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Effectiveness of involving pharmacists in the process of ambulatory health care to improve drug treatment adherence and disease control

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Abstract

Rationale, aims and objectives To evaluate the effectiveness of incorporating the pharmacist into the ambulatory health care team to increase the proportion of patients with type 2 diabetes mellitus (T2DM) and/or hypertension who adhere to their drug regimen and to improve disease control.

Methods A non-randomized clinical trial was carried out in patients with T2DM and/or hypertension from two primary care clinics. Patients from one of the clinics comprised the intervention group (IG) who received 'counselling' from the pharmacist. The control group (CG) was comprised of patients who attended another clinic and received the usual care. Adherence was measured by counting pills; hypertension control was evaluated by blood pressure and diabetes control by blood glucose. Statistical analysis was carried out by intention to treat using generalized linear models.

Results There were 440 patients included. There was no difference in the proportion of IG and CG patients who adhered to treatment according to baseline measurements. An increase in the proportion of adherence at baseline and final determination was observed in both groups (IG 71–80%, $P = 0.006$ and CG 72–87%, $P = 0.000$). Generalized linear models showed a 55% or higher probability of IG patients achieving control of hypertension in comparison with the CG. Patients from the IG with T2DM have 13% more possibility of achieving glycaemic control than those of the CG.

Conclusion Counselling offered by the pharmacist proved to be effective for improving drug adherence of diabetic and hypertensive patients in ambulatory health care.

Introduction

Lack of adherence with drug treatment causes ~125 000 deaths a year [1] and represents a serious public health problem. Studies carried out in both ambulatory and hospitalized patients from different socio-economic levels who suffer from chronic diseases such as type 2 diabetes mellitus (T2DM), hypertension, hypercholesterolaemia, heart failure and mental disorders have shown an adherence rate between 50% and 65%. Lack of adherence causes patients to receive suboptimal treatments, experience complications, have worsening of their signs and symptoms and have an increase in the number of doctor visits, emergency services and hospitalizations [2,3]. Demographic characteristics of patients, medication costs, number of drugs and doctor actions have also been described as factors that influence lack of patient adherence [4]. It has been documented that patients with chronic diseases (T2DM, hypertension, dyslipidemia and congestive heart failure) who report between 80% and 100% adherence to drug treatment are less prone to be hospitalized when compared with patients with low levels of adherence [3].

In Mexico, where the prevalence of chronic diseases is high (9.2% T2DM and 31% for hypertension in populations >20 years of age) [5], the quality of health care is a priority. In the Instituto Mexicano del Seguro Social (IMSS), the health care institution that provides medical care to 30.41% of the Mexican population [6], it has been noted that only ~21% of patients with T2DM who receive primary medical care [family medicine clinics (FMC)] are under metabolic control [7]. Despite the fact that 98% of the patients reported having understood the instructions given by their doctor and having a good relationship with the doctor, only 54%

comply with the prescribed drug treatment. These findings have been associated with a low educational level and lack of disease-related information [8].

Regarding hypertension, it has been found that 44% [9] to 77.5% of patients who adhere to the instructions provided by their doctor manage to achieve controlled blood pressure levels [10]. It should be mentioned that only 20.5% of patients with this disease have optimal and high normal levels [9].

There is sufficient literature-based evidence that documents the impact of different interventions whose aim has been to improve treatment adherence. Some of these interventions have been educational and others behavioural [11]. Systematic reviews have shown that, in general, these strategies have a minimum positive effect [1], although when interventions are performed under controlled conditions, almost 40% may be associated with a significant increase in adherence, whereas <50% of patients showed clinical improvement. The most effective interventions have been those that include a combination of different strategies such as family counselling, self-reporting of adherence, reminders, etc. [2]. In Mexico, the experience in the IMSS reveals that educational, participatory and traditional strategies directed at patients with T2DM have had a favourable impact on adherence and metabolic control, with the results of participatory strategies being superior [12,13].

Pharmacists are a potential link between the patient and doctor and have a relevant position in conveying to patients the importance of adhering to the prescribed treatment, such that this would impact on health results. However, in Mexico, the pharmacist has not been routinely considered as part of the health care team in public institutions of the health system. Particularly in the IMSS, which provides 'prepaid' medical care and includes dispensing medications, there are no pharmacists who participate in providing care. Therefore, the aim of this study was to evaluate the effectiveness of incorporating the pharmacist as a support member of the health team at the ambulatory health care level so as to increase the proportion of patients with T2DM and/or hypertension who adhere to their drug regimen; and as a secondary objective, to explore the improvement in disease control.

