

53 - RELATIONSHIP BETWEEN FISSUE GLYCEMIA AND AUTONOMICAL MODULATION OF THE HEART RATE OF POST-MENOPAUSE WOMEN WITH DIABETES MELLITUS TYPE 2

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INTRODUCTION

Diabetes mellitus (DM) is one of the most common metabolic disorders in the world, with 90% of cases being type 2 (DM2) (KORC, 2003), characterized by long duration, slow progression and premature coronary heart disease (NITA et al, 2012). Increased survival of diabetic subjects increases the chances of development of chronic complications of the disease, such as macroangiopathy, retinopathy, nephropathy, and neuropathies, which are closely associated with the time of exposure to hyperglycemia, which can be very debilitating to the individual and are very costly to the health system (SBD, 2015).

Autonomic neural imbalance is a serious complication of long-term diabetes patients and may progress to diabetic autonomic neuropathy (NAD), which begins with degeneration of small nerve fibers in the sympathetic and parasympathetic branches. The clinical manifestations of these complications include postural hypotension and persistent tachycardia, in addition to being associated with a high mortality rate (ROY & GATATAK, 2013). These neural changes may precede the clinical diagnosis of autonomic neuropathy and are directly related to a worse prognosis (FREEMAN, 1991).

The study by Vinik & Ziegler (2007) showed that heart rate variability (HRV) is a method capable of pointing to disorders that may precede NAD. The HRV analyzes the periodic oscillations of the heartbeat intervals (iR-R), which allows us to explore the dynamic changes in the central rhythmic regulatory modulation of the heart and the functioning of the ANS (MITCHELL, 2012), which gives it great significance in several conditions clinical and functional. The relevance of the information, added to the ease, reproducibility and low cost to acquire the data, justifies the clinical evaluation of the autonomic cardiac function through this method (VANDERLEI et al, 2009).

The associations between autonomic imbalance and various pathological conditions are well established, and the reduction in HRV has been related to compromised and predictive mortality (PAL et al, 2014). Thus, evaluations of autonomic heart rate modulation present a potential for the detection of autonomic imbalance in its sub-clinical and asymptomatic stages (FLEISCHER, 2012), being an important clinical application tool for the diagnosis, prognosis and therapeutic intervention of cardiac autonomic neuropathy in diabetics (SUBBALAKSHMI, ADHIKARI & JEGANATHAN, 2014).

The monitoring of the biochemical profile, such as the investigation of the contributing factors to altered values, is of important relevance for the adoption of appropriate therapeutic strategies (CAMBRI et al., 2008), especially with regard to postmenopausal women's health care, where a high prevalence of high fasting blood glucose levels is observed (SBC, 2005), where hypoestrogenism is an important factor in reducing cardiovascular risk and increasing cardiovascular risk because it is related to increased body fat, reduced lean mass and worsened glycemic control (PAFFENBARGE et al., 1993), as well as contribute to worsening of the autonomic function (EARNEST et al., 2008).

Persistent hyperglycemia has been an important etiological factor in relation to the complications of DM2, provoking progressive autonomic dysfunction parallel to the development of NAD (POP-BUSUI, 2010). In this sense, Bassi et al. (2015) pointed out that individuals with DM2 who did not have good glycemic control presented greater loss in both linear and non-linear indices of HRV when comparing with those who had better control. On the other hand, Nayak et al. (2013) observed that diabetics who were on regular treatment with insulin and oral hypoglycemic agents did not correlate with the diagnosis of NAD and the time of exposure to the disease.

Thus, studying fasting glycemia and HRV in postmenopausal women with type 2 diabetes represent important clinical tools to evaluate the impact of DM2 on the integrity of the autonomic system, thus contributing to the management of the therapeutic strategies of this population. Thus, the aim of the study was to analyze the relationship between fasting glycemia and autonomic heart rate modulation of postmenopausal women with DM2

METHODOLOGY

The present study was conducted in the city of Marília-SP, formed by women in the age group between 50 and 85 years, with DM2 for more than 3 years and without menstruation for at least 12 months. No patient presented amputations and / or prosthesis use in limbs; severe coronary disease; hypotension or severe hypertension; uncontrolled congestive heart failure; unstable angina; uncontrolled diabetes; unstable dysrhythmia; uncontrolled systemic arterial hypertension. The procedures used in this research will obey the Criteria of Ethics in Research with Human Beings according to resolution n. 466/12 of the National Health Council. This research was approved by the Research Ethics Committee of the University of Marília-SP (UNIMAR), under protocol no. 2,083,537 / 2017, which follows the criteria established by the resolution.

