Clinical and Experimental Health Sciences

A Prospective Study Concerning the Effect of Pharmaceutical Care Services on Patients with Heart Failure

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ABSTRACT

Objective: Heart failure (HF), caused by an abnormality in cardiac function, is the inability of heart tissue to pump blood or deliver sufficient oxygen, resulting in abnormal diastolic volume. Drug-Related Problems (DRPs) can cause significant but preventable morbidity and mortality once specific medication errors and their contributing factors are identified. The aim of this prospective study is to determine the effect of pharmaceutical care in patients with heart failure in a Turkish hospital.

Methods: A total of 160 patients with heart failure (80 patients in the control group, 80 patients in the intervention group) were examined at a university hospital. The results of the Pharmaceutical Care Survey were evaluated in accordance with the objective of the study. In addition, using the Pharmaceutical Care Network Europe (PCNE) classification system V8.01, the role and importance of the clinical pharmacist in identifying, preventing and resolving drug-related problems encountered during the treatment of two groups was assessed. The number and causes of potential DRPs were taken into scrutiny.

Results: Comparing the results of the Pharmaceutical Care Survey in both groups at the end of the 6th month, the study group shows a significant improvement in the rates of "forgetting to take medication" (2.9%) and "experiencing any side effects from your drug" (4.5%). Compared to other problems, ineffectiveness of the drugs used in treatment was reported as the most common drug-related problem (n=23; 28.7%) in the study group (p<.05). 72.5% of the proposed interventions were accepted and the problem was found to be resolved in 31% of the patients.

Conclusion: In this study, it is discussed that clinical pharmacists can play an active role in resolving DRPs in heart failure patients. It is therefore can be predicted that the training of information and warnings conveyed by the clinical pharmacist to the intervention group will make a significant contribution to the health of the patient within the framework of pharmaceutical care.

Keywords: Clinical Pharmacy, Drug-related problem, Heart Failure, Pharmaceutical Care

1. INTRODUCTION

Heart failure (HF) is a serious, life-threatening chronic condition associated with certain filling and drainage abnormalities in heart structure, function, rhythm, or conduction that rupture (1, 2). Chronic diseases are the main cause of morbidity and mortality worldwide. The prevalence of heart failure varies mainly between adult and elderly populations with a treatment approach that slows disease progression and relieves patients' symptoms (3).

Preclinical heart failure is four times more common than symptomatic heart failure. The criteria for diagnosing chronic heart failure (CHF) were established in accordance with the guidelines for the diagnosis and treatment of heart failure published by the European Society of Cardiology in 2016, emphasizing that self-care is an essential part of HF management and the drugs used in the pharmacotherapy of heart failure (4, 5, 6).

For HF pharmacotherapy, the drug related problem (DRP) is one of the main problems that need to be defined, identified and used to solve the situation. The DRP is defined as the effect of a disease that is intended to be achieved with medication treatment, with an existing or potential negative situation stemming from the drug itself. Because DRPs deal with current or potential problems and can be identified as side effects or drug failures, the grading of the urgency of the situation in terms of resolution depends on potential injuries, harms, and the risk rate of that harm to the patient,

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which correlates primarily with the Rational drug use (RUD) concept. This is also a key point where clinical pharmacists have an important role to play when it comes to involving patient care pharmacists in DRP therapy with other healthcare professionals (7, 8). Many studies have shown that pharmaceutical care reduces PRM status by 50-80% by reducing the number of adverse drug reactions (ADRs), length of hospital stay and maintenance costs (9, 10) .

The aim of the present study is to identify the clinical pharmacist's role in the prevention and elimination of drug-related problems, particularly in patients with heart failure, in a full-capacity university hospital setting, which was attempted to determine with a Pharmaceutical Care Survey (ordered by the classification of the European Association of Pharmaceutical Care Network (PCNE)) (11).

2. METHODS

This was a prospective study that randomly enrolled 160 adult patients of both genders. Patients in the study group were admitted to the hospital with a diagnosis of heart failure, who were hospitalized, and discharged. At discharge, the patients in the study group were randomly divided into two subgroups of 80 and designated as the control and intervention groups

The patients' registration sequence numbers during their hospital stay were processed in the random number generator program and the random numbers generated by the program were organized and the first 80 patient groups were assigned as a control group and the second 80 patient groups as an intervention group.

Simultaneously, the PCNE classification (version 8.01) was performed for both groups to monitor DRPs, and the validated "Pharmaceutical Care Survey" was used to assess the role and contribution of the clinical pharmacist in improving its measuring criteria (12).

