# 54 - ANALYSIS OF THE AUTONOMOUS FUNCTION OF POST-MENOPAUSE WOMEN WITH DIABETES MELLITUS TYPE 2

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INTRODUCTION

Diabetes can alter the functioning of the autonomic nervous system (ANS) by damaging the afferent inputs, which leads to cardiac autonomic neuropathy (CAN), thereby interrupting an important component of cardiovascular regulation and contributing to an increased incidence of cardiovascular diseases in patients with Type 2 Diabetes Mellitus (T2DM), such as heart attack, sudden cardiac death and silent ischemia (ROY & GHATAK, 2013). In addition, it also affects many other segments of the population such as the elderly, patients with hypertension and metabolic syndrome (MS). When previously diagnosed, it indicates an unfavorable cardiovascular risk profile (TANG et al, 2014). During progression of CAN, the parasympathetic nerve fibers that innervate the heart are affected before sympathetic nerve fibers leading to reduced heart rate variability (HRV) (TARVAINEN et al, 2014).

Predominant symptoms may include nausea, vomiting, gastroparesis, involuntary diarrhea, postural hypotension, difficulty urinating and sexual dysfunction (FLEISCHER, 2012), as well as persistent tachycardia, exercise intolerance, silent myocardial infarction, and even increased incidence of accidents ischemic stroke (MICHEL-CHAVEZ et al 2015, LIU et al, 2016). However, the duration of diabetes is an independent factor for the development of CAN for both types of diabetes, and in addition, inadequate glycemic control favors its progression (DIMITROPOULOS, TAHRANI & STEVENS, 2014). The prevalence of CAN can vary from 20 to 73% in patients with T2DM, being influenced by factors such as age and sex. However, even with such a high prevalence and severe impact for cardiovascular events, little attention is paid to its diagnosis, which leads to a lack of specific treatment to prevent or delay progression (LIU et al, 2016). In addition, among patients with T2DM, the prevalence of hypertension is high, which in turn contributes to the increased prevalence of cardiac autonomic dysfunction, reducing blood pressure variability and altering baroreflex sensitivity (COLLIES et al, 2009).

Considering the importance of CAN diagnosis, Ewing et al. (1980) proposed a test battery for evaluation of autonomic function, using tests that evaluate cardiovascular reflexes, but which may reflect damage elsewhere in the autonomic nervous system, both the sympathetic and parasympathetic pathways. The test battery comprises a total of five analyzes, where three evaluate the heart rate (HR) response that predominantly reflect the function of the parasympathetic branch of the ANS and two analyzes that evaluate the blood pressure (BP) response, mainly assessing the sympathetic function (EWING & CLARKE, 1982; BOER, MOCELIN & MATSUDO, 1998). Thus, because CAN represents a significant cause of morbidity and mortality in patients with T2DM and is associated with a high risk of cardiac arrhythmias and sudden death, possibly related to silent myocardial ischemia, its diagnosis has important clinical and prognostic relevance (POPs) -BUSUI, 2010). In addition, studies that contribute to identify the prevalence and clinical characteristics of patients with T2DM and diagnosis of CAN allow a better understanding of the complexity of the present conditions in order to establish safe treatment goals. Thus, the objective of the study was to assess the prevalence of CAN in postmenopausal women with T2DM.

METHODOLOGY

The sample consisted of women aged between 50 and 85 years, without menstruation for at least 12 months (BURGER et al, 1995), with diagnosis of T2DM for at least 3 years. We initially included in the study all patients diagnosed with T2DM with medical referral for the practice of Hydrogynastics to the Laboratory of Physical Evaluation and Sports Practice of Unimar (LAFIPE-UNIMAR).

Patients with an inability to understand and respond to simple verbal command were not included in the study; amputations and / or prosthesis use in limbs; sequelae of stroke; Parkinson's disease; fractures in lower limbs and / or spine after age 60; severe coronary disease; incapacitating labyrinth; otitis; hydrophobicity; skin lesions; hypotension or severe hypertension; uncontrolled congestive heart failure; unstable angina; uncontrolled diabetes; unstable dysrhythmia; uncontrolled systemic arterial hypertension and foot deformity. The procedures used in this research obeyed Ethics Criteria in Researches with Human Beings according to Resolution Nº. 466/12 of the National Health Council, being approved by the Research Ethics Committee of the University of Marília, under protocol nº. 2,012,517/2017

This is a cross-sectional observational study. The patients were submitted to an evaluation that consisted of anamnesis and history of diseases, anthropometry and autonomic function test battery. Data were collected in two days, the first day being used for anamnesis and history of diseases and anthropometry with waist circumference (WC), body weight and height for calculating body mass index (BMI), for classifications of central and general obesity, respectively. On the second day, the protocol for analysis of the autonomic and diagnostic function of CAN was performed, which is composed by the following tests: active postural change (MPA), which evaluates variations of HR and systolic BP, valsalva maneuver (MVal) and (EWING & CLARKE 1982; EWING et al., 1985). In the present study, the use of a non-invasive approach was performed in the presence of aortic stenosis. Qualitative variables were described by the absolute and relative frequency distribution. SPSS software version 19.0 for Windows was used.

