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Research Article

The role of pharmacists' interventions in improving drug-related problems, blood pressure, and quality of life of patients with stage 5 chronic kidney disease

Peri[1], Azizah Nasution[2], Alwi Thamrin Nasution[3]

1 *Pirngadi Hospital, Medan, Indonesia*
2 *Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia*
3 *Rasyida Kidney Specialist Hospital, Medan, Indonesia*

Corresponding author: Azizah Nasution (azizah@usu.ac.id)

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Abstract

This six-month cohort study analyzed the impact of pharmacy interventions (PI) on drug-related problems (DRPs), blood pressure (BP), and quality of life (QoL) among patients with stage 5 chronic kidney disease (CKD) (n = 83) admitted to Pirngadi Hospital, Medan, Indonesia period February to July 2021. DRPs, BP, and QoL of the patients were analyzed before and after PI. DRPs were analyzed applying PCNE version 9, BP scores were extracted from the patients' medical records. Their QoL was assessed using a WHOQoL questionnaire. The impacts of PI on the incidence of DRPs, BP, and the patients' QoL were analyzed applying Wilcoxon Signed Rank and Friedman test in the SPSS program version 23.0. The number of DRPs was significantly reduced from 470 before PI to 162 following PI (p = 0.000). The patients' QoL improved significantly from 40 ± 9.87 before PI to 69 ± 12. 45 after PI, p = 0.000. PI is crucial to improve the outcomes of CKD patients.

Keywords

Pharmacy intervention, stage 5 CKD, DRPs, blood pressure, QoL

Introduction

Chronic kidney disease remains a leading global health problem due to its high morbidity and mortality, high treatment costs, and poor clinical outcomes. About one in ten of the world's population or 850 million people globally suffer from CKD (WHO/WKD 2020). In Indonesia, the prevalence of CKD was about 3.8%. The Indonesian Renal Registry (2018), 2018 indicates large increase in the number of new and active hemodialysis patients in Indonesia. In 2017, the number of new patients was 30,831 and the active hemodialysis patients reached 77,892, while in 2018 number of new patients increased to 66,433 with 132,142 active hemodialysis patients (Panma and Rohmawati 2021).

Patients with CKD always suffer from comorbidities and complications including hypertension, diabetes mellitus, kidney stones, infection, anemia, and hyperphosphatemia that can worsen the patients' QoL if not treated appropriately. These comorbidities and complications require complex management which tend to result in

increased costs of illness, DRPs, interference with clinical outcomes, reduce the patients' QoL, and even death (Ernst and Grizzle 2001; Ruths et al. 2007; Adumisilli and Adepu 2014; Van Mil et al. 2017). Therefore, a multi-disciplinary approach is crucial in which pharmacists can play an important role in improving clinical outcomes.

Many studies on DRPs and clinical outcomes in the management of CKD have been undertaken in different parts of the world. These include a study conducted in Nigeria which identified 234 DRPs in which inappropriate drug selection and drug interactions were the most frequently occurring problems (Adibe et al. 2017). Another study found that DRPs frequently experienced by CKD patients undergoing hemodialysis were indications without therapy (5.9%), therapy without indications (20%), inappropriate drug prescriptions (21.2%), and drug interactions (20%) (Diputra et al. 2020). Additionally, a study conducted in a tertiary care teaching hospital in South India identified a total of 337 DRPs, predominantly drug interactions (60%). Studies on CKD in Indonesian hospitals are still limited and need to be highlighted. More studies are required to identify and resolve problems associated with the disease management to improve outcomes.

In response to the above problems, the present study was conducted to analyze the impacts of PI on DRPs, BP, and QoL of hemodialysis patients with stage 5 CKD undergoing hemodialysis admitted to Dr. Pirngadi hospital, Medan, Indonesia.

