

PHARMACEUTICAL CARE AND ANTI-HYPERTENSION TREATMENT AT TRF-HT PATIENTS UNDERGOING REGULAR HEMODIALYSIS. A STUDY AT HEMODIALYSIS ROOM, DR HARYOTO HOSPITAL, LUMAJANG, EAST JAVA, INDONESIA

Sri Any Sulistyowati¹, Budi Suprapti¹, Benny Gufron²

¹Department of Clinical Pharmacy, Faculty of Pharmacy, Airlangga University, Surabaya

²Dr Haryoto Hospital, Lumajang

ABSTRAK

Pharmaceutical care penting bagi pasien yang mendapat terapi obat, terutama pasien dengan gangguan ginjal terminal disertai hipertensi (TRF-HT) yang menjalani hemodialisis (HD). Kondisi patofisiologis penderita HT dan penggunaan obat anti hipertensi (AHT) merupakan kombinasi yang potensial menimbulkan permasalahan terkait penggunaan obat (DRPs). Tujuan penelitian adalah mengkaji jenis-jenis DRPs pada pasien TRF-HT yang menjalani HD dan mengkaji intervensi PC serta intervensi yang diterima dokter, perawat, dan penderita. Penelitian ini merupakan observasional analitik tipe kohort prospektif. Setiap pasien TRF-HT yang menjalani HD reguler akan disertai dengan implementasi PC dan pemberian obat AHT selama 8 minggu. Sampel diambil sebanyak 36 pasien TRF-HT yang mendapatkan implementasi PC setiap menjalani HD. Frekuensi HD paling banyak 2 kali setiap minggu. Ditemukan 275 DRPs dengan sebagian besar penderita dapat mengalami >1 DRPs terkait penggunaan obat AHT. Klasifikasi dan prosentase DRPs menurut American Society Health-System Pharmacist (AHSP) 1998 adalah sebagai berikut: indikasi tidak diikuti 4%, ketidaktepatan pemilihan obat 3%, dosis subterapeutik 1%, gagal mendapatkan pengobatan 27%, overdosis 4%, efek samping obat (ESO) 37%, interaksi obat 24%, dan pengobatan tanpa indikasi 0%. Seratus intervensi PC pada dokter dengan rincian konsultasi 75%, komunikasi 9%, dan saran 16%. Intervensi PC pada penderita atau keluarga penderita berupa konseling informasi edukasi (KIE) sebanyak 219 kali, 84% KIE diterima. Penderita TRF-HT yang menjalani HD reguler dan pemberian AHT berpotensi mengalami DRPs, serta PC meningkatkan terapi obat secara tepat. (FMI 2013;49:186-192)

Kata kunci: hemodialisa, obat antihipertensi, pharmaceutical care, DRPs

ABSTRACT

Pharmaceutical care is important for patients who received drug therapy, especially patients with terminal renal failure with hypertension (TRF-HT) who underwent hemodialysis. Pathophysiological conditions of HT patients and usage of anti-hypertensive medications (AHT) is a combination that raises potential problems related to drug (DRPs). The purpose of the study was to assess the types of DRPs TRF-HT in patients undergoing HD and assessed PC intervention and interventions received doctor, nurses, and patients. This study was prospective observational cohort analytic type. Each patient underwent TRF-HT regular HD would be accompanied by the intervention of the PC and AHT medication for 8 weeks. Samples were taken by 36 TRF-HT patients who got intervention of PC every undergoing HD. HD frequency maximum of 2 times per week. Discovered 275 DRPs with the majority of patients can experience >1 DRPs related AHT drug. Classification and percentage of DRPs according to the American Society of Health-System Pharmacist (AHSP) 1998 is as follows: untreated indication 4%, 3% improper drug selection, sub therapeutic dosage 1%, failure to receive medication 27%, overdosage 4%, adverse drug side reaction (ESO) 37%, drug interaction 24%, medication use without indication 0%. One hundred of PC intervention doctor with details of consultation 75%, communication 9%, and suggestions 16%. PC intervention in patients or families patients in form counseling information education as much as 219 times, 84% IEC accepted. TRF-HT patients who underwent regular HD and administration of AHT potentially experiencing DRPs and PC improves drug therapy appropriately. (FMI 2013;49:186-192)