Subjects and methods

We conducted a non-randomized clinical trial in two FMC affiliated with the IMSS in Mexico City, selected by convenience. Both clinics were similar with regard to number of doctors, clinical, laboratory and imaging services and type of population they serve. In order to avoid contamination of the intervention, patients from one of the FMC received the intervention [intervention group (IG)] and the other FMC patients represented the control group (CG).

We included patients with an established diagnosis of T2DM and/or hypertension who received a medical consultation in either of the selected FMC and who agreed to participate, providing verbal consent, using consecutive sampling. We did not include patients who received care at the emergency department, laboratory, imaging services, reproductive health or preventive medicine or who had other medical conditions that did not allow them to be responsible for taking their medications. Also excluded from the study were patients with mental disorders and pregnant women. Those patients who refused to participate in the study were eliminated, and those who were lost during follow-up were included in the analysis.

The intervention consisted of the incorporation into the health team of two experienced pharmacists during each shift (morning and evening) and whose activity was the creation of a new service referred to as 'counselling' and aimed at patients with T2DM and/or hypertension.

CG patients received the usual care and, in addition, were given a brochure with 'basic' information on the proper use of antihypertensive and antidiabetic drugs at the time their medications were dispensed at the pharmacy.

The sample size was estimated using the formula for binary outcome measures with uniform allocation [14] considering adherence as the primary outcome. The assumptions were as follows: increase of 20% of patients with treatment adherence in the IG vs CG, $\alpha = 0.05$, $\beta = 0.20$; allocation ratio 1:1 and withdrawal of 10%. The required sample size was 109 patients per group. The recruitment period was 7 months (June 2005–December 2005) and there was a 6-month follow-up for each patient.

The primary result variable was the increase in the proportion of patients with T2DM and/or hypertension who adhered to their drug treatment. This outcome was measured by pill count; the percentage of adherence was calculated from the remaining pills in the container compared with the number of pills prescribed. Adherence was considered when medication use was between 80% and 110% [15]. Reasons for of lack adherence were classified as 'intentional' when the patient deliberately stopped drug treatment for the following reasons:

- Drugs cause health problems or make the patient feel unwell.
- Patient feels good without medication.
- Patient switched to an alternative treatment.
- Drug effects were cancelled by alcohol consumption.
- Patient required the drug when feeling unwell.
- Patient tired of taking the drug.

Unintentional reasons for lack of adherence were as follows:

- Not having the drug.
- Forgetting to take the drug.
- Directed by a non-treating doctor.

As secondary variables, we considered the definition of control of T2DM as glycaemic values ≤130 mg dL^{-1} and control of hypertension when blood pressure levels were ≤140/90 mmHg [16,17].

Study description

All patients were recruited by six trained nurses who circulated through the waiting rooms of the clinics to identify patients with diabetes and/or hypertension. In cases where patients agreed to participate and gave their verbal consent, the nurse carried out a structured interview and included a data sheet (age, gender, marital status, education and occupation), medical history and history of use of antidiabetic and/or antihypertensive medications.

Intervention

Patients included in the IG received an individual 'counselling' session by the pharmacist after the medical visit during which time the importance of taking each of the drugs was explained. Information was provided on the actions to be taken in the event that the

patient forgets to take one or more doses during the day or if the patient experiences any adverse reactions. All questions were answered and information was provided to the patient about medication schedules regarding food and meal times. During this time, the pharmacist reinforced the importance of diet and exercise and, in the case of patients with hypertension, on reducing salt intake. As part of the 'counselling', the pharmacist transcribed the prescription to pictograms by using a computer program that was developed expressly for this protocol in order to provide understandable information to the patient regarding quantities, schedules and duration of each of their treatments. At the conclusion of the 'counselling', the patient then proceeded to the pharmacy (which is integrated within the FMC) to fill their prescriptions.

Patients in the CG received their usual medical care and, when presenting to the FMC pharmacy, were given a brochure with hypoglycaemic and/or antihypertensive drug information as suggested reading for 'information relevant to your health', in addition to asking the patient to retain the information in order to refer to it as often as necessary.