Methods

This six-month prospective analytical cohort study was conducted to analyze the impact of PI on DRPs, BP, and QoL of hemodialysis patients with stage 5 CKD (n = 83) admitted to Pirngadi hospital period February to July 2021. DRPs, BP, and QoL of the patients were analyzed before and after PI. Ethical clearance was obtained from the Ethics Committee, Faculty of Medicine, University of Sumatera Utara no. 567/KEP/USU/2021. Inclusion criteria were patients with stage 5 CKD admitted to Pirngadi hospital during the period February to July 2021. The minimum number of stage 5 CKD patients required in this study was 15–30 persons (Gay et al. 2009). All of the patients involved in the study signed informed consent before the study was started. The Patient characteristics were assessed using a self-designed questionnaire. DRPs were analyzed applying PCNE version 9 classification system which included 3 problems, 9 causes, 4 intervention categories, and 3 alternative statuses of intervention (Schindler et al. 2021). Blood pressure of the patients was extracted from the patients' medical records before PI, and 1, 2, and three months after PI. Their QoL was assessed using a WHO-QoL questionnaire comprising physical, psychological, social, and environmental factors. The patients' QoL was grouped into 5 categories (very poor = 0–20; poor =21–40; fair, 41–60; good, 61–80; very good, 81–100. The patient characteristics were analyzed descriptively. The incidence of DRPs occurring in each patient was analyzed based on their medical conditions, the drugs provided, functions of organs assessed from laboratory results and reliable literatures (Anderson et al. 2002; Baxter and Preston 2010; Chatfield 2015; Rose 2015; Ashley et al. 2018). The impact of PI on the incidence of DRPs, BP, and QoL of the patients was analyzed applying a Wilcoxon Signed Rank and Friedman test in the SPSS program version 23.0.

Results

Patient characteristics

Patient characteristics during the study period are shown in Table 1. As shown in Table 1, the mean age of the patients was 48.93±11.61 (years). Most (65.0%) of them were males. More than three quarters (81.92%) of the patients graduated from senior high school. More than half (60.24%) of the patients were routinely admitted to the hospital for hemodialysis.

Incidence of DRPs in the management of patients with stage 5 CKD

In terms of problems, the incidence of DRPs in the management of patients with stage 5 CKD before and after interventions is shown in Table 2. Overall, 470 DRPs were recorded before intervention, with a mean of 5.73 ± 2.20, which was significantly reduced to 1.90 ± 1.04 after intervention, $\alpha = 0.000$. The most common DRPs experienced by the patients with stage 5 CKD in the treatment effectiveness category (P.1) were sub-optimal drug effects with 239 inciden-

Table 1. Patient characteristics during the study period.

Gender		Age		Education		Duration hemodialysis	
Variable	Number (%)	Variable	Number (%)	Variable	Number (%)	Variable	Number (%)
Male	54 (65.06)	≤40	18 (21.68)	Primary school	3 (3.61)	<1	7 (8.44)
Female	29 (34.94)	41–50	22 (26.50)	Junior high school	5 (6.04)	1–5	50 (60.24)
		51–60	29 (34.93)	Senior high school	68 (81.92)	>5	26 (31.32)
		61–70	11 (13.28)	University	7 (8.43)		
		71–80	2 (2.41)				
		Over 81	1 (1.20)				
Total	83 (100.00)	Total	83 (100.00)	Total	83 (100.00)	Total	83 (100.00)
						Total	**83 (100.00)**

Table 2. Incidence of DRPs based on problems before and after interventions.

Code	Problems	Incidence of DRPs			Wilcoxon test (Asymp.Sig)
		Before PI	After PI	% reduction	
P	**Overall DRPs**	**470**	**162**	**65.53**	
P.1	**Treatment effectiveness**	**385**	**152**	**60.51**	0.000
P1.1	No drug effect	42	10	76.19	
P1.2	Sub-optimal drug effects	239	87	63.59	
P1.3	Untreated symptoms/ indications	104	55	47.11	
P.2	**Safety**	**83**	**8**	**90.36**	
P2.1	Adverse drug reaction (ADRs) events	83	8	90.36	
P.3	**Others**	**2**	**2**	**0**	
P3.1	Problems with cost-effectiveness	2	2	0	

ces, followed by untreated symptoms (104 cases), and no drug effect (42 cases) before PI. However, after PI, sub-optimal, untreated, and no effect problems were reduced by as much as 63.59%, 47.11%, and 76.19%, respectively.

As also listed in Table 2, the number of ADRs (P2.1), included under safety problems (P2), was also significantly reduced from 83 cases before PI to 8 cases after PI, a reduction of 90.36%.

The incidence of DRPs before and after intervention by cause is listed in Table 3. With regards to causes, an inappropriate combination of drugs (C1.4) was most frequently experienced by the patients as shown in Table 3. Overall, the 5 highest incidences of DRPs by cause before PI in decreasing order were inappropriate drug combinations (173 cases), incomplete drug treatment (106 cases), under-administration of drugs by a health professional (37 cases), too low dose (19 cases), and incorrect patient use of drugs (14 cases). Following PI, incidences of inappropriate drug combinations, incomplete drug treatment, drug under-administered by a health professional, too low dose, and incorrect patient use of drugs were significantly reduced by as much as 83.23%, 24.52%, 100%, 94.73%, and 78.57%, respectively, $\alpha = 0.000$.

