

Full Length Research paper

Impact of medication therapy management (MTM) program on the clinical outcomes and the quality of life

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To evaluate the impact of a medication therapy management (MTM) program on the clinical outcomes and the quality of life (QoL) of a group of elderly patients with type 2 diabetes mellitus (DM). The study was conducted in a community pharmacy in Aracaju, Brazil, from February to November 2009. A quasi-experimental, longitudinal, prospective study was conducted by intervention. The group patients received medication therapy management from a clinical pharmacist. A sample of convenience was obtained for patients of both genders aged from 60 to 75 years. Monthly visits were scheduled over 10 months. At these consultations, sociodemographic, clinical data were obtained. QoL assessment was conducted using a generic instrument—the *Medical Outcomes Studies 36-item Short Form Survey (SF-36®)*. In total, 34 completed the study. The mean age of the patients was 65.9 (4.7) years. In total, 117 DRPs were identified. Patients' baseline and final evaluation measures for glycosylated hemoglobin, capillary blood glucose, blood pressure, and waist circumference were significantly different ($p < 0.05$). The domains of QoL assessed by the SF-36® also show s significant differences between patients' baseline and final evaluation scores. The co-responsibility and active participation on the part of the elderly may have helped pharmacotherapy achieve its clinical and humanistic aims.

Key words: Medication therapy management, diabetes mellitus, elderly.

INTRODUCTION

Diabetes mellitus (DM) is a chronic health condition and relevant risk factor to cardiovascular diseases, especially in elderly (Wermeille et al., 2004). In practice, the treatments involve counseling on behaviour change by family physicians and primary care teams, and referral to exercise specialists and registered dieticians and drug therapy (Assunção et al., 2002; Chatterjee et al., 2012). Management of elderly patients with DM is more difficult because of certain inherent characteristics of this age group, such as the presence of comorbidities, pathophysiological changes associated with old age, and

cognition loss, resulting in polypharmacy.

Polypharmacy increase the susceptibility to adverse drug reactions in elderly patients and they find it difficult to understand the disease and its treatment (Vinks et al., 2009; Cranor and Christensen, 2003; Paolisso, 2010). Taken together, these circumstances often produce poor control of blood glucose levels and a high incidence of drug-related problems (DRPs) that negatively affect the quality of life (QoL) of these patients (Cranor and Christensen, 2003; Fornos et al., 2006). Growing evidence demonstrates that models of diabetes care which involve pharmacists are able to contribute to improved patient outcomes (Armor et al., 2009).

Since 1990s, pharmaceutical practice has been moving from a technical to a social paradigm, with services becoming patient-focused (Li, 2003). The practice of

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pharmaceutical care has been defined by Hepler and Strand (1990) as “the responsible provision of pharmacotherapy, with the goal of achieving defined therapeutic outcomes in health and the improvement of quality of life of the population. In last years, pharmaceutical care services had a logical extension called medication therapy management (MTM) that is defined as “the optimization therapeutic outcomes through improved medication use” and “reduce the risk of adverse events, including adverse drug reactions (de Oliveira et al., 2010). Although there were some studies about MTM in Brazil, this practice is unusual in community pharmacies. Thus, the aim of this study was to develop and implement a pilot community pharmacy MTM program and evaluate its impact on the clinical outcomes and the QoL of a group of elderly patients with type 2 DM.

METHODS

Design and study site

This study was a prospective trial pilot (single group) study conducted by intervention in a single community pharmacy in Aracaju, Brazil, from February to November 2009. Study approval was obtained from the Ethics Committee in Research of the University Hospital of the Federal University of Sergipe (Protocol n° 0137.0.107.000-07).

Patient selection

We recruited a convenience sample through referrals of eligible patients from the University Hospital clinic. This comprised patients of both genders aged from 60 to 75 years. Included were patients who were eligible if they had a confirmed diagnosis of type 2 DM according to the American Diabetes Association (ADA, 2005) and were taking antidiabetic medications. We excluded patients unable to attend scheduled visits, and patients who missed more than 3 consecutive visits (Al Mazroui et al., 2009; Garção and Cabrita, 2002). The target population was recruited over approximately 2 months. All patients agreeing to participate in the study signed a consent form in accordance with Resolution CNS n° 196/96.

