Metabolic control and medication adherence in people with diabetes *mellitus*

Controle metabólico e adesão medicamentosa em pessoas com diabetes *mellitus*

José Claudio Garcia Lira Neto[1]
Andréa Pereira da Silva[1]
Márcio Flávio Moura de Araújo[2]
Marta Maria Coelho Damasceno[3]
Maurício Batista Paes Landim[1]
Roberto Wagner Júnior Freire de Freitas[4]

Keywords
Patient compliance; Medication adherence; Diabetes *mellitus*, type 2; Biomarkers; Primary health care

Descritores
Cooperação do paciente; Adesão à medicação; Diabetes *mellitus* tipo 2; Marcadores clínicos; Atenção primária à saúde

Submitted
December 11, 2016

Accepted
April 12, 2017

Corresponding author
José Cláudio Garcia Lira Neto
BR 343, km 3,5, 64800-000, Floriano, PI, Brazil.
jclira@live.com

DOI
http://dx.doi.org/10.1590/1982-0194201700024

Abstract

Objective: To relate adherence to oral antidiabetics and metabolic control of people with Type 2 Diabetes *mellitus*.

Methods: An analytical study conducted with 201 participants, of both sexes, aged over 18 years with diagnosis of type 2 diabetes mellitus, cared for in the basic health units. Sociodemographic, anthropometric and clinical variables related to medication adherence and metabolic control were analyzed. Morisky's test was used to evaluate adherence to medication therapy.

Results: Only 23.9% of the participants were considered adherents to medication treatment, showing better levels of glycated hemoglobin ($p = 0.048$), fasting glycemia ($p < 0.001$), and total cholesterol ($p = 0.028$).

Conclusion: A relationship between adherence to oral antidiabetics and some variables of metabolic control was identified, such as glycated hemoglobin, fasting glycemia and total cholesterol. Medication adherence should be increasingly encouraged among people with Diabetes *mellitus*.

Resumo

Objetivo: Relacionar a adesão aos antidiabéticos orais e o controle metabólico de pessoas com Diabetes *mellitus* tipo 2.

Métodos: Estudo analítico, realizado com 201 participantes, de ambos os sexos, com idade acima dos 18 anos e diagnóstico de Diabetes *mellitus* tipo 2, acompanhados em unidades básicas de saúde. Foram analisadas variáveis sociodemográficas, antropométricas, clínicas, relacionadas à adesão medicamentosa e ao controle metabólico. Para verificar a adesão à terapêutica medicamentosa utilizou-se o Teste de *Morisky*.

Resultados: Apenas 23,9% dos participantes foram considerados aderentes ao tratamento medicamentoso, e estes apresentaram, significativamente, melhores níveis de hemoglobina glicada ($p=0,048$), glicemia de jejum ($p<0,001$) e colesterol total ($p=0,028$).

Conclusão: Houve relação entre a adesão aos antidiabéticos orais e algumas variáveis do controle metabólico, como hemoglobina glicada, glicemia de jejum e colesterol total. Dessa forma, a adesão medicamentosa deve ser, cada vez mais, incentivada entre as pessoas com Diabetes *mellitus*.

[1]Universidade Federal do Piauí, Floriano, PI, Brazil.
[2]Universidade da Integração Internacional da Lusofonia Afro-Brasileira, Redenção, CE, Brazil.
[3]Universidade Federal do Ceará, Fortaleza, CE, Brazil.
[4]Fundação Oswaldo Cruz, Fortaleza, CE, Brazil.

Conflicts of interest: there are no conflicts of interest to declare.

Introduction

Diabetes *mellitus* (DM) is a complex, epidemic disease complex that currently affects more than 415 million people around the world. A large proportion of these people (81%) live in developing countries, such as Brazil, where this disease affects more than 14.3 million people.[1-3]

The incidence of cases of the most common subtype, type 2 diabetes *mellitus* (T2DM), has been increasing in Brazil, especially due to the increase in variables such as adiposity, sedentary lifestyle, and consumption of sugar and saturated fat. In addition, this situation exacerbates low fiber consumption, and the aging of the population.[3]

Currently, in order to minimize the impact of the imbalance due to the illness, researchers and clinicians have increasingly sought to focus their actions and establish care based on the control of metabolic biomarkers of people with this common chronic disease.[4-6] Thus, the use of the term, metabolic control (MC), was established, which means to achieve adequate levels of different markers. In this study, these were adjusted to be: glycated hemoglobin (HbA1c), fasting glycemia (FG), low density lipoprotein (LDL), high density lipoprotein (HDL), total cholesterol (TC), triglycerides (TG), and blood pressure (BP) in people with DM, both for the correlation between DM as well as for the easy requisition of these tests in the Basic Health Units of Brazil.

