# ROLE OF PHARMACISTS IN REDUCING DRUG-RELATED PROBLEMS IN HEMODIALYSIS OUTPATIENTS

## ROMAULI LUMBANTOBING[1], RANI SAURIASARI[2], RETNOSARI ANDRAJATI[2]*

[1]Department of Pharmacy, Universitas Kristen Indonesia Hospital, Jakarta, Indonesia. [2]Department of , Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia. Email: andrajati@farmasi.ui.ac.id

## ABSTRACT

**Objectives:** Hemodialysis outpatients have a higher risk of developing drug-related problems. Pharmacists play a key role in identifying and preventing these drug-related problems. This study aimed to assess the effect of pharmacist intervention on the number and types of drug-related problems in outpatients undergoing hemodialysis at Indonesia Christian University Hospital.

**Methods:** This pre- and post-prospective study was conducted from January 2013 to June 2013. We evaluated 86 patients who were prescribed 804 drugs.

**Results:** A total of 337 drug-related problems were identified (41.86% of the total drugs prescribed). The types of drug-related problems identified were as follows: Failed therapy (18.69%); sub-optimal therapy (52.23%); indication of non-administration of therapy (2.37%); and non-allergic adverse drug effects (26.71%). The physicians received 59 recommendations, and the patients received 278 recommendations. These recommendations resulted in a decrease in ineffective drug therapy or therapeutic failure (18.69-0%), sub-optimal therapy (52.23-21.36%), indications of non-administration of drug (2.37-2.08%), and non-allergic adverse drug effects (26.71-9.20%). The factors that significantly affected the occurrence of drug-related problems were hemodialysis frequency, number of comorbidities, and number of drugs prescribed. Patients undergoing hemodialysis 3 times a week were more likely to experience a decrease in drug-related problems than those undergoing hemodialysis twice a week (odds ratio 26.33, 95% confidence interval 2.710-255.884).

**Conclusions:** Pharmacist intervention could decrease drug-related problems in hemodialysis patients.

**Keywords:** Role of pharmacists, Drug-related problems, PCNE-6.02, Hemodialysis, Outpatient.

## INTRODUCTION

A drug-related problem is a drug therapy-associated event that disrupts or potentially disrupts the achievement of the desired therapeutic outcome [1]. Sequential drug administration, simultaneous drug administration, or both; low adherence to treatment regimens; and drug interactions may lead to drug-related problems [2]. Drug-related problems generally occur in patients with renal failure and in hemodialysis outpatients. Patients with chronic renal failure undergoing hemodialysis therapy have a higher risk of drug-related problems because hemodialysis outpatients are more likely to have comorbidities such as diabetes mellitus, hypertension, coronary artery disease, and infections, necessitating complex therapies such as five or more drugs, with 12 or more medication doses per day. In addition, some drugs used for the treatment of patients undergoing hemodialysis require monitoring and dose adjustment [3].

Patients undergoing chronic hemodialysis therapy generally have low medication adherence. Therefore, in some studies, the incidence of adverse drug reactions was higher in patients with chronic renal failure than in those without renal failure [3]. Manley *et al.* (2005) identified 1593 drug-related problems in 395 chronic renal failure patients undergoing hemodialysis [4]. Another study conducted in Dr. Ramelan Naval Hospital in Surabaya, Indonesia, investigated drug-related problems in hemodialysis outpatients in Indonesia. The prevalence rate of failure to obtain drug prescriptions was 32.20%, overly low dose was 20.34%, drug-related side effects was 14.41%, untreated indications was 5.93%, overly high dose was 3.39%, and therapy without indication was 1.70% [5].

Even though polypharmacy and high risk for adverse drug-related problems are common in hemodialysis outpatients, few studies have investigated drug-related problems in this population. As a provider of pharmacy services, a pharmacist is responsible for managing drug-related problems by identifying these problems, implementing solutions in the form of interventions, and taking action proactively to prevent their occurrence [6].