RESULTS

The mean age of the sample was 66.1 ± 8.3 years, the time of diagnosis of T2DM was 10.3 ± 7. The main comorbidities associated with DM2 were: 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%.

Table 1 shows the frequency distribution of the performance classification in cardiac autonomic tests. It was observed that a large part of the sample presented normal HR and SBP responses in the MPA test (88% and 84% respectively), as well as in

the MVal HR response (64%). On the other hand, in the MASR, 60% of the sample presented abnormal HR response, and in the HAND test the adjustment of the DBP was more distributed among the classifications (40% abnormal, 36% normal and 24% borderline). When observing the frequency distribution of the diagnosis of CAN by means of the autonomic test, 60% of the sample was within the atypical classification (Table 2).

**Table 1:** Distribution of absolute (f) and relative frequency of performance classification in cardiac autonomic tests.

| Test | Classification | *f* | % |
|---|---|---|---|
| **MPA HR** | Normal | 22 | 88 |
| | Borderline | 3 | 12 |
| | Abnormal | 0 | 0 |
| **MPA SBP** | Normal | 21 | 84 |
| | Borderline | 4 | 16 |
| | Abnormal | 0 | 0 |
| **MVal HR** | Normal | 16 | 64 |
| | Borderline | 4 | 16 |
| | Abnormal | 5 | 20 |
| **MASR HR** | Normal | 6 | 24 |
| | Borderline | 4 | 16 |
| | Abnormal | 15 | 60 |
| **HAND DBP** | Normal | 9 | 36 |
| | Borderline | 6 | 24 |
| | Abnormal | 10 | 40 |

Note: Active postural change (MPA), valsalva maneuver (MVal), respiratory sinus arrhythmia maneuver (MASR) and isometric manual grip contraction (HAND); heart rate (HR), systolic blood pressure (SBP); diastolic blood pressure (DBP).

Table 2: Distribution of absolute (f) and relative frequency of the diagnosis of cardiac autonomic neuropathy by cardiac autonomic test.

| NAC Diagnostic | *F* | % |
|---|---|---|
| **Normal** | 4 | 16,0 |
| **Early** | 4 | 16,0 |
| **Definite** | 1 | 4,0 |
| **Severe** | 1 | 4,0 |
| **Atypical** | 15 | 60,0 |
| **Total** | 25 | 100,0 |

.Note: Cardiac autonomic neuropathy (NAC).

## DISCUSSION

Observing the tests that investigate HR adjustments, the MPA test showed a normal response in 88% and borderline in 3% of the sample. MVal showed an abnormal HR response in 20%, borderline in 16% and normal in 64% of patients. However for MASR an abnormal response was observed for 60%, borderline for 16% and normal for 24%. These results point to the important impact of the presence of T2DM and other associated comorbidities on the function of the parasympathetic branch of the ANS on the heart (EWING & CLARKE, 1982; BOER, MOCELIN & MATSUDO, 1998), suggesting persistent tachycardia related to the reduction of HRV at rest (LIU et al, 2016).

Regarding the PAS response to the MPA test, abnormal behavior was observed in 40%, borderline in 24% and normal in 36% of the patients. For PAD, 40% presented abnormal response, 36% normal and 24% borderline. The abnormal responses SBP and DBP are indicative of neuronal damage in the sympathetic branch, mainly affecting the baroreflex sensitivity (COLLIES et al, 2009; POP-BUSUI 2010), which suggests the development of postural hypotension as a clinical symptom (FLEISCHER, 2012).

Regarding the diagnostic evaluation of the autonomic tests, it was observed that only 16% of the sample was classified as normal, that is, without NAC. On the other hand, 84% of the patients studied presented some degree of autonomic dysfunction, which may be strongly associated with the time of exposure to hyperglycemia (DIMITROPOULOS, TAHRANI & STEVENS, 2014). Regarding the degrees of autonomic dysfunction to classify NAC by means of the cardiovascular reflex tests, 16% of the patients presented NAC at an early stage. However, considering the defined, severe and atypical stages that are related to a higher degree of cardiac autonomic compromise (ERWING & CLARKE, 1982), 68% of the patients presented CAN in these advanced stages. The main mechanism of injury to ANS in T2DM is related to the deleterious effect of hyperglycemia in insulin-dependent tissues (FLEISCHER, 2012), thus inadequate glycemic control favors its progression (DIMITROPOULOS, TAHRANI & STEVENS, 2014).