The term MC assists in the staging of both T2DM and its related health problems. The inadequate MC of T2DM applies, directly, for example, to cardiovascular problems, which are responsible for 75% of all global deaths. Indirectly, it helps to chronicle pre-existing health problems which decrease productivity, due to irreversible and incalculable damages.[2,3]

Due to the concomitance of chronic pathologies and the stage of discovery of the disease, pharmacological measures are practically unavoidable for good MC in people with T2DM. In such cases, oral antidiabetic (OAD), anti-lipemic and antihypertensive agents are usually used to maintain control of changes related to the disease, and to prevent the development of possible chronic complications (nephropathy, retinopathy, and neuropathy). Therefore, it is necessary that the subjects who have the disease are adherent to the prescribed therapy.[7,8]

Previous studies in the northeastern and southeastern regions of Brazil have shown worrying rates of nonadherence to OAD treatment in people with T2DM, but without assessing the impact of that on MC disease and other health indicators.[5,9] In addition, international publications have not been able to agree on the association between OAD adherence and good MC in individuals with DM.[10-12] These facts demonstrate a real research problem, as evidence is needed to support program planning of specific care, representing a new contribution of knowledge in the nursing context.

Adherence to the use of OAD may influence MC, in part or as a whole. Thus, investigations should be conducted, both to broaden the discussion on vulnerability points of MC and its implications in individuals with T2DM in primary care, and to design effective prevention strategies that may help to curb the relentless increase of this disease. Particularly in Northeastern Brazil, a region that faces multidimensional adversities that affect diseases in general and that presents high rates of individuals diagnosed with DM, a small scientific production on MC has begun, especially regarding its relationship with T2DM. Thus, the objective of this study was to relate adherence to OADs and MC of individuals with T2DM.

Methods

This was a descriptive, epidemiological, analytical, quantitative study, conducted in 17 primary health care services in Floriano, in the state of Piauí- Brazil, between 2013-2015.

The sample consisted of 201 participants, older than 18 years, of both sexes, with a medical diagnosis of T2DM. The inclusion criteria were: 1) to be on OAD treatment for at least six months; and, 2) enrolled in the care program of the Family Health Strategy of the municipality for individuals with DM. Individuals taking insulin and pregnant wom-

en were excluded, since these factors directly impact a change in the metabolic variables investigated.

Subjects were recruited during nursing consultations of individuals with DM. Initially, after agreeing to participate in the study, and soon after signing the Terms of Free and Informed Consent form, participants were interviewed individually in a private room, and a semi-structured questionnaire was administered, composed of questions related to sociodemographic data (age, sex, skin color, religion, marital status, job situation and economic class), anthropometric data (weight, height, nutritional status and waist circumference), and clinical conditions (use of alcohol and/or tobacco). At the time, the degree of adherence to medication therapy was also investigated, using the adapted Morisky's Test.[13]

For categorization of economic class, the parameters established by the *Brazilian Association of Research Companies* (Associação Brasileira de Empresas para Pesquisa - ABEP)[14] were used. The nutritional status of participants was classified as: eutrophic (18.5 - 24.9 kg/m²), overweight (25.0 - 29.9 kg / m²), and obese (≥30.0 kg/m²), according to the Body Mass Index (BMI).[15] Regarding waist circumference (WC), the appropriate values were considered according to sex, which were ≤ 94cm for men and ≤80cm for women.[16]

The use of alcohol and tobacco was self-reported. Those who reported alcohol intake on two or more days of the week, in amounts exceeding 30g of alcohol for men (equivalent to a 650ml bottle of beer or two doses of 50ml brandy), and 15g for women were considered to be alcoholics; they were identified as smokers if they smoked at all, regardless of the number of cigarettes.[17] In turn, the physical exercise variable was also evaluated according to the self-report of the participants, being therefore classified as sedentary those who reported practicing less than 90 minutes of weekly physical activities.[18]

The Morisky's test is originally composed of four questions that aim to evaluate patient behavior in relation to the habitual use of the medicine. For our survey, the model already validated and adapted to Brazil was used, which adds two questions, in order to estimate treatment adherence with greater precision. The subject who answered "yes" to at least one of the questions proposed in the test was considered nonadherent to the medication treatment.[13]

At the second meeting, previously scheduled by the researchers at the time of administration of the questionnaire, the participants had been fasting and blood samples were collected to determine the following variables: HbA1c, FG, TG, HDL and LDL cholesterol, to investigate MC. In addition, the BP was checked using the palpatory/auscultatory method, with three measurements performed to ascertain their mean.