The MTM program

The MTM program comprised monthly visits scheduled over 10 months; each lasted 40–60 min. The 9 steps of good practice of MTM were followed: (1) establishment of a pharmacist–patient therapeutic relationship; (2) collection, analysis, and interpretation of relevant information; (3) identification and classification of DRPs;

(4) establishment of drug therapy goals with the patient; (5) determination of viable drug therapy alternatives; (6) selection of the best drug therapy alternative; (7) developing a plan of care; (8) implementation of an individual plan and monitoring of the same; and (9) follow-up (Hepler and Strand, 1990). For the identification of DRPs, the *Pharmacists' Work-Up of Drug Therapy* model was used. This classifies DRPs into Necessity (DRPs 1 and 2), Effectiveness (DRPs 3 and 4), Safety (DRPs 5 and 6), and Compliance (DRPs 7) (Strand et al., 2004). At this stage of the process, the description of DRPs was based on information provided by the patients, for example, the problem or condition of the patient, the medication(s) involved, and the association of the medication(s) with the patient's

problem. This identification requires clinical skills, a thorough knowledge of the patient as a person, as well as knowledge of the drug and the illness, good communication skills, and a systematic care process (Strand et al., 2004).

During the MTM program, educational interventions aimed at personal transformation were conducted and the patient's “critical awareness” was encouraged. These were inspired by the approach of participatory social orientation proposed by Freire (1983). Educational measures included oral and written instructions (with folders and slides). Patients were informed about DM and its complications; appropriate drug dosages, side effects, and medication storage. Changes in lifestyle particularly with regard to diet and physical exercise were stressed, as was the importance of the management of the signs and symptoms of DM through self-monitoring (Al Mazroui et al., 2009; American Diabetes Association, 1996). These educational interventions were reinforced at each encounter with the patient. Moreover, changes in pharmacotherapy were discussed with the patients and physicians when necessary. All such changes were suggested in view of the recommendations of the American Diabetes Association (ADA, 2005). It is important to highlight that pharmacists alone could not alter pharmacotherapy: patients were referred to their physician for therapy adjustment.

A detailed assessment of the pharmacotherapy was carried out after each interview, looking at the characteristics of each of the drugs in depth. This assessment was always made with regard to the characteristics and problems of each individual patient. Pharmacists assessed the safety and effectiveness of both drugs and lifestyle, coming to the conclusion of whether or not one or more DRPs had arisen or were likely to arise. Then a strategy was determined to solve the problem (Fornos et al., 2006).

Data collection

At each of the consultations, sociodemographic, clinical, and pharmacotherapeutic data were obtained. This included data on levels of capillary blood glucose, and blood pressure (BP), and measurements of Body Mass Index (BMI) and waist circumference (Sociedade Brasileira de Diabetes. Diretrizes da Sociedade Brasileira de Diabetes, 2007; Lipschitz, 1994; World Health Organization, 1998). Therefore, glycosylated hemoglobin (HbA1c) was obtained to patients at baseline (first interview) and at the end of the study (10-months). QoL evaluation was performed using a generic instrument—the *Medical Outcomes Studies 36-item Short Form* (SF-36®; Portuguese version) Ciconelli et al., (1999). This is administered twice at the start and end of the 10-month period of the program (Freire P 1983). This instrument has 8 domains, which assess functional capacity, physical aspects, pain, general state of health, vitality, social, emotional, and mental health aspects. Each domain was measured on a scale of 0 to 100, with scores closer to 100 representing a better QoL. In this study, the concept of QoL was defined like a multidimensional construct, which comprises physical, mental, and social aspects as well as the perception of the general wellbeing of the individual (Hepler and Strand, 1990).

Statistical analysis

Data collected were double entered and then analyzed using the BioEstat® database (Version 5.0, National Council for Scientific and Technological Development [CNPq], Brazil). Statistical analyses were conducted: these included frequency, mean, and standard deviation (SD).

