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Effectiveness of Pharmacotherapy Follow-Up for the Control of Hypertensive Patients in Community Pharmacies: EMDADER-HTA Study

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SUMMARY. **The present study was designed to evaluate the effect of pharmacotherapy follow-up (PFU) on blood pressure (BP) readings, total cholesterol (TC) levels and cardiovascular risk (CVR) in patients with hypertension and/or hypercholesterolemia, at community pharmacies in Spain. The study was carried out in 18 community pharmacies in Spain with 6 months of PFU. Measurements were taken at: start, 6, 12, and 24 weeks. Hypertensive patients aged 35-74 attended with a prescription for at least one drug indicated primarily for the treatment of hypertension were included. A total of 117 patients completed the study. There were statistically significant increases in the achievement of hypertension targets (23.9%, $p < 0.001$). There were decreases in the average Wilson-Grundy CVR (-1.5%), CVR SCORE (-0.5%), systolic and diastolic BP (-7.6 mm Hg) (-3.3 mm Hg) and TC (-14.6 mg/dL). PFU carried out by community pharmacists in hypertensive patients attending community pharmacies in Spain improves BP, TC and can achieve BP, TC and CVR reduction.**

INTRODUCTION

Hypertension (HTN) is one of the leading cardiovascular risk factors and a significant direct cause of morbidity and mortality in developed countries [1], where it affects more than 40% of the adult population [2]. In Spain, the prevalence of HTN amongst adults is approximately 35%, increasing to 40% in the middle-aged population and up to 68% in the over-65s, affecting around 10 million adults throughout the country [3]. It is estimated that 24% of the population of developed countries and up to 80% of developing countries will be hypertensive by 2025 [2]. Hypertension is involved in the deaths of an estimated 40,000 people over the age of 50 in Spain each year [4].

In Spain, it is estimated that the main cardiovascular risk (CVR) factors, such as HTN and hypercholesterolaemia, are controlled in just 10% of patients with a high or very high CVR [5]. This indicates that strategies should be put in place to help increase the number of patients who achieve their therapeutic targets. Community pharmacists, in collaboration with other healthcare professionals, could help to improve clinical outcomes for patients with chronic illnesses.

A number of studies have shown that by carrying out pharmacotherapy follow-up (PFU), community pharmacists can detect, prevent and resolve negative outcomes associated with medication (NOM). This, in turn, will help to improve the results of therapeutic interventions in patients with HTN [6-10] and overall outcomes for patients [10-17]. It will also increase the number of patients with high CVR who achieve their therapeutic targets for arterial blood pressure [18-20]. However, other studies have not found that pharmacist intervention is of any benefit for

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more important health outcomes [21,22], and have concluded that more studies need to be carried out to assess pharmacist intervention [23].

The aim of this study is to evaluate the effect of PFU on blood pressure readings and the achievement of therapeutic targets for blood pressure in hypertensive patients attending community pharmacies in Spain. The secondary aim is to calculate the percentage of patients who achieve their total cholesterol (TC) targets, and the percentage whose absolute CVR is reduced.

METHODOLOGY

Study Type

Quasi-experimental uncontrolled before and after study carried out in 18 community pharmacies in Spain. The study was designed by researchers at the University of Granada and a number of expert PFU pharmacists were recruited to take part. The study population was made up of patients diagnosed with HTN who attended the 18 pharmacies to collect antihypertensive drugs. The patients were recruited between January 2007 and January 2008. Each patient underwent PFU for a period of 6 months, with variables measured at the start, at 4-6, 12, and 24 weeks.

Inclusion and Exclusion Criteria

Patients aged between 35 and 74 diagnosed with HTN were included in the study. They attended the community pharmacies during the study period with a prescription for at least one drug indicated primarily for the treatment of HTN. The following patients were excluded from the study: patients who attended the pharmacy with prescriptions for other people, who were pregnant, with BP > 180/110 mm Hg, with a history of myocardial infarction < 3 months before, attending a cardiac rehabilitation program, or with a terminal illness.

Sample Group

According to the EMDADER-CV [24] study, an estimated 66% of patients have not achieved their therapeutic BP targets before PFU. Assuming that 50% achieve that target after pharmacist intervention, with a confidence level of 95% and a statistical power of 94% (beta error of 6%), 114 patients were required for the sample group. In order to cover for possible losses due to patients leaving the study or difficulties in the follow-up, and to increase the sensitivity of the analysis, an additional 15% was added to the sample group, bringing it up to 131 patients.