The reference values used for the analysis of the laboratory tests were: a) HbA1c ≤7%; B) FG <100mg/dL; C) TC ≤200mg/dL; D) TG ≤150mg/dL; E) HDL ≥60mg/dL; F) LDL <100mg/dL and; G) BP ≤130x≤85mmHg.[3,19,20]

After the first laboratory analysis, some blood samples were insufficient to reveal the values of each variable that composed MC, requiring a new sample. However, due to the refusal of some participants to collect the blood material for the second time, in those cases where the first collection was not sufficient, some missing data may be observed in the results.

Descriptive analysis was used to describe sociodemographic, anthropometric, clinical data, referring to MC and prevalence of participants who were or were not adherent to OADs.

The data were tabulated in Excel, version 2010, and analyzed in the free statistical software, Epi-Info, version 3.5.3 (Atlanta, USA). Initially, measures of central tendency were calculated. In the analysis of the normality of the variables, the Bartlett test was adopted. Based on this information, parametric tests (t-test) or non-parametric tests (Kruskal-Wallis test) were used. In the association of variable proportions, the Chi-square test and Fisher's test were used in the case of 2x2 tables. A 95% confidence interval and significance level of 0.05 were adopted for all analyses.

National and international norms guiding ethics in research involving human beings were respected in all steps of this study. The data collection was initiated only after approval of the research project by the Research Ethics Committee of the Federal University of Piauí, under protocol 485.420.

Results

Among the 201 participants, the majority were female (72.6%), of mixed skin color (68.7%), religious (95.0%), married/in a stable union (50.2%), owned their home (91.5%), were retired (50.8%), and had a low educational level, as the mean time of study was 4.7 years (SD ± 4.34). Ages ranged from 19 to 96 years, with a mean of 63.1 years (SD ± 12.5). When the sample was stratified by economic class, classes B and C prevailed (52.7%), and the retirement income was the main source of income (44.5%).

Regarding the anthropometric and clinical data, excess weight was prevalent in 71.6% of the sample: 38.8% and 32.8% were overweight or obese, respectively. The WC was elevated in 62.0% of those investigated, and a sedentary lifestyle was present in 71.1% of the participants. Tobacco and alcohol use were reported by 10.9% and 12.4% of the sample, respectively. In addition, only 23.9% of diabetics (n = 48) were considered adherent to OAD treatment.

Regarding the laboratory data for MC analysis, the table below summarizes the main information (Table 1).

Most of the patients did not present safe values for FG, HbA1c and TG at the time of data collection. Regarding the LDL and CT rates, 33.8% and 47.6% of the sample, respectively, showed values above those recommended by guidelines and consensus statements. In turn, the HDL was decreased in 88.5% of diabetics. The blood pressure conditions were adequate in most of the patients investigated (70.6%), with a mean of 129.1x76.3 mmHg (SD ± 17.98x10.7).

Medication adherence was associated with other variables of the study, and the results showed that obese people were the ones with the lowest OAD medication adherence, showing a statistically significant relationship (p = 0.047).

Table 2 shows the associations between metabolic control and medication adherence. Patients classified as adherent to medication treatment showed a better control of their HbA1c (p=0.048), FG (p <0.001) and CT (p = 0.028) rates, demonstrating a statistically significant association between them.