Student's paired *t* test was used for continuous normally distributed variables in clinical and humanistic outcomes between baseline and end of study and *p* < 0.05 was used to indicate a significant difference. The Cohen's *d* test was applied for

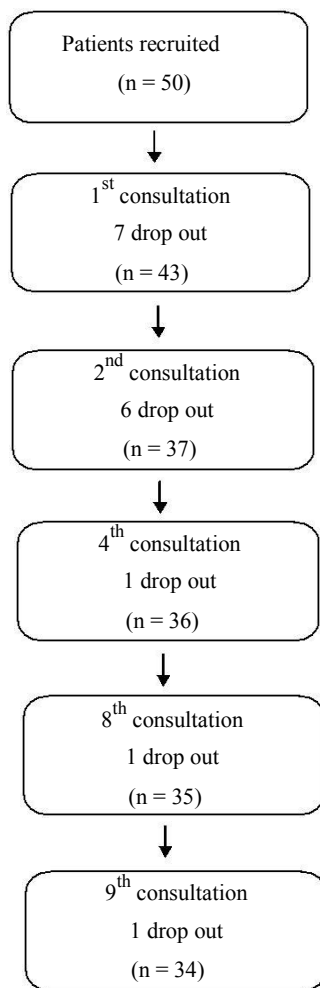


Figure 1. Patient abandonment during a community pharmacy study in Aracaju, Brazil, February to November 2009.

measuring significant effect size for all variables of QoL.

RESULTS

In total, 50 patients were invited to participate in the MTM program pilot, and of these, 34 completed the study (drop out rate = 32%). The reasons reported for dropping out were: lack of interest (50%; n = 8), loss of contact (18.75%; n = 3), moving to another city (12.5%; n = 2), limited mobility (12.5%; n = 2), and hospitalization (6.25%; n = 1) (Figure 1).

The mean patient age was 66 years, and approximately half were female and had not finished high school. The median of DM diagnosis time was 12 years. Most of elderly (76.5%, n = 26) were retired and had access to the public (44.1%, n = 15) and private (41.9%, n = 14) health care service. Their medications mainly were

Table 1. Sociodemographic characteristics of elderly patients (n = 34) attending at a community pharmacy in Aracaju, Brazil from February to November 2009.

Age (years)*	65.9 (4.7) *
Gender	% (n)
Female	52.9 (18)
Male	47.1 (16)
Marital status	
Married	73.5 (25)
Single	11.7 (4)
Divorced	8.8 (3)
Widow	5.9 (2)
Level of education	
Literate	5.9 (2)
Elementary school	50.0 (17)
High School	23.5 (8)
College	20.6 (7)
Profession	
Retired	76.5 (26)
Homemaker	11.8 (n = 4)
Employment relationship	5.9 (n = 2)
Others	5.9 (2)
Access to health service	
Public	44.1 (15)
Private	41.9 (14)
Both	14.7 (5)
Diagnostic Time	
	13.5 (9.9)*
Up to 10 years	35.3 (n = 12)
10 to 20 years	35.3 (n = 12)
>20 years	29.4 (n = 10)

Risk Factors for Diabetes

Hypertension ^a	79.4 (n = 27)
Family history	70.9 (n = 24)
Increased waist circumference	58.8 (n = 20)
Dyslipidemia	47.0 (n = 16)
Sedentarism	47.0 (n = 16)
Neuropathy	8.8 (n = 3)
Nephropathy	2.9 (n = 1)
Retinopathy	2.9 (n = 1)
Tobacco smoking	2.9 (n = 1)

* Mean (standard deviation (SD)) ; ^a BP greater than 140/90mmHg

acquired in Farmácia Popular do Brasil for low cost. Regarding risk factors, a majority had family history of DM, hypertension and, central obesity (Table 1).

Table 2. Drug-related problems (DRPs) identified (n = 117) and resolved in elderly patients at a community pharmacy in Aracaju Brazil, according to the Pharmacist Workup Drug Therapy classification (February to November 2009).

Necessities related to the medications	Type of DRP	DRP Real	DRP Potential	Total n (%)
		Identified (Resolved)	Identified (Resolved)	
Indication	1	6(5)	5(4)	25 (21.4)
	2	13(10)	1(1)	
Effectiveness	3	10(8)	0(0)	40 (34.2)
	4	25(24)	5(3)	
Safety	5	9(8)	5(5)	22 (18.8)
	6	6(6)	2(2)	
Compliance	7	25(20)	5(5)	30 (25.6)
Total		94(81)	23(20)	117

Table 3. Clinical parameters in the baseline and final evaluation of elderly patients (n = 34) at a community pharmacy in Aracaju Brazil, February to November 2009.

