Revista de Ciências Farmacêuticas Básica e Aplicada
Journal of Basic and Applied Pharmaceutical Sciences

Rev Ciênc Farm Básica Apl., 2012;33(3):409-414
ISSN 1808-4532

Monitoring biochemical markers during pharmacotherapeutic follow-up of type 2 diabetic patients

Luciana Macatrão Nogueira Nunes[1*]; Thiago Moreira de Olinda[1]; Marta Maria de França Fonteles[1]; Miguel Nasser Hissa[2]; Silvânia Maria Mendes de Vasconcelos[3]; Daniel Freire de Sousa[1]; Maria Goretti Rodrigues de Queiroz[1]

[1]Department of Clinical and Toxicological Analysis, Faculty of Pharmacy, Dentistry and Nursing (FFOE), Federal University of Ceará (UFC), Fortaleza, CE, Brazil.
[2]Department of Endocrinology, Faculty of Medicine, Federal University of Ceará, Fortaleza, CE, Brazil.
[3]Department of Physiology and Pharmacology, Faculty of Medicine, Federal University of Ceará, Fortaleza, CE, Brazil.

ABSTRACT

Loss of the modulatory role of the endothelium may be an important factor in the development of diabetic vascular diseases such as cardiac, cerebral and peripheral vascular disease, as evidenced by changes in the serum lipid profile: increased triglycerides (TG), total lipoprotein cholesterol (TC) and low-density lipoprotein (LDL-C), and reduced high-density lipoprotein (HDL-C). This article describes a longitudinal intervention study conducted at the Center for Research in Diabetes and Endocrinometabolic Diseases of the Federal University of Ceará (UFC, CE, Brazil), in which 58 patients with type 2 diabetes (DM2) were monitored by recording biochemical parameters during two sessions of laboratory tests, and through monthly interview-based pharmacotherapeutic follow-up. The study lasted one year and was approved by the human research ethics committee of UFC. The data collected were analyzed with the aid of the program SPSS 11.0. Hypertension was present in 54.4% of patients with DM2, 64% were sedentary and overweight, 44.7% reported having relatives with cardiovascular disease and 59.5% had a family history of diabetes. The serum levels of fasting glucose, TG, TC and LDL-C and the systolic and diastolic blood pressure were reduced after the active follow-up and monitoring of patients. This result reinforces the importance of the role of the pharmacist in the control of biochemical parameters, improvement of patients' quality of life and prevention of complications.

Keywords: Pharmacotherapeutic monitoring. Diabetes mellitus. Biochemical parameters.

Corresponding Author: Luciana Macatrão Nogueira Nunes - R. José Vilar, 2085 - Fortaleza - Ceará - Brazil - Zip code:60040-430 - phone: 55(85)3366-8269 - fax: 55(85)3366-8262 - e-mail: lucianamacatrao2@yahoo.com.br

INTRODUCTION

Diabetes mellitus (DM) is regarded as a serious public health problem on account of its growing prevalence and chronic macro/microvascular complications, which generate direct and indirect costs, impair the productivity and quality of life of the patients and increase the rates of morbidity and mortaliy (Afonso et al., 2003; Plácido, Fernandes & Guarido, 2009). The loss of the modulatory role of the vascular endothelium may be an important factor in the development of diabetic vascular diseases (Vanhoutte, 2010; Vriese et al., 2000; Wiernsperger, Nivoit & Bouskela, 2007) such as retinopathy, peripheral and autonomic neuropathy, nephropathy and atherothrombotic diseases that result in cardiovascular, cerebrovascular and peripheral vascular impairment (American Diabetes Association, 2007). These disorders are characterized by alterations in lipid levels: increases in serum triglycerides (TG), total lipoprotein cholesterol (TC) and low-density lipoproteins (LDL-C), and reduction in serum level of high-density lipoprotein (HDL-C) (Abdel-Gayoum & Musa, 2009; Torre, 2005).

