The relationship between polipharmacy, chronic complications and depression in individuals with Type 2 Diabetes Mellitus

A RELAÇÃO ENTRE POLIFARMÁCIA, COMPLICAÇÕES CRÔNICAS E DEPRESSÃO EM PORTADORES DE DIABETES MELLITUS TIPO 2

RELACIÓN ENTRE POLIFARMACIA, COMPLICACIONES CRÓNICAS Y DEPRESIÓN EN PORTADORES DE DIABETES MELLITUS TIPO 2

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ABSTRACT

The objectives of this study were: to characterize the polipharmacy in subjects with Type 2 Diabetes Mellitus (DM2) and to verify the correlation between polipharmacy and number of medications for DM2 complications with depression indicators (Beck Depression Inventory (BDI) and urinary cortisol (CORT) levels). A sample composed of 40 patients with DM2 from the Diabetes League of HCFM-USP was analyzed for depression indicators (CORT and BDI) in addition to evaluation for polipharmacy and number of DM2 complications. The results showed oral hypoglycemic agents, insulins, antihypertensives, diuretics, lipid-lowering drugs and thrombolytics are the most frequent medications used. In this sample, 75% used from 5 to 8 medicines daily and 12.5% used more than eight medicines/day; all of them used to take each medication at least 3 times daily. Between 1 and 3 DM2 complications were observed in 60% of the individuals and 22.5% showed more than 3 DM2 complications. No significant correlations were observed between depression indicators (BDI and CORT), number of medications and DM2 complications. However, positive correlation was observed between CORT and daily frequency of medication (Spearman, r=0.319, p=0.019).

KEY WORDS

Hydrocortisone.
Depression.
Diabetes Mellitus, Type 2.
Nursing.
Polypharmacy.

RESUMO

Os objetivos deste estudo foram: caracterizar a polifarmácia entre portadores de Diabetes Mellitus tipo2(DM2); e correlacionar polifarmácia e número de complicações do DM2 com indicadores de depressão (Inventário de Depressão de Beck[IDB] e cortisol urinário[CORT]). A amostra foi composta por 40 pacientes da Liga de Diabetes do HCFM-USP, avaliados quanto aos indicadores de depressão (CORT e IDB) e quanto à prática de polifarmácia e número de complicações do DM2. Os resultados mostraram que os medicamentos utilizados foram: antidiabéticos orais, insulinas, anti-hipertensivos, diuréticos, anti-lipêmicos e trombolíticos. No grupo estudado, 75% fizeram uso diário de 5 a 8 medicamentos, e 12,5% de 8 medicamentos/dia ou mais; todos fizeram no mínimo 3 tomadas diárias, 60% tinham entre 1 e 3 complicações do DM2, e 22,5% tinham 3 ou mais. A correlação entre os indicadores de depressão(IDB e CORT), o número de medicamentos e o número de complicações do DM2 não foi estatisticamente significante. No entanto, houve correlação positiva entre CORT e número de tomadas diárias de medicamentos (Spearman,r=0.319, p=0.019).

DESCRITORES

Hidrocortisona.
Depressão.
Diabetes Mellitus Tipo 2.
Enfermagem.
Polimedicação.

RESUMEN

Fueron objetivos de este estudio: caracterizar a la polifarmacia entre portadores de Diabetes Mellitus tipo 2 (DM2) y correlacionar la polifarmacia y el número de complicaciones de la DM2 con indicadores de depresión (Inventario de Depresión de Beck [IDB] y cortisol urinario [CORT]). La muestra fue integrada por 40 pacientes de la Liga de Diabetes del HCFM-USP evaluados respecto de los indicadores de depresión (CORT e IDB) y también en cuanto a la práctica de polifarmacia y número de complicaciones de la DM2. Los resultados mostraron que los medicamentos utilizados fueron: antidiabéticos orales, insulinas, antihipertensivos, diuréticos, antilipemiantes y trombolíticos. Dentro del grupo estudiado, 75% de los pacientes utilizaban diariamente entre 5 y 8 medicamentos, un 12,5% de la muestra hacía uso de 8 medicamentos/día o más; todos hicieron como mínimo tres tomas diarias, el 60% presentaba entre 1 y 3 complicaciones de la DM2 y el 22,5% presentaba 3 o más. La correlación entre los indicadores de depresión (IDB y CORT) y el número de medicamentos y de complicaciones de la DM2 no fue estadísticamente significativa. Sin embargo, hubo correlación positiva entre CORT y la cantidad de tomas diarias de medicamentos (Spearman, r=0.319, p=0.019).

