Drug Therapy Monitoring in Patients with Type 2 Diabetes and Hypertension

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Abstract: The aim of this paper is to detect, prevent and resolve DRP (drug-related problems) and NOM (negative outcomes associated with medication) in hospitalized patients with DM2 (type 2 diabetes) with HTN (hypertension) in a tertiary care clinic. Descriptive cross-sectional interventional study is used. DTM (drug therapy monitoring) was conducted in 73 patients using data obtained from clinical histories and interviews. NOM were detected based on symptoms and laboratory test results. The statistical significance was 0.05. It can be found that 23 DRP were detected, primarily in the category “likelihood of adverse effects” (30.43%) causing NOM in the “non-quantitative safety problem” category. The NOM detected were related to safety (62%), effectiveness (24.5%) and necessity (13.5%). Of the 68.57% of pharmacist interventions accepted, 48.57% were resolved and 20% were not resolved. A simple linear correlation ($r = -0.34$) analysis indicated a weak association between patient age and severity of NOM. DTM made it possible to detect suspected DRP and NOM, which were then prevented or resolved, improving the control of HTN and DM2 and helping ensure better drug therapy outcomes for patients.

Key words: Drug therapy monitoring, type 2 diabetes mellitus, hypertension, pharmacist intervention.

1. Introduction

Diabetes is a very common metabolic disorder, an extremely serious disease and major cause of disability and death. Pharmacists play a key role in DTM (drug therapy monitoring) by detecting, preventing and resolving NOM (negative outcomes associated with medication). The Dader method is a key tool in this process [1]. Once DRP (drug-related problems) and NOM have been detected, pharmacists conduct the interventions necessary to resolve them and then evaluate the outcome [2].

According to the WHO (World Health Organization), more than 220 million people worldwide had diabetes in 2010 (a 46% increase since 2000), and it is estimated that this will increase to 300 million by 2025 [3].

The global prevalence of diabetes among adults over

18 years of age was 9% in 2014 [4]. In 2012, an estimated 1.5 million deaths were directly caused by DM2 (type 2 diabetes) [5]. More than 80% of DM2 deaths occur in low and middle-income countries. WHO projects that diabetes will be the seventh leading cause of death in 2030 [6]. A healthy diet, regular physical activity, maintaining a healthy body weight and avoiding tobacco use can prevent or delay DM2 onset [7].

DM2 is the most common form of diabetes, representing 80~90% of cases, and a serious health problem in both developed and developing countries [8]. Most cases of DM2 occur in the context of metabolic syndrome, a combination of DM2, HTN (hypertension), elevated cholesterol, triglycerides and/or uric acid, and obesity [8].

In addition to its high prevalence, DM2 is responsible for high morbidity and mortality rates. The associated cost of the disease is also high, primarily

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because of its chronic complications. There is also a high incidence of DM2-related NOM. The total cost of those NOM can be as high as 177.4 billion dollars per year [9].

According to Orozco [10], approximately a quarter of the world population is hypertensive and the prevalence of DM2 in the adult population is around 6~8%.

Pharmacists are drug experts with the opportunity to see chronic patients five times as frequently as other health professionals. Because of this higher degree of accessibility, they can be valuable members of multidisciplinary teams responsible for the care of chronic patients [11].

Pharmaceutical care, specifically DTM (where pharmacists are responsible for patients' drug-related needs), could help deliver better health outcomes for DM2 patients with HTN through the detection, prevention and resolution of NOM [12].

In light of all the above, tertiary care clinics are now focusing their efforts on reducing the impact of these complex diseases. A proposal was, therefore, made to implement a DTM service for patients with DM2 and HTN. The primary aim of this study was to detect, prevent and resolve DRP and NOM in hospitalized patients with DM2 and HTN in a tertiary care clinic using the Dader method.

2. Methods

This descriptive interventional cross-sectional prospective study was conducted between November 2012 and January 2013 in a tertiary care clinic in Barranquilla, Colombia. A simple randomized method was used to draw a sample from a population of patients diagnosed with DM2 with HTN. For an accuracy of 5% and confidence level of 95%, a sample of 73 patients was required. Hospitalized patients of both sexes aged 18 or over with the required diagnosis were asked to participate and those who agreed signed an informed consent. The Dader method of drug therapy monitoring defined by the Third Consensus of

Granada was used [13]. A simple randomized sample was drawn from patients who met the inclusion criteria. The study was conducted in accordance with the guidelines set out in the Declaration of Helsinki [14].

The first stage of the study consisted of talking to the participants, providing a clear, precise and concise explanation of the study aim and duration and how much time each participant would need to devote to the study. The study participants were also given details of the study procedures and it was stressed that they were free to continue or withdraw from the study whenever they deemed appropriate, and that the information obtained would be kept confidential. Finally, the participants were told that they would need to sign an informed consent form as a means to protect their rights as patients.