Keywords: hemodialysis, antihypertension drugs, pharmaceutical care, DRPs

Correspondence: Sri Any Sulistyowati, Department of Clinical Pharmacy, Faculty of Pharmacy, Airlangga University, Dharmawangsa Dalam Surabaya 60286 – Indonesia, <http://www.ff.unair.ac.id>, e-mail: srianysuliatyowati@gmail.com

INTRODUCTION

In hemodialysis patients, hypertension provides higher cardiovascular risk (Hopkins & Bakris 2009). As one of pathophysiological conditions of terminal renal failure patients (TRF) HD is a complicating factor in the control of major blood pressure (BP). Predialysis target

of TD recommended by NKF-KDOQI is <140/90 mmHg (Agarwal 2010, DiPiro et al 2011). Usage of AHT drugs in patients with HD potentially cause drug related problems (DRPs) that issues related to the use of the drug, this is because HD process can affect the pharmacokinetics and pharmacodynamic characteristics of the drug and pathophysiological conditions TRF HD

patients is a major complicating factor in the control of TD (Stemer & Lemmens-Gruber 2011). To prevent and to solve the emergence of DRPs are required clinical pharmacy with the concept of Pharmaceutical Care (PC) so the expectations to optimize therapy and minimize the ESO with rational drug therapy which safe, appropriate, cost-effective and can be realized (Hughes et al 2001).

PC is a process where pharmacists in collaboration with the patient and other professionals in designing, implementing and monitoring a therapeutic plan that will produce specific therapeutic outcomes for patients (Rovers & Currie 1998). The basic principles and practices in accordance with American PC statement Pharmacist Association (APhA) and American Society of Health-System Pharmacist (ASHP) is a paradigm changes from product orientation to patient orientation. Generally the patient care process in a PC consists of three steps that must be done by a pharmacist which includes assessment phase of data collection, determination of drug related needs (DRNs) patients and identification of DRPs, Care Plan phase includes setting goals of therapy, the accuracy intervention and responsibility resolve DRPs and prevent the development of DRPs and follow-up evaluation phase with a focus on real patient outcomes (Cipolle et al 1998).

Clinical pharmacy with the concept of PC is expected to improve rational drug therapy that is safe, precise, and cost-effective clinical pharmacy so the main goal is to optimize therapy and minimize drug side effects (ESO) is reached. The aim of this study was to examine the types of DRPs were using AHT drugs, and assessed and received interventions by the doctors, nurses and patients. Based on the above problems, the aims of this study was to examine types of DRPs as a result of drug use AHT, assess interventions and interventions received by the doctors, nurses and patients.

MATERIALS AND METHODS

This research was prospective cohort observational analytic type to the implementation of the PC whenever the patient undergoing HD to TRF-regular HD patients with HT who received AHT drugs. This research was conducted in the Hemodialysis room Dr. Haryoto Lumajang with 2 week observation period began on 5 October 2012 and the implementation of the PC for 8 weeks which began on October 30, 2012 until January 22, 2013. Inclusion criteria were patients with regular TRF-HD that has pre-dialytic TD > 140/90 mmHg and using AHT drugs and be willing to follow the research and has signed a letter of consent (informed consent).

Exclusion criteria were patients with HD frequency <1 time per week. Drop-out (DO) criteria was not undergoing hemodialysis patient again and died at the time of the study.