DESCRIPTORES

Hidrocortisona.
Depresión.
Diabetes Mellitus Tipo 2.
Enfermería.
Polifarmacia.

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INTRODUCTION

Diabetes Mellitus is a widespread chronic disease. According to the International Diabetes Federation, it affects approximately 140 million people throughout the world and it is estimated to reach 300 million by 2025[1].

In Brazil, Diabetes Mellitus prevalence in the population between 30 to 69 years old is of 7.6%, representing 10 million people. Within these people, 90% are carriers of Diabetes Mellitus Type 2 (DM2) [2]. A more recent study developed in Ribeirão Preto using more restricted glycemic limits according to current recommendations, demonstrated a prevalence of 12.1% in similar population[3].

Chronic complications from the disease include macroangiopathy, microangiopathy and peripheral and autonomic neuropathies [4].

The United Kingdom Prospective Diabetes Study (UKPDS) was the most important multicentric study carried out with DM2 carriers. It demonstrated that the lower the glycated hemoglobin (A1c) level, the lower the risk on developing complications from such infirmity[4], which disable the individual to perform routine and productive activities, generating costs for society.

DM2 demands the polypharmacy practice for its metabolic control. Polypharmacy is a term used to describe the daily multiple use of medications by a patient (5 or more)[5]. Some studies have characterized users of this practice[5-6].

One study affirms that individuals that tend to practice polypharmacy are of old age, females, under poor health condition and showing symptoms of depression[6]. Another study presents results showing that elder women with educational level up to junior high school are more tendentious to the practice. In this sample, 91% used some type of medication, 33% of them used it with no medical prescription and 27% showed evidences of polypharmacy[5].

In another knowledge sphere, some studies demonstrate higher prevalence of depression in -DM2 carriers[7-8]. One of these studies performed a systematic review between 1990 and 2001 on MEDLINE and LILACS databases, showing that depression symptoms are related to glycemic decompensation, to an increase and higher severity of complications resulting from DM2 and the elevated impact on the routine life of DM2 carriers[7].

Another study that aimed at identifying depression symptoms by the Beck Depression Inventory (BDI) in carriers of DM2, demonstrated that 68.12% of the sample of 59 DM2 carriers showed depression symptoms higher than the cut-off point score established by the instrument. These results were related to females (p=0.002), older age (p<0.001) and lower educational level (p=0.024)[8].

In order to understand these interrelations, literature shows that as from a stressing agent, the hypophyseal adrenocortical axis can be activated, increasing synthesis and the liberation of cortisol, a hyperglycemia hormone that basically damages metabolic control in DM2 carriers leading individuals to depression[9].

Starting from that, this study aims to investigate if the practice of polypharmacy among DM2 carriers is a stressing agent capable of influencing the hypophyseal adrenocortical axis, leading this population to depression and, consequently to the inefficient control of DM2.

Hence, three indicators were used: two regarding depression measuring, one subjective (BDI)[10], and another objective (urinary cortisol (CORT)); and one third indicator regarding metabolic decompensation measuring that demonstrates DM2 control (A1C).

OBJECTIVES

Characterize polypharmacy among DM2 carriers. Relate polypharmacy and the number of chronic complications of DM2 with depression symptoms indicators (BDI and CORT).

Some studies demonstrate higher prevalence of depression in Diabetes Mellitus Type 2.

METHOD

This is a cross-sectional descriptive study. Data were collected from DM2 carriers in the Diabetes Control League clinics of the General Hospital of the University of Medicine of São Paulo Endocrinology Discipline.

Mandatory inclusion criteria for this study were the following: DM2 carriers at any evolution phase of the disease; being 18 or older due to peculiarities regarding DM2 and depression and to ensure ethical aspects of the research; not using any anti-depressive medications or anti-anxiety agents for a period of at least one month before accepting to participate in this research, in order to avoid possible humor or neuro-chemicals and hormones influence; accepting to participate in this research and proceed with a written agreement by signing a *Free and Informed Consent Form* (registered under protocol 468/2005 in the Research Ethics Committee of the Nursing School of the University of São Paulo).