Data were obtained and measured in the following stages:

(1) Stage I: detect DRP and NOM in patients treated for DM2 with HTN: the clinical histories of patients diagnosed with both conditions, based on clinical laboratory results (blood sugar levels) and measurements (blood pressure), were reviewed. Patients were interviewed to collect data on signs, symptoms and prescribed medications;

(2) Stage II: determine the number of drugs linked to the appearance of DRP and NOM: each patient's current health status was determined. If the presence of a NOM was confirmed, the drug involved was identified. In this way, the prescribed medications responsible for NOM could be determined;

(3) Stage III: evaluate the acceptance rate of pharmacist interventions and degree of resolution of NOM: once the NOM were detected, the pharmacist intervention was sent in writing to the healthcare team (doctor/nurse/patient) who decided whether or not to accept it. Patient follow-up was then conducted to determine if the intervention was accepted and whether or not the health problem was resolved [15].

In cases of non-quantitative safety problems, the

algorithm defined by Naranjo et al. [15] was used to determine whether or not the adverse reactions could be attributed to the drugs [16].

Once NOM were detected, pharmacist interventions were conducted to resolve or prevent health problems in the patients. The interventions were divided into two categories:

- (1) pharmacist-patient interventions;
- (2) pharmacist-patient-doctor interventions.

The tools used to gather data were those validated by the Pharmaceutical Care Research Group of the University of Granada, Spain, which have been used to conduct drug therapy monitoring studies internationally.

The Student's *t*-test was used to compare means of the quantitative variables (age, average hospital stay, duration of monitoring, use of drugs). For normally distributed variables, the Chi-square test was used to perform non-parametric tests (sex, age, etc.).

3. Results

The 73 patients were interviewed (54.8% male, 45.2% female). 68.5% of participants were over 60 years of age, and 24.66% were between 45 and 59. The most prevalent diagnosis was HTN (59%), followed by DM2 with HTN (36%) and DM2 only (5%) (Table 1).

Table 2 shows that the most frequent DRP were in the "likelihood of adverse effects" (32.43%),

"non-adherence" (16.22%) and "personal characteristics" (13.51%) categories. More NOM were detected among males (64.87%) than females (35.13%). The NOM identified most frequently were non-quantitative safety problems (62%), followed by NOM related to necessity (untreated health problems (13.5%)) and quantitative ineffectiveness (13.5%), and finally non-quantitative ineffectiveness (11%). With regard to the severity of safety-related NOM, 30.43% were moderate in both men and women and 21.74% were severe in men (Table 3).

Table 4 shows the number of drugs administered to 29 of the 73 patients in the study who had NOM, with 3 patients who had been prescribed 11 drugs. The therapeutic groups affected by the drugs were the alimentary tract and metabolism, and blood and blood forming organs, both with 30%.

Table 5 shows the drugs involved in the appearance of NOM, including losartan (27%) followed by furosemide (19%). The most frequent NOM were non-quantitative safety problems (62.16%), followed by quantitative ineffectiveness and untreated health problems (both 13.5%).

Table 6 shows the outcomes of the pharmacist interventions. 35 pharmacist interventions were conducted as a result of the suspected DRP and NOM detected. 68.57% were accepted and 31.43% were not accepted.

Table 1 Sex, age and clinical diagnosis of patients included in the drug therapy monitoring trial.

Items	Sex				Total	
	Male		Female			
	Number	Percentage (%)	Number	Percentage (%)		
Sample size	73					100
Age (years) mean±SD	63.3 ± 13.93		69.66 ± 15.01			
Age						
≥ 60 years	50	26	24	32.88		68.5
45~59 years	18	11	7	9.59		24.66
25~44 years	5	3	2	2.74		6.85
Total	73	40	33	45.20		100
Clinical diagnosis						
HTN	I10		43			59
DM2 and HTN	E11/I10		26			36
DM2	E11		4			5

Source: data obtained from the initial interview and clinical histories.

Table 2 Types of DRP (drug-related problems) and NOM (negative outcomes associated with medication) by sex y category.