Follow-up

All patients had three follow-up sessions with a nurse. During the first two encounters aimed to reinforce the intervention and to prevent loss of follow-up, the nurse reinforced the advice to the patients in the IG given by the pharmacist during the prior visit. For patients in the CG, the nurse invited them to review the brochure regarding medication information for their condition. The first follow-up session was completed during the fourth week after having reviewed baseline adherence information. The second and third follow-up visits were carried out at 1 month and 2 months after the first follow-up visit. For carrying out measurements of adherence during the third follow-up appointment, the nurse contacted the patient via telephone 2 days prior to the date of the scheduled medical appointment in order to remind the patient to arrive for the visit with the containers containing the remaining medication and a copy of the prescription provided by the doctor during the last visit. If a patient did not attend their medical appointment, a telephone call was made by the nurse to schedule an appointment at the patient's home in order to complete a measurement of adherence. For baseline and final measurement of pill use, the nurse reviewed the date of the last prescription, which had to agree with the date of the last doctor visit recorded in the medical record, counted the remaining pills and reviewed the number of pills that had been given to the patient by the pharmacy and the number of pills that the patient was instructed by the doctor to take according to the prescription.

Statistical analysis

Intention to treat (ITT) analysis was performed. Binary variables were summarized as proportions and χ^2 was used to compare between-group differences. For mean differences between groups, we used Student's *t*-test for independent samples. Results were considered significant when two-tailed *P*-value was <0.05. ITT analysis included patients who answered at least the initial questionnaire and had baseline measurements. Losses (cases assigned but did not complete the intervention and/or did not have a final evaluation) were treated with the imputation method to which the last measurement obtained was assigned and was considered to remain unchanged. Multivariate analysis was used to estimate the difference of the average change between groups (differences in differences) [18] and was calculated according to the regression equation:

$$C = \beta 0 + \beta 1 \text{ intervention group} + \beta 2 \text{ time (before-after)} + \beta 3 \text{ group * time (1)} + \beta \text{jCov}$$

where β1 measured the average change (mean difference) within each group (control and intervention), β2 measured the average change after the intervention and the effect of the intervention on the patient was observed in β3 that measured the difference in the average change between groups.

The regression model included the covariables of adherence and time of evolution, which was based on prior studies and was limited to the measured study variables that were statistically significant according to bivariate analysis. The effect of the intervention on disease control (binary outcome, 1 = yes, 0 = no) was measured using a generalized linear model (as an alternative for logistic regression) [19] for each result variable, both in the group of patients with T2DM as well as those with hypertension and was controlled by the covariables. The process for model selection started with the fully specified model that included adherence and disease duration. A backwards model selection approach was then used to remove one predictor at a time from the model based on their *P*-values. Odds ratios for covariates were calculated as the exponential of the estimated coefficient for that variable and confidence intervals using robust variance estimators.

To perform the analysis, Stata v.12.0 (Stata/SE 12.0, Stata Corporation, College Station, TX, USA) and SPSS for Windows v.18 (SPSS Inc., Chicago, IL, USA) were used. The investigation protocol was authorized by the National Scientific Research Committee of the IMSS.

Results

There were 440 patients included in the study: 48% in the IG ($n = 211$) and 52% in the CG ($n = 229$). Differences were found between groups according to certain demographic characteristics such as age, education and occupation. Diagnosis of T2DM with hypertension as the principal disease was more frequent than being diagnosed with only one of these diseases. A greater proportion of the patients from the IG had some type of concomitant disease. In the IG, obesity and hypercholesterolaemia were predominant and osteoarthritis and obesity in the CG (Table 1).

In the IG, time of diagnosis of hypertension was on average 3 years less (9.9 ± 9 IG vs 12 ± 9, $P = 0.01$) and no difference was seen between groups according to the time of diabetes evolution. Patients from the IG had a lower SBP average (141 ± 20 vs 149 ± 19, $P = 0.001$) and DPB (89 ± 11 vs 92 ± 15, $P < 0.05$).

In the baseline measurement, there was no significant difference when comparing the proportion of patients with adherence or reasons for lack of adherence between groups. In the final measurement, difference was observed in the proportion of lack of adherence between groups, but not in the proportion of intentional or unintentional reasons (Table 2).

In both groups, a significant increase was observed between baseline and final measurement within group (71–80%, $P = 0.006$ IG and 72–87%, $P < 0.001$ CG; data not shown).

According to the condition of adherence, there was a significant decrease in blood pressure at baseline and final measurements in both groups and in blood glucose only in adherent patients (Table 3).

Multivariate analysis showed that the effect of the intervention on disease control in patients with hypertension, regardless of their adherence to drug therapy and duration of their disease, favours a 55% greater possibility of patients from the IG to achieve disease control compared to the CG. In the case of patients with diabetes, it was reported that there is a >13% possibility that patients intervened reach glycaemic control compared with the CG, independent of their adherence to drug therapy and disease duration (Table 4).