Data were collected throughout the period of 09/28/2005 to 03/08/2006 in a location that ensured privacy to each collaborator, informing them to preferably not bring any companions (family or friend), to answer the research instruments and receive guidelines regarding CORT doses.

The amount of subjects composing the study was determined by the sample calculation and the alpha risk was lower or equal to 5% and beta risk lower or equal to 20% of committing a type 1 or first class mistake. A forty-carriers of DM2 sample was considered for a 2-tailed hypothesis for an independent and non-parametric test.

CORT dosages (objective indicator of depression symptoms) were measured through the biochemical 24-hour urine exam, using electro-immune test[11].

Applied questionnaires and instruments were composed of:

• Socio-Demographic Data Collection Questionnaire: elaborated to characterize Gindividuals of the research regarding socio-demographic data (gender, age, marital status, origin, religion/faith presence and practice, level of education, individual income, family income, income *per capita* and people who are in charge of the income for the whole family).

• DM2 Data Collection Questionnaire: data in this instrument provided information about therapeutic and clinical conditions contemplating: DM2 duration, self-assessment of DM2 impact over routine life (assessment through alpha-numeric scale from 0 to 10, where 0 (zero) is equivalent to no impact and 10 (ten) to maximum impact), lifestyle (smoking[12], alcoholism[13], physical activity and eating habits), anthropometric data (weight, height, body mass index (BMI), waist circumference (WC), and waist hips ratio (WHR)), pharmacology, dealing with the disease (daily control method for the disease and hypoglycemic crisis), and biochemical control of the disease (A1c).

In order to analyze lifestyles regarding smoking and drinking, two specific instruments[12-13] were used as follows.

The Fagerström test aims at assessing the nicotine dependency degree as from the individual's affirmative answer regarding the smoking habit, consequently, the probability of this individual to show abstinence syndrome if, eventually, he stops smoking; it is composed of 6 questions, the first and fourth questions have 4 alternatives rating from 0 to 3 points and the other questions have 2 alternatives rating from 0 to 1 points. The sum of these points, when there are scores above or equal to 6 points, demonstrates great dependency on nicotine and higher chances of showing abstinence syndromes when stopping it. Although not validated, this test is recommended by the National Cancer Institute of the Department of Health (INCA in Brazilian acronyms)[12].

The Cage test identifies if the individual is an alcoholic or not. It was validated for Portuguese in 1983 and is composed of 4 questions, where affirmative answers are equivalent to 1 point while negative answers do not add or subtract points from the score, because they are equivalent to zero. The classification occurs after the sum of the points acquired in the affirmative answers. Therefore, when the score is 0 to 1, the individual is not an alcoholic, when the score is 2 points; the individual shows high risk of becoming an alcoholic and when the score is between 3 and 4 points, the individual is an alcoholic[13].

In order to analyze anthropometric data, reference values alleged by the Brazilian Association for the Study of Obesity and the Metabolic Syndrome[14] were uses as follows:

• Regarding BMI: Individuals with values <18.5 were considered thin, individuals with values between 18.5 ├ 25 were considered normal, individuals between 25 ├ 30 were considered overweight, individuals with values between 30 ├ 40 were considered obese, and individuals with values ≥40 were considered severely obese;

• Regarding WC: Women with values ≤ 80 were considered normal, women with values > 80 were considered having central obesity; men with values ≤ 95 were considered normal and men with values > 95 were considered with central obesity;

• Regarding WHR: Women with values ≤ 0.80 were considered normal, women with values > 0.80 were considered having central obesity; men with values ≤ 0.90 were considered normal and men with values > 0.90 were considered with central obesity;

To analyze A1c the Performance Liquid Chromatography (HPLC) method alleged by the Interdisciplinary Group of A1c standardization of FENAD (National Federation of Diabetes Associations and Entities) was used, where values above 7% were considered as altered[15].

