Effect of supervised integrated exercise on heart rate variability in type 2 diabetes mellitus

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Abstract

Background: Heart rate variability (HRV) reflects autonomic nervous system modulation of cardiac activity. There is a relationship between degrees of physical activity, HRV changes and the risk of cardiovascular disease.

Aim: To study the effect of a supervised integrated exercise programme on HRV in type 2 diabetes mellitus (DM).

Methods: The study group consisted of 48 patients (27 males, mean age 62±7 years) with type 2 diabetes, of whom 28 underwent a special exercise programme whereas the remaining 20 did not and served as the control group. The supervised integrated exercise programme was applied for a period of 9 months. Deep breathing time domain HRV (difference between the shortest and the longest R-R interval over one minute) was measured at baseline and after 3, 6 and 9 months.

Results: A significant improvement in the HRV values was observed with increasing duration of exercise (13.03 ± 1.08) beats/min at baseline versus 16.5 ± 1.11 beats/min at 9 months, p <0.001) whereas HRV decreased in the control group (14.85 ± 1.15 beats/min at baseline vs. 14.30 ± 1.75 at 9 months, p <0.05). Favourable changes in HRV in the exercise group were gender-dependent and were significant in males (12.4 ± 1.76 beats/min at baseline vs. 16.18 ± 1.91 at 9 months, p <0.001) whereas in females only a trend towards HRV improvement was observed. The HRV changes were also age-dependent and were more pronounced in younger patients than in the elderly. The metabolic parameters of diabetes control (blood glucose and glycosylated haemoglobin levels) significantly improved in the exercise group and significantly worsened in the control group.

Conclusions: Regular supervised integrated exercise significantly improves HRV in patients with type 2 DM, which may favourably influence their long-term prognosis.

Key words: diabetes, heart rate variability, exercise

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Introduction

Heart rate variability (HRV) is a non-invasive electrocardiographic marker, reflecting the effects of the autonomic nervous system (ANS) on the sinus node of the heart [1]. Heart rate variability expresses the total amount of variations of both instantaneous heart rate (HR) and R-R intervals. Heart rate variability has recently become a popular non-invasive research tool in cardiology. Recent studies have shown that decreased fluctuation of R-R intervals is not noise, but implicates an increased risk of arrhythmic events and an increased mortality rate in patients with a previous myocardial infarction (MI) [2]. Time and frequency domain measures of HRV have provided prognostic information and also made it possible to perform non-invasive studies on the significance of changes in the regulation of HR behaviour.

Address for correspondence:

HS Nagaraja PhD, Department of Human Biology, International Medical University (IMU), Plaza Komanwel, Bukit Jalil, Kuala Lumpur, Malaysia, tel.: 603 8656 7228, fax: 603 8656 7229, e-mail: hsnagaraja@rediffmail.com **Received:** 12 June 2006. **Accepted:** 03 January 2007. In population studies decreased HRV has been of predictive value for mortality among healthy adults [3]. Among the diverse conditions associated with decrease in HRV are MI, congestive heart failure (CHF) and diabetes mellitus (DM) [4]. Several studies indicated that diabetic patients have reduced HRV [4-7]. Abnormal HRV in diabetes represents an increased risk for ventricular arrhythmias, as well as total cardiovascular morbidity and mortality [8].

Although data on the effects of physical training on autonomic control in healthy subjects remain controversial, the mortality reduction observed in physically active subjects compared with sedentary persons strongly suggests that exercise is beneficial. Individuals who engage in regular physical activity have a lower prevalence of cardiovascular risk factors. Accordingly, exercise is considered an important adjuvant therapy in risk factor modification [9]. Hence, there is still a need to demonstrate to the community and physicians the numerous benefits of regular physical training. Regular exercise training is capable of modifying the autonomic balance. Recent studies showed that even a single bout of maximal exercise is able to positively affect the autonomic balance of normal subjects for up to 24 h. Longitudinal studies have shown that exercise training increases HRV in various conditions such as coronary artery disease (CAD) [10], acute MI [11], cardiac rehabilitation patients [12], in patients on haemodialysis [13] and in healthy young and older adults [14]. However, very few prospective studies have assessed the effects of exercise training on HRV in type 2 diabetes patients. Hence the present research work was taken up with the aim of studying the effects of integrated exercises on HRV in patients with type 2 diabetes mellitus. Our research hypothesis was that integrated exercise training might increase HRV in diabetic patients.

Methods

Fifty-five type 2 DM patients who attended a diabetes camp held in the hospital were included in this study. Patients were interviewed and then invited for a baseline clinical examination. General physical examination, including height, body weight, waist-hip ratio, blood pressure, pulse rate, respiratory rate and complete systemic examination, was performed. Detailed examination for pulmonary vascular disease, cerebral vascular disease and CAD was also done.