Table 1. Analysis of the metabolic variables of individuals with Type 2 Diabetes *mellitus*

Variables	n(%)	Mean ± SD*	Minimum	Maximum
Fasting glycemia	164	135.0 ± 55.5	69.0	398.0
Normal	51(31.1)			
Altered	113(68.9)			
HbA1c	164	7.97 ± 2.0	3.6	14.6
Normal	47(28.7)			
Altered	117(71.3)			
Triglycerides	165	182.8 ± 95.9	65.0	503.0
Normal	76(46.1)			
Altered	89(53.9)			
LDL	160	119.7 ± 44.3	11.0	303.2
Normal	106(66.2)			
Altered	54(33.8)			
HDL	148	48.8 ± 10.8	25.0	111.0
Normal	17(11.5)			
Altered	131(88.5)			
Total cholesterol	147	204 ± 44.3	106.0	398.0
Normal	77(52.4)			
Altered	70(47.6)			
Blood pressure	201	SBP 129.1 ± 17.9	90.0	223.0
		DBP 76.3 ± 10.7	50.0	120.0
Normal	142(70.6)			
Altered	59(29.4)			

*SD - standard deviation; HBA1C - glycated hemoglobin; HDL - high density lipoprotein; LDL - low density lipoprotein; SBP - systolic blood pressure; DBP - Diastolic blood pressure

Table 2. Association of metabolic control and medication adherence in individuals with Type 2 Diabetes *mellitus*

Variables	Morisky test		p-value*
	Adherent n(%)	Nonadherent n(%)	
HbA1c			0.048
Normal	17(38.6)	30(25.0)	
Altered	27(61.4)	90(75.0)	
Fasting glycemia			<0.001
Normal	24(54.5)	27(22.5)	
Altered	20(45.5)	93(77.5)	
Triglycerides			0.533
Normal	20(45.5)	56(46.3)	
Altered	24(54.5)	65(53.7)	
LDL			0.154
Normal	31(73.8)	75(63.6)	
Altered	11(26.2)	43(36.4)	
HDL			0.267
Normal	6(15.4)	11(10.1)	
Altered	33(84.6)	98(89.9)	
Total cholesterol			0.028
Normal	26(66.7)	51(47.2)	
Altered	13(33.3)	57(52.8)	
Blood pressure			0.435
Normal	33(68.8)	109(71.2)	
Altered	15(31.2)	44(28.8)	

*p-value Fisher exact test; HBA1C - glycated hemoglobin; HDL - high density lipoprotein; LDL - low density lipoprotein

Discussion

The study was limited to the analytical aspect; therefore it was not possible to establish causal re-

lationships, even in those items in which a statistically significant association was found. In addition, the study has *missing data* due to refusal of some participants to allow blood to be collected for a second time, in cases in which the first collection was not sufficient enough for laboratory analysis. However, the results are clinically relevant because they contribute to the identification of individual characteristics and clinical aspects of patients who were nonadherent to treatment.

The information contained in the screening survey indicates the multidimensionality of the impacts caused by nonadherence to OADs, and supports the design of intervention strategies in cases in which a lack of adherence to medication treatment is found associated to the instability of clinical markers linked to the control of the T2DM. This guides the practice of nurses and other health professionals who care for people with the disease. In addition, understanding the phenomenon of nonadherence can sensitize nursing professionals about which variables are relevant during their approach to the care of the patients, who present difficulties regarding adherence to treatment, demonstrating a care based on evidence, supporting the care in different scenarios, such as primary health care, home care or hospital care. Likewise, this research indicates the need to use instruments that measure medication adherence, both to predict the efficacy of the recommendations and the prescribed treatment, as well as to manage appropriate care.

In this study, the majority of patients with T2DM were female, with a mean age of 63.1 years and a low educational level; this profile demands primary health care services, similar to other investigations [6,8,21] Age is one of the barriers for treatment adherence, mainly due to cognitive and functional changes, which progress with the age, and which can interfere in the comprehension of information about the disease, generating a deficit in self-care.[11]

In the evaluation of anthropometric and clinical measures, overweight, sedentary lifestyle and elevated WC were present in 71.6%, 71.7% and 62.0% of the sample, respectively, in agreement with the literature.[5,22] These figures show the food imbalance in the western world and the failures generated by lack of adequate stimulation to the regular practice of physical exercises, triggering important alterations in patients' metabolic control.

