Heart rate recovery in exercise test in diabetic patients with and without microalbuminuria

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Original Article

Abstract

BACKGROUND: Diabetes mellitus (DM) has a lot of complications such as macrovessel and microvessel disease. Another complication of DM is cardiac autonomic neuropathy (CAN), which have effect on automatic nervous system of heart. Failure in heart rate slowing after exercise is a presentation of this abnormality.

METHODS: We selected diabetic patients and divided them to case and control group based on microalbuminuria. Case group comprised of diabetic patients with microalbuminuria and control group included those without microalbuminuria. Patients in both groups exercised on treadmill using Bruce protocol and heart rate was measured in first and second minutes in the recovery period.

RESULTS: We selected 35 patients with microalbuminuria (case group) and 35 without microalbuminuria (control group) among diabetic patients. No statistically significant difference was seen in sex and age between case and control groups. Heart rate recovery in the first minute of recovery in the case and control groups did not show significant difference; but in the second minute of recovery, it was significantly higher in control group (97 ± 19.4 vs. 101.9 ± 12.4 beat per minute, P = 0.04).

CONCLUSION: In this study we evaluated the heart rate recovery or deceleration in diabetic patients with albuminuria and without microalbuminuria in recovery phase after exercise test. We found out that heart rate recovery at the second minute in the case and control groups has statistically significant difference but at the first minute, it did not.

Keywords: Diabetes Mellitus, Exercise Test, Heart Rate Recovery

Introduction

Diabetes mellitus (DM) is one of the most important causes of morbidity and mortality in the word especially in Middle East, hot spot area for this disease,[1] and diabetic nephropathy is one of the most disabling complications of DM.

About 25% of type 1 diabetic patients will be affected by renal insufficiency, while it is 5% to 10% in type 2. Microalbuminuria is the first sign of progression to kidney disease and proteinuria. 50% of people with type 1 diabetes are affected by microalbuminuria and about 20% by proteinuria; and progress to the end stage renal failure and diabetic nephropathy in patients with type 2 diabetes is similar to patients with type 1 diabetes.[2-4]

The risk of cardiovascular disease (CVD) in patients with type 2 diabetes mellitus with microalbuminuria is two or three times more than patients without the albuminuria. However, if a patient has proteinuria, cardiovascular risk increases to 10 times. The survival of type 2 diabetic patients with renal failure is short after the beginning of the dialysis.[3] Many of these patients will die with cardiovascular events rather kidney problem.[5]

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The reasons for such close relationships between nephropathy and cardiovascular disease is not definitely determined, but autonomic nervous system disorders that occur more in nephropathic patients can explain this issues.[6] Cohen et al. showed that fasting blood sugar has independent and strong relationship with abnormal heart rate recovery (HRR) after exercise, even in nondiabetic levels.[7] The result of Framingham study[5] has also shown that the low HRR, that means sympathetic and parasympathetic nervous system disorder are seen in diabetic patients. Another studies expressed that the low HRR following the exercise test had an independent relationship with the high prevalence of CVD and all-cause mortality in diabetic men.[8,9] Therefore, HRR can help the diagnosis and prediction of early stage of CVD and cardiac autonomic neuropathy (CAN) in diabetic patients.[10] We examined HRR, as a sign of cardiac autonomic function, in albuminuric (case group) versus non-albuminuric (control group) diabetic patients.

Materials and Methods

This case-control study was done in diabetic patients in Al-Zahra and Noor University Hospitals, and Isfahan Endocrine, Metabolism and Cardiovascular Research Center in 2011. All patients signed the consent form for participating in the study.

Inclusion criteria were type 1 or 2 diabetic patients without history of angina pectoris, myocardial infarction or stroke in 6 months ago. Exclusion criteria were history of coronary artery bypass graft (CABG) in 3 months before entry to this study, heart failure New York Heart Association (NYHA) class 3 or 4, severe peripheral vessel disease, inability to complete exercise test, history of hospitalization, poor compliance for follow up and serum creatinine more than 3 mg/dl.

Case group included diabetic patients with microalbuminuria and control group consisted of diabetic patients without microalbuminuria. Exercise test was done for both groups by Bruce protocol in Noor Hospital and heart rate was recorded at first and second minute after termination of exercise in recovery period.