Because it represents a significant cause of morbidity and mortality in patients with T2DM, the study and diagnosis of CAN represents important clinical and prognostic relevance (POP-BUSUI 2010), which can help to better understand the degenerative effects of the disease, allowing better strategies to combat control within health care.

## CONCLUSION

The high prevalence of CAN among postmenopausal women with T2DM indicates the importance of therapeutic strategies in the glycemic control of these patients, since this is directly related to the damage to the ANS. In addition, the high prevalence of comorbidities increases the cardiovascular risk of these patients considerably.

## REFERENCES

1.BOER, C.A.A.; MOCELIN, A.J.; MATSUO, T. Validação dos testes de Ewing para avaliação de disfunção autonômica. Arq Neuropsiquiatr, v.56, n.2, p.250-254, 1998.

2.BURGER HG, et al. The endocrinology of the menopausal transition: a cross-sectional study of a population-based sample [comment]. J Clin Endocrinol Metab. 80:3537–45, 1995.

3.COLLIES, S.R.; CARHART JR, R.; FRECHETTE, V.; TOBIN, M.M.; BENNETT, N.; LUCKENBAUGH, A.N.; FERNHALL, B. Cardiac autonomic function and baroreflex changes following 4 weeks of resistance versus aerobic training in individuals with pre-hypertension. Acta Physiol, v.195, p.339–348, 2009.

4.DIMITROPOULOS, G.; TAHRANI, A.A.; STEVENS, M.J. Cardiac autonomic neuropathy in patients with diabetes mellitus. World J Diabetes, v.15, n. 1, p.17-39, 2014.

5.EWING DJ, CAMPBELL IW, CLARKE BF. The natural history of diabetic autonomic neuropathy. Q J Med. 193:95-108, 1980.

6.EWING, D. J.et al., The value of cardiovascular autonomic function tests: 10 years experience in diabetes, Diabetes Care, 8 (5), 491-8, 1985.

7.EWING, D.J.; CLARK, B.F. Diagnosis and management of diabetic autonomic neuropaty. Br Med J, v.285,p.916-918, 1982.

8.FLEISCHER J. Diabetic Autonomic Imbalance and Glycemic Variability. Journal of Diabetes Science and Technology, v.6, n.5, p.1207-1215, 2012.

9.LIU, Y.; LIU, S.; ZHENG, F.; CAI, Y.; XIE, K.; ZHANG, W. Cardiovascular autonomic neuropathy in patines with type 2 diabetes. J Diabetes Investig, v.7, p. 615–621, 2016.

10.MICHEL-CHÁVEZ, A.; ESTANOL, B.; GIEN-LÓPEZ, J.A.; ROBLES-CABRERA, A.; HUITRADO-DUARTE, M.H.; ,MORENO-MORALES, R.; BECERRA-LUNA, B. Variabilidade da freqüência cardíaca e da pressão arterial sistólica em diabéticos com diagnóstico recente. Arq Bras Cardiol.. 2015.

11.POP-BUSUI, R. Cardiac autonomic neuropathy in diabetes. Diabetes Care, v.33, n.2, p.434-441, 2010.

12.ROY, B.; GHATAK, S. Métodos Não-Lineares para Avaliar Mudanças na Variabilidade da Frequência Cardíaca em Pacientes com Diabetes Tipo 2.Arq Bras Cardiol, v.101, n.4, p.317-327, 2013.

13.TANG, Z.H.; et al. Bayesian estimation of cardiovascular autonomic neuropathy diagnostic test based on short-term heart rate variability without a gold standard. BMJ Open, v.4, p. 1-9, 2014.

14.TARVAINEN, M.P.; et al. Cardiac autonomic dysfunction in type 2 diabetes – effect of hyperglycemia and disease duration. Frontiers in Endocrinology. v.5, n.130, p.1-9, 2014.

ANALYSIS OF THE AUTONOMOUS FUNCTION OF DIABETIC TYPE 2 POST MENOPAUSAL WOMEN

Autonomic neural imbalance is a serious complication of long-term diabetes patients and may progress to autonomic cardiac neuropathy (NAC). Thus the objective of the study was to analyze the prevalence of NAC in postmenopausal women with type 2 diabetes mellitus (DM2). The sample consisted of 25 women aged 50 to 85 years. The autonomic function was evaluated by a battery of tests that evaluated the cardiovascular reflexes of heart rate (HR) and systolic (SBP) and diastolic (DBP) blood pressure. Only 16% of the sample presented normal autonomic function, and 84% of the patients presented a diagnosis of NAC some degree of autonomic dysfunction, which indicates a high risk of cardiovascular complications in the population of postmenopausal women with DM2. The high prevalence of NAC among postmenopausal women with DM2 indicates the importance of therapeutic strategies in the glycemic control of these patients, since this is directly related to the damage to the autonomic nervous system. In addition, the high prevalence of comorbidities considerably increases the cardiovascular risk of these patients.