Table 1 Demographic and clinical characteristics of the study patients

	IG	CG	
Characteristics	*n* = 211	*n* = 229	*P*-value
Age (years), mean ± SD	58 ± 10	62 ± 10	<0.001
Gender	*n* (%)	*n* (%)	
Female	159 (75.3)	179 (78.1)	NS
Education	*n* = 209	*n* = 229	<0.001
Elementary school or lower	95 (45.5)	153 (66.8)	
Secondary school or higher	114 (54.5)	76 (33.2)	
Occupation	*n* = 210	*n* = 229	0.02
Housewife	92 (43.8)	135 (58.9)	
Services, shopkeeper	94 (44.8)	52 (22.7)	
Retired, unemployed	24 (11.4)	42 (18.4)	
Civil status	*n* = 211	*n* = 229	NS
Married	124 (58.8)	152 (66.4)	
Single, divorced or widowed	87 (41.2)	77 (33.6)	
Principal disease	*n* = 211	*n* = 229	NS
T2DM	54 (25.5)	62 (27.0)	
Hypertension	74 (35.0)	77 (33.6)	
T2DM and hypertension	83 (39.3)	90 (39.3)	
Co-morbidities	*n* = 211	*n* = 229	
With concomitant disease	119 (56.4)	110 (48.0)	0.08
Obesity	59 (49.6)	35 (31.8)	0.006
Hypercholesterolaemia	51 (42.9)	28 (25.4)	0.006
Osteoarthritis	13 (10.9)	46 (41.8)	<0.001
Cardiopathy or nephropathy	30 (25.21)	31 (13.5)	NS

CG, control group; IG, intervention group; NS, not significant; SD, standard deviation; T2DM, type 2 diabetes mellitus.

Discussion

The results of the study revealed that the percentage of adherence was within the upper limits reported in the literature for chronic conditions (55–73%) [3]. This result may be due to the method of measuring adherence because it may have overestimated actual adherence behaviour [20].

The method of pill count can be imprecise because patients occasionally may not bring the remaining medication to their appointments; however, despite this limitation, it is a practical method to be used in a considerable number of patients. Although other methods of measuring adherence such as electronic systems (Medication Monitoring System), serological measurements of the drug, etc., can be more accurate, they are expensive and difficult to implement in routine clinical practice.

One of the more common reasons for lack of adherence to drug therapy in patients was unintended, 'not having the drug'. This result suggests the importance of having an efficient and permanent supply system particularly in health services that include provision of drugs ('prepaid' services); this situation has been reported in a previous study [9]. Another aspect necessary to strengthen drug adherence is the implementation of mechanisms to remind patients to take their medications and to maintain strategies aimed at educating and motivating patients. Reports in the literature have shown that the most effective interventions to improve adherence and to promote positive changes in clinical variables have been 'complex' interventions that include one or more components of information: counselling, reminders and self-monitoring, among others [2].

An important outcome worth mentioning is that a positive change in adherence was demonstrated in the two studied groups.

Table 2 Proportion of lack of adherence and reasons

	IG	CG	IG	CG
	n = 211 *n* (%) Basal	*n* = 229 *n* (%)	*n* = 211 *n* (%) Final*	*n* = 229 *n* (%)
Lack of adherence	62 (29.3)	64 (27.9)	41 (19.4)	28 (12.2)
Intentional reasons	26 (42.0)	25 (39.0)	22 (53.7)	13 (46.4)
The medication causes health problems or makes patient feel unwell	13 (50.0)	12 (48.0)	10 (45.5)	5 (38.5)
Patient feels good without medication	6 (23.0)	11 (44.0)	2 (9.1)	2 (15.4)
Too many drugs	–	–	3 (13.6)	1 (7.7)
Patient takes medication when not feeling well	–	–	7 (31.8)	2 (15.4)
Others	7 (27.0)	2 (8.0)	0 (0.0)	3 (23.0)
Unintentional reasons	36 (58.0)	39 (61.0)	19 (46.3)	15 (53.6)
Not having the drug	18 (50.0)	8 (20.5)	3 (15.8)	2 (13.3)
Patient forgot to take medication	16 (44.4)	31 (79.5)	14 (73.7)	13 (86.7)
Patient directed by a non-treating doctor	2 (5.6)	0 (0.0)	2 (10.5)	0 (0.0)

*Mann–Whitney *U* 0.034.

CG, control group; IG, intervention group.

