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COST MINIMIZATION ANALYSIS OF ANTIHYPERTENSIVE DRUG USE IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HEMODIALYSIS

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ABSTRACT

Hypertension is the primary cause of Chronic Kidney Disease (CKD), as it damages blood vessels in the kidneys. The most commonly used management for hypertension as monotherapy includes Calcium Channel Blockers (CCB) such as Amlodipine and Angiotensin Receptor Blockers (ARB) such as candesartan. Patients with CKD undergoing hemodialysis depend on dialysis machines, which impacts their economic burden. Therefore, a cost analysis review of drugs with the same therapeutic goals is necessary. This was a non-experimental study with a descriptive design. Data were collected through retrospective purposive sampling from January to December 2023 using medical records and payment data for inpatient treatments with hemodialysis that met the inclusion criteria. Direct medical costs included antihypertensive, other medication, service and facility fees, and medical support costs. Of the 100 samples that met the inclusion criteria from January to December 2023, amlodipine was the most commonly used antihypertensive (56%), followed by candesartan (38%). The average direct medical costs were IDR 184.350 for Amlodipine and IDR 561,339 for candesartan. The patient characteristics by gender showed a higher percentage of males (52%) than of females (48%). By age, the majority were in the late adult group (67%), whereas the elderly accounted for (33%). The Amlodipine group achieved more significant cost minimization than the candesartan group. Future studies should examine the potential of amlodipine in reducing the economic burden of limited resources.

Keywords: antihypertensive, CMA, CKD

INTRODUCTION

Chronic Kidney Disease (CKD) is a significant medical and public health concern. CKD also contributes to the onset of other diseases such as cardiovascular diseases and diabetes, and is a leading cause of morbidity and early mortality (Liyanage *et al.*, 2022). According to the 2023 Indonesian Health Survey (SKI), the prevalence of CKD, based on physician diagnoses in Indonesia, is highest in Lampung (0.30%), followed by Gorontalo (0.29%) and Central Sulawesi (0.28%) (SKI, 2023). CKD can be caused by various factors, including infection (pyelonephritis), metabolic disorders (such as diabetes), urinary tract obstructions, immunological disorders, primary tubular disorders (nephrotoxins), congenital abnormalities that lead to decreased Glomerular Filtration Rate (GFR), and a history of hypertension (Narsa *et al.*, 2022).

Hypertension is the most commonly encountered condition in CKD patients (Cahyo *et al.*, 2021). It is estimated that 25 million Indonesians suffer from CKD, caused by hypertension and diabetes (Azalea and Andayani, 2016). Hypertension persists for a long time and causes vascular sclerosis. Sclerotic lesions that occur in the small arteries, arterioles, and glomeruli lead to nephrosclerosis. These lesions occur because of plasma

leakage through the intimal membrane of blood vessels, resulting in the formation of fibrinoid deposits in the media layer of blood vessels, accompanied by progressive thickening of the blood vessel walls, causing vasoconstriction and vascular obstruction. The obstruction that occurs in the arteries and arterioles will lead to glomerular damage and tubular atrophy, resulting in nephron damage, which causes chronic kidney failure (Syukria Agussalim *et al.*, 2022).

CKD patients undergoing lifelong hemodialysis are dependent on dialysis machines, which inevitably increases the economic burden (Tandah *et al.*, 2019). Therefore, it is necessary to review the medication costs to alleviate this economic burden. In this context, considering the choice of drugs with the same therapeutic goal, a cost analysis review of these medications is warranted. Cost Minimization Analysis (CMA) is used to compare two or more interventions with the same objective. CMA focuses on determining the drug with the lowest daily cost (Faramitha, Prihartanto and Destiani, 2019).

Cost Minimization Analysis (CMA) is the simplest method for a cost-effectiveness analysis. The AMiB is a pharmacoeconomic study used to compare two or more types of health interventions that have been shown to have comparable, similar, or equivalent outcomes. If two therapies or two (types, brands) drugs are clinically equivalent, all that needs to be compared is the cost of performing the intervention (Indonesia, 2013). In this study, the researchers will perform a CMA on the use of antihypertensive drugs (Amlodipine and Candesartan) in patients with CKD undergoing hemodialysis therapy.

METHODS

Research Design

This was a non-experimental descriptive study. Data were collected through purposive sampling using a retrospective method for the period from January to December 2023, utilizing medical records and payment data from inpatient hemodialysis treatments that met the inclusion criteria. The direct medical cost categories included antihypertensive costs, costs of other medications, service and facility fees, and medical support costs.

Inclusion Criteria

1. Patients aged 18–75 years.
2. Inpatients were hospitalized for more than 3 days and received antihypertensive therapy with amlodipine and candesartan.
3. Patients with complete medical records.

