JPPM
eISSN: 2383-4498
Journal of Pharmacoeconomics & Pharmaceutical Management
Tehran University of Medical Sciences

Cost-Effectiveness Analysis of Antihypertensive Therapy in Outpatient Hypertension Patients at Hospital X in Wajo Regency

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Citation Rahmah Safitri A, Ibrahim. I, Adhayanti A. Cost Cost-Effectiveness Analysis of Antihypertensive Therapy in Outpatient Hypertension Patients at Hospital X in Wajo Regency, Journal of Pharmacoeconomics and Pharmaceutical Management. 2023; 9 (3): 29-35

Running Title Cost-Effectiveness Analysis of Antihypertensive Therapy

Article Type Research Paper

Abstract

Background Hypertension is a chronic disease that cannot be cured and can only be controlled but requires long-term treatment, even for life. The variety of antihypertensive treatments makes it necessary to adjust the choice of treatment not only in terms of effectiveness, but also in terms of cost. Therefore, a pharmacoeconomic approach is needed, namely Cost Effectiveness Analysis (CEA) to compare the effectiveness of therapy and costs of several alternative therapies used.

Materials and Methods This research is observational using a descriptive research design through a pharmacoeconomic analysis approach, namely Cost-Effectiveness Analysis. The data collection technique was retrospective by accessing data from medical records of outpatient hypertension patients who met the inclusion criteria. Data taken for cost-effectiveness analysis are data on antihypertensive effectiveness and direct medical costs.

Results The combination of two antihypertensive drugs Calcium Channel Blocker (CCB) and Angiotensin II Receptor Blocker (ARB) with an ACER value of IDR 2,996 is the most cost-effective compared to the other combination groups.

Conclusion The combination of two antihypertensive drugs Calcium Channel Blocker (CCB) and Angiotensin II Receptor Blocker (ARB) with an ACER value of IDR 2,996 is the most cost-effective compared to the other combination groups.

Keywords Hypertension, Pharmacoeconomics, Cost-Effectiveness Analysis

Received; Accepted 2023 04.04.2023; 25.09.2023

Introduction

Indonesia is currently facing changes in disease risk factors or what is known as the epidemiological transition. This condition is marked by a shift in disease risk factors that were originally communicable to non-infectious. Changes in socio-economic patterns, modifications to the structure of society and the environment have also contributed to the emergence of this phenomenon. Some people still live an unhealthy lifestyle including smoking, eating fatty foods, lack of exercise and drinking alcohol are considered risk factors for non-communicable diseases. In the 21st century it is predicted that there will be an increase in the frequency of non-communicable diseases which is a major challenge in the health sector in the future [1].

Non-Communicable Diseases (NCD) are a public health challenge and are the largest contributor to global mortality rates. The world's population's attention to NCD has increased significantly along with the frequency of its occurrence which continues to increase [2]. According to the World Health Organization, NCD is responsible for 70% of the total deaths in the world, or 39.5 million of 56.4 million deaths. Cardiovascular disease is responsible for 45% of total NCD deaths, accounting for 17.7 million of 39.5 million deaths. One of the causes of cardiovascular disease is hypertension [3].

Hypertension is a chronic condition that can significantly increase the risk of cardiovascular disease. Blood pressure levels that are high and far from normal are considered hypertension. A person with normal blood pressure must have a blood pressure of 120/80 mmHg. If above 140/90 mmHg, WHO says they suffer from hypertension (Amal et al., 2021). The World Health Organization (WHO) estimates that 22% of the world's population currently suffers from hypertension. However, only less than a fifth of sufferers treat their hypertension, the rest do not take any action to control their blood pressure. Regions with the highest prevalence of hypertension are in Africa which reaches 27%, Southeast Asia ranks third with a prevalence of 25% of the total population [4].