The roles assumed in the association of physicians and clinical pharmacists for both groups are as follows: Physicians performed the clinical follow-up of the control group after discharge. Apart from their binding recommendations, they gave no further information. To the study design, there was no further information attempt by clinical pharmacists on this group.

In the intervention group, in addition to the doctors' usual clinical follow-ups, the clinical pharmacists repeated their information on the drug related problems in the PCNE classification and applied the "Pharmaceutical Care Survey", which would measure the improvement in patient monitoring.

The first step in the study was the discharge step of the patients. Three further steps were created to enable outpatient follow-up after discharge. These steps are referred to as:

1. Month Interval Outpatient Polyclinics: This is the step of following the routine control and recommendations of all patients summoned by doctors one month after discharge. The doctors performed routine examinations for all patients in the control and study groups. In addition to medical interventions, clinical pharmacists informed only 80 patients verbally in the intervention group about their prescription medications, gave them dietary advice, and answered patient questions. Standardization to ensure the readability of patient-pharmacist verbal interactions was accomplished by adapting the Pawson review protocol questions as communication tools, e.g. *"what works, for whom, in what circumstances, in what respects, to what extent and why"* (13,14). They also applied the "Pharmaceutical Care Survey" to patients.

3. Month Interval Clinical Pharmacy Department Communication: Clinical pharmacists attempted to answer questions and **inform** patients **over the phone** about the disease and their medications by calling patients in the intervention group.

6. Month Interval Routine Outpatient Clinics: In the fourth step of the study, the procedure carried out in the second step (month 1) was repeated again by the same team.

While the cardiologist performed a classic standard practice clinical assessment in both groups, the clinical pharmacist applied the PCNE classification system and a Pharmaceutical Care Survey.

3.1. Ethical Aspects

The study was approved by the Ethics Committee of Non-Interventional Clinical Investigations of Istanbul Medipol University (approval number 186 and date 16.05.2017).

3.2. Statistical Analysis

The descriptive statistics included the average, standard deviation, lowest and highest values. The number of DRPs was presented as an (%). The independent samples t-test was employed for the analysis of quantitative independent data. Categorized data were analyzed using the Chi square or Fisher exact test when required. A confidence interval of 95% and p value of <.05 were considered significant. The SPSS 22.0 statistical software package was used for all statistical analyses.

3. RESULTS

The aim of the present study is to identify drug-related problems, especially in patients with heart failure, to plan interventions for these problems, and to evaluate the effect of the clinical pharmacist in the cardiology room considering the acceptability/rejection of the interventions.

The gender distribution was 45% females and 55% males and 36% females and 64% males in the accompanying

intervention group. Gender distribution was not statistically significant at the p=.261 levels.

According to the Pharmaceutical Care Survey, patient responses to questions were converted to percentages of frequency and statistically evaluated using the chi-square test. Table 1 summarizes the differences in patient responses to Questions (Qs) 2, 4, 5, 7, 8, 9 and non-significance between the two groups is indicated.

Statistically significant differences were calculated for the remaining questions (p<.05). More specifically, compared to the control group, the intervention group was more likely not to forget to take their medication and was more aware of the importance of taking it. (Q1); experienced side effects of their medications (Q3); paid attention to changes in their body weight (Q6); and they were better informed and more aware of developing a productive cough (Q10).

As for the control and intervention groups, the detailed DRP data mentioned below, collected from the Pharmaceutical Care Survey, were reassessed at the end of the 6-month interval.

According to this assessment, 2 patients (2.9%) in the intervention group answered yes and 67 patients (97.1%) answered no due to the condition "forgot to take medication". On the other hand, 29 patients (36.2%) in the control group answered yes and 51 patients (63.7%) answered no.

The responses of the patients in the intervention group to the parameter "experience of side effects of the recommended drug" were "yes" in 3 patients (4.5%) and "no" in 64 (95.5%) patients, while these values were at 39 patients (48.8%) of the control group answered yes and 41 (51.2%) patients answered no.

The answers to the question "diet-related body weight gain" were as follows: 19 (29.2%) of the patients in the intervention group yes, 46 (70.8%) no; 43 (53.8%) of the patients in the control group answered yes and 37 (46.2%) no.

The responses to the question "development of a productive cough" are as follows: 16 (23.2%) of the intervention group answered yes, 53 (76.8%) no; 35 (43.8%) of the control group answered yes, 45 (56.2%) no. A statistically significant difference in the development of the "no" and "yes" answers to these question parameters was found between the groups and is shown in Table 1.

As shown in Table 2, when examining patient-reported reasons for DRPs, the most common in the control group were inappropriate medications or combinations of medications, while in the intervention group no medication was prescribed despite the current indication.