• Beck Depression Inventory (BDI) [16]: subjective indicator of depression symptoms that, according to its description, refer to a

> […] Depression self-assessment measure, with no diagnosis purpose, however serving as assessment complement; composed of 21 symptoms and attitudes categories characterized from depression manifestations. Each category consists of a series of different intensity degrees of manifestations, reflecting the intensity of the symptom (from neutrality to maximum severity), in numeric scales from 0 to 3 points. Categories involve humor, vegetative, social withdrawal, and cognitive and irritability manifestations. Depression symptoms involve the following categories according to the order they appear in the instrument: Sadness, pessimism, failure sensation, lack of satisfaction, guilty sensation, punishment sensation, self-depreciation, self-accusation, suicidal ideas, crying crisis, irritability, social isolation, indecision, body image distortion, work inhibition, sleep disorder, fatigue, appetite loss, weight loss, somatic anxiety, and reduction in libido. To assess the score obtained in applying the inventory, the sum of points from all categories must be performed for later result verification. [...] Studies recommend that results must be classified into three different levels of score: from 0 to 15 points, absence of depression symptoms; scores above 15 points and bellow 20 points indicate a dysphoria state; and scores above 20 points indicate suggestive depression diagnosis [...][17].

In order to analyze the internal consistence of BDI, a Cronbach Alpha of 0.920 was used, indicating a great reliability index. The index was maintained even when some of its domains were withdrawn, proving a minimum coefficient of 0.915. It is important to stand out that the domain *Suicidal Ideas* was eliminated from the analysis, since they showed zero variance.

RESULTS

The sample was constituted by 60% of women, 45% of elders (60 years old or older); the age median was 56.5, where the minimum and the maximum were, respectively, 21 to 90 years old, and the average of age was 59.8 with standard deviation of ± 13.6 years old.

The group was composed of 52.5% in a stable relationship, 22% of widowers, 15% of unmarried and 10% of separated /divorced; 37.5% from the interior of the state of São Paulo, 32.5% from the Great area of São Paulo, and 30% from other States.

The whole sample (100%) affirmed having a religion and/or faith, and within them 77.5% affirmed to practice it.

The median in the school education level was of 8 years old. the minimum and maximum were, respectively, from 0 to 20 years, the average was 7.6 with standard deviation of ± 4.8 years of study, 2.5% of the sample was illiterate.

Individual income varied from 1 to 20 minimum salaries in 85% of the sample. The others had no own income and 34% of the sample were family income providers. Family income varied from 1 to 15 minimum salaries and the *per capita* income of 0.3 to 5 with median of 1.6 minimum salaries.

The characterization of the sample is presented as follows under various clinical aspects of DM2 (Table 1).

Table 1 - Characterization of the group studied according to clinical aspects - São Paulo - 2005 - 2006

Variables and Categories	N	%
DM2 Duration (Average / ± SD / Median, in years)	13.7 / ± 9.9 / 11.0	
Number of complications that are consequences of DM2		
3 or more	16	42.5
1 or 2	14	37.8
None	7	18.9
Self-assessment of the impact of dm2 on daily life (Average / ± SD / Median)	5.8 / ± 2.5 / 6.0	
Physical activity practice		
No	28	70.0
Yes	12	30.0
Practicing frequency of physical activity		
5 times per week	7	58.3
3 times per week	4	33.3
7 times per week	1	8.3
Following nutritional guidelines		
No	22	55.0
Yes	18	45.0
Alcoholism		
No	37	92.5
Yes	3	7.5
Higher probabilities of having alcoholism. according to cage		
No	35	87.5
Yes	5	12.5
Smoking		
No	25	62.5
Yes	15	37.5
Higher probabilities of abstinence syndrome by nicotine. according to Fagerström		
Yes	12	80.0
No	3	20.0
Use of medications		
Yes	40	100.0
Number of medications used		
5 or more medications per day	35	87.5
4 medications per day	4	10.0
3 medications per day	1	2.5
Medication frequency		
Up to 3 times per day	21	52.5
4 times per day	19	47.5
Using exogenous insulin		
No	21	52.5
Yes	19	47.5
Glycemic control performance		
No	34	85.0
Yes	6	15.0
Presence of hypoglycemic crisis		
No	31	77.5
Yes	9	22.5
Frequency of hypoglycemic crisis		
Once per month	6	66.7
8 times per month	2	22.2
Longer than one month interval	1	11.1
Body mass index (Average / ± SD / Median. in kg/m^2)	28.3 / ± 4.3 / 28.3	
Waist circumference alteration		
Female	19	78.0
Male	10	77.0
Waist-hip ratio alteration		
Female	24	100.0
Male	16	100.0
Glycated hemoglobin (Average / ± SD / Median, in percentages)	9.1 / ± 2.2 / 9.2	

The Spearman correlation test between BDI scores and CORT dosages demonstrate a statistically significant and positive correlation between the two variables. In other words, as the BDI score increases, higher the CORT dosage, and vice-versa, according to what is demonstrated in Figure 1.

