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Assessment of Autonomic Neuropathy in Patients with Diabetes Mellitus by Measurement of Heart Rate Turbulence and Heart Rate Variability

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Abstract

Background Heart rate variability (HRV) and heart rate turbulence (HRT) illustrate regulation of the heart by autonomic nervous system (ANS). The autonomic nervous system plays an important role not only in physiological situations, but also in various pathological settings such as diabetic neuropathy Diabetic autonomic neuropathy is a serious and common complication of diabetes.

Objective To determine the association between HRT, HRV and diabetes control monitored by concentrations of HbA1c.

Methods In 52 patients with diabetes mellitus type II of either sex attending Cardiac Care Unit (CCU) in Al-Kadhimya Hospital, 24-hour Holter ECG monitoring was performed to evaluate time domain HRV parameters (SDNN, SDNNI, SDANN, rMSSD, pNN50) and HRT parameters (TO and TS). HBA1c was measured in all patients. Regression analysis was performed to evaluate the association between tested parameters.

Results Significant correlation has been observed between TO and SDNN, SDNNI and SDANN. TS correlated significantly with SDNN, SDNNI, SDANN, rMSSD, pNN50. We noted no correlation between HbA1c and HRV or HRT parameters.

Conclusion We concluded that HRV time domain parameters correlate with HRT in patients with diabetes mellitus. Diabetes control estimated on basis of HbA1c value did not show correlation with HRV and HRT.

Key words Heart rate turbulence HRT, Heart rate variability HRV, Diabetic Autonomic Neuropathy. HbA_1c.

Introduction

Heart rate variability (HRV) and heart rate turbulence (HRT) reflect the functional status of the autonomic nervous system [(1,9)]. In recent years noninvasive techniques based on the electrocardiogram (ECG) have been used as markers of autonomic modulation of the heart, these include HRV and heart rate turbulence (HRT), a new method based on fluctuations of sinus rhythm cycle length after a single premature ventricular contraction. Diabetic autonomic neuropathy is a serious and common complication of diabetes mellitus (DM) [(12)]. Dysfunction of the autonomic nervous system is associated with increased risk of mortality in patients with diabetes.[6] Autonomic neuropathy is characterized by early and widespread neuronal degeneration of small nerve fibers of both sympathetic and parasympathetic tracts [(3,5)]. Its clinical manifestations are ubiquitous with functional impairment and include postural hypotension and persistent tachycardia [3]. Once clinical manifestations of diabetic autonomic neuropathy (DAN) supervene, the estimated 5-year mortality is approximately 50% [3,5,6,10]. Thus, early subclinical detection of autonomic dysfunction is important for risk stratification and subsequent management [3]. Analyses of short-term and/or long-term HRV have been proven useful in detecting DAN [9-12]. In neuropathy associated with DM characterized by alteration of small nerve fibers, a reduction in time domain parameters of HRV seems not only to carry negative prognostic value but also to precede the clinical expression of autonomic neuropathy [5,7,13]. In diabetic patients without evidence of autonomic neuropathy, reduction of the absolute power of low frequency (LF) and high frequency (HF) during controlled conditions was also reported [3,11]. Thus, the initial manifestation of this neuropathy is likely to involve both efferent limbs of the autonomic nervous system [1].

In the present study we analyze correlations between HRV and HRT parameters and HbA1c in patients with diabetes mellitus.

Methods

The study group consisted of 52 patients with non-insulin depended DM, attending Cardiac care Unit in Al-Kadhimia Hospital. Clinical characteristics of the studied patients are shown in table 1.