Table 3 shows the types of DRP. According to the results, all patients required intervention for a problem related to the medication they were taking that was relevant to their disease. The adverse drug event that occurred was the most common DRP (50%) with a statistically significant difference (p<.05) compared to all other problem types in the control group. Inadequate drug response was the most common DRP (28.7%) with a statistically significant (p<.05) compared to the remaining problem types in the study group. Cost-related problems were not identified in any of the patients.

Of the interventions of this study, 72.5% were accepted, 6.2% were not accepted, and 21.2% were included in the other category.

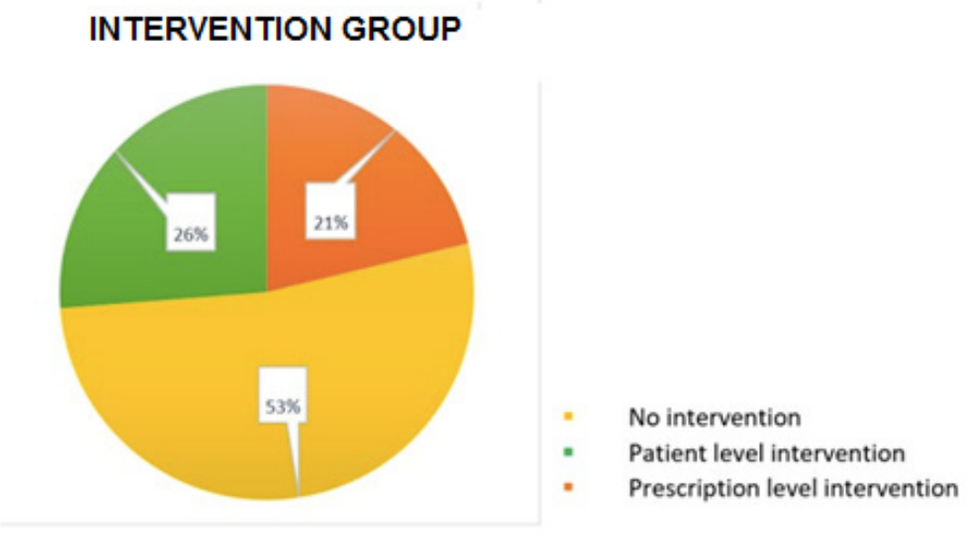

Figure 1. *Types of clinical pharmacist intervention*

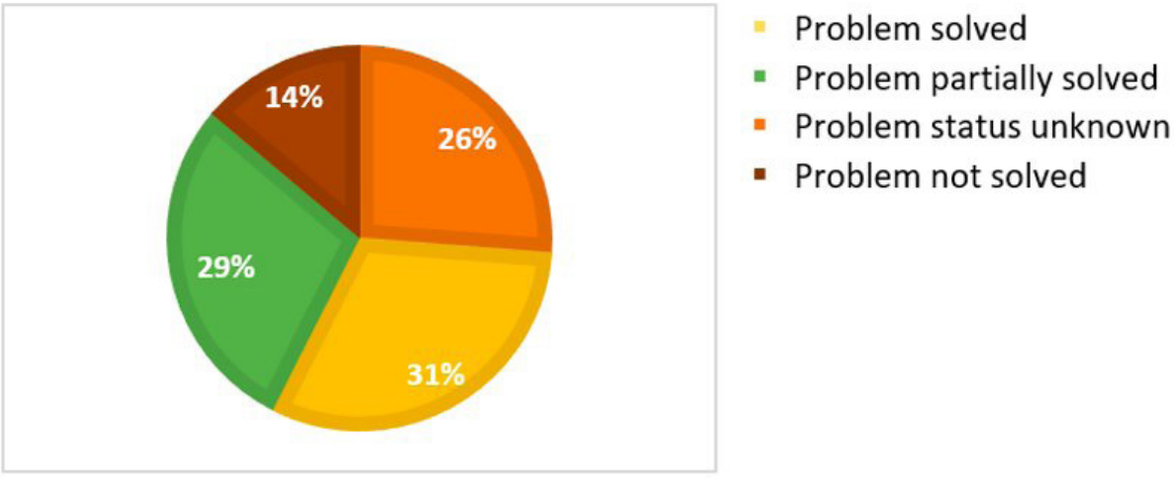

Figure 2. *Clinical Pharmacist Intervention Results*

Table 1. *Comparison of the Sixth-Month Pharmaceutical Care Survey*

		Intervention		Control		p
		n	%	n	%	
Have you ever forgotten to take your medicine or preferred not to take it?	Yes	2	2.9%	29	36.2%	p<.05
	No	67	97.1%	51	63.7%	
Do you know what you need to do when you miss a dose of your medicine?	Yes	51	83.6%	61	76.2%	p>.05
	No	10	16.4%	19	23.8%	
Have you experienced any side effects from your medication?	Yes	3	4.5%	39	48.8%	p<.05
	No	64	95.5%	41	51.2%	
Do you have a blood test regularly?	Yes	54	94.7%	73	91.2%	p>.05
	No	3	5.3%	7	8.8%	
Do you smoke?	Yes	6	8.8%	13	16.2%	p>.05
	No	62	91.2%	67	83.8%	
Have you observed any changes in your weight several times?	Yes	19	29.2%	43	53.8%	p<.05
	No	46	70.8%	37	46.2%	
Have you observed any swelling or increased swelling in your ankles?	Yes	40	63.5%	46	57.5%	p>.05
	No	23	36.5%	34	42.5%	
Have you noticed any shortness of breath or an increase in your breathing problems during exercise?	Yes	56	82.4%	64	80.0%	p>.05
	No	12	17.6%	16	20.0%	
Have you noticed any shortness of breath or an increase in your breathing problems during sleep at night?	Yes	34	52.3%	46	57.5%	p>.05
	No	31	47.7%	34	42.5%	
Do you have a productive cough?	Yes	16	23.2%	35	43.8%	p<.05
	No	53	76.8%	45	56.2%	

Table 2. *Causes of DRPs in Control and Study Groups*

		Intervention		Control	
		n	%	n	%
C	Inappropriate drug	0	0.0%	2	2.5%
	Inappropriate combination of drugs or drugs and herbal medication	6	7.5%	21	26.2%
	No drug treatment in spite of existing indication	20	25.0%	13	16.2%
	Numerous drugs are prescribed for indication	0	0.0%	1	1.2%