The medications used were: oral anti-diabetes, insulin, anti-high blood pressure, diuretic, antilipemic and thrombolytic. In the group studied, 75% made daily use of 5 to 8 medications and 12.5% 8 medications/day or more; all subjects took at least 3 medications/day; and 60% had between 1 to 3 DM2 complications and 22.5% had 3 or more.

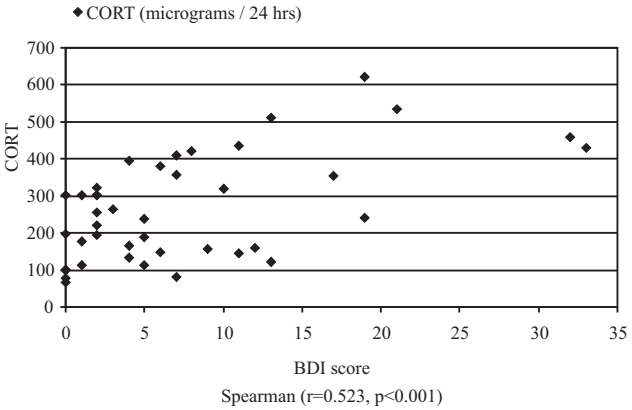


Figura 1 - Correlation between BDI and CORT (micrograms / 24 hrs) in carriers of DM2 - São Paulo - 2005 - 2006.

The correlation between the number of medications and depression indicators (BDI and CORT) were not statistically significant (Spearman, r=0.129, p=0.427; and r=-0.019. p=0.905, respectively).

A similar situation occurred between the number of DM2 complications and these same depression indicators (Spearman, r=0.045, p=0.785; and r=0.084, p=0.605, respectively).

The correlation between the frequency of taking medications/day and depression indicators did not evidenced significant statistically correlation with BDI (Spearman, r=0.179, p=0.270).

However, calculations with CORT demonstrated positive and significant statistically correlation (Spearman, r=0.319, p=0.019), in other words, as medication intake frequency/day increases, the same occurs to CORT levels. Figure 2 shows the distribution of DM2 carriers according to the frequency in which medications are taken daily and CORT levels.

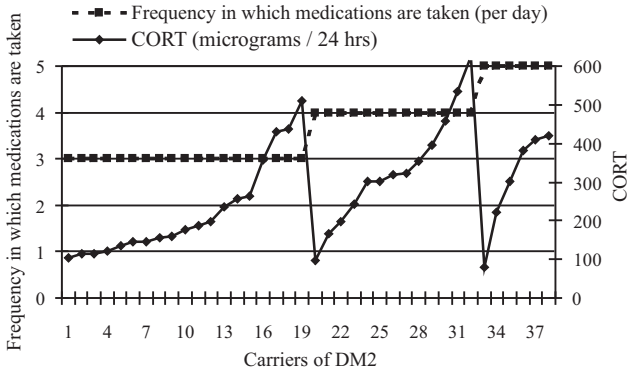
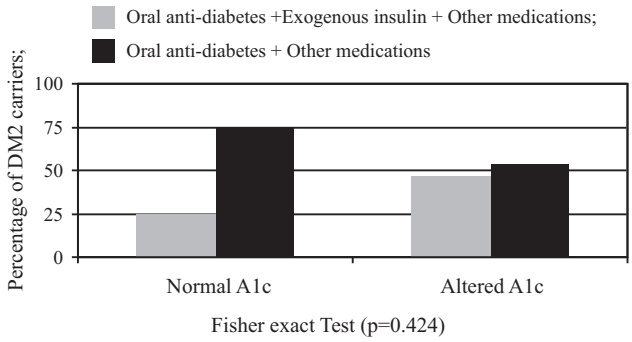


Figure 2 - DM2 carriers' distribution according to the frequency in which medication are taken (per day) and CORT (micrograms / 24 hrs). São Paulo, 2005 – 2006

In Figure 3, firstly the study group was subdivided into two subgroups per individuals with normal A1c and another with altered A1c. Afterwards, the correlation of exogenous insulin use with the presence of A1c levels alterations in each subgroup was analyzed.