Data were collected on the time of diagnosis of DM2, age, blood pressure and body mass index (BMI). In order to obtain fasting glucose data, the measurements in a biochemical reflectance spectrophotometry analyzer (Accutrend Plus, Roche Diagnostics) will be performed. The reference values recommended by the American Diabetics Association (ADA, 2010) will be adopted for the classification of fasting blood glucose (GL) concentrations.

For analysis of resting HRV, 20 minutes were used lying in the supine position. The heart rate (HR) and the instantaneous iR-R were recorded during the protocol, using a digital validated telemetry system (GAMELIN, BERTHOIN, BOSQUET, 2006), which consists of a transmitter positioned in the height of the xiphoid process and a monitor / receiver (Polar RS800CX, Polar Electro Oy, Kempele, Finland).

The data were transmitted to a computer using Polar Pro Trainer software (version 5) and converted into text files that were analyzed only the series with more than 95% of sinus beats, with 256 stable points being selected (Software Kubios HRV, version 2.0, University of Kopio, Finland). In the time domain the following statistical calculations were made: mean and standard deviation of the iR-R (iRR and SDNN) in milliseconds (ms); standard deviation of HR, square root of squared mean of the differences between successive normal intervals (RMSSD), expressed in ms. The last two indices are representative of the

parasympathetic modulation (VANDERLEI et al, 2009)

For the analysis in the frequency domain, the cubic splines interpolation method with frequency of 4 Hz was applied and the spectral power density of the most stable segment was calculated through the Fast Fourier Transform (FFT) that decomposes the signal into the following bands: high frequency (HF - High Frequency - 0.15 to 0.4 Hz) corresponding to respiratory and vagus (parasympathetic) modulation of the heart; low frequency (LF - 0.04 to 0.15Hz) that represents sympathetic and parasympathetic modulation, but with the predominance of sympathetic; and the LF / HF ratio representing the sympatho-vagal balance (VANDERLEI et al, 2009). The LF and HF data will be presented in absolute values (ms²) and in normalized unit (nu). The normalized data will be calculated by dividing the power spectral density of a given band by total power, subtracting the very low frequency band and multiplying by 100 (MALLIANI, 1999).

The mean and standard deviation for the quantitative variables and the relative (%) and absolute (f) frequency distribution for the qualitative variables were used to describe the variables that represent the general characteristics of the sample. The distribution of normality was verified by the Shapiro-wilk test. To analyze the correlation between the quantitative variables, the Pearson (parametric) and Spearman (non-parametric) correlation test was applied. The significance level adopted was 5% and the data were analyzed in SPSS software, version 19.0 for Windows.

RESULTS

The mean age of the sample was 66.1 ± 8.3 years, the time of diagnosis of DM2 was 10.3 ± 7. HR and HRV values were: HR = 69.4 ± 11 bpm; iRR = 880 ± 129 ms; SDNN = 26.3 ± 14.9; RMSSD = 16.9 ± 9.8; LF (ms²) = 203.8 ± 278.1; HF (ms²) = 101.2 ± 88.6; LF (n.u.) = 57.6 ± 24.1; HF (n.) = 42.3 ± 24.1; LF / HF = 2.404 ± 2.572. Regarding the frequency distribution of risk factors, the sample presented: Systemic arterial hypertension = 88.0%; Central obesity (CC) 84.0%; Arthrosis = 56.0%; General obesity (BMI) = 56.0%; Dyslipidemia = 48.0%; Osteoporosis = 20.0%; Arthritis 16.0%. As for the simultaneity of risk factors, we found: A factor = 4%; Two factors = 36.0%; Three factors = 40.0%; Four factors = 20.0%.