Clinical parameter	Baseline mean (SD)	Final mean (SD)	p*
Glycosylated hemoglobin (%)	8.9(2.1)	6.9(0.9)	< 0.001*
Capillary glucose (mg/dL)	230.9(103.3)	176.4(76.5)	0.005*
Systolic BP (mmHg)	148.5 (19.7)	128.9(14.7)	< 0.001*
Diastolic BP (mmHg)	83.1(12.1)	76.1(9.8)	< 0.001*
BMI (kg.m ⁻²)	27.9 (3.8)	28.1(4.0)	0.089
Waist measurement (cm)			
Men	98.3(10.8)	96.6(10.4)	0.003*
Women	100.3 (9.4)	96.3(13.9)	0.036*

*Statistical significance: p < 0.05; BP = blood pressure; BMI = body mass index.

In this study, the median of medication used was 6, and 28 patients (82%) used 5 or more medications, resulting in polypharmacy. The most widely used medications were for the cardiovascular system (41.9%, n = 89), specifically inhibitors of the renin-angiotensin system (10.8%, n = 23) and medications which regulate the alimentary tract and metabolism (33.9%, n = 72). Medication mainly used in the treatment of DM comprised 32% (n = 68). The most commonly used oral antidiabetics were metformin, and glibenclamide.

In total, 117 DRPs were identified, with a mean of 3.4 (1.9) DRPs per patient. The largest DRP category was Effectiveness (Table 2). Of the total DRPs detected, 94 (80%) were actual and 23 (20%) potential. During patient follow-ups, 101 DRPs (86.3%) were resolved, with 81 actual and 20 potential DRPs.

A total of 500 drug therapy interventions were performed and documented. These included advice to the doctor to cease medications causing adverse reactions (23%), adjusting medication intervals (15%), explanation of the importance of improving adherence to

treatment, (11%), request to the doctor to increase the dose to improve the effectiveness of pharmacotherapy (10%) and information to seniors on managing self-medication (6%). Furthermore, 48.5% of the resolved DRPs required decisions from physicians. Thus, a cooperative working relationship between the research pharmacist, doctors and patients were key to solving and preventing DRPs in pharmacy. As a result, physicians accepted all recommendation for changes to the medication regimen.

In addition, 360 educational interventions were documented by the pharmacist. The most frequent were: advice on changes in lifestyle (14%), explanations about the importance of storage of medicines (12%), counseling on the disease (10%) and clarification of concerns about administration of medications (dose, time, duration of treatment and route of administration) (10%).

At the end of the MTM program the patients' mean HbA1c decreased 2.0%, a significant difference between the baseline and final evaluation (Table 3). Of these 73.5% (n = 25) patients achieved the target HbA1c

Table 4. SF36® Quality of life domain scores at baseline and final evaluation for 34 elderly patients at a community pharmacy in Aracaju, Brazil from February to November 2009.

Domain	Baseline mean (SD)	Final evaluation mean (SD)	p* ^h
Functional capacity	68.8 (26.2)	74.5 (23.8)	0.022*
Physical aspects	61.7 (42.3)	78.7 (38.5)	0.003*
Pain	57.3 (26.3)	71.3 (32.1)	0.003*
General state of health	66.6 (17.2)	71.3 (20.1)	0.026*
Vitality	65.0 (16.6)	76.9 (19.9)	<0.001*
Social aspects	82.7 (26.0)	86.7 (22.4)	0.235
Emotional aspects	67.6 (42.2)	78.4 (39.2)	0.127
Mental health	66.8 (21.6)	78.6 (18.2)	<0.001*

*Statistical significance: $p < 0.05$.

of <7% (Wubben and Vivian, 2008). There were also significant improvements in mean capillary blood glucose measurements, BP (systolic and diastolic), and waist circumference, before and after the MTM program. It is noteworthy that 56% ($n = 19$) of the patients achieved capillary blood glucose control (<200 mg/dL), 62% ($n = 21$) exhibited BP improvement, and 26.5% ($n = 9$) achieved waist circumference control (for men <102 cm and for women <88 cm) (Ferreira et al. 2006; Funnell and Brown 2008). For BMI, a baseline of 53% ($n = 18$) of the elderly were classified as overweight and 47% ($n = 16$) as eutrophic, with no statistically significant difference ($p < 0.05$) at the end of the study. Changes in clinical parameters are shown in Table 3.