More than 50% of the mortality in patients with type 2 diabetes (DM2) is related to cardiovascular disease and the incidence of cerebrovascular and coronary artery disease is two to four times higher in DM2 patients than in the general population (Kumar, 2010). Evidence from randomized clinical trials shows that tight glycemic control based on the reduction of glycated hemoglobin (HbA_{1c}) reduces long-term DM microvascular complications (Furtado & Polanczyk, 2007).

Pharmacotherapeutic follow-up, a component of pharmaceutical care, is essential in the treatment of diabetes, as it is a disease caused by the highly complex interplay of genetic, physiological and environmental factors that vary from individual to individual, and because it is commonly associated with other medical conditions, especially in certain groups such as the elderly. It should also be taken into account that people of all ages and socio-economic conditions are included in the patient profile (Kirwin et al., 2010). Thus, pharmacists can help improve

results by identifying, resolving and, more importantly, preventing problems that may be generated by drug therapy (Consenso Brasileiro de Atenção Farmacêutica, 2002; Planas et al., 2005). Flores (2005) showed that a pharmaceutical care program offered in the Brazilian public health service resulted in an average fall of about 50mg/dL in blood glucose and that the activities developed by the multidisciplinary team were able to maintain these levels during the observation period of six months. Cani (2011) showed that knowledge of diabetes, use of medication, adherence to pharmacological treatment, correct use of insulin application techniques and capillary blood glucose monitoring all increased significantly in the intervention group, namely those DM2 patients who received pharmacotherapeutic monitoring and individualized education about type 2 diabetes for 6 months. In the same study, the mean glycated hemoglobin reading decreased significantly in the intervention group, but not in the control group who received normal care.

Thus, this study was conducted to assess the impact of pharmacotherapeutic follow-up on type 2 diabetic patients, by monitoring biochemical markers for endothelial dysfunction and glycemic control (fasting glucose, HbA1c, TC, HDL-C and LDL-C and TG).

MATERIAL AND METHODS

The study consisted of a longitudinal intervention performed at the Research Center for Diabetes and Endocrine/Metabolic Diseases Research of the Federal University of Ceará (UFC, Brazil). This Center has an interdisciplinary team of doctors, nurses, pharmacist and other members, available for the discussion of cases. The study lasted one year (June 2006 to June 2007).

The study included patients older than 30 years, of both sexes, with type 2 diabetes and being treated with hypoglycemic agents and / or change of lifestyle. For the duration of the study they did not participate in any other research. At the beginning, there were 101 patients in the group, but 43 patients left before the end: 9 quit, 2 died, 4 lost contact and 28 joined other projects. Thus, 58 patients concluded the study.

For the pharmacotherapeutic follow-up, an adaptation of the Dáder method (offer of service, first interview, clinical situation status, study phase, assessment, intervention, intervention result, new situation status and successive interviews) was used (Machuca et al., 2003). Each month, the patients were followed up by the pharmaceutical researchers and informed about the importance of adhering to the treatment. Data on comorbidities and risk factors were obtained by self-report in interviews with patients.

The data collection tools used were questionnaires and laboratory tests (fasting glycemia, TC, HDL-C, LDL-C and TG). The latter were carried out twice: at the first interview and after three months of follow-up. Blood samples were collected after 12 hours fasting and processed by kinetic, enzymatic and colorimetric methods based on commercial kits (Labtest). Body mass index (BMI) was calculated, and systolic (SBP) and diastolic pressure (DBP) was measured. Blood was collected from patients by a pharmacy technician and the serum of patients was transferred to the Laboratory of Clinical and Toxicological Analysis (LACT) of FFOE, UFC, where the biochemical tests were performed by a pharmaceutical researcher and an intern (pharmacy student). The reference values used for laboratory parameters were those described in the 3rd Brazilian Guidelines on Dyslipidemia and Guideline of Atherosclerosis Prevention, Department of Atherosclerosis of Brazilian Society of Cardiology (2001) and in the guidelines of the Brazilian Society of Diabetes (2009). The test results were input into a suitable model, previously tested by the LACT, and given to patients during their next visit. The test used was chi-square. Data were analyzed by the chi-squared test, using SPSS 11.0, organized in tables and and discussed with reference to the literature concerning DM.