The research instrument used was Document Medical Patients (DMK), patient medication record card (Patient Medication Report/PMR), patient observation sheets, leaflets treatment of hypertension in patients with HD, DRNs related questionnaires, comprehension, and compliance DRPs and copy of the PC implementation. Each arrival of patients who fulfilled the inclusion criteria will be performed the patient data collection. Identification drug related needs (DRNs), the identification and classification of actual and potential DRPs AHT due to drug use, made an implementation plan PC to intervene PC. PC intervention conducted to: doctor form of communication, consultation, information and recommendations, nurses form of communication, information and advice and patient form of in the IEC patient or families of patients, monitoring and evaluation of drug therapy outcomes AHT. IEC which was performed to patients patient families was conducted continuously during the implementation of the PC as needed, monitoring (follow-up) and evaluation of drug therapy outcomes AHT. Monitoring and evaluation was performed by bedside monitoring, routine measurement of BP predialysis and postdialysis, routine measurement of weight and predialysis and postdialysis DMK regularly saw patients and laboratory data which available, as well as an interview during IEC. The results of the monitoring and evaluation of the patient was recorded in the observation sheet. This whole process was recapitulated in copy of PC. The collected data was grouped according to the research objectives and processed with the aim of analyzed patient demographics, analyzed the type and percentage of DRPs and interventions performed analyzes and which was acceptable to doctors, nurses and patients.

RESULTS

Each patient underwent TRF-HT regular HD would be accompanied by the intervention of the PC and AHT medication for 8 weeks during period 30 October 2012 to 22 January 2013. According to inclusion and exclusion criteria, samples were taken by 36 TRF-HT patients who got intervention of PC every undergoing HD. HD frequency maximum of 2 times per week (67%) for 4 hours. During PC implementation each patient received one recipe per month, may change. The average each patient received 2 to 4 times recipes. AHT drug profiles are shown in Table 3 and Table 4.

Table 1. Demographic data of patients

Characteristic of patients		Number (%) ^a
Gender	Male	23 (64)
	Female	13(36)
Age	21-30	2(6)
	31-40	7(19)
	41-50	14(39)
	51-60	10(28)
	61-70	3(8)
Education	SD/ SR	16(45)
	SMP	6(17)
	SMA	7(19)
	S1	7(19)
Profesion	Jobless	6(17)
	Privat sector	21(58)
	PNS	6(17)
	Retired	3(8)
Insurers Cost	Jamkesmas	18(50)
	Askes	12(33)
	Jamkesda	6(17)

Note: ^aPercentage of the total number of samples (36 patients)

Table 2. Etiologic diagnosis and patient comorbidities

Patients Diagnosis		Number (%) ^a
Etiology	Polycystic kidney	3(8)
	Primary Glomerulopati	1(3)
	Uric Acid Nephrophaty	1(3)
	Diabetic Nephrophaty	3(8)
	SLE Lupus Nephrophaty	1(3)
	HKD	27(75)
Comorbidities	Hepatitis A	1(3)
	DM with Hepatitis A	1(3)
	Hepatitis B	1(3)
	Hipertensi with DM	1(3)
	Hypertension	3(8)
	Without comorbidities	29(80)

HKD: hypertensive kidney disease

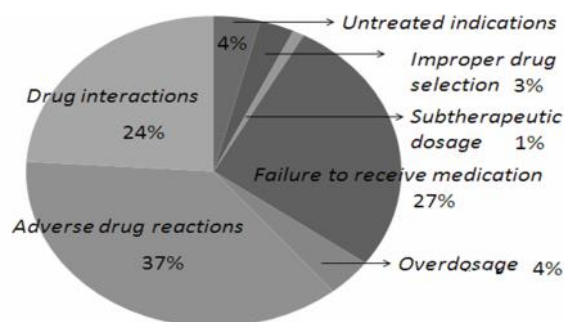


Figure 1. Classification Type and Percentage DRPs experienced by patients during the PC to total DRPs (275 DRPs).

DRPs identification results related to the use of AHT drugs during the implementation of the PC found 275 DRPs. Each patient experienced a 1 DRPs related to

drug use AHT. The type and number of DRPs experienced by patients during the implementation of the PC shown in Figure 1, Table 5 and Table 6 with the classification of DRPs by ASHP 1998.