The SF-36® scores for each domain are shown in Table 4. A significant difference was observed between the baseline and final evaluation in the domains of functional capacity, physical aspects, pain, general state of health, vitality, and mental health. For the domains of social and emotional aspects, mean scores increased but the difference was not statistically significant. Regarding the magnitude of the effect size showed an intermediate effect for domains of vitality ($d = 0.6494$; $r = 0.3088$) and mental health ($d = 0.5908$; $r = 0.2833$).

DISCUSSION

In Brazil, few Pharmaceutical care studies evaluated the improvements in clinical and humanistic outcomes. These studies usually were carried out with a small number of patients ($n=30-64$), on blood pressure control and in communities, pharmacies and ambulatories (Castro and Correr, 2007; Lyra et al., 2007). Then, DM MTM pilot program successfully implemented, representing an innovative approach in health care services delivered in community pharmacy in Brazil and may be extended more broadly.

The socio-demographic characteristics, type of access to health services, levels of polypharmacy, and risk

factors presented by the elderly in this program suggest that the study sample was typical of an elderly population of type 2 diabetes patients (Wermeille et al., 2004; Cranor and Christensen, 2003; Al Mazroui et al., 2009; Castro and Correr, 2007; Cranor et al., 2003; Clifford et al., 2005). In this study, the proportion of patients who experienced some form of DRPs is similar to the findings of Rao et al. (2007) but is higher than values reported in other studies (Doucette et al., 2005; Paulino et al., 2004). One reason for this high rate in our study may have been the presence of a pharmacist qualified to identify and resolve DRPs (Rao et al., 2007). In this study, the mean DRP value per patient was close to the values found by Fornos et al. (2006) and Roozendaal and Krass (2009). These results demonstrate the high prevalence of DRPs in elderly patients with type 2 DM, and this emphasizes the need for pharmacotherapeutic follow-up of these patients (Zhou et al., 2009).

Finally, the category of DRPs most commonly found in this study - effectiveness - corroborates data found by Fornos et al. (2006) but differs from most previous studies (Wermeille et al., 2004; Roozendaal and Krass, 2009; Zhou et al., 2009). This discrepancy may be partially explained by the lack of standardization in DRP classification. Although the elderly patients had a mean of 14 years of type 2 DM diagnosis, they still used mainly hypoglycemic first choice for the treatment of DM, such as metformin and glibenclamide (Sociedade Brasileira de Diabetes, Diretrizes da Sociedade Brasileira de Diabetes, 2007). Probably, the clinical inertia has been one of the factors that influenced in a greater frequency of DRPs effectiveness.

The positive impact of pharmaceutical interventions on the values of most of the clinical variables was an important result of this study. For HbA1c, the reduction of 2.0% was higher than that seen in other recent research and the same is true for reductions in BP and capillary blood glucose seen in this study (Wermeille et al., 2004; Fornos et al., 2006; Al Mazroui et al., 2009; Clifford et al., 2005).

Furthermore, the large proportion of patients who achieved the clinical goals for DM shows that pharmaceutical interventions can provide clinically relevant differences for these patients (American Diabetes Association, 2005). According to the UK Prospective Diabetes Study (1998), a reduction of at least 0.5% in HbA1c levels leads to an estimated 18.5% reduction in microvascular complications and a 10.5% lowering of DM-related mortality. Regarding BP, the difference of 10/5 mmHg seen in the present study would lead to a reduction of 44% in the risk of stroke, a 37% lowering of the risk of microvascular complications, and a 32% reduction in DM-related mortality (UK Prospective Diabetes Study Group, 1998).