This project was approved by the Ethics and Research Committee of the UFC Hospital Complex, COMEPE N 58/06.

RESULTS

The characteristics of the patients and their mean BMI, blood pressure and laboratory test results, at the start and after 3 months' intervention, are shown in Table 1. Women were 58% of the participants in our study. The mean age of the subjects was 55.4 years and 41% were aged 51 to 64. The mean time since the DM diagnosis was less than 10 years.

Table 2 shows the risk factors for cardiovascular diseases (CVD) presented by the 101 patients at the beginning of the study. Regarding family history, 44.7% of the patients had a relative with CVD, while 59.5% had DM in the family. Hypertension was observed in 54.5% of the DM2 patients, 63.3% were sedentary, 40.6% smoked and 16.8% were alcoholic.

Slight reductions were observed in the mean values of BMI, SBP and DBP after three months. There was also a modest improvement in blood test results: reduction in fasting glycemia, TG, TC and LDL-C and increase in HDL-C. The patients were told about these results and encouraged to keep on with the treatment.

We realized that it was necessary to help the patients to improve their lifestyle: eating healthy food, doing physical exercise, stopping smoking and drinking less alcohol. They were encouraged to eat fruit and vegetables, substitute olive and other vegetable oils for animal fat and butter, eat little red meat and increase fiber intake. The physical exercise was promoted as a tool for improving glycemic control, losing weight and reducing the risk of CVD.

In relation to the drugs used, antidiabetic drugs were taken by 93.9% of the patients; insulin was used less frequently than biguanides or sulfonylureas. The second most frequently used drugs were those affecting the cardiovascular system (52%). Among drugs that interfere with the electrolyte balance (20.4%), hydrochlorothiazide was used the most. Antilipidemic drugs, such as sinvastatin and atorvastatin, were taken by 13.3%. Other drugs used were: central nervous system drugs (11.2%); non-steroidal anti-inflammatory drugs (7.1%) and gastrointestinal drugs (5.1%). It should be emphasized that 82% of patients were taking more than one drug.

We advised all of the polymedicated patients about searching for complementary medical specialties, drug intake (dose, frequency and route of administration) and so forth in order to prevent medication-related problems (MRP) due to pharmaceutical interventions. The most widely practiced form of intervention was the pharmacist-patient type (90.3%), such as planning a balanced diet and encouraging physical activity. Of these interventions, 50% were accepted and 40.3% were rejected. The medical-pharmaceutical patient interventions consisted of changes in drug class and in the time of drug administration, adding up to a total of 16% of the interventions, 9.7% of which were accepted.

Table 1. Characteristics of the patient sample and mean values of BMI, blood pressure and biochemical markers. Fortaleza, CE, June 2006 to June 2007 (n=58).

Parameters	Beginning	After 3 months
Male (%)	42.0	
Age (years)	55.4 ± 11.9	
Time of disease (years)	5.7 [0.2-22]	
SP (mmHg)	137.7 ± 19.1	132.5 ± 18.1
DP (mmHg)	82.7 ± 10.1	81.0 ± 8.6
BMI (kg/m2)	28.7 ± 4.6	28.6 ± 4.7
Glycemia (mg/dL)	183.6 ± 73.3	169.7 ± 87.3
TG (mg/dL)	182.4 ± 148.1	110 ± 54.8
TC (mg/dL)	166.6 ± 35.9	133.7 ± 45.6
HDL-C (mg/dL)	35.4 ± 21.8	39.0 ± 12.6
LDL-C (mg/dL)	99.7 ± 29.1	71.0 ± 37.0

UFC, Fortaleza, Ceará, Brazil.