The level of intervention provided by the pharmacist and its status are listed in Table 4. The 470 cases were grouped into 4 levels comprising prescribers, patient, drug, and other levels. Overall, 100% of PI were accepted by the prescribers or patients. The three most common problems requiring intervention by the pharmacist were associated with patient counseling (155 cases), discussions with prescribers (125 cases), and suggestions to the prescribers (98 cases). As much as 11.06% of the PI suggested by the pharmacist were accepted and completely implemented by the prescribers, while 54.46% of the PI were accepted and partially implemented. In contrast, 34.48% of the PI were accepted but not implemented.

Table 3. Incidence of DRPs before and after intervention by cause.

Code	Causes (C)	Number of causes			Wilcoxon test (Asymp. Sig)
		Before PI	After PI	% Of Reduction	
C	**Overall causes**	**470**	**162**	**65.53**	0.000
C.1	**Drug Selection**	**280**	**109**	**61.07**	
C1.4	Inappropriate combination of drugs, drug and herbal remedies, or drugs and herbal supplements	173	29	83.23	
C1.5	Inappropriate duplication of therapeutic group or active ingredient	1	0	100	
C1.6	No or incomplete drug treatment despite existing indication	106	80	24.52	
C.3	**Dose selection**	**25**	**1**	**96.00**	
C3.1	Too low dose	19	1	94.73	
C3.2	Too high dose	6	0	100	
C.4	**Treatment duration**	**1**	**0**	**100**	
C4.2	Too long duration	1	0	100	
C.6	**Process of drug administration**	**54**	**2**	**96.29**	
C6.1	Inappropriate timing of administration or dosing intervals by a health professional	17	2	88.23	
C6.2	Under-administration of drugs by a health professional	37	0	100	
C.7	**Patient-related**	**21**	**3**	**85.71**	
C7.1	Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	6	0	100	
C7.7	Inappropriate timing/ dosing interval	1	0	100	
C7.8	Patient uses drug incorrectly	14	3	78.57	
C.9	**Others**	**90**	**47**	**47.78**	
C9.2	Other causes	90	47	47.78	

Table 4. Intervention provided by the pharmacist according to level of intervention.

Intervention	Code	Classification	Number of PI	%
I.1 At prescriber level	I1.3	Intervention suggested to prescribers	98	20.85
	I1.4	Intervention discussed with prescribers	125	26.59
I.2 At patient level	I2.1	Patient counseling	155	32.97
I.3 At drug level	I3.2	Dosage changed	40	8.51
	I3.4	Changed instruction for use	21	4.46
I.4 Other intervention	I4.1	Other intervention	31	6.62
		Total	**470**	**100**
Status of PI	**Code**	**Classification**	**Number PI**	**%**
1. Accepted	A1.1	Accepted and completely implemented	52	11.06
	A1.2	Accepted and partially implemented	256	54.46
	A1.3	Accepted but not implemented	155	34.48
		Total	**470**	**100**

Clinical outcomes

One of the outcomes measured in this study was BP. Changes in BP of the stage 5 CKD patients undergoing hemodialysis before and after intervention are shown in Table 5. The present study indicated that the BP of patients with stage 5 CKD was not significantly different before and after pharmacy intervention, $p = 0.069$.

Table 5. Changes in BP of the patients before and after intervention.

Evaluation	BP		
	Mean BP	Wilcoxon test (Asymp. sig)	Friedman test (Asymp. sig.)
Before PI	141 ± 18.48	0,517	0.069
Follow up 1 (1 month after PI)	141 ± 19.10		
Follow up 1	141 ± 19.10	0,455	
Follow up 2 (2 months after PI)	144 ± 21.89		
Follow up 2	144 ± 21.89	0,874	
Posttest (3 months after PI)	143 ± 20.39		
Before PI	141 ± 18.48	0,091	
After PI	143 ± 20.39		

Association among number of DRPs with BP and QoL of the patients before and after interventions is shown in Table 6. The second outcome analyzed in this study was QoL. The present study proved that patients' QoL improved significantly from 40 ± 9.87 before PI to 69 ± 12. 45 after PI, p = 0.000. By number of DRPs, the CKD patients experienced 1 to 13 incidences. Association among number of DRPs with BP and QoL of the stage 5 CKD patients undergoing hemodialysis before and after PI are presented in Tables 5 and 6, respectively.

Table 6. Association among number of DRPs with BP and QoL of the patients before and after intervention.