Exclusion Criteria

1. Patients not using antihypertensive medications.
2. Patients who were discharged from medical advice or deceased.

Study Time and Location

This study was conducted at the Undata Regional General Hospital in Palu from April to June 2024.

Data Collection and Analysis Techniques

Patient examination data were analyzed using IBM SPSS version 29. The data analysis in this study used a quantitative approach in the form of a retrospective cross-sectional study. After the data were collected, they were analyzed by calculating the average direct medical costs per patient. The data are presented as total costs, percentages, and significant differences through p-values. A significant relationship was indicated if the chi-square analysis result was $p < 0.05$.

Ethical Considerations

The study was conducted after obtaining approval from the Ethics Committee of the Faculty of Medicine at Tadulako University with approval number 5296/UN28.1.30/KL/2024.

RESULTS AND DISCUSSION

The variety of antihypertensive alternatives used in hypertension therapy makes the economic aspect one of the factors that must be considered when choosing the appropriate therapy, but in accordance with the patient's purchasing power.

Based on research conducted at Undata Regional General Hospital in Palu, the patient data distribution included characteristics, medications used, and direct cost components. Data of patients with hypertension undergoing hemodialysis were obtained from the inpatient medical records department. Subsequently, cost minimization was identified based on the choice of treatment with CCB and ARB. This study used a retrospective data collection method from January to December 2023, involving a total of 100 patients. This study adopted a hospital perspective. The patient characteristics are presented in **Table I**.

Table I. Characteristics of Chronic Kidney Disease Patients Undergoing Hemodialysis

Characteristics	n	Percent (%)
Gender		
Male	52	52
Female	48	48
Age (years)		
Late adults (40-59)	67	67
Elderly (>60)	33	33
Antihypertensives		
Amlodipine	86	56
Candesartan	58	38

In **Table I**, the distribution of patients by gender shows a predominance of males, which is consistent with the results of Tandah *et al*., (2019) and Wijaya, Ryshang Bathari and Wiedyaningsih, (2023), where males were more dominant than females.

The patient age distribution was mostly within the 40-59 years range. This finding aligns with the research by Saadah and Yanti, indicating that this age group is more likely to undergo hemodialysis. Generally, this age range begins to exhibit physiological changes that gradually lead to deterioration, including hormonal changes that affect health and psychological conditions, thus increasing the risk of depression Saadah and Hartanti, (2021) and Pasaribu, Sefti and Rina, (2021). Furthermore, certain risk factors, such as smoking and alcohol consumption, can lead to rapid or progressive decline in renal function, causing various complaints (Yulianto *et al*., 2020). The dominant antihypertensive used was amlodipine (56%) compared to candesartan (38%). The dose of amlodipine used was 10 mg, and the dose of the drug candesartan was 16 mg.

Table II. An overview of the use of other groups and types of drugs used by CKD patients with hemodialysis

No	Group	Type	n	Percent (%)
1	Beta-blocker	Bisoprolol	48	17
2	Strong Diuretic	Furosemide	44	15
3	Statin	Atorvastatin	44	15
4	Proton Pum Inhibitor	Omeprazole	29	10
5	Antypiretics	Paracetamol	20	7
6	Antiplatelet	Clopidogrel	21	7
		Miniaspi	18	6
7	Benzodiazepine	Alprazolam	13	5
8	Ace inhibitor	Ramipril	11	4
		Captopril	4	1
9	Nootropic	Citicoline	8	3
10	Opioid	Codein	7	2
11	Mukolitik	Asetil sistein	7	2
12	Antirematik	Allopurinol	3	1
13	Mineral	KSR	4	1
	TOTAL		**288**	**100**

Table II shows the use of other groups and types of drugs was dominated by the beta-blocker class of bisoprolol (17%). Bisoprolol is commonly added to therapy for hypertensive patients with a high risk of heart disease and diabetes. Bisoprolol is a beta-blocker that is widely used as an antihypertensive agent, heart rate controller, and agent to improve cardiac ejection fraction (Jaya, Veryanti and Kartika, 2021).

Research conducted by Wu *et al.* compared bisoprolol with carvedilol in patients undergoing hemodialysis. The use of bisoprolol in hemodialysis patients can minimize the risk of mortality, which is caused by the risk of heart failure and ischemic stroke (Wu *et al.*, 2021). However, another study by Foch *et al.* showed the opposite result. A comparison between bisoprolol and other antihypertensives showed no significant differences in terms of the risk of obesity or erectile dysfunction. These data support further consideration of the use of bisoprolol in the treatment of patients with hypertension (Foch *et al.*, 2022).