In a study conducted in the Netherlands by Klopotowska *et al.* [7], pharmacist participation in the intensive care unit resulted in 659 recommendations of 1173 prescribed drugs, with a 74% physician acceptance rate. Pharmacist intervention for the prevention of drug-related problems can reduce the cost of healthcare, save lives, and improve the patients' quality of life [8-10]. To date, no studies conducted in Indonesia have investigated the prevalence of hemodialysis in outpatients because the data available on the number of hemodialysis outpatients are incomplete. However, the number of hemodialysis outpatients in Indonesia is expected to increase.

This study was conducted at Indonesia Christian University General Hospital (RSU UKI), which has been providing hemodialysis services since 2004, with a consistent annual increase in the number of hemodialysis outpatients. In 2010, UKI Hospital provided hemodialysis services to an average of 65 outpatients per month, and this number increased to an average of 76 patients per month in 2012. On average, every hemodialysis patient received five different classes of therapeutic drugs. This study aimed to identify drug-related problems, and assess the effect of pharmacist intervention on the number and types of drug-related problems in hemodialysis outpatients at Indonesian Christian University General Hospital.

## METHODS

This study was an experimental study with a pre-post design. Pre-tests were conducted to determine the initial patient status for comparison with the patient status after the recommendation(s) had been implemented. This study was conducted in the internal disease hemodialysis room of the Indonesia Christian University Hospital, Jakarta, from January 2013 to June 2013. The data were retrieved for the period from March 2013 to May 2013.

### Sample

This study sample consisted of 86 hemodialysis outpatients who were prescribed 804 drugs. Three physicians were involved in the study: The physicians on duty in the specialist practicing room, internal disease polyclinic room, and hemodialysis room, who were willing to receive recommendations. The inclusion criteria for the study sample were outpatients undergoing hemodialysis and age ≥20 years.

### Data collection

Before being given to patients, the prescriptions from the physicians were first analyzed to identify potential drug-related problems. When drug-related problems were present, the researchers communicated the problems to the physicians and provided appropriate recommendations to resolve the problems. The researchers assessed the results of these recommendations by monitoring changes in drug therapy in the prescription note or in the patients' medical records. A decline in the number of drug-related problems was defined as implementation of the pharmacist-recommended drug therapy by the physicians. When the drug-related problems occurred because of improper use of drugs by the patients or because of the personality or behavior of the patient, the researchers provided recommendations to the patients in accordance with the problem. The effects of the recommendations given to the patients were assessed on the basis of a change in patient behavior in terms of drug usage, which was determined from information provided by the patients and their family, and the observations of the researchers. A decline in the number of drug-related problems was defined as a change in patient behavior in accordance with the researchers' recommendations.

## RESULTS

### Patient demographics

This study included 45 (52.33%) male and 41 (47.67%) female patients, aged 22-75 years old. The 41-60-year-old patient group had the most patients (48.84%).

### Clinical characteristics of hemodialysis outpatients

The etiologies of renal failure in the study patients were as follows: Diabetes mellitus, 35 patients (40.70%); hypertension, 30 patients (34.88%); infections and other causes, 9 patients (10.47%); and polycystic kidney disease, 3 patients (3.49%), others 9 (10.47%). Regarding the duration of hemodialysis, the 0-12-month group had the highest number of patients with 38 patients (44.19%), followed by the 13-24-month group with 17 patients (19.77%) and the ≥25-month group with 31 patients (36.05%). Regarding the weekly frequency of hemodialysis, the highest number of patients underwent dialysis twice a week (81 patients, 94.19%), followed by 3 times a week (5 patients, 5.81%).

### Comorbidities in hemodialysis outpatients

Of the 86 hemodialysis outpatients, 37 (42.02%) had <3 comorbidities and 49 (56.98%) had ≥3 comorbidities.

### Types of comorbidities in hemodialysis outpatients

Anemia was the most common comorbidity in hemodialysis outpatients, affecting 76 patients (88.37%), followed by hypertension in 47 patients (54.65%), nausea in 33 patients (38.37%), ascites and edema in 23 patients (26.74%), and cough in 18 patients (20.93%). The complete data are presented in Table 1.