Table 1 presents the correlation test data between fasting blood glucose values and HR and HRV variables. A statistically significant correlation of fasting glycemia with the SDNN (R = -0.422 p = 0.036), RMSSD (R = -0.486 p = 0.014) and HF (ms²) (R = -0.412 p = 0.041) values was observed.

Table 1: Correlation test between fasting blood glucose values and HRV indices.

	Fasting blood glucose (mg/dL)	
	R	p
HR(bpm)	0.373	0.066
iRR (ms)	-0.387	0.056
SDNN (ms)	-0.422	0.036*
RMSSD (ms)	-0.486	0.014*
LF (ms ²)	-0.355	0.082
HF (ms ²)	-0.412	0.041*
LF (nu)	-0.064	0.761
HF (nu)	0.065	0.757
LF/HF	0.031	0.883

Note: * p ≤ 0.05 significant correlation by the test and Pearson. r Pearson correlation coefficient.

DISCUSSION

The prevalence of risk factors in the type 2 diabetic sample of the study showed a marked presence of systemic arterial hypertension (88.0%) and central obesity by CC (84.0%). In a study by Ferreira et al. (2010) with 418 elderly people (70.7 ± 7 years) observed 83.3% of central obesity (CC), 80.4% of arterial hypertension and 19.1% of DM2 in their sample. Likewise, Petersen et al. (2011) found a prevalence of 92.1% of central obesity (CC), 83.8% of hypertensive individuals when studying a group of 204 individuals aged 64.2 + 11.5 years. Rodrigues et al. (2016) found 82.6% of patients with systemic arterial hypertension and abdominal obesity (CC) and 30.4% with DM2 in a sample of 23 subjects (59.8 ± 5.9 years). Observing the simultaneity of risk factors in the present study, 40% of the sample presented three factors and 36% presented two concomitant factors. Ferreira et al. (2010) pointed out 87.3% of the sample with two or more risk factors, while Petersen et al. (2011) and Rodrigues et al. (2016) found 85.0% and 56.5%, respectively, with a diagnosis of metabolic syndrome (more than three risk factors present).

Analyzing the relationship between fasting blood glucose concentrations and HR and HRV values, statistically significant correlation was observed with SDNN (R = -0.422 p = 0.036), RMSSD (R = -0.486 p = 0.014), and HF (ms²) (R = -0.412 p = 0.041). These results indicate that individuals with higher fasting glucose levels, parasympathetic modulation and global HRV tend to be at lower values, in line with the studies of Bassi et al. (2015), I pointed out that individuals with DM2 who did not have good glycemic control actually had greater impairment in both linear and non-linear HRV indices when compared to those with better control. In another study, Liao et al. (1995) who investigated 154 diabetic and 1,779 non-diabetic men and middle-aged women in the ARIC (Atherosclerosis Risk in Communities) study, and found that diabetics had vagal modulation lower than non-diabetic after adjustment for age, ethnicity, and gender. In non-diabetics, an inverse relationship was found between the parasympathetic component of high frequency (HF), insulin and fasting glucose, suggesting that the reduction of vagal tonus may be involved with the pathogenesis of diabetes.

It has been observed that diabetics may present autonomic neuropathy due to neurological degeneration that affects small fibers of the peripheral nervous system and central nervous system, resulting in the reduction of HRV. It is pointed out that these individuals present a reduction of the parasympathetic component due to elevated glycemia exposure (SINGH, LARSON & O'DONNELL, 2000).

The obesity factor may be related to such results, since some studies (GOLDFINE & KAHN, 2003) point out that adiponectin production by the adipose tissue is altered in these individuals, resulting in insulin resistance and consequent increase in serum levels, which increases the activation of the sympathetic nervous system by means of glucose metabolism in the ventromedial hypothalamus (LANDSBERG & YOUNG, 1985). The accumulation of fat mass in the abdominal region is associated with elevated triglycerides (BARD et al., 2001), usually accompanied by a decrease in the concentration of high-density (HDL-c) cholesterol, increasing glucose production, insulin secretion (KUCH et al., 2001), and an increase in the risk of cardiovascular disease and diabetes (LAEDERACH-HOFMANN, MUSSGAY & RUDEL, 2000).