Table 3 Baseline vs final comparison of the surrogate variables in 'adherent' and 'non-adherent' patients and according to study group

	Adherent patients				Non-adherent patients			
	IG		CG		IG		CG	
	Basal *n* = 149	Final *n* = 170	Basal *n* = 165	Final *n* = 201	Basal *n* = 62	Final *n* = 41	Basal *n* = 64	Final *n* = 28
SBP (mmHg)	142 ± 18	124 ± 12*	151 ± 20	129 ± 16*	143 ± 26	124 ± 12*	146 ± 17	133 ± 19*
DBP (mmHg)	89 ± 12	79 ± 7*	94 ± 17	81 ± 9*	92 ± 12	80 ± 8*	90 ± 11	84 ± 10*
Glucose (mg dL^{-1})	197 ± 67	145 ± 40*	184 ± 52	171 ± 65*	205 ± 49	173 ± 72	189 ± 49	198 ± 84

*Mann–Whitney *U*-test, $P < 0.05$.
CG, control group; DBP, diastolic blood pressure; IG, intervention group; SBP, systolic blood pressure.

Table 4 Effect of the counselling by pharmacist (intervention) on control of hypertension or type 2 diabetes mellitus*

	OR	SE	*Z*	*P*-value	95% CI Lower limit	Upper limit
Control of hypertension						
Intervention	1.559	0.2901	2.39	0.017	1.082	2.245
Adherence	2.372	0.5649	3.63	0.000	1.487	3.783
Duration of disease	0.9740	0.0099	–2.57	0.010	0.954	0.993
Constant	2.249	0.6165	2.96	0.003	1.314	3.848
Control of type 2 diabetes mellitus						
Intervention	1.134	0.1640	0.87	0.383	0.8545	1.506
Adherence	1.270	0.3007	1.01	0.312	0.7989	2.020
Duration of disease	0.9905	0.0089	–1.06	0.291	0.9731	1.008
Constant	0.8763	0.2180	–0.53	0.596	0.5381	1.427

*Generalized linear model.
CI, confidence interval; OR, odds ratio; SE, standard error.

It is notable that the increase observed in the CG was greater than what has been described in the literature (5–11%) [1]. This fact suggests that monthly patient monitoring provided by nurses may have had a positive influence on the two groups. According to the literature, the combined effect of interventions and strategies, which include supervision, produces better results [1,4,21].

It is important to emphasize the effectiveness of the intervention on hypertension control as well as glycaemic control of T2DM. Studies performed in other contexts have also reported that the participation of the pharmacist as part of the health team is a positive aspect to achieve control of these chronic conditions [1,22–24]. However, the literature also mentions that it is necessary to explore electronic alternatives to improve adherence. In a systematic review, it was reported that in 67% of the studies in which electronic strategies were evaluated there were successful results, whereas in 52% of the studies in which there was participation of the pharmacists, nurses or doctors there were satisfactory results obtained, mainly with pharmacists [25]. For this reason, it is appropriate to evaluate other alternatives and to jointly analyse all actions that can be performed by the pharmacist in medical ambulatory care.

The study has some limitations. One limitation was lack of randomization of the groups caused by the conditions of actual clinical practice. We must recognize that lack of randomization reduces the power of the study and there is a risk that the treatment groups may not be comparable due to imbalance of the covariates. In this study, age, duration of the illness and treatment adherence were different, but all were included in the regression models. In addition, the presence of a chronic comorbidity makes control of the patients difficult. In our study, the proportion in the presence of concomitant disease did not show statistically significant differences; however, the independent analysis of each of the comorbidities (obesity, high cholesterol and heart disease/nephropathy) showed a higher frequency in the IG and may have underestimated the effect of the intervention.

Another limitation was that the study included three types of patients for both intervention and control groups: patients with T2DM, patients with hypertension and patients with both conditions; the analysis did not discriminate among groups. The sample size was insufficient for carrying out a separate analysis for each type of patients; consequently, a non-differential misclassification bias may have occurred because the distribution of T2DM, hypertension and both conditions was similar.

Follow-up time of patients was shorter than what was reported in other studies [1]. It is known that the longer treatment time decreases the proportion of adherence [26]. Further research is necessary to identify the effect of this type of strategy in the long term.

In conclusion, counselling services offered by the pharmacist proved to be effective in achieving a significant proportion of patients who attained control of hypertension and, although to a lesser extent, also achieved control of T2DM. Furthermore, our results suggest that patient monitoring by nurses contributes to achieving better results in both adherence and disease control. Further evidence is necessary to confirm the relevance of integrating multidisciplinary health teams in primary care.

Consideration should be given to the need for pharmacist counselling and follow-up by nurses on a permanent basis for patients with chronic diseases to reinforce strategies for improving adherence and better disease control.

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