Table 2. Risk factors reported by the study participants. Fortaleza, CE, June 2006 to June 2007 (n = 101).

Risk factors	n (%)
Cardiovascular disease family history	45 (44.7)
Diabetes family history	60 (59.5)
Sedentary lifestyle	64 (63.3)
Alcoholism	17 (16.8)
Smoking	41 (40.6)
Hypertension	55 (54.5)

Fortaleza, Ceará, Brazil.

DISCUSSION

In relation to gender, more women than men participated in the study, corroborating the findings of a study by Goldenberg (1996). This may reflect the fact that women care more about themselves than do men and, historically, women are responsible for the healthcare of the family. Women are more alert to early symptoms and usually seek medical support sooner than men (Couto et al., 2006).

The influence of age on the prevalence of DM and impaired glucose tolerance was described in the Multicentre Study on Diabetes Prevalence in Brazil (Malerbi, 1992), which reported that the prevalence of DM was 2.7% of the population aged 30-59 and 17.4% of those aged 60-69. A similar pattern was found in New Zealand (Joshy, 2009). The mean age of our sample was within the range showing 2.7% DM in the above-mentioned study.

The association between diabetes and hypertension in patients in our study (54.5%) is consistent with that reported by the Brazilian Health Ministry (around 50%), which recommends special care in the treatment of the two conditions in the same patient (Brasil, 2007).

Patients with DM2, even without atherosclerotic disease, have an increased risk of vascular events occurring in the future. The chance of a diabetic patient without previous cardiovascular disease suffering a cardiac event within seven years is estimated at 20% (Furtado & Polanczyk, 2007). Hypertensive patients with DM have a higher risk of developing myocardial infarction, cerebral vascular diseases, angina and amputation than hypertensive patients without DM (Lyra & Cavalcante, 2006).

Smoking was an important risk factor (40.6%) in our sample. The risk of death by CVD in male patients aged > 65 who smoke is twice that in similar non-smoking patients. Cardiovascular benefits due to cessation of smoking may be seen within one year (Christopher, 2008; Ribeiro & Lotufo, 2005).

At the beginning of our study, the patients were overweight (mean 28.7 kg/m^2) and sedentary (64%). Studies show that weight loss in obese and overweight patients reduces the incidence of many risk factors for cardiovascular disease and improves glycemic control (Furtado & Polanczyk, 2007; Wiernsperger et al., 2007). According to a global health report published in 2002 by the World Health Organization, physical inactivity causes 1.9 million deaths per year in the world. This report also showed that physical inactivity is responsible for 16% of DM (Monela-Fernandez, 2005).

The diagnosis of DM may take years and it may be diagnosed only after a complication, such as peripheral neuropathy, retinopathy, sexual impotence or a cardiac or cerebrovascular event, has occurred. In fact, when DM is diagnosed, about half the patients have already developed clinical or laboratory complications. This may be explained by the fact that hyperglycemia develops gradually and is asymptomatic in the early stages (Lyra & Cavalcante, 2006). The mean time for diagnosis in the patients of our sample was 5.7 years.

To achieve adequate metabolic control, patients must have some notion of good nutrition, and the beneficial effects of physical activity on the level of glycemia and lipid profile. They must also know about the actions of the drugs used. These factors play an important role in the improvement of patient health and this information must be imparted carefully by the health team.

A prospective epidemiological study of DM patients showed that a reduction of 0.5% in (raised) HbA_{1-c} corresponds to a reduction of 7% in the risk of myocardial infarction and 12% in the risk of general infarction, reinforcing the association between high glycemia and macro/microvascular complications of type II DM (UKPDS, 1998).

The commonest changes in the lipid profile in type II DM are hypertriglyceridemia and a low level of HDL-C.

Usually, the LDL-C level is normal. However, chronic hypertriglyceridemia leads to a higher rate of oxidation and glycation of LDL-C, increasing atherogenicity (Sociedade Brasileira de Diabetes, 2009). A cohort study of 2,473 DM patients in Canada showed a 55% prevalence of dyslipidemia within 2 years of acquiring the disease. This prevalence rose to 66% after 15 years (Harris, 2005).