Other mechanisms associated with sympathetic activation in obese patients include dyslipidemia (GRASSI et al., 2009) and increased activation of the renin-angiotensin-aldosterone system (RAHMOUNI et al., 2005). The genesis of systemic arterial hypertension is associated with early changes in the autonomic system in some cases (POLITO & FARINATTI, 2003). Results from large epidemiological studies, such as the ARIC that investigated 11,061 men and women (SCHROEDER, 2003), provide strong evidence that vagal modulation is lower in hypertensive than in normotensive individuals.

The present study was based on the hypothesis that postmenopausal women with DM2 with worse control of fasting blood glucose had a worse autonomic modulation of HR due to exposure to persistent hyperglycemia, which was in fact observed. Understanding the clinical reality and understanding the factors that negatively influence autonomic modulation is of utmost importance for health care strategies to be oriented with better efficiency.

CONCLUSION

The study pointed out that the individuals who presented higher fasting blood glucose concentrations showed lower values of parasympathetic modulation on HR and general HRV also decreased.

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RELATIONSHIP BETWEEN FISSUE GLYCEMIA AND AUTONOMICAL MODULATION OF THE HEART RATE OF POST-MENOPAUSE WOMEN WITH DIABETES MELLITUS TYPE 2

The aim of this study was to analyze the relationship between fasting glycemia and autonomic heart rate modulation of postmenopausal women with type 2 diabetes (DM2). This is a cross-sectional observational study. The patients were submitted to a single evaluation consisting of anamnesis and history of diseases, assessment of habitual physical activity, anthropometry, blood biochemistry, blood pressure (BP) and R-R intervals for analysis of heart rate variability (HRV). The data were collected in two days, the first day being used for anamnesis and history of diseases, evaluation of habitual physical activity, anthropometry. On the second day, the biochemical measurements were performed, followed by recording of the R-R intervals and BP measurement in the supine position. Postmenopausal women with a diagnosis of DM2 for at least 3 years were referred to the hydrogymnastics program of the Laboratory of Physical Evaluation and Sports Practice of UNIMAR - University of Marília-SP. It was verified a significant correlation in the values of SDNN (R = -0.422 and p = 0.036), RMSSD (R = -0.486 and p = 0.014), HF (ms²) (R = -0.412 and p = 0.041). It was concluded that the individuals with the highest serum fasting blood glucose concentrations showed lower values of the parasympathetic modulation on HR and general HRV also decreased.

KEY WORDS: Diabetes Mellitus, Menopause; Autonomic Nervous System.

RELATION ENTRE LA GLYCÉMIE DU FISSUE ET LA MODULATION AUTONOMIQUE DU TAUX CARDIAQUE DE FEMMES DIABÉTIQUES DE TYPE 2 APRÈS LAMÉNopause

Le but de cette étude était d'analyser la relation entre la glycémie à jeun et de la modulation autonome de la fréquence cardiaque chez les femmes ménopausées souffrant d'un diabète de type 2 (DT2). Ceci est une étude observationnelle transversale. Les patients ont subi une évaluation unique composée des antécédents médicaux et de l'histoire de la maladie, l'évaluation de l'activité physique, l'anthropométrie, la chimie du sang, la pression artérielle (TA) et l'absorption des intervalles R-R pour l'analyse de la variabilité de la fréquence cardiaque (VRC). Les collectes de données ont été réalisées en deux jours, le premier jour destiné à l'histoire et l'histoire des maladies, l'évaluation de l'activité physique, l'anthropométrie. Le deuxième jour, les mesures biochimiques ont été effectuées, suivies de l'enregistrement des intervalles R-R et de la mesure de la TA en décubitus dorsal. L'étude a inclus des femmes ménopausées atteintes de diabète de type 2 à au moins trois ans, fait référence au programme de gymnastique du laboratoire de l'évaluation physique et la pratique des sports UNIMAR - Université de Marília-SP. corrélation significative n'a été trouvée dans les valeurs SDNN (R = -0.422, et P = 0,036), RMSSD (R = -0,486, P = 0,014), HF (ms²) (R = -0,412, P = 0,041). Il a été conclu que les personnes qui avaient des taux sériques plus élevés de glycémie à jeun, des valeurs plus faibles observées dans la modulation parasympathique sur la HR et VRC généralement aussi diminué.