	Drug dose too low	2	2.5%	1	1.2%
	Drug dose too high	6	7.5%	14	17.5%
	Dosage regimen not frequent enough	2	2.5%	1	1.2%
	Dosage regimen too frequent	3	3.8%	2	2.5%
	Necessary information not provided	1	1.2%	0	0.0%
	Wrong drug, strength or dosage advised	3	3.8%	1	1.2%
	Wrong drug or strength dispensed	1	1.2%	0	0.0%
	Inappropriate timing of administration and / or dosing intervals	4	5.0%	0	0.0%
	Drug under–administered	1	1.2%	0	0.0%
	Drug over-administered	2	2.5%	0	0.0%
	Drug not administered at all	3	3.8%	0	0.0%
	Wrong drug administered	1	1.2%	2	2.5%
	Patient uses less drug than prescribed or does not take the drug at all	3	3.8%	0	0.0%
	Inappropriate timing or dosing intervals	7	8.8%	8	10.0%
	Patient uses the drug in a wrong way	5	6.2%	1	1.2%
	Patient unable to use the drug as directed	1	1.2%	0	0.0%
	Medication follow-up is not done properly	9	11.2%	13	16.2%

Table 3. *Types of problems in control and intervention groups*

		Intervention		Control	
		n	%	n	%
P	No effect of drug treatment	15	18.8%	5	6.2%
	Effect of drug treatment not optimal	23	28.7%	24	30%
	Untreated symtomps or indications	19	23.8%	9	11.2%
	Advers drug event occuring	13	16.2%	40	50%
	Unnecessary drug treatment	4	5%	0	0%
	Unclear problem or complaint	6	7.5%	2	2.5%

4. DISCUSSION

In the study by Roblek et al. (2016), in which DRPs were evaluated in 213 patients with heart failure, 66 clinically significant DRPs were found in 51 patients. As a result of the interventions performed, it was found that the number of patients with DRP at discharge was significantly lower (10 versus 31; p=.0049). The results show the importance of clinical pharmacist intervention to reduce the number of patients with drug-related problems (15).

In another study, Sadik et al. (2005) evaluated the effect of a pharmacist-led pharmaceutical care follow-up program on optimizing pharmacological therapy in 160 patients with heart failure, and at the end of 12 months, enlightened patients were unaffected by the prescribed medications (85 vs. 35) and lifestyle changes (75 vs. 29) showed higher compliance than control patients (16).

In the study by Varma et al. (1999) 83 patients with heart failure were educated about lifestyle changes, monitoring of

their symptoms, and pharmacologic treatments to evaluate the outcome of a pharmaceutical care program. As a result of the 12-month study, it was documented that patients who received training showed better adherence to therapy and increased physical performance (17).