As shown by Hsaio & Salmon (2000), patient education about the disease is an important component of the treatment, as the informed patient understands and contributes to the therapy, reducing the complications of diabetes and improving his/her quality of life. Such education may be provided by personal intervention, mailed materials, and workshops. The final result is adherence to the treatment.

Clifford et al. (2005) and Plácido et al. (2009) report that the involvement of the pharmacist contributes to the improvement of patients, both in blood glucose and blood pressure, regardless of the pharmacotherapeutic changes made, and also conclude that pharmaceutical care can be considered a valuable multidisciplinary component of diabetes care.

In relation to the drugs, the second most used drugs were those affecting the cardiovascular system. This is explained by the strong correlation between DM and hypertension.

The pharmaceutical interventions were carried out in order to solve the MRPs that patients presented during treatment and took into account the health problems that most concerned the patient and the possible priorities as seen by the pharmacist. Thus, in the present study, a total of 146 pharmaceutical interventions were made during pharmacotherapeutic follow-up, corroborating the results of studies by Armour et al. (2004) and Wermeille et al. (2004). In the first of those studies, a significant improvement was seen in the diabetes control and health care of patients, after monthly pharmacotherapeutic monitoring for a period of 9 months, with a total of 106 interventions, and in the second it was demonstrated that pharmaceutical guidance may be effective in the reduction and control of diabetes.

Cioffi et al. (2004) achieved a significant reduction in glycated hemoglobin, systolic and diastolic blood pressure, total cholesterol, triglycerides and microalbumin levels, in the period of 9 to 12 months over which pharmacotherapeutic follow-up took place. Thus, the reductions in the mean values of fasting glycemia, TG, TC, LDL-C, BMI, systolic and diastolic pressure and the increase in HDL-C in the present study reinforce the importance of pharmacists in the analysis of the effectiveness and security of the drugs used. They can also warn of possible cardiovascular complications, in addition to providing effective care for patients with poor glycemic control, expanding their responsibilities within the multidisciplinary team. Similar observations were made by Cani (2011) and Flores (2005).

ACKNOWLEDGEMENTS

We acknowledge the Ceará Research Aid Foundation (FUNCAP), the Center for Research in Diabetes and Endocrinometabolic Disorders and the Laboratory of Clinical and Toxicological Analysis (LACT) of the UFC.

RESUMO

Uso de marcadores bioquímicos no diabetes tipo II como parâmetro de monitorização no Acompanhamento Farmacoterapêutico de pacientes

A perda do papel modulador do endotélio pode ser um fator importante no desenvolvimento de doenças vasculares diabéticas como enfermidade cardiovascular, insuficiência cerebrovascular e vascular periférica que são evidenciadas por alterações no perfil lipídico: aumento do nível sérico de triglicérides (TG), colesterol total (lipoproteínas CT) e de baixa densidade (LDL-c), e redução no nível sérico de lipoproteína de alta densidade (HDL-c). O estudo delineado foi do tipo longitudinal de intervenção realizado no Centro de Pesquisa em Diabetes e Doenças Endócrinometabólicas da Universidade Federal do Ceará – UFC no qual foram monitorados 58 pacientes portadores de diabetes tipo II (DM2) através da análise de parâmetros bioquímicos, realizados durante duas sessões de exames laboratóriais, e do acompanhamento farmacoterapêutico mensal. O estudo teve duração de 1 ano com a aprovação pelo comitê de ética e pesquisa em seres humanos da UFC. Os dados foram analisados pelo programa estatístico SPSS versão 11.0. A hipertensão arterial esteve presente em 54,4% dos pacientes portadores de DM2, 64% eram sedentários e com sobrepeso; 44,7% disseram que tem / tinha parentes com a doença cardiovascular, e 59,5% tinham história diabéticos familiar. Os parâmetros de glicemia de jejum, TG, CT e LDL-c, pressão arterial sistólica e diastólica foram reduzidos após o monitoramento e acompanhamento dos pacientes. Este resultado reforça a importância da atuação do profissional farmacêutico na redução e controle dos índices bioquímicos, melhoria da qualidade de vida desses e prevenção de complicações.