Tabel 3. The type and frequency of prescribing AHT

AHT drug	Regiment	Frequency of prescribing (%) ^a
CCB		
Amlodipin	1x 5mg	8(7.4)
	1x 10mg	67(62)
	2x 10mg	30(27.8)
Nifedipin	1x 20mg	1(0.9)
Diuretic Loop		
Furosemid	2x 40mg	72(66.7)
	2x 80mg	1(0.9)
ACE Inhibitor		
Lisinopril	1x 5mg	6(5.6)
	1x 10mg	42(38.9)
	2x 10mg	18(16.7)
bloker		
Bisoprolol	1x 2.5mg	8(7.4)
	1x 5mg	29(26.9)
ARB		
Telmisartan	1x 80mg	27(25)
	2x 80mg	3(2.8)
Losartan	1x 50mg	1(0.9)
	2x 50mg	1(0.9)
2-adrenergic		
Clonidin	2x 0.15 mg	6(5.6)
Antiadrenergik		
Reserpin	1x 0.25mg	1(0.9)
	2x 0.25mg	1(0.9)
Tiazid		
HCT	2x 25mg	2(1.9)

AHT: antihypertension

^a Percentage frequency of prescribing the total number of prescriptions (108)

HCT: Hydroclorotiazid

Tabel 4. AHT use of the drug as a single agent and combination

Prescribing type	Number (%) ^a
Single	
1 AHT	1 (0.9)
Combination	
2 AHT	25(23.1)
3 AHT	54(50)
4 AHT	22(20.4)
5 AHT	6(5.5)
Total	108 (100)

Each DRP performed 1 PC intervention. There were 2 DRPs experienced by 5 patients have not been performed due to the intervention PC technical problems in the field. The total number of interventions undertaken PC was 319. In detail, there were interventions undertaken PC in Figure 2.

Table 5. The type and number of DRPs experienced by the patients

DRPs types ^a	Number (% ^b)
<i>Untreated indications</i>	11 (30.6)
<i>Improper drug selection</i>	7 (19.4)
<i>Subtherapeutic dosage;</i>	4 (11.1)
<i>Failure to receive medication</i>	75 (208)
<i>Overdosage</i>	10 (27.8)
<i>Adverse drug reactions: ESO^c</i>	
1. <i>Definite</i> score > 8	10 (27.8)
2. <i>Probable</i> score 5-8	29 (80.6)
3. <i>Possible</i> score 1-4	62 (172.2)
4. <i>Doubtful</i> score < 1	1 (2.8)
<i>Drug interactions^d</i>	
1. Actual	27 (75)
2. Potential	40 (111.1)
<i>Medication use without indication</i>	0
Total	275

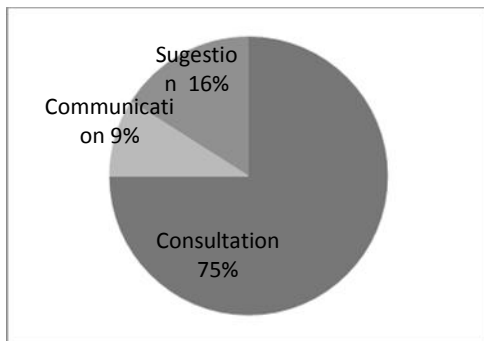
^a DRPs classification according to ASHP 1998^b Percentage of the number of DRPs patients^c Estimated probability of the ESO according to ADR probability scale (Naranjo 1981)^d Drug interaction according to Stockley's Drug Interactions 8Th ed (Karen 2008)

Figure 2. Percentage of PC intervention results to the physician for a PC with a total of 100 interventions PC doctor.

DISCUSSION

The highest prevalence of genital Janis TRF-HT patients undergoing regular HD and get AHT medications was more males (64%) than female gender (36%), the age distribution is at most patients aged 41-50 year (39 %) (Table 1). Distribution of education and obtained a job most people with a low educational level (elementary school) (45%) and private employment (farm laborers, drivers, traders, etc.) (58%). HD treatment costs are very high so most of the cost of underwriting done by insurers. This condition can be explained that the results of cross-sectional surveys and observational prospective cohort studies revealed a

positive relationship between TD with characteristics different of gender, age, culture, and socioeconomic.