Sampling was done by convenience method. The sample size was calculated as 35 subjects in each group in order to compare the two proportionate considering $\alpha = 5\%$, statistical power of 80%, and the 76.6% and 23.4% risk in patients with or without microalbuminuria as mentioned in the literature, respectively.[11]

Diabetic patients were enrolled and physical examination was done for all patients by a cardiologist who referred them to the laboratory for measurement of urine analyses, microalbuminuria, and urine creatinine after 12 hours fasting. The albumin to urine creatinine ratio (ACR) was calculated and ACR 30-300mg was defined as microalbuminuria.

Based on microalbuminuria, patients were classified to two groups. Then, patients were referred to exercise test department but technician did not know about patient history and laboratory Data. Patients exercised to the maximum expected effort as they can do. All exercise data such as patient's symptoms, heart rate and electrocardiogram were recorded. Recovery period included walking phase with the speed of 1.9km/h and 0% grade of treadmill. Patient's heart rate (HR) was measured and recorded in 2 minutes. Heart rate recovery (HRR) or heart rate deceleration was calculated as below:

Predicated Maximum HR = 220 - age (year) $\pm$ 10 beat per minute

HRR = peak HR - HR at 1st min recovery: Normal > 12 beat per minute

HRR = peak HR -HR at 2nd min recovery: Normal > 22 beat per minute

Heart rate drop more than 12 and 22 beat per minute (BPM) in the first and second minute, respectively, were considered normal response whereas lower values were considered abnormal. Research data were recorded in a questionnaire sheet and approved by cardiologists and statisticians and were analyzed by SPSS software version 18 (SPSS, Inc., Chicago, IL) using chi-square and Student's t-test.

Results

Among diabetics, we selected 35 patients with microalbuminuria (case group) and 35 without microalbuminuria (control group) with regard to inclusion and exclusion criteria. Among 70 participants, 11 patients excluded (4 in case and 7 in control), due to inability of running enough, or other exclusion criteria. Patient's age was between 16 and 65 years. The average age of patients was 49.9 $\pm$ 9.5 years. The average age of microalbuminuric patients was 50 $\pm$ 11.5 years and in non-microalbuminuric patients it was 49.9 $\pm$ 6.8 years (P = 0.96). 35.5% of subjects with microalbuminuria (11 person) and 32.1% subjects (9 of person) without microalbuminuria was male and the rest were female. There was no statistically

significant difference in sex and age between case and control groups.

The average duration of exercise test in all of the patients was 8.5 ± 2.5 minutes, but in two groups (case and control) it was 9.1 ± 2.9 and 7.7 ± 1.5 minutes, respectively (Figure 1), with a statistically significant difference (P = 0.024). Average heart rate in peak exercise in the case and control groups was 142.7 ± 25.6 and 157.5 ± 20.6 beat per minute (Figure 2) and the difference between them was statistically significant (P = 0.02).

HRR in the first and second minutes was within normal limit in both groups (Table 2) but HRR in the case group was insignificantly lower than the control group in both first minute (P = 0.051) and second minute (P = 0.064) (Table 1). Average heart rate in the first minute of recovery in the case group was 119.1 ± 24.6 beat per minute and in the control group it was 126.5 ± 15.8 beat per minute without statistically significant difference (P = 0.18).

In the second minute of recovery, the average heart rate in the case and the control groups was 97 ± 19.4 beat per minute and 101.9 ± 12.4 beat per minute, respectively. It showed that the heart rate recovery from peak to 2nd minute of recovery had statistically significant difference between the two groups (P = 0.04).

HRR in the first minute of recovery was abnormal in 6 patients (10.2%), among whom 4 patients were in the case group and 2 in the control group (12.9% vs. 7.1%). Based on the Fisher's exact test, there was not any significant difference between them (P = 0.67). HRR in the second minute of the recovery in 5 (8.5%) patients was abnormal, which 3 (9.7%) patients were in case group and 2 (7.1%) were in control group without statistically significant difference between the two groups (Fisher's exact test, P = 0.99).
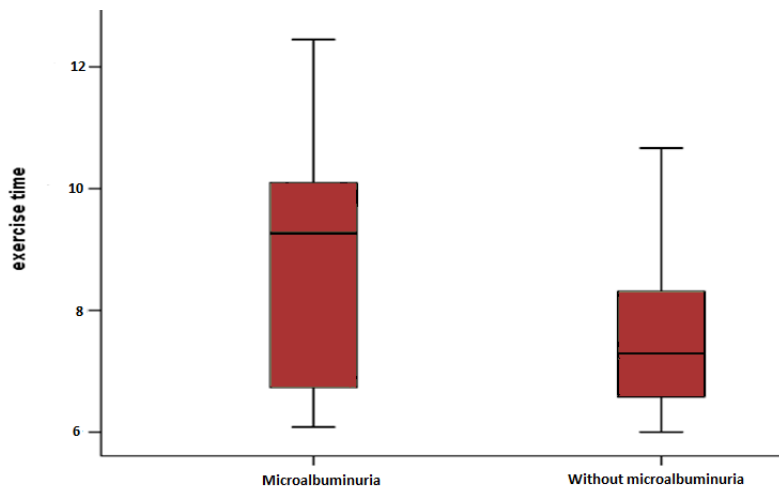