Palavras-chave: Acompanhamento farmacoterapêutico. Diabetes Mellitus. Parâmetros bioquímicos.

REFERENCES

Abdel-Gayoum AA, Musa AS. The effect of glycemic control on serum lipids and calcium – phosphate profiles in patients with type 2 diabetes mellitus. Egypt J Biochem Mol Biol. 2009; 27(1):79-92.

Affonso FS, Cailleaux S, Pinto LFC, Tibiriçá E, Gomes MB. Níveis glicêmicos usados para o diagnóstico de Diabetes mellitus alteram a função endotelial? Estudo em rim isolado de coelhos normais. Arq Bras Endocrinol Metab. 2003;47(6):716-20.

American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2007;27(Suppl 1):S5-S10.

Armour CL, Taylor SJ, Hourihan F, Smith C, Krass I. Implementation and evaluation of Australian pharmacists diabetes care services. J Am Pharm Assoc. 2004;44(4):455-66.

Brasil. Ministério da Saúde. Departamento de Atenção Básica. Área Técnica de Diabetes e Hipertensão Arterial. Hipertensão Arterial Sistêmica (HAS) e Diabetes mellitus (DM): protocolo. Brasília (DF): Ministério da Saúde; 2007.

Cani CG. Impacto da Atenção Farmacêutica no cuidado de pacientes portadores de diabete melito tipo 2 atendidos em hospital de nível terciário de atenção. [Dissertação]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2011.

Cioffi ST, Caron MF, Kalus JS, Hill P, Buckley TE. Glycosylated Hemoglobin, cardiovascular and renal outcomes in a pharmacist-managed clinic. Ann Pharmacother. 2004;38(5):771-5.

Consenso Brasileiro de Atenção Farmacêutica: proposta. Brasília, DF: Organização Pan-Americana da Saúde; 2002. Disponível em:< http://bvsms.saude.gov.br/bvs/publicacoes/PropostaConsensoAtenfar.pdf>. Acesso em: 20 mar. 2011.

Christopher B. Impact of tobacco smoking and smoking cessation on cardiovascular risk and disease. Exp Rev Cardiovascular Ther. 2008;6(6):883-895.

Clifford RM, Davis WA, Batty KT, Davis TM, Fremantle Diabetes Study. Effect of a pharmaceutical care program on vascular risk factors in type 2 diabetes. Diabetes Care. 2005;28(4):771-6.

Couto BM, Albuquerque IL, Medeiros MAS. Uso abusivo de medicamentos por idosos em comunidade de Fortaleza – CE. Braz J Health Promot. 2006;20(1):12-6.

Flores CM. Avaliação da Atenção Farmacêutica ao paciente diabético tipo 2 no município de Ponta Grossa. [Dissertação]. Porto Alegre: Faculdade de Farmácia, Universidade Federal do Rio Grande do Sul; 2005.

Furtado MV, Polanczyk CA. Prevenção cardiovascular em pacientes com diabetes: revisão baseada em evidências. Arq Bras Endocrinol Metab. 2007;51(2):312-8.

Goldenberg P, Franco LJ, Pagliaro H, Silva RS, Santos CA. Diabetes mellitus auto-referido no município de São Paulo: prevalência e desigualdade. Cad Saúde Pública. 1996;12(1):37-45.

Harris SB, Ekoé JM, Zdanowicz Y, Webster-Bogaert S. Glycemic control and morbidity in the Canadian primary care setting (results of the diabetes in Canada evaluation study). Diabetes Res Clin Pract. 2005;70(1):90-7.