Types of DRP	Men	Women	Total	Percentage (%)
Likelihood of adverse effects	7	5	12	32.43
Non-adherence	6	0	6	16.22
Personal characteristics	4	1	5	13.51
Insufficiently treated health problem	3	2	5	13.51
Inappropriate dose, dosage regimen and/or duration	1	3	4	10.81
Interactions	1	2	3	8.11
Incorrect administration of the drug	1	1	2	5.41
Total	23	14	37	100
Sex	Patients with NOM (<i>n</i> = 28)	No. of NOM (<i>n</i> = 9)	Total NOM <i>n</i> = 37 (%)	
	13	1	13 (35.14)	
Male	4	2	8 (21.62)	
	1	3	3 (8.11)	
Subtotal	17	6	24 (64.87)	
Female	9	1	9 (24.32)	
	2	2	4 (10.81)	
Subtotal	11	3	13 (35.13)	
Total	28	9	37 (100)	
Category	Types of NOM	<i>n</i> = 37	Percentage (%)	
Necessity	Untreated health problem	5	13.5	
	Effect of unnecessary medicine	-	-	
Effectiveness	Quantitative ineffectiveness	5	13.5	
	Non-quantitative ineffectiveness	4	11	
Safety	Quantitative safety problem	-	-	
	Non-quantitative safety problem	23	62	
Total		37	100	

Table 3 Types of DRP (drug-related problems) by severity of safety problems.

NOM	Severity <i>n</i> = 23	Male		Female		Total
		Number	Percentage (%)	Number	Percentage (%)	
NQSP	Moderate	7	30.43	7	30.43	60.86
NQSP	Severe	5	21.74	-	-	21.74
NQSP	Mild	3	13.04	1	4.35	17.39
Total		15	65.21	8	34.78	100.00

Correlation coefficient $r = -0.34$

NQSP: non-quantitative safety problem;

Source: data obtained during drug therapy monitoring process.

Table 4 Number of drugs prescribed to patients with DM2 and HTN, and therapeutic groups affected.

No. of drugs prescribed per patient	No. of patients (<i>n</i> = 29)		Total drugs prescribed (<i>n</i> = 204)	Percentage (%)
8	8		64	31
7	5		35	17
11	3		33	16
9	3		27	13
6	4		24	12
4	2		8	4
3	2		6	3
2	1		2	3
5	1		5	2
2	1		2	1
Total	29		204	100
Student's <i>t</i> -test 7 ± 0.88 (6.11~7.88)				
Therapeutic group	Necessity	Effectiveness	Safety	Percentage (%)
A: alimentary tract and metabolism	- ^a	- ^a	11	11(30)
B: blood and blood forming organs	5	- ^a	6	11(30)
C: cardiovascular system	- ^a	9	- ^a	9 (24)
N: central nervous system	- ^a	- ^a	4	4 (11)
D: dermatologicals	- ^a	- ^a	1	1 (2.5)
M: musculoskeletal system	- ^a	- ^a	1	1 (2.5)
Total	5	9	23	37 (100)

-^a: not reported; Based on ATC classification [33].

Source: data obtained during drug therapy monitoring process.

Table 5 Prescribed drugs involved in the appearance of NOM (negative outcomes associated with medication) in patients with DM2 and HTN.

Drug involved in the NOM		Necessity		Effectiveness		Safety		Total n = 37 (%)
		UHP n = 0	EUM n = 0	QI n = 8	NQI n = 7	QSP n = 0	NQSP n = 22	
Losartan		- ^a	- ^a	5	3	- ^a	2	10 (27)
Furosemide		- ^a	- ^a	- ^a	- ^a	- ^a	7	7 (19)
Amlodipine		- ^a	- ^a	3	2	- ^a	1	6 (16)
Metoprolol		- ^a	- ^a	- ^a	1	- ^a	4	5 (14)
Omeprazole		- ^a	- ^a	- ^a	- ^a	- ^a	2	2 (5.41)
Atorvastatin		- ^a	- ^a	- ^a	- ^a	- ^a	1	1 (2.70)
Clopidogrel		- ^a	- ^a	- ^a	- ^a	- ^a	1	1 (2.70)
Isosorbide dinitrate		- ^a	- ^a	- ^a	- ^a	- ^a	1	1 (2.70)
Metformin		- ^a	- ^a	- ^a	- ^a	- ^a	1	1 (2.70)
Sucralfate		- ^a	- ^a	- ^a	- ^a	- ^a	1	1 (2.70)
Vancomycin		- ^a	- ^a	- ^a	- ^a	- ^a	1	1 (2.70)
Enalapril		- ^a	- ^a	- ^a	1	- ^a	- ^a	1 (2.70)
Total		- ^a	- ^a	8	7	- ^a	22	37 (100)

Category	Type of NOM	No. NOM in patients with DM2 and HTN n = 18	Percentage (%) of NOM in patients with DM2 and HTN	No. NOM in patients with DM2 n = 2	Percentage (%) of NOM in patients with DM2	No. NOM in patients with HTN n = 17	Percentage (%) of NOM in patients with HTN	Total
Necessity	Untreated health problem	3	8.11	- ^a	- ^a	2	5.41	13.52
	Effect of unnecessary medicine	- ^a	- ^a	- ^a	- ^a	- ^a	- ^a	- ^a
Effectiveness	Quantitative ineffectiveness	1	2.70	1	2.70	3	8.11	13.51
	Non-quantitative ineffectiveness	3	8.11	- ^a	- ^a	1	2.70	10.81
Safety	Quantitative safety problem	- ^a	- ^a	- ^a	- ^a	- ^a	- ^a	- ^a
	Non-quantitative safety problem	11	29.73	1	2.70	11	29.73	62.16
Total		18	48.65	2	5.40	17	45.95	100