Measurements

Body weight and height were measured by standard methods. A 12-lead ECG was recorded and findings were

noted down. Blood was drawn from the antecubital vein of the seated patients and from the blood samples fasting blood glucose was measured by glucose dehydrogenase method. Glycosylated haemoglobin (HbA_{1C}) was assessed by the immunoterbidimetric method.

Diabetes mellitus patients were classified as having diabetes on the basis of history, regardless of duration of disease or need for anti-diabetic agents. Diabetes was defined as fasting glucose \geq 7.0 mmol/l. Diabetes mellitus patients with CHF, atrial fibrillation, frequent ectopic beats, unstable angina, patients with MI and those diabetes patients who were unable to perform deep breathing test were excluded from this study.

From 55 diabetic patients, twenty-eight were enrolled for the exercise programme, which was conducted under the guidance of a physiotherapist. All 28 diabetes patients were requested to visit the hospital regularly for 5 days per week and practice the exercise daily.

Exercise programme

The training programme included:

- warming up exercise for 5 minutes,
- cycling or treadmill exercise, depending on the exercise capacity of the patients for 30 minutes,
- cooling down exercise for 10 minutes.

The entire duration of the exercise did not exceed 45 minutes for each session on each day.

Twenty diabetes mellitus patients were recruited as a non-exercised group and served as controls. The pharmacological treatment did not differ significantly between the two groups at baseline and there were no major changes during the study.

Seven patients were withdrawn during the study for various reasons. In all, 48 patients completed the study: 20 controls and 28 in the exercised group. An informed consent was obtained from all patients before enrolling in the exercise programme and the study received the approval of the Institutional Ethical Committee.

Heart rate variability analysis

Deep breathing HR test [15] was conducted in a supine position during standard ECG recording. Before beginning the test, the subjects were taught to breathe at a rate of 6 respiratory cycles per minute, 5 s for each inhalation and 5 s for each exhalation. Electrocardiogram was recorded continuously at a speed of 25 mm/s for 60 s while the patients breathed as instructed.

Beat-to-beat alterations in HR were evaluated by the time domain method. The HRV interval (R-R intervals

between adjacent QRS complexes resulting from sinus node depolarisation) was measured manually with a scaled calliper. The R-R interval was measured in each respiratory cycle and an average R-R interval was taken for the measurement of HRV. The variability in HR was calculated as the difference between the shortest and longest R-R intervals and expressed in beats/min. Each patient in the exercise study group was examined every month on a regular basis.

During the follow-up, blood pressure, fasting blood glucose, post-prandial blood glucose and body weight were measured. The study was continued for a period of 9 months. The follow-up HRV in the control group was also measured at the end of 9 months.

Statistical analysis

The results are presented as mean \pm standard deviation or numbers and percentages. For demographics, Fisher's test was employed to observe differences in gender. The Mann-Whitney U test was employed to compare parameters in the exercised and non-exercised groups. The Wilcoxon signed rank test was employed for statistical comparison between the baseline and follow-up measurements of blood glucose, HbA_{1C} and HRV. A stepwise multiple regression analysis was used to determine the main factors influencing HRV. A p value was taken as significant at 5 percent confidence level (p <0.05). The SPSS statistical package was used.

Results

The demographic characteristics of the patients are given in Table I. Comparison between the exercised and control groups for various parameters using Mann-Whitney U test showed that the two study groups were well balanced and individuals in both groups did not differ significantly in age, gender, duration of diabetes, blood pressure, medication or smoking status.

As indicated by the Wilcoxon signed rank test, there was no significant difference in the blood glucose level in both exercise and control groups at the baseline recordings (Table II). However, after 9 months of the exercise programme, a significant decrease in blood glucose level (p <0.001) was seen compared to the baseline levels. The blood glucose level increased significantly (p <0.001) after 9 months in the control patients. The patients who underwent the exercise programme had significantly lower blood glucose levels (p <0.001) than control patients after 9 months of the follow-up period (Table II).

Glycosylated haemoglobin level in the exercised group was significantly lower (p <0.001) than the

Table I. Demographic and clinical characteristics

Parameter	Control group	Exercised group	p <
Gender (M/F)	20 (10/10)	28 (22/6)	0.062
Age [years]	59.45±2.75	61.78±3.10	0.419
Duration of diabetes [years]	7.00±1.44	8.89±1.28	0.063
Diabetes treatment [%]			
insulin	3	6	0.716
sulphonylureas	13	19	1.00
other drugs	3	4	0.351
Hypertension	6	12	0.408
Hypotensive agents	8	6	0.516
Smoking	4	6	0.905

Table II. Glucose, HbA_{1C} level and HRV values before and after exercise programme