Procedure

The general study procedure is shown in Fig. 1. The pharmacist researcher at each community pharmacy told the coordinator which patients met the inclusion criteria. The coordinator checked that these patients met all the inclusion criteria, and told the researchers which patients were to be included in the study.

The pharmacist carried out PFU on the patients using the Dader Method [25] for pharmaceutical care, a systematic PFU process based on the use of pharmacotherapy records to complete a health status form which includes details of all the patient's health problems and drugs used, and their assessment on a specific date. This assessment is used to identify any potential or actual negative outcomes associated with medication and the drug-related problems (DRP) that cause them. Once the DRP and NOM are identified, the necessary interventions should be carried out to resolve them. In this study, PFU was carried out in accordance with a systematic and documented method, in collaboration with patients and physicians. Pharmacists carried out the following steps:

(a) Obtained patient data by interviewing the patient and reviewing their health problems and drug record. The patient provided medical reports and test results. This information was used to complete the assessment form.

(b) Evaluated and identified suspected NOM and DRP: the aim of this stage was to assess if the treatment targets had been achieved.

(c) Conducted an intervention to resolve NOM and DRP: the interventions prevented or resolved NOM and DRP and included interventions aimed at the patient (to modify a problem with lifestyle or use of a medication) or at the doctor (to modify drug therapy in either a quantitative way (modifying dosage or frequency) or a qualitative way (adding or changing a drug).

Variables Related to the Study Objectives

Target BP readings: generally, BP readings should be < 140/90 mm Hg. In patients with DM, renal failure, AMI or stroke, they should be < 130/80 mm Hg. BP readings were taken following international guidelines, after a 5-min rest and using a recently calibrated device (mercury, aneroid or automatic). Each recorded reading was the average of 2 measurements taken while the patient was sitting, over the course of 3-5 min.

Target TC levels: < 200 mg/dL for primary prevention patients and < 175 mg/dL for secondary prevention patients. Plasma concentra-