The etiology of most patients with TRF-HT (Table 2) was hypertensive renal disease (75%) and diabetic nephropathy and polycystic kidney, respectively (8%), and (8%) patients experienced HT as comorbidities (Table 2). HT is an important contributing factor to the speed of progression of renal damage, so untreated HT or poorly controlled can directly damage the kidneys due to hypertensive nephropathy (Levy et al 2004, Saint-Remy & Krzesinski 2005, Ashley & Currie 2009). Management of AHT drug selection algorithm based treatment of hypertension in dialysis patients (NKF 2005). During the implementation of the PC there were 108 times the prescription (Table 3 and Table 4).

The final step of the assessment phase was the identification of drug related problems AHT (DRPs), problems related to drug use continues tarjadi rapidly in patients undergoing regular HD (Manley et al 2003). During the implementation of a PC with a total of 603 meetings discovered 275 DRPs (Table 5). The results showed that each patient can experience related DRPs 1 AHT drug use. The type and number of DRPs experienced by patients during the implementation of the PC shown in Table 5. Classification of DRPs according to ASHP 1998 and the percentage based on number of patients.

DRP untreated indication experienced 30.6% of patients (Table 6). PC interventions undertaken to overcome the patients who have not received the AHT drug was consulting the doctor, this intervention is accepted and patients receive appropriate the AHT drug, respectively clinical condition. DRP improper drug selection experienced 19.4% of patients (Table 6), PC intervention was undertaken consulting physician for 4 DRPs and accepted, while for 1 case of 3 patients experienced that the combination of lisinopril with epoetin until the end of the study has not been done because the PC intervention technical constraints of the field.

DRP subtherapeutic dosage experienced by 11.1% of patients and interventions PC was committed to physician consultation and all received, to 2.8% of patients did not experience a change in prescribing because although the target has not been reached TD predialytic patients experienced white-coat hypertension is Ambulatory Blood Pressure Monitoring (ABPM) <140/90 mm Hg and systolic BP pre-dialytic > 180 mmHg with the condition of the patient is always anxiety and stress every HD (Agarwal 2010).

Table 6. Types and DRPs causing factor

DRP Type *	Causing factor **	Number % ^a
Untreated indication	HT predialysis (+), AHT drug (-)	2 (5.6)
	AHT drug (+), need additional AHT drug	9 (25)
Improper drug selection	Drug combination should be avoided	3(8.3)
	Risk contradiction	3(8.3)
	Combination of excessive drug	1(2.8)
Subtherapeutic dosage	Too low dosage to get desired responses	4(11.1)
Failure to receive medication	Lack of understanding	36(100)
	Less compliance, often forgotten	9(25)
	Purposely not taking medication because of the belief that the drug is not suitable	3(8.3)
	Inventory runs out, empty	9(25)
	No afford to buy drug	1(2.8)
	IFRS no inventory	2(5.6)
	Time to take medication less precise	13(36.1)
	Different company (different formulation)	2(5.6)
Overdosage	Too high dosage, hypotension	5(13.9)
	Too high dosage, hypertension	3(8.3)
	Addition of dosage by patient because effect is less	2(5.6)
ESO ^b	Drug mechanism	
	1. Definite	7(19.4)
	2. Probable	28(77.8)
	3. Possible	61(169.4)
	4. Doubtful	1(2.8)
	Allergic reaction	
	1. Probable	1(2.8)
	2. Possible	1(2.8)
	ESO mechanism unknown certainly	
	1. Definite (past)	3(8.3)
Drug interaction ^c	Pharmacokinetics: absorption potential	1(2.8)
	Pharmacodynamic	
	1. Additive/ synergic	
	- Actual	4(11.1)
	- Potential	1(2.8)
	2. Antagonist/ opposite	
	- Actual	23(63.9)
	- Potential	32(88.9)
	Unknown: potential	6(16.7)
Total		275

* DRPs classification according to ASHP 1998.

** DRPs causing factor according to Cipolle 1998, Rover 1998 & Walker 1999.

^a Percentage of the number of DRPs patients.^b Estimated probability of the ESO according to ADR probability scale (Naranjo 1981)^c Drug interaction according to Stockley's Drug Interactions 8th ed (Karen 2008).