Number of DRPs Before PI	Number of patients	Mean BP	Mean QoL	Spearman Rho test	Correction Coefficient (r-value)	*p*
Before PI						
1	2	146	42	DRPs with BP	r = 0.405	0.000
2	2	130	48			
3	5	133	43			
4	15	130	42			
5	16	141	44			
6	15	146	39			
7	15	146	36	DRPs with QoL	r=-0.329	0.002
8	4	143	39			
9	5	149	40			
12	2	167	28			
13	1	162	28			
After PI						
1	23	133	67	DRPs with BP	r = 0.304	0.005
2	26	144	71			
3	22	149	70			
4	4	159	70	DRPs with QoL	r = 0.156	0.158
5	1	183	69			

There was a significant association between the number of incidences with BP of the patients before PI (r = 0.405), p = 0.000. This result implied that the higher the number of DRPs, the higher the patients' BP. Consistent result was also found in the patients' QoL. The higher the number of DRPs experienced by the patients, the lower their QoL (r = –0,329), p = 0.002.

Discussion

Patient characteristics varied widely in terms of age, education, employment, and the disease duration. These conditions were associated with many complicated factors. A systematic review proved that socio-economic conditions including income or occupational levels, education levels, health insurance, and access to healthcare facilities affect the characteristics of CKD patients as well as the disease morbidity and mortality (Morton et al. 2016).

The present study proved that the incidence of DRPs both before and after PI varies from one category to another. The highest incidence in problem category was therapeutic effectiveness before and after PI 385 and 152 cases, respectively. The major incidence in causes category was inappropriate combination of drugs with 173 occurrences and 155 DRPs that required patient counseling.

A similar previous study conducted in several tertiary hospitals in Nigeria identified 234 drug therapy problems (DTPs) in which inappropriate drug selection/dosing problems and drug interactions were the major sources of DTPs (Adibe et al. 2017). Another more recent study undertaken in an educational tertiary hospital in South India detected 337 DRPs (approximately 2.1 incidences/patient) in the management of 160 patients diagnosed with any stage of CKD, of which the three most frequently occurring DRPs in decreasing order were drug interactions (59.94%), followed by frequency error (11.57%), and indication without drugs (11.28%) (Subeesh et al. 2020). The incidence of DRPs varies from one country to another. Another study on DRPs undertaken on 103 patients with CKD at any stage in a university medical centre, Southwest Ethiopia identified 81 (78.6%) DRPs. The rate of these DRPs was 30.95 per 100 medication orders. In contrast, a study undertaken in the US found a lower incidence of DRPs (6.58 DRPs per 100 medication orders) (Manley et al. 2003).

These studies found a wide range of DRPs experienced by CKD patients across countries due to many complex socio-economic factors, level of education, and medication adherence of the patients in particular countries. A study undertaken in K&D Clinic PGIMS, Rohtak, India proved that CKD patients with a higher education and income had a greater adherence to their medications. On the other hand, patients with lower education levels had lower adherence to their prescribed medications as a result of their limited knowledge about the disease they were suffering and the required treatments (Jain and Meel 2018; Aggarwal et al. 2018). Budgetary limitations on universal health coverage also vary from one country to another, which in turn may result in the wide range in the incidence of DRPs (Agustina et al. 2019).

Chronic high BP in stage 5 CKD patients undergoing haemodialysis must be managed to improve clinical outcomes (Rose 2015). Even though the present study found no significant difference in terms of BP before and after PI, yet avoidance of elevated BP helped to slow the progression of kidney damage. Difficulties in achieving target BPs may be associated with many complex factors, including disease comorbidities and complications, patients' life-

styles, and their adherence to the prescribed medications. Lifestyles and imbalance food intakes could interfere with normal RAAS causing elevated BP in the kidneys (Anderegg et al. 2018; Szabó et al. 2021).

In this study, the QoL of patients with stage 5 CKD must also be considered since they tend to experience decreased physical, mental, and social conditions (WHO, 2016). This present study showed significant improvements in QoL following PI. This finding supported a previous study conducted in the HD centers of three different teaching, government, and private hospitals in South India. It was found that HRQoL scores with regard to "physical functioning, general health, emotional well-being, social functioning, symptom/problem list, and effects of kidney disease" in pharmaceutical care group significantly improved over time compared to those in the usual care group with $p < 0.05$ in all the three centers, which showed an increase in the QoL of CKD patients undergoing hemodialysis after carrying out pharmaceutical care interventions (Mateti et al. 2017).

Conclusions

The present study proves that PI plays an important role in reducing DRPs, improving BP, and increasing patients' QoL. Policymakers should consider this finding to improve management of patients with stage 5 CKD. Sufficient numbers of qualified human resources, especially healthcare providers involved in the management of hemodialysis patients are crucial. These factors should be highlighted and considered by policymakers to improve healthcare.

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