Figue 3 - DM2 carriers percentage distribution, according to the use of exogenous insulin and the presence of alterations in A1c levels. São Paulo, 2005 - 2006

Results demonstrated that in the A1c normal subgroup, 25% of individuals are medicated with exogenous insulin. While in the altered A1c subgroup this percentage is 46.4% (Figure 3). In addition, no association between the use of exogenous insulin with A1c levels alterations in each subgroup were evidenced, according to Fisher Exact Test (p=0.424).

DISCUSSION

Only a few studies tried to investigate the hypophyseal adrenocortical axis[18] activity in the DM2 context. On the other hand, based on theoretical knowledge, it is well-known that CORT levels trigged by a stressing agent can cause depression and hyperglycemia symptoms[9].

Through a stressing agent, whether pleasant or not, holding the subject as reference, this stressing agent acts in the hypophyseal adrenocortical axis, leading the individual to depression, through blocking serotonin receptors $5HT_{1A}$; and the metabolic decompensation, analyzed from the DM2 context perspective, through the stimulation of hepatic glyconeogenesis, protein degradation and increase in the number of glucocorticoid receptors in adipose tissue; and the inhibition of glucose receptors in the adipose and muscle levels (Figure 4).

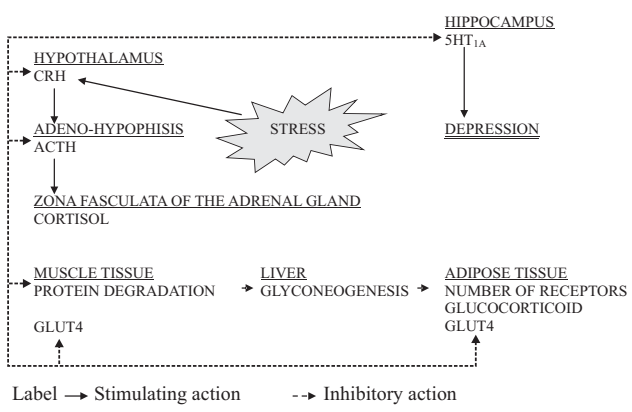


Figure 4 - The intervention between cortisol, depression and diabetes mellitus type 2

The experience of the chronic DM2 condition can be characterized as stress. Chronicity can be measured by the complications resulting from this disease and the practice of polypharmacy. In addition to behaviors that can contribute for the development and severity of the chronic aspect.

As from the results demonstrated (Table 1), verifying that it regards a group that has been experiencing DM2 for at least 10 years was possible, and only 18.9% of these individuals have no complications resulting from DM2 and classified this disease as highly impacting to their routine life.

When analyzing under the lifestyle perspective (Table 1), only 30% performed some type of physical activity, among these, only 8.3% practiced it daily; in addition, 55% affirmed not following nutritional guidelines and 85% do not perform daily glycemic control.

Regarding the anthropometric profile of the group (Table 1), which has BMI average and median of 28.3 with standard deviation of ± 4.3, demonstrating an overweight sample. The female sample has an average WC measure of 88 cm and a fraction of waist-hip ratio of 0.88; the male sample has, respectively, 102 cm and 1.01. It regards people with cardiovascular disease risk, developing DM2 and with tendencies to central obesity [14]. In order to aggravate this chart 12.5% of the group have higher probabilities to show alcoholism and 37.5% affirm being smokers, from these, 80% were characterized as chemical and nicotine dependents.

Polypharmacy practice was verified[5-6] and the frequency of these daily intake of medications has shown itself as a stressing agent, through the perspective of the depression objective indicator (CORT).

The subjective indicator of depression (BDI) was expected to also demonstrate a significant and positive correlation from the statistical point of view with the daily frequency of medication intake.

In face of these results, questionings arouse about the administration of exogenous insulin as a determining variable to control DM2, in regards of medications orally administrated, and that because of this thinking, perhaps interfered in the meaning of the stressing agent for DM2 carriers.

The individual with altered A1c demonstrated to use more exogenous insulin, in comparison to those with normal A1c. However, the use or not of exogenous insulin is indifferent to control metabolic decompensation in DM2. Therefore, it is not a stressing agent with higher or less importance in face of orally administrated medications.

In other words, what determines the increase on CORT levels is exclusively the frequency of daily medication intake, meaning the times individuals daily stop to self-administer medications to control DM2.