In this study, as in the studies by Sadik and Varma et al., the results obtained showed that patient awareness increased, particularly in the intervention group. Patients in the intervention group, who were informed and trained in the field of pharmaceutical care, forgot to take their medication less often than the control group and became more aware of the importance of taking medication. They were found to be more aware of the side effects they may experience associated with drug therapy. They also paid more attention to maintaining their body weight.

In the studies by Chambela et al. (2020) to emphasize the importance of pharmaceutical care in 81 heart failure patients, found that DRPs were reduced in all patients in the intervention group compared to baseline DRPs. The ADR, which was 17.5% at the start of the study, fell to 8.8% at the end of the 12th month. In the control group, the ADRs remained at the same level from the start to the end of the study (18).

In the study by Adriano et al. (2017) found that pharmaceutical care services prevent the development of DRP by 50-80% and reduce the number of ADRs (9). In the study by Winterstein et al. (2002) reported that in a study of patients hospitalized for DRP, about 60% of DRP could be prevented (19). Shastry et al. (2019) evaluated drug interactions and adverse drug reactions in 120 patients with ischemic heart disease and reported that 40% of the adverse drug reactions identified were preventable (20).

In this study, DRPs were shown to completely resolve as a result of the interventions in 31% of patients. For 26% of the patients who underwent the intervention, the results of the interventions are unknown for various reasons.

In the study conducted in the clinical pharmacy unit of Lycksele Hospital in Sweden, interventions for DRPs were performed in 88% of cases. The rate of patients with medication-related problems was 66% (68/103), and the most common DRPs were inappropriate medication use (39/133), drug interaction (21/133), incomplete medication (12/133, and overdose (12/133) (21).

In the study by Dempsey et al. (2017) to identify the important role of pharmacists in 60 patients diagnosed with heart failure and to document the prevalence of problems related to drug therapy, 304 drug-related problems were identified. In 22% of drug-related problems, pharmacists intervened to change the medication regimen. According to the results obtained, all patients in this study required intervention due to some problems with their pharmacotherapies. It was found that 53% of patients in the study group required intervention at the prescribed level. 72.5% of the interventions were successful, while 6.2% did not accept them. Patient-level interventions were performed in 26% of patients. The most common drug-related problems in patients have been reported as an untreated indication or inadequate treatment and drug interactions (22).

In our study, the most common drug-related problem in the group of patients in whom we conducted the drug survey was non-optimal drug response (28.7%). In the uninformed and educated control group, adverse drug reactions (50%) were the most common problem. When examining the underlying causes of drug-related problems, inappropriate drug use or combination of drugs was the most common cause in the control group; non-prescribing of medication despite current indication is the most common reason identified in the intervention group. Our findings are like these studies in relation to the types and causes of drug problems.

The results of these two studies, supported by the Lycksele Hospital Study and Dempsey et al. (2017) point out the importance of advice and information, training and the role of the clinical pharmacist in relation to pharmaceutical care services and show that this makes a positive contribution to the health of the patient. Like the other studies mentioned here, these studies also agree with the results of our present study.

As indicated in Table 1, the collected data from the "Pharmaceutical Care Survey" were reassessed at the end of the 6th month with regard to the control and intervention groups. After that, patients in the intervention group were informed about the parameters "forgetting to take medication", "experience of side effects of the recommended medication, diet-related increase in body weight and occurrence of productive cough". If this information process is counted as training, the positive results in the intervention group are statistically significant compared to the control group.

Drug-related problems are common in most people with various illnesses. Patient education or training is an important criterion in solving drug-related problems. Although patient education does not cover all pharmaceutical care services, it occupies an important place within the clinical pharmacist's services. When evaluating the results, the intervention group treated with medication differed significantly from the control group. This result can be considered a good measure of the importance of pharmaceutical care and the functional benefit of clinical-pharmaceutical services.

In this study, it is argued that clinical pharmacists can play an effective role in improving the DRPs of heart failure patients, and it can be predicted that the information and warning training provided by the clinical pharmacist to the intervention group will make a significant positive contribution for the patient's health as a follow-up of pharmaceutical care.

This study has some limitations. First, it was conducted in a single center with a limited number of patients. Additionally, the limitations here are to only assess the prevalence of DRP-related PCNE criteria's in a single center. Despite the limitations of this study, it also validates the importance

of clinical pharmacy services in identifying, resolving, and preventing DRPs in heart failure consultations. Our DRP findings from this study become more tangible when the extent to which patient education can contribute to treatment is replicated at the multicenter and country levels.

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