**Table 1: Types of comorbidities in hemodialysis outpatients**

| Type of comorbidity | Number of patients of 86 patient (%) |
|---|---|
| Ascites and edema | 23 (26.74) |
| Anemia | 76 (88.37) |
| Body ache | 4 (4.65) |
| Cough | 18 (20.93) |
| Diabetes mellitus | 4 (4.65) |
| Skin disorders | 11 (12.79) |
| Urinary tract disorders | 5 (5.81) |
| Hypertension | 47 (54.65) |
| Lymphadenitis | 5 (5.81) |
| Nausea | 33 (38.37) |
| Shortness of breath | 7 (8.14) |

### Drug therapy of hemodialysis outpatients

Hemodialysis outpatients have a high risk of drug-related problems because they are generally prescribed ≥5 drugs. In this study, 79 patients (91.86%) received ≥5 drug therapies, and 7 patients (8.14%) received <5 drug therapies. Vitamin B complex and Vitamin C 500 mg are generally prescribed to all patients undergoing hemodialysis. In this study, 84 patients (97.67%) received calcium carbonate, 67 patients (77.91%) received ferrous sulfate, 53 patients (61.63%) received sodium bicarbonate, 52 patients (60.47%) received amlodipine, 44 patients (51.16%) received epoetin alfa, 40 patients (46.51%) received folic acid, 30 patients (34.88%) received omeprazole, and 20 patients (23.26%) received captopril. Drug therapy data are shown in Table 2.

Supplements were the most commonly prescribed drug class with 237 drugs (29.48%), followed by antihypertensives (162, 20.15%), antianemics (159 drugs, 19.78%), drugs for bone disorders (88 drugs, 10.95%), metabolic acidosis drugs (53 drugs, 6.59%), and drugs for gastrointestinal disorders (50 drugs, 6.22%). Data on drug therapy by class and frequency are presented in Table 3.

### Drug-related problems in hemodialysis outpatients

The type and number of drug-related problems were identified using Pharmaceutical Care Network Europe V6.02 classification. A total of 337 drug-related problems were identified and classified into four types: Failed therapy 63 (18.69%), suboptimal therapeutic effects 176 (52.23%), indications of non-administration of drug 8 (2.37%), and non-allergic adverse drug effects 90 (26.71%). Data on the prevalence of drug-related problems by type are presented in Table 4.

### Drugs causing drug-related problems before recommendation

Out of 65 drug classes prescribed to hemodialysis outpatients, 12 drug classes caused drug-related problems. The drug that caused the most drug-related problems were $CaCO_3$ with 176 problems (52.23%), followed by ferrous sulfate with 63 problems (18.69%), erythropoiesis-stimulating agents (ESA) with 32 problems (9.50%), and omeprazole with 30 problems (8.90%). The drugs that caused drug-related problems are listed in Table 5.

### Pharmacist recommendations

Since the patients were outpatients, they received 277 pharmacist recommendations (82.20%) compared to the 59 recommendations (17.40%) given to the physicians. The types of recommendations given to prescribers and patients to prevent and manage drug-related problems are described in Table 6. The recommendations included adjustment of dose, frequency of drug administration, time of drug administration by patients, information on drug side effects or the effects of simultaneous drug administration, and drug monitoring recommendations.

### Decrease in the type and number of drug-related problems before and after recommendations

After the implementation of pharmacist recommendations, a decrease was observed in different types of drug-related problems (Table 7):