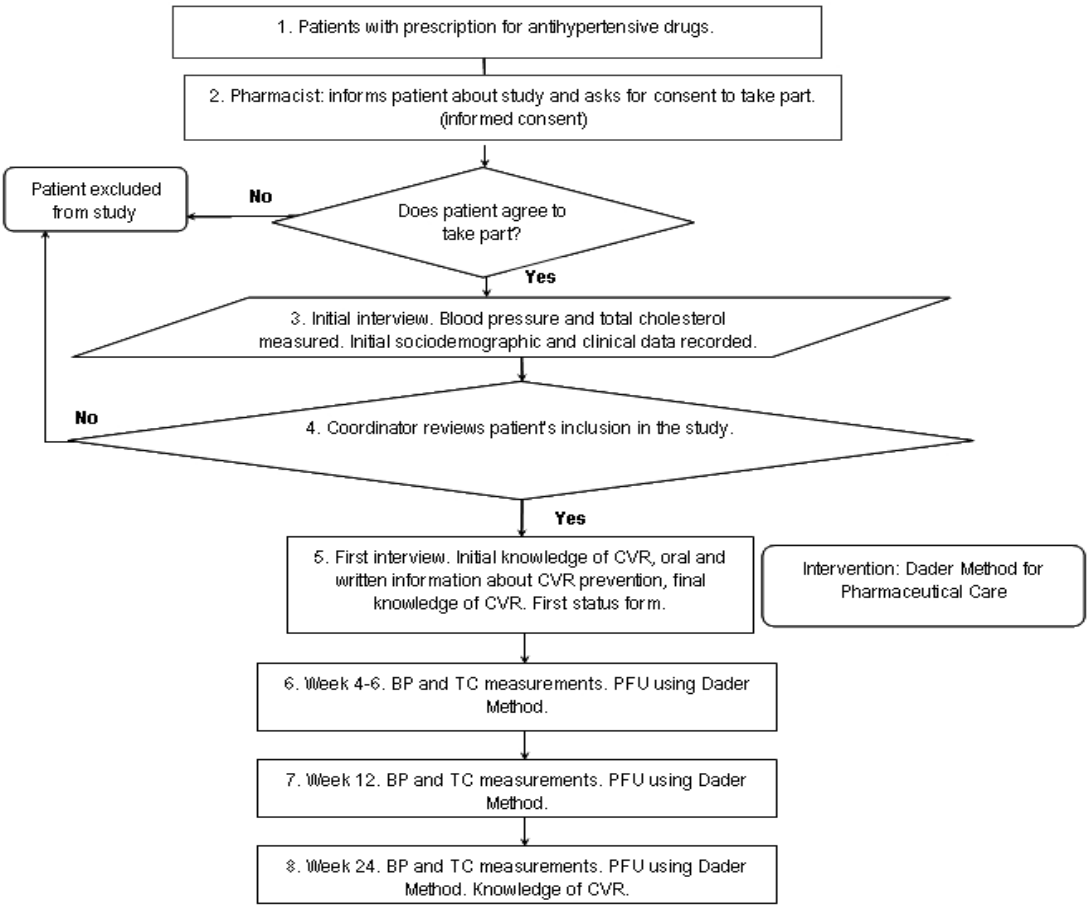

Figure 1. EMDADER-HTA Study: General Procedure.

tions of TC are measured in milligrams per decilitre (mg/dL) and obtained by quantifying the total cholesterol levels in a capillary blood sample taken from the index finger, using an Accutrend GL device.

Statistical Analysis

The statistical analysis was carried out using descriptive measures, the Chi-square test to compare proportions and the Student's t-test to compare averages. Multiple linear regression and principal component analyses were also carried out. All of the analyses were carried out using SPSS version 15.0 (SPSS Inc, Chicago, III). P values < 0.05 were considered statistically significant.

RESULTS

The initial study group was made up of 133 patients recruited in 18 community pharmacies in Spain. Sixteen patients (12%) left the study, so the final group was made up of 117 patients. The average age (SD) of patients in the final study group was 60.2 (9.0), 43.6% (51) were men and 56.4% (66) had high BP. The initial demographic and clinical data for the patients who completed the study are shown in Table 1.

At the start of the study, 51 (43.6%) of the 117 patients had achieved their therapeutic targets for HTN and 44 (37.6%) had achieved their targets for TC (Table 2). After 6 months of PFU, there were statistically significant increases in the percentages of patients who had achieved adequate therapeutic targets for HTN (23.9%, P < 0.001) and TC (15.4%, P = 0.004) (Table 2).

The initial quantitative Wilson-Grundy (W-G) CVR, quantitative CVR SCORE, SBP, DBP and TC were 6.7%, 2.7%, 137.6 mm Hg, 80.8 mm Hg and 209.7 mg/dL, respectively (Table 3).

After 6 months of PFU, there were statistically significant (P < 0.05) decreases in the average WG CVR (-1.5%, CI 95%: -2.43 to -0.69), CVR SCORE (-0.5%, CI 95%: -0.85 to -0.18), SBP (-7.6 mm Hg, CI 95%: -10.31 to -4.88), DBP (-3.3 mm Hg, CI 95%: -4.94 to -1.83) and TC (-14.6 mg/dL, CI 95%: -20.98 to -8.24).

Demographic and Clinical Variables		Group Total (N = 133)		Group Total (N = 117)	
		%	n	%	(n)
Average Age (SD)	59.52	9.43	60.23	9.08	
Sex	Female	54.1	72	54.6	66
	Male	45.9	61	43.6	51
Level of Education	None/Primary	51.9	69	52.1	61
	Secondary	26.3	35	24.8	29
	University/Vocational	21.8	29	23.1	27
Relationship Status	Single	23.3	31	22.2	26
	In a Relationship	76.7	102	77.8	91
Perceived Health Status	Fair, Poor, Very Poor	57.1	76	59	69
	Good, Excellent	42.9	57	41	48
HTN	No	45.1	60	43.6	51
	Yes	54.9	73	56.4	66
Dyslipidaemia	No	51.9	69	51.3	60
	Yes	48.1	64	48.7	57
High CVR (Assessment Not Necessary)	No	74.4	99	73.5	86
	Yes	25.6	34	26.5	31
Diabetes	No	88.7	118	88	103
	Yes	11.3	15	12	14
History of AMI	No	99.2	132	99.1	116
	Yes	0.8	1	0.9	1
Associated Clinical Condition	No	91.7	122	91.5	107
	Yes	8.3	11	8.5	10
Type of CV Prevention	Primary	90.2	120	89.7	105
	Secondary	9.8	13	10.3	12
Type of Associated Clinical Condition	None	91.7	122	91.5	107
	HF-LVH	2.3	3	1.7	2
	Hereditary Dyslipidaemia	3	4	3	4
	Renal Failure	3	4	3.4	4
Clinical Form of CV Disease	None	90.2	120	89.7	105
	Acute Myocardial Infarction	1.8	1	0.9	1
	Angina	5.3	7	5.1	6
	Cerebrovascular Disease	2.3	3	2.6	3
	Peripheral Artery Disease	1.5	2	1.7	2

Table 1. Initial Demographic and Clinical Data for Patients Who Started and Completed the Study. SD: standard deviation; HTN: hypertension; CVR: cardiovascular risk; AMI: acute myocardial infarction; CV: cardiovascular; HF-LVH: heart failure-left ventricular hypertrophy.