KEYWORDS: Menopause. Diabetic neuropathy. Nervous system.

ANALYSE DE LA FONCTION AUTONOME DES FEMMES DIABÉTIQUES DE TYPE 2 POST-MENOPAUS

Le déséquilibre neuronal autonome est une complication grave chez les patients diabétiques à long terme et peut évoluer vers une neuropathie cardiaque autonome (NAC). Ainsi, l'objectif de l'étude était d'évaluer la prévalence des femmes post-ménopausées du CNA avec le diabète de type 2 (DM2). L'échantillon comprenait 25 femmes âgées de 50 à 85 ans. La fonction autonome a été évaluée par une batterie d'évaluation des tests de réflexes cardio-vasculaires, la fréquence cardiaque (HR) et la pression artérielle systolique (SBP) et diastolique (DBP). Seulement 16% de l'échantillon avaient une fonction normale autonome, alors que 84% des patients présentaient un diagnostic de NAC un certain degré de dysautonomie, ce qui indique un risque élevé de complications cardiovasculaires dans la population des femmes ménopausées atteintes d'un diabète de type 2. La prévalence élevée de NAC chez les femmes ménopausées avec DM2 indique l'importance des stratégies thérapeutiques dans le contrôle glycémique de ces patients, puisque cela est directement lié à la lésion du système nerveux autonome. De plus, la forte prévalence des comorbidités augmente considérablement le risque cardiovasculaire de ces patients.

MOTS-CLÉS: Ménopause. Neuropathie diabétique. Système nerveux

ANÁLISIS DE LA FUNCIÓN AUTONÓMICA DE MUJERES POST-MENOPAUSA DIABÉTICAS TIPO 2

El desequilibrio neural autonómico es una complicación grave de los pacientes con diabetes a largo plazo y pueden evolucionar a la neuropatía autonómica cardiaca (NAC). De este modo el objetivo del estudio fue analizar la prevalencia de NAC de mujeres posmenopáusicas con diabetes mellitus tipo 2 (DM2). La muestra se constituyó de 25 mujeres de entre 50 y 85 años. La función autonómica fue evaluada por batería de pruebas que evaluaba los reflejos cardiovasculares de la frecuencia cardíaca (FC) y presión arterial sistólica (PAS) y diastólica (PAD). El 16% de la muestra presentó una función autonómica normal, siendo que el 84% de las pacientes presentaron diagnóstico de NAC algún grado de disfunción autonómica, lo que indica un alto riesgo de complicaciones cardiovasculares en la población de mujeres posmenopáusicas con DM2. La alta prevalencia de NAC entre mujeres posmenopáusicas con DM2 indica la importancia de las estrategias terapéuticas en el control glucémico de estas pacientes, pues este se relaciona directamente con el daño al sitema nervioso autónomo. Además, la alta prevalencia de comorbilidades eleva de forma considerable el riesgo cardiovascular de estas pacientes.

PALABRAS CLAVE: Menopausia. Neuropatía diabética. Sistema nervioso.

ANÁLISE DA FUNÇÃO AUTONÔMICA DE MULHERES PÓS-MENOPAUSA COM DIABETES MELLITUS TIPO 2

O desequilíbrio neural autonômico é uma complicação grave de pacientes com diabetes em longo prazo e podem evoluir para neuropatia autonômica cardíaca (NAC). Deste modo o objetivo do estudo foi analisar a prevalência de NAC de mulheres pós-menopausa com diabetes mellitus tipo 2 (DM2). A amostra foi constituída de 25 mulheres com idade entre 50 a 85 anos. A função autonômica foi avaliada por bateria de testes que avaliação os reflexos cardiovasculares da frequência cardíaca (FC) e pressão arterial sistólica (PAS) e diastólica (PAD). Apenas 16% da amostra apresentou função autonômica normal, sendo que 84% das pacientes apresentaram diagnostico de NAC algum grau de disfunção autonômica, o que indica um alto risco de complicações cardiovasculares na população de mulheres pós-menopausa com DM2.A alta prevalência de NAC entre mulheres pós-menopausa com DM2 indica a importância das estratégias terapêutica no controle glicêmico destas pacientes, pois, este se relaciona diretamente com o dano ao sistema nervoso autônomo. Além disto, a alta prevalência de comorbidades eleva de forma considerável o risco cardiovascular destas pacientes.

PALAVRAS-CHAVE: Menopausa. Neuropatia Diabética. Sistema Nervoso.