**Table 2: Classes and frequency of drugs prescribed to hemodialysis outpatients**

| Drug class | Drug | Number of patients of total patients (%) |
| --- | --- | --- |
| Anemia | hemapo/recormon | 44 (51.16) |
| Anemia | Fe sucrose | 8 (9.30) |
| Anemia | Ferrous sulfate | 67 (77.91) |
| Anemia | Folic acid | 40 (46.51) |
| Metabolic acidosis | Sodium bicarbonate | 53 (61.63) |
| Bone disorders | CaCo3/Ca acetate | 84 (97.67) |
| Bone disorders | Calcitriol/active Vitamin D | 4 (4.65) |
| Antihypertensive | Amlodipine | 52 (60.47) |
| Antihypertensive | Nifedipine | 5 (5.81) |
| Antihypertensive | Diltiazem | 5 (5.81) |
| Antihypertensive | Bisoprolol | 22 (25.58) |
| Antihypertensive | Captopril | 20 (23.26) |
| Antihypertensive | Imidapril | 1 (1.16) |
| Antihypertensive | Lisinopril | 1 (1.16) |
| Antihypertensive | Perindopril | 1 (1.16) |
| Antihypertensive | Ramipril | 1 (1.16) |
| Antihypertensive | Clonidine | 5 (5.81) |
| Antihypertensive | Irbesartan | 9 (10.47) |
| Antihypertensive | Telmisartan | 7 (8.14) |
| Antihypertensive | Valsartan | 13 (15.12) |
| Vasodilators | Isosorbide dinitrate | 9 (10.47) |
| Cardiac glycoside | Digoxin | 1 (1.16) |
| Antiarrhythmic | Amiodarone | 1 (1.16) |
| Diuretic | Furosemide | 14 (16.28) |
| Anticholesterol | Simvastatin | 4 (4.65) |
| Antidiabetic | Gliquidone | 5 (5.81) |
| Antidiabetic | Insulin | 2 (2.33) |
| Antigout | Colchicine | 1 (1.16) |
| Antibiotic | Ciprofloxacin | 2 (2.33) |
| Antiplatelet aggregation | Acetyl salicylic | 5 (5.81) |
| Antiplatelet aggregation | Clopidogrel | 5 (5.81) |
| Benzodiazepine | Alprazolam | 4 (4.65) |
| Benzodiazepine | Lorazepam | 2 (2.33) |
| Antihistamine-H2 | Cimetidine | 1 (1.16) |
| Antihistamine-H2 | Ranitidine | 9 (10.47) |
| Proton pump inhibitor | Omeprazole | 30 (34.88) |
| Antacid | Antacids | 2 (2.33) |
| Antacid | Sucralfate | 5 (5.81) |
| Laxative | Laxadine | 2 (2.33) |
| Analgesic | Neuralgin | 2 (2.33) |
| Analgesic | Paracetamol | 4 (4.65) |
| Supplement | Albumin | 3 (3.49) |
| Supplement | Hemobion | 9 (10.47) |
| Supplement | Kalitake | 3 (3.49) |
| Supplement | Ketosterol | 2 (2.33) |
| Supplement | KSR | 2 (2.33) |
| Supplement | ProRenal | 13 (15.12) |
| Supplement | Renogard | 3 (3.49) |
| Supplement | Sangobion | 1 (1.16) |
| Supplement | Theragram | 2 (2.33) |
| Supplement | Virinon | 1 (1.16) |
| Supplement | Vitamin B12 | 8 (9.30) |
| Supplement | Vitamin E/fundamin E | 1 (1.16) |
| Supplement | Biosanbe | 1 (1.16) |
| Supplement | Neurobion | 5 (5.81) |
| Supplement | Neurodex | 11 (12.79) |
| Supplement | Sohobion/neurobion IV | 86 (100.00) |
| Supplement | Vitamin C 500 mg (IV) | 86 (100.00) |
| Antihistamine-H1 | Cetirizine | 3 (3.49) |
| Antihistamine-H2 | Diphenhydramine | 1 (1.16) |
| Dopamine antagonist | Domperidone | 4 (4.65) |
| Receptor antagonist, 5-HT3 | Ondansetron | 4 (4.65) |
| Mucolytic | Fluimucil | 1 (1.16) |
| Mucolytic | Cough syrup | 5 (5.81) |
| Mucolytic | Benadryl | 1 (1.16) |

The number of non-effective or failed therapy cases decreased from 63 (18.69%) to 0 (0%), suboptimal therapeutic effect cases decreased from 176 (51.92%) to 72 (21.24%), cases with indication of non-treatment decreased from 8 (2.36%) to 7 (2.06%), and patients experiencing non-allergic adverse drug effects decreased from 90 (26.55%) to 31 (9.14%).