DISCUSSION

PFU results in a significant increase in the percentage of patients who achieve adequate therapeutic targets for BP and TC. PFU involves a series of key strategies for improving BP control. These strategies include educating the patient about the disease and drugs, treatment adherence and lifestyle changes, and conducting interventions related to the need for, effectiveness and safety of drugs. In cases where a patient's treatment regimen needs to be modified, the physician will always be consulted.

A number of studies have shown that pharmacist intervention can improve the results of drug therapy in hypertensive patients [6-9,26]. The degree of achievement of therapeutic targets for BP and TC is very different in controlled clinical studies than in medical practice. In the EMDAD-

Therapeutic Target Variables (N = 117)	Initial		6 Months of PFU		Difference	P [a]
	%	n	%	n	%	
Achievement of HTN Targets [b]	43.6	51	67.5	79	23.9	< 0.001 (SS)
Achievement of TC Targets [c]	37.6	44	52.9	62	15.4	0.004 (SS)
Smokes	7.6	9	5.9	7	-1.7	0.625
Exercises	66.6	78	72.6	85	5.9	0.039 (SS)
Adequate Qualitative Knowledge of CVR	82.0	96	97.4	114	15.3	< 0.001 (SS)

Table 2. Changes in Therapeutic Targets Over 6-Month Study Period. [a]: McNemar's test; [b]: Blood pressure < 140/90 mmHg in patients with uncomplicated hypertension and < 130/80 mmHg in patients with diabetes, chronic kidney disease, or a history of myocardial infarction or stroke; [c]: Total cholesterol < 200 mg/dL in patients without cardiovascular disease and < 175 mg/dL in patients with cardiovascular disease. PFU: pharmacotherapy follow-up; HTN: hypertension; CVR: cardiovascular risk; SS: statistically significant.

Variables (N = 117)	Initial Value (Mean)	Final Value (Mean)	Difference	(CI 95%)	P [a]
Quantitative WG CVR (%)	6.7	5.1	-1.5	(-2.43 to -0.69)	<0.001 (SS)
Quantitative CVR SCORE (%)	2.7	2.2	-0.5	(-0.85 to -0.18)	0.003 (SS)
SBP (mmHg)	137.6	130.0	-7.6	(-10.31 to -4.88)	<0.001 (SS)
DBP (mmHg)	80.8	77.4	-3.3	(-4.94 to -1.83)	<0.001 (SS)
TC (mg/dL)	209.7	195.0	-14.6	(-20.98 to -8.24)	<0.001 (SS)
BMI (kg/m^2)	29.2	28.9	-0.3	(-0.50 to -0.09)	0.004 (SS)
CVR Education - Knowledge	8.7	8.5	-0.2	(-0.44 to 0.02)	0.085

Table 3. Initial and Final Clinical Values for Patients Who Completed the Study. P: between final and initial values. [a] McNemar's test. WG CVR: Wilson-Grundy cardiovascular risk; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; BMI: body mass index; CI 95%: confidence interval of 95%; SS: statistically significant; mmHg: millimetres of mercury; mg/dL: milligrams per decilitre; kg/m^2: kilograms per square meter.

ER-CV randomised clinical trial, Amariles *et al.* [24] found that just 30% of patients achieve their therapeutic targets for BP and TC, and less than 20% achieve the targets for both risk factors. In that study, which compared the effect of a PFU programme with the usual care process in 40 community pharmacies in Spain (N = 714), there was a significant increase of 19.6% (P < 0.001) in the percentage of patients who achieved their therapeutic target for BP in the intervention group: 52.5% of patients achieved adequate BP targets. Furthermore, at the end of the 8-month study, the patients who underwent PFU also achieved reductions in SBP (-11.3 mm Hg, P < 0.001) and DBP (-4.3 mm Hg, P < 0.001), with final average values of 134.2 and 79.0 mm Hg, respectively. These results are quite similar to those of this EMDADER-HTA study, possibly because both studies used the Dader Method for PFU, and despite their different sample sizes (117 *vs.* 714) and durations (6 *vs.* 8 months). This study found a higher percentage of controlled patients (67 *vs.* 52.5%). This is because of the higher initial percentage (43.6 *vs.* 32.9%), which may also be due to the higher average age of patients in the EMDADER-CV 24 study (60.2 (9.0) *vs.* 63.0 (8.3) years).