In the present study, BMI was the only clinical variable which showed no significant difference before and after intervention. This may be because lack of power this pilot study and compared to younger patients, the elderly are less likely or less capable of performing physical activities that minimize weight gain (Abbatecola et al., 2008). It is also worth highlighting other healthcare professionals such as doctors, nutritionists, and physical trainers are needed to support lifestyle change in elderly patients (Ahrens et al., 2003; Guimarães and Ciolac, 2004).

Although there was reduction in the clinical parameter of waist circumference, measurements did not reach the cutoff recommended by the World Health Organization (WHO, 1998). However, while waist circumference is one of the most widely used indicators for measuring the centralized distribution of adipose tissue in individual and collective assessments (WHO, 1995) differences in body composition between different age and racial groups hinder the development of universal cutoff points (Ferreira et al., 2006).

In this study, the inclusion of educational interventions was considered fundamental to the success of the MTM program. As part of this approach, it was important for the elderly to assume an active role in their educational development. Similar findings were reported in a recent systematic review of 4 studies; the review showed a significant improvement in pharmacotherapeutic outcomes amongst elderly patients who used an individualized education provided by a pharmacist (George et al., 2008). According to the National Standards for Diabetes Self-Management Education (2008) (Funnell and Brown, 2008) there are basic guiding principles for the development of these interventions, and this resource also discusses the need for continued support to sustain the progress made by participants of educational programs, stating that education about DM is effective in improving both patients' clinical outcomes and QoL.

In this study, improvements in patient QoL scores were probably the result of the effectiveness of educational interventions, and of greater patient contact with their clinical pharmacists. The results from the SF-36 analysis are similar to those found by Elnour et al. (2008) and Al

Mazrouiu et al. (2009). These data also support the use of this generic QoL instrument for the evaluation of the impact of education programs for DM patients (Brown et al., 2000). For the social aspects and emotional aspects domains, improvement was observed, but the differences were not statistically significant. In the case of social aspects it was noted that there were high baseline scores, reflecting a possible ceiling effect in this domain. Polypharmacy, a characteristic of the sample studied, may have contributed to the lack of positive impact on the emotional aspects domain scores (Lyra et al., 2007). The results of effect size (Cohen's *d*) and the improvement of the physical aspect, pain, vitality and mental state of patients suggest that the changes associated with the program have put to practical significance. Despite the results show the improvement in functional capacity and general health status of patients, we could not prove the influence of the program due to the small magnitude of size effect.

Limitations

In this study, the dropout rate was relatively high. However, the reported reasons for this were consistent with other studies (Garção and Cabrita, 2002; Lee et al., 2006). According to Martinez-Perez (2004) the abandonment of monitoring programs reflects poor patient knowledge about their illness. In this study, elderly patients' lack of experience in receiving care from pharmacists could have been the main reason for their drop out of the service. MTM program abandonment rates and their causes are important indicators and need to be taken into account when developing appropriate strategies for the design of the studies in this area.

In this pilot, 10 months was considered an adequate evaluation period. However, since pilot studies like this one cannot be used for more than hypothesis generation, new long-term studies are now necessary to validate the clinical and humanistic benefits demonstrated in this study. The limitations of a pilot program (1 research site and the small sample size) should be considered when developing future studies; more patients and pharmacies are needed. Moreover, the inclusion of a control group and the evaluation of the economic impact of this service should be included in future research to increase the robustness and reliability of the results.

Regarding QoL assessment, although the SF-36 has been frequently used in MTM research, several studies have criticized the lack of specificity and sensitivity of this instrument for this function (Billups et al., 2000; Malone et al., 2001; Kheir et al., 2004). Thus the development of an instrument designed to specifically measure the impact on QoL as a result of MTM services could optimize the detection and evaluation of positive results from this program (Schultz, 2001; Pickard and Hung,

2006).

Conclusion

This pilot study at a community pharmacy in Brazil demonstrated that MTM interventions coupled with an educational program led to improvements QoL scores and clinical parameters for a group of elderly patients. From the results obtained it could be suggested that community pharmacists may play a valuable role in health care provide to patients with type 2 diabetes by focusing on optimizing the benefits of pharmacotherapy. Future studies are needed for to enhance the methodology used, including the following: evaluation of MTM structure and process; construction, validation and standardization of research tools; correct randomization; description of the sample size; impact of educational interventions; and evaluation of economic results.

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