Figure 1. Exercise duration in case (microalbuminuria) and control (without microalbuminuria) groups
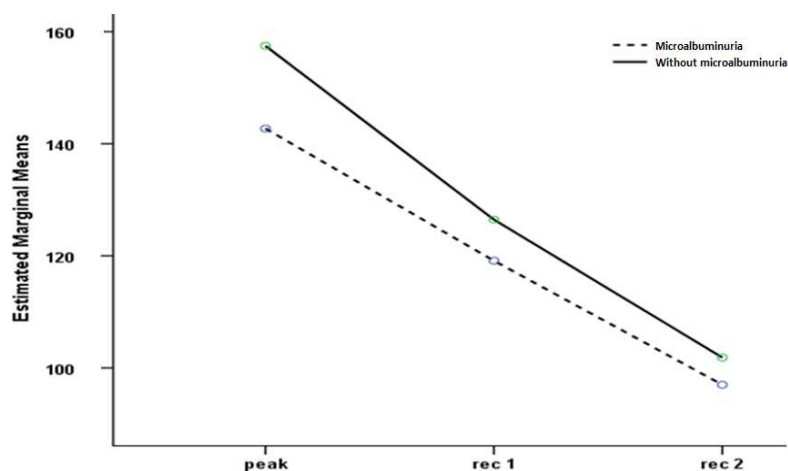

Figure 2. Mean of heart rate (beat per minute) changes from peak to first (rec 1) and second (rec 2) minute recovery time in case and control groups

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Table 1. The mean and standard deviation of heart rate in the peak phase and in the first and second minute of recovery

Time	Groups	Heart Rate (BPM)	P
Peak	With microalbuminuria	142.7 ± 25.6	0.020
	Without microalbuminuria	157.5 ± 20.6	
First minute recovery	With microalbuminuria	119.1 ± 24.1	0.180
	Without microalbuminuria	126.5 ± 15.8	
HRR first minute	With microalbuminuria	23.6 ± 13.0	0.051
	Without microalbuminuria	31.0 ± 15.5	
Second minute recovery	With microalbuminuria	97.0 ± 19.4	0.260
	Without microalbuminuria	101.9 ± 12.4	
HRR second minute	With microalbuminuria	45.7 ± 17.1	0.064
	Without microalbuminuria	55.6 ± 23.0	

BPM: Beat per minute; HRR: Heart rate recovery
Data are presented as mean ± standard deviation

Table 2. Heart rate recovery results in nephropathic and non-nephropathic groups

	Group	With microalbuminuria n (%)	Without microalbuminuria n (%)	P
First minute	Normal	27 (87.1)	26 (92.9)	0.67
	Abnormal	4 (12.9)	2 (7.1)	
Second minute	Normal	28 (90.3)	26 (92.9)	0.99
	Abnormal	3 (9.7)	2 (7.1)	

Discussion

We compared the heart rate recovery following exercise test in diabetic patients with and without microalbuminuria. The mean value of maximum heart rate in the case group was significantly lower than control group but their heart rates recovery to appropriate values was similar to non-microalbuminuric patients.

In our study, heart rate in the case group could not reach the expected target heart rate appropriately (220 – age ± 10 BPM). Heart rate dramatically decreased in control group and reached to normal values in first and second minutes of recovery time. As shown in table 1, the mean of HRR in case group was lower than values of control group, which is in line with findings of a recent study in Poland.[12]

Diabetes as a complex disease can have variable effects on nervous system. Some presentations of its effects on cardiac system are resting tachycardia, exercise intolerance, orthostatic hypotension, prolonged QT interval, silent ischemia, and sudden cardiac death.[13] Subclinical diabetic autonomic neuropathy can appear one to two years after abnormality in HRR and the preliminary sign of cardiac autonomic neuropathy (CAN) is the decreased HRR. Although CAN could be presented even one or two year after presence of diabetes, but it usually develops in patients who have had diabetes for 20 years or more.[14] Therefore, this is not unexpected that we did not find any significant abnormal finding between the two groups.

Conflict of Interests

Authors have no conflict of interests.

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