Parameters		Control group	Exercised group	
Blood glucose [mmol/l]				
	baseline	10.68±0.69	11.21±1.21	
	after 9 months	11.51±1.23**	9.52±1.02* **	
HbA _{1C} [%]				
	baseline	8.64±0.64	8.58±0.42**	
	after 9 months	8.93±0.44 [◆]	7.18±0.25***	
HRV [beats/min]				
	baseline	14.85±1.15	13.03±1.08*	
	after 9 months	14.30±1.75 [•]	16.50±1.11***	

*p <0.001 – exercise group vs. non-exercise group, *p <0.05; ** p <0.001 – baseline vs. 9 months follow-up in exercise and nonexercise group

control group at the start of the study. After 9 months of integrated exercise, HbA_{1C} level decreased significantly (p <0.001) compared with the baseline values and was significantly lower than in controls (p <0.001). In the control group, there was a significant increase in HbA_{1C} after 9 months of follow-up (Table II).

Baseline HRV was significantly lower (p < 0.001) in the exercised group than in controls. A significant improvement in HRV (p < 0.001) was observed in the exercised group after regular practice of supervised integrated exercise after 9 months (Table II). Comparison of the follow-up HRV between the exercise group and controls showed that there was a significant (p < 0.001) improvement in HRV in those who underwent the training programme. In the control group, a significant decrease in HRV (p < 0.05) after 9 months was found.

Table III. Gender-related differences in HRV in the exercised group

HRV [beats/min]	Male (n=15)	Female (n=13)	
HRV – baseline	12.40±1.76	15.33±1.50	
HRV – 9 months	16.18±1.91	17.66±1.96	

* p <0.001 – baseline vs. 9 months follow-up

Table IV. Follow-up HRV (beats/min) in different age groups in exercised patients

Groups [years]	Baseline HRV	HRV 9 months	р
50-59 (n=10)	14.66±1.45	17.91±1.67	0.043
60-69 (n=10)	12.30±1.64	16.00±1.63	0.039
>70 (n=8)	11.00±1.26	14.50±1.04	0.085

Table V. Standardised coefficients for exercise, age and diabetes

Predictors	Standardised coefficient beta	t	R	Significance
Exercise	0.795	5.185	0.505	0.001
Age	-0.011	-0.137	0.600	0.892
Duration of diabetes	-0.105	-1.371	0.909	0.178

Stepwise regression analysis; dependent variable – HRV after 9 months

Both male and female patients showed an improvement in mean HRV with regular exercise (Table III); however, the difference was significant only in males (p <0.001) whereas in females only a trend towards HRV improvement was observed. When HRV was compared between different age groups (50-59, 60-69 and >70 years) in the exercised patients, there was a significant increase in HRV in 50-59 (p <0.05) and 60-69 age groups (p <0.05), but not in the elderly (Table IV).

When a stepwise multiple regression was employed for the different variables, exercise alone accounted for 50.5% (R=0.505) of the variations in HRV after 9 months of follow-up (Table V). When age – another predictor – was added, the contribution of exercise increased to 60% (R=0.600). All other remaining predictors contributed to 90.9%. Thus, exercise having 50.5% contribution in variability indicated the greater contributions of the predictor. Co-linearity for the excluded variables was >0.276, confirming that the co-linearity was not a problem for this model. The coefficient for exercise was the greatest (standardised coefficient beta = 0.795) (Table V), showing the greater "pull" by exercise than any other predictors (age, duration of diabetes, medications etc.) on HRV.

Discussion

Heart rate variability with deep breathing is the simplest and most widely performed measure of autonomic function. This test produces a sensitive, specific and reproducible indirect measure of vagal cardiac function.

Analysis of HRV in our study showed that there was a slow progressive and significant improvement in the mean HRV with increasing duration of exercise. Longitudinal studies have shown that exercise training increases HRV in various conditions inluding CAD [10], acute MI [11], cardiac rehabilitation patients [12], in patients on hemodialysis [13] and in healthy young or older adults [14]. Contrary to this, the recent study by Scott et al. [16] showed that cardiac parasympathetic activity was not enhanced with endurance training.

Only a few prospective studies, however, have assessed the effects of exercise training on HRV in type 2 DM patients. The recent study by Loimaala et al. [17] reported a trend towards increasing values of HRV in the exercised group and they also observed that resting HR decreased significantly with exercise in the study group, which suggests that vagal tone was increased after training.

In our study, diabetics who underwent supervised integrated exercise showed a significant increase in HRV from the baseline measures compared to the control patients. The patients who did not undergo the training programme did not show any improvement in HRV but actually presented a decrease in mean HRV, which might be due to the natural course of the disease which affects the cardiac autonomic function. Both male and female diabetic patients showed a progressive improvement in mean HRV with regular exercise. The improvement was significant in males whereas in females it did not reach statistical significance, which may be due to the small sample size in the study. These results suggest that both male and female diabetics had beneficial effects on their cardiovascular autonomic function with regular integrated type of exercise.