Patients without sinus rhythm, after myocardial infarction and those with left ventricular systolic dysfunction in echocardiography (EF<50%) were excluded. All patients underwent 24-hour Holter monitoring (3-channel recorders Schiller MT 101, Swiss). Holter ECG was firstly analyzed automatically, followed by manual correction by the operator. HRV was analyzed in the time domain in accordance with standards all artifacts, arrhythmias, pauses and conduction disturbances were eliminated. The following HRV parameters were analyzed:

• SDNN: Standard deviation of all NN (normal-normal) intervals

• SDNNI: Mean of the standard deviations of all NN intervals for every 5-minute segments of the entire recording

• SDANN: Standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording

• rMSSD: The square root of the mean of the sum of the squares of differences between adjacent NN intervals

• pNN50: NN50 (50% of NN) count divided by the total number of all NN intervals

In patients with premature ventricular beats (PVC) we analyzed HRT parameters, which are the turbulence onset (TO) and the turbulence slope (TS).

The TO is the percentage difference between the heart rate immediately following PVC and the heart rate immediately preceding PVC. It is calculated using the equation:

$TO = ((RR1 + RR2) - (RR{-2} + RR{-1})) / (RR{-2} + RR{-1}) * 100$ with RR-2 and RR-1 being the first two normal intervals preceding the PVC and RR1 and RR2 the first two normal intervals following the PVC.

The TS is the steepest slope of a linear regression line through five consecutive measurement points in the averaged tachogram. We used filters which exclude RR intervals with the following characteristics were excluded from the HRT calculation using special filters:

1. R-R < 300 ms
2. R-R > 2000 ms
3. Difference to the preceding sinus interval > 200 ms
4. Difference to the reference interval (mean of the 5 last sinus intervals) >20%

In addition, we limit the HRT calculations to PVCs with:

a. a minimum prematurity of 20% and

b. a post-extrasystole interval which was at least 20% longer than the normal interval.

Glycosylated hemoglobin (HbA1c) level was measured in all patients for evaluation of glycaemic control.

Table1. Demographic features of the patient group.

Parameter	N(%) or mean ± SD
Number of patients (n)	52
Gender (females/males) (n%)	34 (65%) M / 18 (35%) F
Age (years) (mean±SD)	62.6 ± 9.2 years
Duration of diabetes (mean±SD)	7 ± 3.6 years
Hemoglobin A1c concentrations (mean±SD)	8.64% ± 2.84%
Insulin therapy (n %)	17(32%)
Oral antidiabetic agents: sulphonylureas (n %)	35(32%)

Results

The HbA1c level was from 5.9% to 10.2% (mean 8.64% ± 2.84%) In 11 (20%) patients the HRT parameters could not be computed (appear ventricular beats did not or ventricular beats did not meet criteria of HRT analysis). HRV parameters calculated in subgroup in whom it was not been possible to calculate HRT did not differ significantly from remaining studied group.

Correlation coefficients between HRT parameters and HbA1c are shown in table 3.

A significant correlation between TO and SDNN, SDNNI and SDANN was observed. On the other hand, TS correlated significantly with SDNN, SDNNI, SDANN. rMSSD, pNN50 (Table 2). No correlation was noticed between HbA1c (table 1) and HRV or HRT parameters (Table 2).

Table 2. HRV values and correlation coefficients between HRV and TO, TS, HbA1c

HRV parameter	Value ±SD	TO		TS		HbA1c	
		r	p	r	p	r	p
SDNN	130±33	-0.33	0.005	0.52	0.001	-0.12	NS
SDNNI	46±16	-0.21	0.01	0.48	0.003	-0.14	NS
SDANN	122±29	-0.26	0.003	0.42	0.001	-0.12	NS
rMSSD	31±13	-0.12	NS	0.36	0.005	-0.18	NS
pNN50	9±8	-0.14	NS	0.32	0.005	-016	NS

Table 3. HRT values and correlation coefficients with HbA1c.

HRT parameter	Value	HbA1c	
		r	p
TO	-1.1 ±1.4	0.18	NS
TS	12.1 ±9.5	-0.12	NS

Discussion

HRT is the physiological, biphasic response of the sinus node to premature ventricular contractions. The underlying mechanisms of HRT are an autonomous baro-reflex. It consists of a short initial acceleration followed by a deceleration of the heart rate causes a brief disturbance of the arterial blood pressure. If the autonomic control system is impaired, this reaction is either weakened or entirely missing [(1,9)].