Hsaio LCD, Salmon JW. Predicting Adherence to Prescription Medication Purchase Among HMO Enrollees With Diabetes. J Manag Care Pharm. 2000;5(4):336-41.

Joshy G, Porter T, Lievre CL, Lane J, Williams M, Lawrenson R. Prevalence of diabetes in New Zealand general practice: the influence of ethnicity and social deprivation. J Epidemiol Community Health. 2009;63:386-90. DOI:10.1136/jech.2008.078873

Kirwin JL, Cunningham RJ, Sequist TD. Pharmacist recommendations to improve the quality of diabetes care: a randomized controlled trial. J Manag Care Pharm. 2010;16(2):104-13.

Kumar V, Abbas A, Fausto N, Aster J. Robbins and Cotran Pathologic Basis of Disease. 8th ed. Philadelphia: Saunders Elsevier; 2010.

Lyra R, Cavalcante N. Diabetes mellitus. Rio de Janeiro: Editora Diagraphic; 2006.

Machuca M, Fernández-Llimós F, Faus MJ. Método Dáder. Guía de seguimiento Fármacoterapéutico. Grupo de Investigación en Atención Famacêutica. Granada: Universidade de Granada; 2003. Disponível em: http://www.atencionfarmaceutica-ugr.es/index.php?option=com_remository&Itemid=62&func=select&id=11

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

Monela-Fernandes CA, Nardo Junior NN, Tasca RS, Pelloso SM, Cuman RKN. A importância da associação de dieta e de atividade física na prevenção e controle do diabetes mellitus tipo 2. Acta Sci Health Sci 2005;27(2):195-205.

Plácido VB, Fernandes, LPS, Guarido CF. Contribuição da Atenção Farmacêutica para pacientes portadores de diabetes atendidos no ambulatório de endocrinologia da UNIMAR. Rev Bras Farm. 2009;90(3):258-263.

Planas LG, Kimberlin CL, Segal R, Brushwood DB, Hepler CD, Schlenker BR. A pharmacist model of perceived responsibility for drug therapy outcomes. Soc Sci Med. 2005;60(10):2393-2403.

Ribeiro RC, Lotufo PA. Hipertensão Arterial: Diagnóstico e tratamento. São Paulo: Sarvier; 2005.

Sociedade Brasileira de Diabetes. Diretrizes da sociedade brasileira de diabetes [Internet]. 2009 [citado 2011 out 22]. Disponível em: http://www.lojavirtualsbd.com.br/ >.

Sociedade Brasileira de Cardiologia. III Diretrizes Brasileiras Sobre Dislipidemias e Diretriz de Prevenção da Aterosclerose do Departamento de Aterosclerose da Sociedade Brasileira de Cardiologia. Arq Bras Cardiol. 2001;77(Suppl 3):1-48.

Torre, JB. Como abordar a dislipidemia da pessoa com diabetes tipo 2. Revista Port Clin Geral. 2005;21:606-16.

UK Prospective Diabetes Study Group (UKPDS). Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes. Lancet. 1998; 12;352(9131):854-65.

Vanhoutte PM. Regeneration of the endothelium in vascular injury. Cardiovasc Drugs Ther. 2010;24(4):299-303.

Vriese AS, Verbeuren TJ, Voorde JV, Lameire NH, Vanhoutte PM. Endothelial dysfunction in diabetes. Br J Pharmacol. 2000;130(5):963-74.

Wermeille J, Bennie M, Brown I, McKnight J. Pharmaceutical care model for patients with type 2 diabetes: Integration of the community pharmacist into the diabetes team - a pilot study. Pharm World Sci. 2004;26(1):18-25.

Wiernsperger N, Nivoit P, Bouskela E. Microcirculation in obesity: an unexplored domain. An Acad Bras Ciênc. 2007;79(4):617-38.

Recebido em 18 de outubro de 2011.

Aceito para publicação em 1 de fevereiro de 2012.