This present research aimed at pointing out the importance of rationally adopting a pharmacology therapy, since it can trigger collateral events apart from those once predicted, or through chemical components interactions. In addition, to reaffirm that the absolute number of medications in use or the absolute number of resulting complications in DM2 were not determinants of the eventual manifestation of depression symptoms, but, mostly probable, the meanings printed within these events.

CONCLUSIONS

Results demonstrated that DM2 carriers practice polypharmacy. However, neither the amount of medication daily taken, nor even the use of exogenous insulin, are configured as stressing agents; it is the frequency in which these medications are daily taken.

REFERENCE

1. Gruber W, Lander T, Leese B. The economics of diabetes and diabetes care. Brussels, Belgium: International Diabetes Federation; 1998.

2. Malerbi DA, Franco IJ. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in the urban brazilian population age 30-69 years. The Brazilian Cooperative Group on the Study of Diabetes Prevalence. Diabetes Care. 1992;15(11):1509-16.

3. Laquata ATCG, Montenegro RM, Vianna LAL, Souza RAHG, Lanna CMM, Lucas JCB, et al. Prevalence of diabetes mellitus and impaired glucose tolerance in the urban population aged 30-69 years in Ribeirão Preto (São Paulo), Brazil. Sao Paulo Med J. 2003;121(6):224-30.

4. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complication in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352(9131):837-53.

5. Rozenfeld S. Prevalência, fatores associados e mau uso de medicamentos entre os idosos: uma revisão. Cad Saúde Pública. 2003;19(3):717-24.

6. Flores LM, Mengue SS. Uso de medicamentos por idosos em Região do Sul do Brasil. Rev Saúde Pública. 2005;39(6):924-9.

7. Moreira RO, Papelbaum M, Appolinário JD, Matos AG, Coutinho WF, Meirelles RMR, et al. Diabetes mellitus e depressão: uma revisão sistemática. Arq Bras Endocrinol Metab. 2003; 47(1):19-29.

8. Ricco RC, Miyazaki MCOS, Silva RCMA, Góngora DVN, Perozim LM, Cordeiro JA. Depressão em pacientes adultos portadores de doenças crônicas: diabetes mellitus e hepatites virais. HB Cient. 2004;7(3):156-60.

9. Graeff FG, Brandão ML, Tomaz C. Neurobiologia das doenças mentais. São Paulo: Lemos; 1993.

10. Gorenstein C, Andrade LHSG, Zuardi AW. Escalas de avaliação clínica em psiquiatria e psicofarmacologia. São Paulo: Lemos; 2000. p. 89-95.

11. Fréjaville JP, Kamoun P. Manual de exames de laboratório. São Paulo: Atheneu; 1989.

12. Instituto Nacional do Câncer (INCA). Coordenação Nacional de Controle do Tabagismo e Prevenção Primária de Câncer. Ajudando seu paciente a deixar de fumar. Rio de Janeiro; 1997. p. 18-23.

13. Masur J, Monteiro MG. Validation of the "Cage" alcoholism screening test in a brazilian psychiatric inpatient hospital setting. Brazilian J Med Biol Res. 1983;16(2):215-18.

14. Associação Brasileira para o Estudo da Obesidade e da Síndrome Metabólica (ABESO). [homepage na Internet]. São Paulo; 2009. [citado 2008 mar. 20]. Disponível em: http://www.abeso.org.br

15. Grupo Interdisciplinar de Padronização da Hemoglobina Glicada A1c. A importância da hemoglobina glicada (A1c) para a avaliação do controle glicêmico em pacientes com diabetes mellitus: aspectos clínicos e laboratoriais. São Paulo: Federação Nacional das Associações e Entidades de Diabetes (FENAD); 2004.

16. Gorenstein C, Andrade LHSG, Zuardi AW. Escalas de avaliação clínica em psiquiatria e psicofarmacologia. São Paulo: Lemos; 2000.

17. Costa ALS. Processos de enfrentamento do estresse e sintomas depressivos em pacientes portadores de retocolite ulcerativa idiopática. São Paulo: A. L. S. Costa; 2003. p. 46-8.

18. Cameron BJ, Kronfol Z, Greden JF, Carroll BJ. Hypothalamic-pituitary-adrenocortical activity in patients with diabetes mellitus. Arch Gen Psychiatry. 1984;41(11):1090-5.

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