RP failed to receive medication 208% (Table 6) which means that each patient experienced > 1 DRPs (Table 6). Intervention PC done to overcome these DRPs was IEC to patients or patients' family and then do continuous monitoring began early evaluation by the end of the study. PC intervention doctor form of information about the availability of prescription the AHT drug to the patient and ask the patient, 100% of this intervention is accepted by a doctor. DRP overdosage is one of the causes of hypotension and the emergence of ESO (Table 6). PC intervention was performed to the doctor for consultation and suggested lowering the dose of the AHT drug to the patient in the form of IEC. The results of the consultation in the form of a PC intervention are

all accepted, the proposal received 20% which is decrease in the dose of amlodipine 20 mg daily that the doctor prescribed to 10 mg per day according Guideline NKF/KDOQI in 2005, the reason for the rejection of this proposal is that the target has not been reached predialysis BP and clinically when dose of amlodipine lowered cardiovascular disorders will occur more harm patients. PC intervention to patients families of patients in the form of oral hygiene IEC, taking appropriate the drug prescribed dose.

DRPs ESO is the most often experienced by patients. Clinical situation did not desirable because of the drug can not be distinguished from manifestations of disease

because non-specific manifestations of ESO, so any clinical condition suspected to be due to ESO's clinical condition, so that an assessment is done by using ADR probability scale to establish the classification of ESO (Naranjo et al 1981). ESO assessment results showed that each patient can experience 1 ESO (Table 5). Clinical signs of drug interactions were not common but could be a cause of morbidity (Walker & Edwards 1999). As a result of the mechanism of interaction pharmacokinetics and pharmacodynamic AHT drug-AHT drug, AHT drug-other drugs, AHT drug-food and drinks, AHT-herbal medicine can cause adverse effects, among others, the outcome of therapy becomes more dangerous because of the increased toxicity of the drug, or decline in the effectiveness of drugs and the presence of beneficial effects, such as the use of AHT drugs in combination is more potent to reach TD on target when compared to the use of AHT drugs singly (Baxter 2008). In this study, the DRP drug interactions (186%) with details of the actual DRP 75% and potential DRP 111% (Table 5 and Table 6). PC intervention given to overcome AHT drug-consumption habits interactions was IEC about restriction of Na⁺ and the choice of food (DASH) (NKF 2010). The results of the PC intervention conducted there were 12 accepted and 15 rejected rejection reason was because people can not change the consumption habits both the type and amount so that there are 5 until the end of the study patients who never achieve the predialysis BP on target.

AHT drug-AHT drug interactions (11%) cause hypotension. PC interventions undertaken to overcome the DRP include consultation doctor and patients and the IEC to the patient or family. The results of the PC intervention in the form of consulting all received and accepted IEC to patients 7 and 1 rejected, the reason for rejection was because people was not have gauges TD and distance between home and remote health facilities hard to reach. From the discussion above shows that each of DRPs also conducted PC intervention to resolve DRPs and prevent the continuation of DRPs. Collaboration pharmacists as executor PC with doctor in the management of clinical therapy could improve clinical outcomes of patients (Isetts et al 2003). PC intervention of the nurse was not performed because was not obtained during the study DRPs related to the role of nurses. To the extent end of the study there were 3 DRPs that has not been done in the field of intervention because technical constraints. The final stage of the PC was followed-up evaluation of monitoring-evaluation is being conducted since the beginning of the implementation of the PC, the focus of this stage was the actual patient outcomes with the aim to assess the results of the PC interventions that have been carried out with see and communicate with the patient or family patients about what happened to the

patient. From this stage if DRPs still unfinished new or emerging DRPs will be done early stages again and so on which is a cycle in the PC.

CONCLUSION

Patients TRF with HT which undergoing regular HD and get AHT drugs may experience DRPs and very difficult to achieve appropriate predialysis BP expected target. It required the involvement of the pharmacist as the Renal Pharmacist specializing in Nephrology Team as medication and executive educator PC With a PC, pharmacists could contribute to resolve or minimize the problem in medicine, including understanding and patient compliance While the implementation of clinical pharmacy (Clinical Pharmacology) by concept PCs that are expected to improve rational drug therapy is safe, appropriate, cost-effective and does not have a standard operating procedure (SOP) standard.

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