**Table 3: Class of drugs prescribed to hemodialysis outpatients**

| Class of drugs | Number of prescriptions (%) |
|---|---|
| Anemia | 159 (19.78) |
| Metabolic acidosis | 53 (6.59) |
| Bone disorders | 88 (10.95) |
| Antihypertensive | 162 (20.15) |
| Anticholesterol | 4 (0.5) |
| Antidiabetic | 7 (0.87) |
| Antigout | 1 (0.12) |
| Antibiotic | 2 (0.25) |
| Anticoagulant | 10 (1.24) |
| Anxiolytics | 4 (0.5) |
| Benzodiazepine | 2 (0.25) |
| Gastrointestinal | 50 (6.22) |
| Analgesic | 6 (0.75) |
| Supplements | 237 (29.48) |
| Antihistamine-H1 | 4 (0.5) |
| Antinausea | 8 (1) |
| Mucolytic | 7 (0.87) |
| Total | 804 (100.00) |

**Table 4: Type and number of drug-related problems in hemodialysis outpatients of Indonesia Christian University Hospital**

| Type of problems | Number of problems (%) |
|---|---|
| Failed therapy | 63 (18.69) |
| Suboptimal therapeutic effect | 176 (52.23) |
| Effect of wrong medication | 0 (0.00) |
| Indication of non-administration of drug | 8 (2.37) |
| Non-allergic adverse drug effect | 90 (26.71) |
| Allergic adverse drug effect | 0 (0.00) |
| Toxic effect | 0 (0.00) |
| Total | 337 (100.00) |

**Table 5: Drugs that caused drug-related problems in hemodialysis outpatients**

| Drug names | Number of drug-related problems before recommendation (%) |
|---|---|
| Amlodipine | 6 (1.78) |
| Acetylsalicylic acid | 1 (0.3) |
| Perindopril | 1 (0.3) |
| CaCO3 | 176 (52.23) |
| Clonidine | 2 (0.59) |
| ESA | 32 (9.5) |
| Furosemide | 8 (2.37) |
| Irbesartan | 7 (2.08) |
| Omeprazole | 30 (8.9) |
| Ferrous sulfate | 63 (18.69) |
| Valsartan | 4 (1.19) |
| Active Vitamin D | 7 (2.08) |

ESA: Erythropoiesis-stimulating agent

**Decrease in the types and number of drug-related problems according to recommendation target**

The type and number of drug-related problems according to the recommendation target are shown in Table 8. Before recommendation, 337 drug-related problems were identified, and after pharmacist recommendations were provided to physicians, this number went down to 59 (17.40%). The 277 recommendations to patients reduced the number of drug-related problems to 168 (49.85%).

**Decrease in the number of drug-related problems according to drug**

The number of drug-related problems caused by amlodipine decreased from 6 (1.78%) to 0 after implementation of pharmacist

recommendations. Similar decreases were observed for acetylsalicylic acid, perindopril, clonidine, furosemide, irbesartan, omeprazole, ferrous sulfate, and valsartan. CaCO3 caused the most drug-related problems with 176 problems (52.23%), which decreased to 77 problems (22.85%) after pharmacist recommendations were implemented. ESA administration caused 32 (9.50%) drug-related problems, and this number did not decrease after implementation of the recommendation to use it for correction of hemoglobin levels. Similarly, drug-related problems caused by active vitamin D did not decrease after application of the pharmacist recommendation. Data on the number of drug-related problems before and after recommendation are presented in Table 9.