MOTS CLÉS: Diabète sucré, ménopause; Système nerveux autonome.

RELACIÓN ENTRE GLICEMIA DE JEJUM Y LA MODULACIÓN AUTONÓMICA DE LA FRECUENCIA CARDÍACA DE MUJERES POST-MENOPAUSA DIABÉTICAS TIPO 2

El objetivo del estudio fue analizar la relación entre la glucemia de ayuno y la modulación autonómica de la frecuencia cardíaca de mujeres posmenopáusicas con diabetes del tipo 2 (DM2). Se trata de un estudio observacional transversal. Las pacientes fueron sometidas a una única evaluación que consiste en anamnesis e historial de enfermedades, evaluación de la actividad física habitual, antropometría, bioquímica de la sangre, presión arterial (PA) y captación de los intervalos R-R para analizar la variabilidad de la frecuencia cardíaca (VFC). Las colectas de datos se realizaron en dos días, siendo el primer día destinado a anamnesis e histórico de enfermedades, evaluación de la actividad física habitual, antropometría. En el segundo día se realizaron las medidas bioquímicas, seguida del registro de los intervalos R-R y medida de la PA en la condición de reposo en la posición supina. Se incluyeron en el estudio mujeres posmenopáusicas con diagnóstico de DM2 a por lo menos 3 años, encaminadas al programa de hidrogenástica del Laboratorio de Evaluación Física y Práctica Deportiva de la UNIMAR - Universidad de Marília-SP. Se verificó una correlación significativa en los valores de SDNN (R = -0,422 y p = 0,036), RMSSD (R = -0,486 y p = 0,014), HF (ms²) (R = -0,412 y p = 0,041). Se concluyó que los individuos que presentaron mayores concentraciones séricas de glucemia de ayuno, se observaron menores valores de la modulación parasimpática sobre la FC y VFC general también disminuida.

PALABRAS CLAVE: Diabetes Mellitus, Menopausia; Sistema Nervioso autónomo.

RELAÇÃO ENTRE GLICEMIA DE JEJUM E A MODULAÇÃO AUTONÔMICA DA FREQUÊNCIA CARDÍACA DE MULHERES PÓS-MENOPAUSA COM DIABETES MELLITUS TIPO 2

O objetivo do estudo foi analisar a relação entre a glicemia de jejum e a modulação autonômica da frequência cardíaca de mulheres pós-menopausa com diabetes do tipo 2 (DM2). Trata-se de um estudo observacional transversal. As pacientes foram submetidas a uma única avaliação que consiste em anamnese e histórico de doenças, avaliação da atividade física habitual, antropometria, bioquímica do sangue, pressão arterial (PA) e captação dos intervalos R-R para análise da variabilidade da frequência cardíaca (VFC). As coletas de dados foram realizados em dois dias, sendo o primeiro dia destinado para anamnese e histórico de doenças, avaliação da atividade física habitual, antropometria. No segundo dia foram realizadas as medidas bioquímicas, seguida do registro dos intervalos R-R e medida da PA na condição de repouso na posição supina. Foram incluídas no estudo mulheres pós-menopausa com diagnóstico de DM2 a no mínimo 3 anos, encaminhadas ao programa de hidrogenástica do Laboratório de Avaliação Física e Prática Esportiva da UNIMAR - Universidade de Marília-SP. Foi verificada correlação significativa nos valores de SDNN (R = -0,422 e p=0,036), RMSSD (R = -0,486 e p=0,014), HF(ms²) (R= -0,412 e p= 0,041). Concluiu-se que os indivíduos que apresentaram maiores concentrações séricas de glicemia de jejum, observou-se menores valores da modulação parassimpática sobre a FC e VFC geral também diminuída.

PALAVRAS-CHAVE: Diabetes Mellitus, Menopausa; Sistema Nervoso Autônomo.