-a: not reported; UHP: untreated health problem; EUM: effect of unnecessary medicine; QI: quantitative ineffectiveness; NQI: non-quantitative ineffectiveness; QSP: quantitative safety problem; NQSP: non-quantitative safety problem.

Source: data obtained during drug therapy monitoring process.

Table 6 Outcomes of pharmacist interventions sent to doctors, nurses and patients, and avoidability of negative outcomes associated with medication.

	Method of communication				Health problem			
	Orally and/or in writing to doctor	Orally and/or in writing to caregiver	Number of patients with interventions <i>n</i> = 35	Percentage (%) of patients with interventions	No. of patients with HP resolved	Percentage (%) of patients with interventions whose HP were resolved	No. of patients with unresolved HP	Percentage (%) of patients with interventions whose HP were not resolved
Pharmacist interventions <i>n</i> = 35								
Pharmacist patient doctor								
Accepted without modification	23 (65.71)	1 (2.86)	24	68.57	17	48.57	7	20.00
Rejected by the doctor with reasons	5	0	5	14.29	3	8.57	2	5.71
Rejected by the doctor without reasons	6	0	6	17.14	4	11.43	2	5.71
Subtotal	34	1	35	100	24	68.57	11	31.42
Interventions accepted: 24 (68.57)								
Interventions not accepted: 11 (31.43%)								
Avoidability of NOM			<i>n</i> = 35	Percentage (%)				
Not avoidable			25	71.43				
Avoidable			10	28.57				
Total			35	100				

HP: health problems.

Source: data obtained from the pharmacist intervention sheet.

4. Discussion

This drug therapy monitoring study consisted of three stages: the detection, analysis and resolution of DRP and NOM linked to DM2 and HTN, both causes of cardiovascular and renovascular disease. The sample group consisted of more men (54.79%) than women, unlike that of the study by Pérez [17], who reported a higher percentage of women. Most of the participants were 60 years of age or older (68.5%). It could be inferred that DM2 risk factors increase with age, as insulin secretion decreases at a rate of approximately 0.7% per year [18].

The most prevalent diagnosis was HTN only (58.90%), followed by DM2 with HTN (35.62%) and DM2 only (5.48%). The efficacy of the doctor-pharmacist collaboration studied is consistent with the findings of previous studies on the role of pharmacists in the treatment of DM2, HTN [19-22] and metabolic syndrome [23]. The results of this study are also consistent with others on the monitoring of HTN [24], DM2 [25] or HTN and DM2.

A simple linear correlation analysis was used to determine the strength of linear association between the variables studied. The correlation coefficient calculated was -0.34 , indicating a weak association between patient age and NOM severity. A negative coefficient also indicates an inverse relationship between these variables. The interval estimate for the number of drugs that caused NOM was 6~8, with a 95% confidence interval. This shows that a higher number of prescribed drugs is not directly linked to the number of patients with NOM.

The DTM service detected 35 suspected NOM. A similar study by Marcel [26] detected 89 NOM, confirming the need to implement DTM programs in high-risk patient groups.

Pharmacist interventions were conducted in just 47.95% of the 73 patients included in the sample group. 68.57% of the 35 pharmacist interventions were accepted and 31.43% were not accepted, showing a

high level of acceptance of the DTM service among patients and doctors. This teamwork helps to improve the clinical condition of chronic patients such as diabetics, as found in previous studies [27-29].

Of the 35 NOM detected, 71.43% were unavoidable and 28.57% were avoidable. Studies in both outpatient [30] and hospital settings have shown that most NOM detected could be avoided, up to 70% in some cases [31, 32]. Through opportune interventions, NOM could be avoided altogether [33].

5. Conclusions

Pharmacotherapeutic follow-up is a professional service that improves the care of diabetic patients with hypertension. It was identified that men predominate with these pathologies, with an age greater than 60 years. Pharmaceutical interventions were used as a solution strategy for NOM, where medical and pharmaceutical professionals were involved. Identifying 35 suspicions of NOM, which reached a high level of acceptance of the drug therapy monitoring process service in patients and medicals. Being avoidable the 28.57% in the hospital environment.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper. This study is part of José Francisco Castro Bolívar's doctoral thesis and the doctorate program of the University of Granada.

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