HRV describes variations of both instantaneous heart rate and RR intervals. Depressed HRV can be used as a predictor of risk after acute myocardial infarction (MI) and as an early warning sign of diabetic neuropathy [(10,12)]. Correlations between HRT and HRV parameters was observed in large populations of patients after myocardial infarction [(7,13)]. Our study confirms this significant correlation between HRT and time domain HRV in patients with diabetes mellitus. Interestingly is the lack of correlations between time domain HRV parameters or HRT and HbA1c level. Previous studies have shown decreased heart rate variability in diabetic patients as a result of diabetic neuropathy, but frequency of occurrence of neuropathy has not correlate directly withHbA1c [(8,10,12, 13)].

References

1. Barthel P, Schmidt G, Schneider R, Bigger JT, Donis JH. Heart Rate Turbulence in Patients With and Without Autonomic Dysfunction. *J Am Coll Cardiol*, 2007; 33(Suppl. A): 136A.
2. Bellavere F, Balzani I, De Masi G, Carraro M, Carenza P, Cobelli C, Thomaseth K. Power spectral analysis of heart rate variation improves assessment of diabetic cardiac autonomic neuropathy. *Diabetes*, 2002; 41:633-640.
3. Bianchi A, Bontempi B, Cerutti S, Gianoglio P, Comi G, Natali Sora MG. Spectral analysis of heart rate variability signal and respiration in diabetic subjects. *Med Biol Eng Comput*, 2000; 28: 205-211.
4. Ewing DJ, Neilson JMM, Traus P. New method for assessing cardiac parasympathetic activity using 24-hour electrocardiograms. *Br Heart*, 2004; 52: 396-402.
5. Ewing DJ, Campbell IW, Clarke BF. The natural history of diabetic autonomic neuropathy. *Q J Med*, 2000; 193: 95-108
6. Gerritsen J, Dekker JM, TenVoorde BJ, Moraes RS. Impaired autonomic function is associated with increased mortality especially in subjects with diabetes, hypertension, or a history of cardiovascular disease. *Diabetes Care*, 2001; 24: 1793-1798.
7. Ghuran A, Reid F, La Rovere MT, Lombardi F, Sousa MR, Ribeiro JP. Heart rate turbulence-based predictors of fatal and nonfatal cardiac arrest (The Autonomic Tone and Reflexes After Myocardial Infarction Sub study). *Am J Cardiol*, 2002; 89: 184-190.
8. Malpas SC, Maling TJB. Heart rate variability and cardiac autonomic function in diabetes. Diabetes. 2001; 39:1177-1181.
9. Schneider R, Barthel P, Schmidt G. Methods for the Assessment of Heart Rate Turbulence in Holter-ECGs. *J Am Coll Cardiol*, 2006; 33(Suppl. A): 351A.
10. Smith S. Reduced sinus arrhythmia in diabetic autonomic neuropathy: diagnostic value of an age related normal range. *Br Med J*, 2002; 285: 1599-1601.
11. Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology. Heart Rate Variability Standards of Measurement, Physiological Interpretation, and Clinical Use. *Circulation*, 2006; 93: 1043-1065.
12. Vinik AI, Maser RE, Mitchell BD, Birkett C. Diabetic autonomic neuropathy. *Diabetes Care*, 2003; 26: 1553-1576.
13. Yap YG, Camm J, Schmidt G, Rodriguez AE, Jimenez J. Heart rate turbulence is influenced by heart rate, age, LVEF, NYHA class, diabetes and frequency of ventricular ectopics in patients after acute myocardial infarction-EMIAT substudy. *J Am Coll Cardiol*, 2001; 37(suppl. 2): A1-A648.

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