Regression test resulted in significant $0.000 < \alpha = 0.05$ indicating that at least one estimated value of $\beta$ is not equal to 0 (Tables 10 and 11). The linear regression analysis resulted in model $Y = 1552 - 0578$ (hemodialysis frequency) $+ 0.252$ (number of diseases) $+ 0.420$ (number of drugs before the recommendation). This means that if the frequency of hemodialysis increases by 1, the number of drug-related issues will be decreased by 0.578, assuming a constant number of diseases and drugs. If the number of comorbidities is increased by one, the number of drug-related problems will increase by 0.252, assuming that the disease and the number of drugs remain constant. The number of drug-related problems will increase by 0.420 if the number of drugs is increased by one, assuming that the disease and the number of drugs remain constant. Confounding variables were statistically tested against the decreases in the number of drug-related problems: Sex, age, number of drugs prescribed, weight, frequency of hemodialysis, and number of comorbidities. The factors that significantly affected the occurrence of drug-related problems were hemodialysis frequency, number of comorbidities, and number of drugs prescribed. Patients undergoing hemodialysis three times a week were more likely to experience a decrease in drug-related problems than those undergoing hemodialysis twice a week (odds ratio 26.33, 95% confidence interval 2.710-255.884).

## DISCUSSION

### Decrease in drug-related problems

Drug-related problems were evaluated by first identifying the drug-related problems according to the category of Pharmaceutical Care Network Europe V6.2 [1]. A total of 804 drugs were evaluated, resulting in the identification of 337 drug-related problems and 337 pharmacist recommendations for the prevention or management of these drug-related problems. After evaluation, we found that 110 (32.45%) drug-related problems could not be managed. These drug-related problems were because of economic reasons such as lack of insurance coverage for the drugs and examinations required by the patients because they were not listed in the insurance formulary.

Various studies have shown that pharmacists are able to identify and manage drug-related problems. Pharmacist recommendations for preventing drug-related problems are instrumental to reducing the cost of healthcare, saving lives, and improving patients' quality of life [8]. Prevention of overdose by pharmacists can improve patient safety and decrease the risk of drug toxicity and side effects. Optimization of the drug administration schedule may reduce the risk of drug interactions and side effects, optimize therapeutic effects, and increase patient acceptance of polypharmacy. Pharmacists also play a role in the selection of drugs for achieving maximal therapeutic effectiveness, minimal toxicity, and optimal cost-effectiveness [11].

CaCO3 resulted in the highest number of drug-related problems likely because it interacted with other drugs, thereby reducing their levels and effects. Another contributing factor was the lack of monitoring of blood calcium content because the high cost of this test made it unaffordable to patients. The National Health Security and Certificate of Financially-challenged citizen do not cover ESAs in the security formulary, resulting in the correction of anemia

**Table 6: Types of recommendations given to physicians and hemodialysis outpatients**

| Drug | Type of drug-related problem | Type of recommendation | Recommendation target |
|---|---|---|---|
| Amlodipine | Therapy effectiveness | Change administration time | Patients |
| Amlodipine | Drug-related problems | Reduce administration frequency | Physicians |
| Amlodipine | Drug-related problems | Avoid combination | Physicians |
| Amlodipine | Drug-related problems | Monitor | Physicians |
| Perindopril | Drug-related problems | Reduce dosage | Physicians |
| CaCO3 | Therapy effectiveness | Change administration time | Patients |
| CaCO3 | Therapy effectiveness | Perform Ca, P, PTH examination | Patients |
| CaCO3 | Drug-related problems | Stop administration | Physicians |
| Clonidine | Drug-related problems | Reduce administration frequency | Physicians |
| ESA | Drug-related problems | ESAs benefit | Patients |
| Furosemide | Drug-related problems | Monitor interaction | Physicians |
| Irbesartan | Drug-related problems | Monitor interaction | Physicians |
| Omeprazole | Drug-related problems | Reduce administration frequency | Physicians |
| Ferrous sulfate | Therapy effectiveness | Change administration time | Patients |
| Valsartan | Drug-related problems | Monitor interaction | Physicians |
| Active Vitamin D | Therapy effectiveness | Changed medicine | Patients |