Rosinach & García-Jiménez [8] carried out a 2-year quasi-experimental uncontrolled single-centre before and after study in a community pharmacy in Spain in order to analyse the effect of PFU on drug therapy in uncontrolled hypertensive patients in order to achieve therapeutic targets for BP. The study yielded good results in terms of the percentage of controlled patients. Initially, 23% of patients in the study group were controlled, but at the end of the 2-year period PFU had resulted in good BP control in 70% of patients. There were also significant average reductions in SBP and DBP (-18.6 mm Hg, P < 0.001 and -9.3 mm Hg, P < 0.001, respectively). These results are better than the ones obtained in the EMDADER-HTA and EMDADER-CV studies [24]. This may be because the study was three times longer than the EMDADER-CV study [24] and four times longer than the EMDADER-HTA study, and because the sample size of the study by Rosinach & García-Jiménez [28] was very small, making it difficult to compare with the other two.

The Dader Method for PFU was also used in a quasi-experimental before and after study carried out by Molina *et al.* [9] in a community pharmacy in Spain with a sample group of 49 patients over a 6-month period. The aim of that study was to determine the effect of pharmacist intervention, healthcare education or PFU on BP values. 87.5% of patients in that sample group, who all had uncontrolled BP, managed to achieve their target BP as a result of PFU. This percentage of patients with controlled BP was higher than the one achieved in the EMDADER-HTA study (67.5%), the EMDADER-CV study 24 (52.5%) and the study by Rosinach & García-Jiménez [8] (70%). The reductions in average SBP and DBP were also greater (-24.8 and -7.6 mm Hg, respectively). This could be because 100% of the patients in the sample group were uncontrolled at the start of the study. Despite these quantitative differences, all of these studies which used the Dader Method for PFU in community pharmacies, including the EMDADER-HTA study, improve the results of pharmacological treatment in hypertensive patients [6-9,26].

The impact of pharmacist intervention in the control of CVR factors is analysed by Santschi *et al.* [27] in a systematic review and meta-analysis of randomised trials. Pharmacist interventions carried out in 19 studies in a total of 10,479 patients were associated with significant reductions in SBP/DBP (-8.1 mm Hg, CI 95%: -10.2 to -5.9 / -3.8 mm Hg, CI 95%: -5.3 to -2.3). The results obtained are very similar to those of the other studies that have used the Dader Method of PFU, especially the EMDADER-HTA study (SBP/DBP: -7.6 *vs.* -8.1 mm Hg / -3.3 *vs.* -3.8).

A controlled randomised trial by Morgado *et al.* [28] to assess if a 9-month hospital pharmacist care program could improve BP control evaluated 197 patients. At the end of the study, 63% of patients in the intervention group (n = 98) had achieved their BP targets. Significant reductions in SBP/DBP were also achieved (-6.8 mm Hg, P = 0.006 / -2.9 mm Hg, P = 0.020), and the results in the intervention group were always better than those in the control group. Again, these values are very similar to, albeit lower than, the ones obtained in the EMDADER-HTA study (BP/SBP/DBP: 67.7 *vs.* 63% / -7.6 *vs.* -6.8 mm Hg / -3.3 *vs.* -2.9 mm Hg), where the interventions were not carried out by clinical pharmacists in a hospital setting, but by community pharmacists in 18 community pharmacies. Despite these small quantitative differences, the evidence indicates that clinical intervention by a pharmacist, regardless of their place of work, leads to improved BP results.

One possible limitation of this study is that it did not include a control group which could have been used to compare the results with patients who did not undergo PFU.

CONCLUSIONS

The EMDADER-HTA study, carried out by community pharmacists in patients with HTN attending community pharmacies in Spain, has increased the effectiveness of antihypertensive treatment by 24%, allowing 7 out of 10 hypertensive patients to achieve their BP targets. Furthermore, thanks to the PFU process, the number of patients with controlled TC increased by 15%. As a result, BP and TC interventions have led to a direct improvement in cardiovascular risk, which decreased by 0.5% according to the SCORE system and 1.5% according to the Wilson-Grundy system.

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