test experienced chest pain during the test. The other exercise parameters in TMT test positive and negative patients were mostly similar.

TABLE NO :- 1 COMPARISON OF LIPID PROFILE, HbA1C AND DURATION OF DIABETES IN TMT POSITIVE AND NEGATIVE PATIENTS

S.No	Parameters	TMT Negative (36) (mean±sd)	TMT Positive (14) (mean±sd)
1	LDL(mg/dl)	118.53±31.44	106.64±24.365
2	HDL(mg/dl)	35.89±3.37	35.57± 3.61

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3	VLDL(mg/dl)	24.22±5.83	30.50±5.61
4	Cholesterol(mg/dl)	181.42±30.54	172.71±25.82
5	Triglycerides(mg/dl)	121.11±28.93	152.71±28.04

TABLE NO:- 2 COMPARISON OF EXERCISE PARAMETERS IN TMT TEST POITIVE AND NEGATIVE PATIENTS

S.NO	EXERCISE PARAMETERS	TMT NEGATIVE PATIENTS (mean value)	TMT POSITIVE PATIENTS (mean value)
1.	Max HR (per min.)	166.54±15.5	164.6±16.5
2.	Change in HR(per min.)	75.6±22.8	73.2±21.8
3.	MaximumSBP(mmHg)	170.9±12.2	169.5±8.8
4.	Change inSBP(mmHg)	47.8±24.5	45.8±21.3
5.	Duration of TMT(secs)	624.3±80.6	521.9±57.8
6.	Chest Pain	Nil	1
7.	Dyspnea	Nil	Nil
8	Syncope	Nil	Nil
9	Arrhythmias	Nil	Nil
10	Hypotension	Nil	Nil

DISCUSSION

Coronary atherosclerosis is one of the most common and chronic complications of diabetes mellitus. A recently observed and focused aspect of coronary artery disease is its silent and asymptomatic presentation.

- The present study was aimed at the asymptomatic presentation of coronary artery disease in the form of silent myocardial ischaemia in asymptomatic diabetes mellitus patients. It consisted of two aspects; first the prevalence of silent myocardial ischaemia in asymptomatic patients with type 2 diabetes mellitus. Secondly to correlate ECG changes with symptoms, if any, during exercise.

This study consisted of 50 known asymptomatic type 2 diabetics without clinical and electrocardiograpic evidence of coronary artery disease and were evaluated for the prevalence of silent myocardial ischaemia by using exercise treadmill testing.

Among 50 patients, TMT was positive in 14 (28%) and was negative in 36 (72%). Out of 14 positive 11 were males and 4 were females. The prevalence of silent myocardial ischaemia in type 2 asymptomatic diabetes mellitus was found to be 28% (14/50).

A study9 by Gupta SB et al in India found that 38.3% of diabetics without prior coronary artery disease had silent myocardial ischaemia on exercise test. Sukhija R et al10, found that silent myocardial ischaemia was seen in 14 (46.7%) out of 30 diabetics by using treadmill test. DIAD study48 found that a total of 113/522 patients (22%) had silent ischaemia using stress testing in asymptomatic patients with type 2 diabetes mellitus. One more study done by Sargin H11 found that 62/500 patients (12.4%) had silent myocardial ischaemia in patients with type 2 diabetes mellitus by using exercise electrocardiogram. So the present study is an agreement with that diabetics have a higher prevalence of silent myocardial ischemia.

We observed that prevalence of silent myocardial ischemia increases with duration of diabetes mellitus. We found 25 patients with diabetes duration equal to or less than 5 years, TMT was positive in 3 (12%). 13 patients with diabetes duration between 6-10 years. TMT was positive in 3 (23.1%). 8 patients with diabetes duration between 11 and 15 years TMT positive in 5 (62.5%). 4 patients with diabetes duration between 16 and 20 years TMT was found to be positive in 3 (75%). In our study Mean duration of DM in TMT positive patients was 11.6 yrs whereas in TMT negative patients was 5.6 yrs. Our results are similar to study conducted by12 Farood A, who conducted a study on 500 type 2 diabetics and found that patients with silent myocardial ischemia has significant relationship with duration of diabetes. They observed that mean duration of diabetes was 15 years in patients with positive stress test and 8 years in patients with negative stress test. Study by Sargin H49 including 500 patients with type 2 diabetes mellitus with normal resting ECG found that, 62 (12.4%) patients had asymptomatic coronary artery disease on exercise treadmill testing. The abnormalities of exercise test were associated with longer duration of diabetes ($p<0.005$).

Lipid abnormalities are very common in type 2 diabetes and are it has great influence on coronary artery disease. In the present study, we found average total cholesterol in TMT positive and negative cases was 172.7 mg% and 181.4 mg% respectively. Mean triglyceride in TMT positive and negative cases 152.7 mg% and 121.1 mg% respectively. Mean LDL was 117.3 mg% in TMT positive cases and 120.0 mg% in TMT negative cases. Mean HDL was 35.6 mg% in TMT positive cases and 35.9 mg% in TMT negative cases. Statistically significant value of $p=0.001$ was found in triglycerides levels between both the groups. The same results were observed in previous study done by Mathura KC et al 13which found that dyslipidemia was very common in type 2 diabetics and the most common abnormality seen was increased serum triglyceride levels in (73.3%) patients. The next common abnormality was decreased serum HDL levels, both seen in 66.7% patients. Coronary artery disease had a stronger correlation with high levels of triglycerides. Another study from India, conducted by Agarwal R 14 found that CAD had strong correlation with high levels of triglycerides (0.82) and low HDL (-0.81). Another study done by Achari V15 found that triglyceride levels were elevated in 28 treadmill positive cases compared to 15 treadmill negative cases ($p<0.01$).

The increased levels of glycosylated hemoglobin indicated poor glycemic control and it has great influence on coronary artery disease. In the present study we found average HbA1c (%) in TMT positive and negative cases was 9.9 and 8.1 respectively. Statistically significant value of $p=0.001$ was found in HbA1c (%) levels between both the groups. DeLuca AJ et al 16found that among those who had diabetes mellitus, silent myocardial ischaemia was present 27 of 54 patients (50%) who had HbA1c level > or = 7.6% and in 39 of 137 (28%) with HbA1c level ($p<0.005$). In a study, conducted by Gautam Ravipathi et al17 there was significant increasing trend of HbA1c levels over the increasing number of coronary vessels involvement with CAD ($p<0.0001$).

In our study we found that the performance of exercise was poor in patients who had positive stress test as compared with patients with negative stress test. The mean duration of exercise was 624.3 secs, in patients with negative stress test which was significantly higher than the mean duration of exercise in positive patients i.e. 521.9 secs. Study done by Airaksinen K18 and co worker showed that exercise tolerance is decreased in young diabetics. Our study also confirms the same findings.

CONCLUSION We conclude that the prevalence of silent myocardial ischaemia is more common in diabetics and it increases with duration of type 2 diabetes mellitus. Hypertriglyceridemia and poor glycemic control (HbA1c levels) are strong clinical predictors of silent myocardial ischaemia. There are multiple means by which silent MI can be

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documented but exercise treadmill test is most important and useful method. Despite the many recent advances in technology related to diagnosis and treatment of cardiovascular disease, the exercise test remains an important diagnostic modality. Its widespread availability and high yield of clinically useful information makes it an important screening tool for more expensive and invasive procedures. Early screening of patients with type 2 diabetes mellitus for evidence of silent myocardial ischaemia may prevent catastrophic cardiac events.

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