ESA: Erythropoiesis-stimulating agents

**Table 7: Type and number of drug-related problems before and after the implementation of pharmacist recommendations**

| Type of recommendation | DRP before recommendation (%) | DRP after recommendation (%) |
|---|---|---|
| Failed therapy | 63 (18.69) | 0 (0) |
| Suboptimal therapeutic effect | 176 (52.23) | 72 (21.36) |
| Effect of wrong medication | 0 (0) | 0 (0) |
| Indication of non-administration of therapy | 8 (2.37) | 7 (2.08) |
| Non-allergic adverse drug effect | 90 (26.71) | 31 (9.2) |
| Allergic adverse drug effect | 0 (0) | 0 (0) |
| Toxic effect | 0 (0) | 0 (0) |
| Total | 337 (100) | 110 (32.64) |

DRP: Drug-related problems

**Table 8: Types and number of drug-related problems according to the recommendation target**

| Type of drug-related problems | Recommendation target | | | |
|---|---|---|---|---|
| | Physicians | | Patients | |
| | DRP before recommendation (%) | DRP after recommendation | DRP before recommendation (%) | DRP after recommendation (%) |
| Failed therapy | - | - | 63 (18.69) | 0 |
| Less optimal therapeutic effect | 3 (0.88) | 0 | 173 (51.34) | 72 (21.36) |
| Effect of wrong medication | - | - | - | - |
| Indication of non-administration of therapy | 1 (0.29) | 0 | 7 (2.08) | 7 (2.08) |
| Non-allergic adverse drug effect | 55 (16.22) | 0 | 35 (10.39) | 31 (9.20) |
| Allergic adverse drug effect | - | - | - | - |
| Toxic effect | - | - | - | - |
| | 59 (17.40) | 0 | 278 (82.49) | 110 (32.64) |
| Differences in DRP before and after recommendation | 59 (17.40) | | 168 (49.85) | |

DRP: drug-related problems

with blood transfusions, which have many adverse effects. Active Vitamin D is needed if the patient's blood calcium level is <8.8 mg/dL. However, since Vitamin D is expensive, most patients do not take it despite low blood calcium levels. The results of analysis showed that the number of drugs, comorbidities, and frequency of hemodialysis affected the number of drug-related problems before the recommendation.

**CONCLUSION**

A total of 337 (41.86%) drug-related problems were identified. The Wilcoxon statistical test revealed a significant change in the number of drug-related problems from before to after implementation of pharmacist recommendations. Factors that significantly influence the occurrence of drug-related problems are hemodialysis frequency, number of comorbidities, and number of drugs prescribed. Patients undergoing hemodialysis three times a week are likely to have fewer drug-related problems than those undergoing hemodialysis twice a week (odds ratio 26.33, 95% confidence interval 2.710-255.884). We would recommend that pharmacists should play an active role in monitoring drug-related problems in the hemodialysis room, and collaborate with other health workers to ensure optimum and integrated treatment of hemodialysis patients. Future studies should evaluate external changes in the patients' conditions after pharmacists assume a more active role in hemodialysis therapy management. The effectiveness of providing information on drug therapy through audiovisual aids in the hemodialysis room should also be investigated since most hemodialysis patients spend 4-5 hrs there.

**Table 9: Decrease in the number of drug-related problems after recommendation, according to drug**

| Drug | Number of drug-related problems before recommendation (%) | Number of drug-related problems after recommendation (%) |
|---|---|---|
| Amlodipine | 6 (1.78) | 0 (0) |
| Acetylsalicylic acid | 1 (0.30) | 0 (0) |
| Perindopril | 1 (0.30) | 0 (0) |
| CaCO3 | 176 (52.22) | 77 (22.85) |
| Clonidine | 2 (0.59) | 0 (0) |
| ESA | 32 (9.50) | 32 (9.5) |
| Furosemide | 8 (2.37) | 0 (0) |
| Irbesartan | 7 (2.08) | 0 (0) |
| Omeprazole | 30 (8.90) | 0 (0) |
| Ferrous sulfate | 63 (18.69) | 0 (0) |
| Valsartan | 4 (1.19) | 0 (0) |
| Active Vitamin D | 7 (2.08) | 7 (2.08) |
| Total | 337 (100.00) | 109 (34.43) |