Table III Comparison of Amlodipine and Candesartan Unit Prices Used at Undata Regional General Hospital, Palu.

Table III. List of Prices for Amlodipine and Candesartan

No	Drug Name	Formulation	Unit Price
1.	Amlodipine	Tablet	IDR 713
2.	Candesartan	Tablet	IDR 1,195

Table III lists the prices of amlodipine and candesartan used at the Undata Regional General Hospital, Palu. Candesartan has a higher cost (IDR 1,195) per tablet than amlodipine (IDR 713). This is consistent with the research of Riannur *et al.* (2020), where the price of amlodipine was lower (IDR 4,354) than that of candesartan (IDR 33,778). Another study by Erlita et al. compared the combination of amlodipine with irbesartan and candesartan. The combination of amlodipine and irbesartan was found to be cheaper, with an IDR of 5,991,007 for a 3-day hospital stay, compared to the amlodipine and candesartan combination, which cost an IDR of 10,025,676 for a 5-day hospital stay (Erlita, Kumala and Sarnianto, 2022).

The average direct medical costs for patients treated with amlodipine and candesartan are presented in **Table IV**.

Table IV. Direct Medical Cost Averages for CKD Patients with Hemodialysis

No	Therapy Cost	Amlodipine n = 77	Candesartan n = 26	P value
1.	Antihypertensive Cost	IDR 60,403	IDR 24,053	0,01
2.	Cost of Other Medications	IDR 12,262,105	IDR 12,347,295	0,32
3.	Facility Service Cost	IDR 921,852	IDR 1,221,907	0,21
4.	Supportive Medical Service Cost	IDR 950,553	IDR 1,001,553	0,21
	TOTAL	IDR 14,194,913	IDR 14,594,808	0,34
	Average	**IDR 184,350**	**IDR 561,339**	**0,02**

To calculate the average direct medical cost, a normality test was performed. The normality test obtained 0.174 a 0.05 of amlodipine (0.174), which means that the data were normally distributed, and 0.200 > 0.05, which also means that the candesartan drug data were normally distributed. The antihypertensive costs of amlodipine and candesartan were significantly different (p value of 0.01 < 0.05). However, the cost of other drugs, facility services, and supporting services are > 0.05, which means that they are not significantly different. From the calculation results of the four components of direct medical costs, the average cost of other medications that incurred the highest expenses, both in the amlodipine and candesartan groups. The average direct medical costs for amlodipine amount to IDR 184,350, which is lower than that for candesartan at IDR 561,339 with a p-value of 0.01 <0.05, which means that it is significantly different between amlodipine and candesartan costs. This aligns with the research by Santi Perawati, where the average direct medical costs for amlodipine were notably lower, totaling IDR 613,028,326, compared with IDR 27,488,835 for candesartan. The difference in direct medical costs is attributed to the duration of hospital stay and level of care during hospitalization (Perawati, Andriani and Utaka, 2021).

Another study, which is also in line with the results of this study, was conducted by Riannur, where amlodipine drugs were more cost-minimizing with an average use of amlodipine IDR 190,008, while candesartan was IDR 221,940 (Riannur *et al.*, 2020). The mechanism of action of amlodipine as an antihypertensive agent involves inhibiting calcium channels, thus causing smooth muscle relaxation that enhances the production of Nitric Oxide (NO), leading to a reduction in blood pressure (Tiyas, 2021). Amlodipine is a fully substituted dialkyl 1,4-dihydropyridine-3,5-dicarboxylate derivative used in the treatment of hypertension, and stable and chronic angina. It is a Dihydropyridine calcium channel blocker and a cytochrome P450 3A inhibitor. Its selectivity towards peripheral blood vessels, associated with a lower incidence of myocardial depression and cardiac conduction abnormalities compared to other calcium channel blockers, underscores its therapeutic profile (Naito *et al.*, 2015).

On the other hand, the mechanism of action of candesartan involves the inhibition of angiotensin II receptors on smooth muscle, which leads to vasodilation and subsequently decreases blood pressure (Wahyuni, 2018). This study has several limitations, including the separate recording of treatment costs and other supporting costs, making it prone to inconsistencies in the patient data. The duration of medication use was not recorded, and blood pressure checks were not conducted every time or hour. In fact, there were some patients whose blood pressure checks were not recorded. In addition, the difficulty in accessing all patient data, both in terms of cost and medication recording, is due to the fact that the Undata Hospital still uses a manual recording system.

CONCLUSION

Based on a cost minimization analysis of antihypertensive drug use in chronic kidney disease patients undergoing hemodialysis from January to December 2023, it was

found that the amlodipine group achieved greater cost minimization than the candesartan group.

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