Our study showed that HRV in different age groups (50-59 years, 60-69 years and >70 years) in exercised diabetic patients was higher after 9 months of regular practice. The previous study by Levy et al. [18], who studied the effect of endurance training on HRV at rest in healthy young and older men, observed that exercise training increased HRV at rest by 68% in the older subjects and by 17% in the younger subjects. Thus, exercise training in the older subjects tends to reverse, at least in part, the age-related deficits in the parasympathetic tone. Our observation confirms the earlier reports from many similar studies [14, 19, 20].

The decrease in HbA_{1C} level after 9 months of regular exercise compared to the baseline level and the control group is in agreement with the previous studies by Loimaala et al. [17] and Canche et al. (21), who showed a similar significant decrease in HbA_{1C} level with exercise training in type 2 DM patients. This confirms that the regular integrated type of exercise in diabetes improves the blood glucose homeostasis and diabetes control.

Chronic hyperglycaemia is an important aetiological factor that leads to various complications of DM. Large randomised clinical trials of subjects with type 2 DM have conclusively demonstrated that a reduction in chronic hyperglycaemia prevents or delays macrovascular and microvascular complications such as neuropathy, nephropathy and retinopathy. Skeletal muscles are the major site for metabolic fuel consumption in the resting state and the increased muscle activity during vigorous aerobic exercise greatly increases fuel requirements. For diabetic individuals, exercise is useful for lowering plasma glucose during and following exercise and to increase insulin sensitivity. Therefore, regular exercise is effective in the reduction of hyperglycaemia and also has multiple positive benefits including cardiovascular risk reduction.

In summary, the present study showed that regular supervised integrated exercise significantly improved HRV and also reduced HbA_{1C} in type 2 DM patients. Regular integrated exercise may have beneficial effects on the autonomic control of the heart and these effects may have clinical importance in preventing sudden cardiac death in diabetics. More epidemiological data in a large sample of patients are needed to confirm that these beneficial effects observed in the autonomic and metabolic variables after the supervised integrated exercise period have favourable effects on the clinical outcome in diabetes.

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Wpływ specjalnego programu ćwiczeń fizycznych na zmienność rytmu serca u chorych z cukrzycą typu 2

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Streszczenie

Wstęp: Zmienność rytmu serca (HRV) odzwierciedla wpływ autonomicznego układu nerwowego na czynność serca. Udokumentowana jest zależność pomiędzy stopniem aktywności fizycznej, zmianami HRV i ryzykiem sercowo-naczyniowym.

Cel: Ocena wpływu specjalnego programu ćwiczeń fizycznych na wartości HRV u chorych z cukrzycą typu 2.

Metodyka: Grupę badaną stanowiło 48 chorych (27 mężczyzn, średni wiek 62±7 lat) z cukrzycą typu 2, spośród których 28 poddano 9-miesięcznemu kontrolowanemu treningowi fizycznemu (jazda na cykloergometrze rowerowym), zaś u pozostałych 20 nie stosowano takiego treningu i stanowili oni grupę kontrolną. Czasowe parametry HRV (różnica pomiędzy najkrótszym a najdłuższym odstępem R-R oceniana podczas głębokiego oddychania przez 1 min) oznaczane były na wstępie oraz po 3, 6 i 9 mies. treningu.

Wyniki: Parametry HRV uległy istotnej poprawie w grupie stosującej kontrolowany trening fizyczny (13,03±1,08 uderzeń/min przed treningiem *vs* 16,5±1,11 uderzeń/min po 9 mies. ćwiczeń, p <0,001), podczas gdy w grupie kontrolnej parametry HRV uległy pogorszeniu (14,85±1,15 uderzeń/min przed rozpoczęciem badania *vs* 14,30±1,75 po 9 mies., p <0,05). Korzystne zmiany HRV w grupie ćwiczącej dotyczyły przede wszystkim mężczyzn (12,4±1,76 uderzeń/min na wstępie *vs* 16,18±1,91 po 9 mies., p <0,001), podczas gdy u kobiet obserwowano trend do poprawy HRV. Zmiany HRV były również zależne od wieku i były mocniej wyrażone u osób młodszych niż u chorych w wieku podeszłym. Metaboliczne parametry wyrównania cukrzycy (stężenie glukozy i hemoglobiny glikozylowej) uległy istotnej poprawie w grupie ćwiczącej i istotnemu pogorszeniu w grupie kontrolnej.

Wnioski: Regularny nadzorowany wysiłek fizyczny istotnie poprawia parametry HRV u chorych z cukrzycą typu 2, co może mieć korzystny wpływ na ich odległe rokowanie.

Słowa kluczowe: cukrzyca, zmienność rytmu serca, trening fizyczny

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