ESA: Erythropoiesis-stimulating agent

**Table 10: Relationship between drug-related problems and confounding variables**

| Confounding variables | Asymptotic significance (2-sided) | Decision | Conclusion |
|---|---|---|---|
| Sex-DRP | 0.059 | >0.05, $H_0$ accepted | No correlation |
| Age-DRP | 0.694 | >0.05, $H_0$ accepted | No correlation |
| Total PP-DRP | 0 | <0.05, $H_0$ rejected | There is correlation |
| Frequency of hemodialysis-DRP | 0 | <0.05, $H_0$ rejected | There is correlation |
| Weight-DRP | 0.529 | >0.05, $H_0$ accepted | No correlation |
| Number of drugs-DRP | 0 | <0.05, $H_0$ rejected | There is correlation |

DRP: Drug-related problems

**Table 11: Logistic regression test results**

| Confounding variables | Asymptotic significance (2-sided) | Decision | Conclusion |
|---|---|---|---|
| Sex-DRP | 0.372 | >0.05, $H_0$ accepted | No correlation |
| Age-DRP | 0.916 | >0.05, $H_0$ accepted | No correlation |
| Total PP-DRP | 0.114 | >0.05, $H_0$ accepted | No correlation |
| Frequency of hemodialysis-DRP | 0.005 | <0.05, $H_0$ rejected | Correlation exits |
| Weight-DRP | 0.782 | >0.05, $H_0$ accepted | No correlation |
| Number of drugs-DRP | 0.297 | >0.05, $H_0$ accepted | No correlation |

DRP: Drug-related problems

## REFERENCES

1. Pharmaceutical Care Network Europe Foundation. Classification For Drug - Related Problems. V6.2 (revised 14-01-2010vm). PCNE; 2010.
2. Tozawa M, Iseki K, Iseki C, Oshiro S, Higashiuesato Y, Yamazato M, *et al.* Analysis of drug prescription in chronic haemodialysis patients. Nephrol Dial Transplant 2002;17(10):1819-24.
3. Hassan Y, Rowa JR, Aziz NA, Ghazali R. Drug use and dosing in chronic kidney disease. MRCP Clinical Pharmacy Programme. Penang: School of Pharmaceutical Science, University Sains Malaysia; 2009.
4. Manley HJ, McClaran ML, Overbay DK, Wright MA, Reid GM, Bender WL, *et al.* Factors associated with medication-related problems in ambulatory hemodialysis patients. Am J Kidney Dis 2003;41(2):386-93.
5. Irawati YW. Kajian Drug Related Problem Pada Panatalaksanaan Pasien Hemodialisis Di RSALDR Ramelan Surabaya. Thesis. Yogyakarta: Universitas Gajah Mada; 2009.
6. Aslam M, Chik KT, Adji P. Farmasi Klinik. Jakarta: PT.Elex Komputindo; 2003.
7. Klopotowska JE, Kuiper R, van Kan HJ, de Pont AC, Dijkgraaf MG, Lie-A-Huen L, *et al.* On-ward participation of a hospital pharmacist in a Dutch intensive care unit reduces prescribing errors and related patient harm: An intervention study. Crit Care 2010;14(5):R174.
8. Alderman CP, Farmer C. A brief analysis of clinical pharmacy interventions undertaken in an Australian teaching hospital. J Qual Clin Pract 2001;21(4):99-103.
9. Bosma L, Jansman FG, Franken AM, Harting JW, Van den Bemt PM. Evaluation of pharmacist clinical interventions in a Dutch hospital setting. Pharm World Sci 2008;30(1):31-8.
10. Kopp BJ, Mrsan M, Erstad BL, Duby JJ. Cost implications of and potential adverse events prevented by interventions of a critical care pharmacist. Am J Health Syst Pharm 2007;64(23):2483-7.
11. Arnold FW, McDonald LC, Newman D, Smith RS, Ramirez JA. Improving antimicrobial use: Longitudinal assessment of an antimicrobial team including a clinical pharmacist. J Manag Care Pharm 2004;10(2):152-8.