The medication adherence identified was low, a convergent or divergent aspect of the publications on the subject.[8,22] Low adherence may be associated with age, educational and socioeconomic level, complex therapeutic regimens, and/or lack of follow-up and control of the disease.[13,23] This context suggests better involvement of the patient regarding the issues related to knowledge, attitudes and practices related to T2DM, considering simplified therapeutic schemes, dynamic forms of health education, as well as strategies related to the inclusion of technologies that stimulate medication adherence, a key element in the process of empowering individuals with this disease.[5,10,11]

The overweight participants were less compliant to the therapeutic regimen (p=0.047). Those with adiposity alone may already show a lack of adherence to the proposed dietary plan, a replicable aspect in terms of medication, in individuals with T2DM. In addition, poor knowledge about care based on the percentage of adiposity in the body, can accentuate some pre-existing metabolic and cardiovascular problems.[21,23]

When analyzing the MC, composed by seven items (BP, FG, HbA1c, LDL, HDL, CT and TG), only three (LDL, CT and BP) presented adequate mean values. In the sample, the glycemic components (HbA1c and FG), which are key pieces in T2DM control, were at high levels, in accordance with the findings of other national surveys.[5,22] The analysis of the glycemic variables is important to reveal the treatment instituted and significantly influence the MC. Regarding lipid values, both TG and HDL were shown to be uncontrolled in relation to established standards. When irregular, these cholesterol ranges accelerate the onset of cardiovascular complications and deregulate MC in T2DM patients. Searching to study the association between adherence to treatment of T2DM and MC, researchers have identified TG elevation as the main problem for the control of metabolic biomarkers, especially influenced by poor diet.[23] When analyz-

ing the HDL decreased in 88.5% of the investigated population, the present research was similar to another study, of analogous methodology. The HDL cholesterol is undoubtedly the major protector against the onset of cardiovascular comorbidities, which in turn are most associated with T2DM-related dysregulations.[6] The findings also indicate a proximity to HDL levels and overweight, as well as sedentary lifestyle found in this study, which indicates a tendency to poor adherence to prescribed guidelines in the health care units regarding T2DM management.

Regarding blood pressure conditions, when crosschecks were performed between BP data and Morisky's test results, no significant association was found. It is noteworthy, however, that BP levels were high among study participants. Thus, the main comorbidity associated with T2DM, arterial hypertension, also receives special attention in the health care units, where BP control is intensified, especially by the prescription and distribution of antihypertensive medications, with positive impacts on MC and minimizing the risks of coronary diseases.[12] As a limitation on the inclusion of BP data, in the present study, the Ambulatory Blood Pressure Monitoring (ABPM), named as a gold standard for the investigation of BP values, was not used as a measurement method.[19] Due to the nature of the study, the inclusion of this method would have led to an even greater amount of missing data.

In the present investigation, patients adhering to OADs presented better HbA1c (p=0.048), FG (p<0.001) and CT (p=0.028), considering the significant correlation of the findings. The analysis of the relationship of these variables coincides with another research study.[22] These data can be explained by the close relationship between T2DM and the onset of dyslipidemias, diseases that lead to metabolic lack of control that progressively bring irreparable damage to the clinical condition of patients with diabetes. In turn, dyslipidemias are treated in the Primary Care Units by means of anti-lipids, which are often adjuvants in the control of T2DM, generating normalization of lipid bands, such as CT.

In addition, patients adhering to OAD treatment also tend to follow a regular diet, exercise, and maintain control over the disease. [6,21-23] For other correlations, those that were not significant, the inconsistency in the literature does not indicate robust measures for solution of the conflicts between the adequate levels of the metabolic variables and the adherence to T2DM treatment. Thus, it is fundamental to incorporate other strategies and tools for controlling biomarkers linked to the metabolism of subjects with T2DM. These tools are divided into health promotion actions, by means of health planning and, above all, revealed by cost-effectiveness studies, which should be stimulated more.

Conclusion

Female patients, with a mean age of 63.1 years and low levels of education, were in the majority in the present study. In addition, most of the participants were sedentary, with elevated WC, and poorly controlled levels of HbA1c, FG, TG, and HDL. Only 23.9% of the participants showed adherence, according to the Morisky Test. This picture predominated in individuals with an excess weight. In turn, when adherent, they also obtained better levels of HbA1c, FG and CT.

Acknowledgements

The authors acknowledge the financial support from Research Foundation for the State of Piauí (FAPEPI) by means of the shared management in health of the Research Program for the Unified Health System (PPSUS)

Collaborations

Lira Neto JCG contributed to analysis, data interpretation and article writing. Silva AP and Araújo MFM contributed to the relevant critical review of the intellectual content. Damasceno MMC, Landim MBP and Freitas RWJF contributed to the study design and final approval of the version to be published.

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