Riskesdas (2018) states that hypertension is a NCD with the greatest frequency, with a total of 185,857 cases diagnosed in health facilities. The percentage of hypertension in Indonesia aged ≥18 years was 34.1%, where South Kalimantan had the highest prevalence, namely 44.1%, and Papua, with the lowest prevalence, namely 22.2%. Meanwhile, South Sulawesi occupies the 13th position, namely 31.9% [5]. The incidence of hypertension in Wajo Regency is 7,500 people, while data from Hospital X in Wajo Regency recorded 2,915 cases of increased blood pressure that occurred from January to December 2022 who carried out outpatient care.

Hypertension is a chronic condition that cannot be recovered but can be controlled but requires long-term or even lifelong treatment. The variety of antihypertensive treatments makes alternative treatments need to be considered not only in terms of treatment, but also in terms of costs. The price of various antihypertensive drugs is a crucial component for decision makers in determining treatment options for people with hypertension. Therefore, a pharmacoeconomic approach is needed in selecting effective antihypertensive treatment both from a cost and pharmacological perspective. The pharmacoeconomic method that can be used in evaluating hypertension treatment guidelines is the Cost Effectiveness Analysis (CEA). The advantage of CEA is that it can recommend the most effective treatment in terms of cost and pharmacology. Generally, CEA can assess the cost-effectiveness of treatment, for example cost-effectiveness in terms of lowering blood pressure [6].

Understanding pharmacoeconomic concepts is important for many parties including the pharmaceutical industry, policy makers and clinical pharmacy. For policy makers such as in hospitals, pharmacoeconomics can help in determining whether a drug should be included in the hospital formulary or a drug should be removed from the hospital formulary because it is not cost-effective compared to other drugs, choosing which health care program to use and formulate other strategic policies related to health care [7].

Material and Methods

This research is an observational study using a descriptive research design with a pharmacoeconomic analysis approach using the Cost-Effectiveness Analysis (CEA) method. This research was conducted at X Hospital in Wajo Regency with a population of hypertensive patients undergoing outpatient treatment at X Hospital in Wajo Regency from July to December 2022 and meeting the inclusion and exclusion criteria. The sampling technique in this study was carried out by non-random sampling with a purposive sampling technique. The inclusion criteria in this study were as follows: (1) Stage 2 hypertension patients aged ≥18 years who were undergoing outpatient care at X Hospital in Wajo Regency for the period July-December 2022; (2) Patients with complete medical record data and cost details; (3) Patients registered as BPJS patients; (4) Patients routinely carry out examinations for 3

consecutive months; (5) Patients with a diagnosis of hypertension with or without comorbidities; and (6) Patients taking the same combination of two oral antihypertensives for at least 3 consecutive months to control the effectiveness of the antihypertensive drugs used. The exclusion criteria in this study were: (1) Patients who did not have complete data (missing or illegible); (2) Patients receiving monotherapy or a combination of more than two drugs; (3) Patients who do not carry out routine examinations; and (4) Hypertensive patients during pregnancy. The data collection technique was carried out retrospectively by accessing data from the medical records of outpatient hypertension patients from July to December 2022 at the Medical Record Installation section. Medical record data includes the patient's identity (medical record number, gender and age), blood pressure, diagnosis, comorbidities and the name of the drug given and recorded on the data collection sheet. While the data for costs, namely direct medical costs which include the cost of antihypertensive drugs and costs including the cost of routine checks obtained from the Outpatient Pharmacy Installation and the BPJS section at Hospital X in Wajo Regency. The data that has been collected will be processed descriptively in tabular form in the Microsoft Excel application for further analysis using the ACER (Avarage Cost-Effectiveness Ratio).

Data analysis: The data that has been processed will be analyzed based on the following calculations:

(1) Calculation of direct medical costs where all costs needed by the patient during outpatient treatment every month; (2) Calculation of the effectiveness of drug use can be seen from the decrease in the patient's blood pressure, and (3) Calculation of the cost-effectiveness analysis of the use of antihypertensive drugs can use the ACER (Avarage Cost-Effectiveness Ratio) formula.

Results

Characteristics of outpatient hypertension patients at the Internal Medicine Polyclinic at Hospital X in Wajo Regency for the period from July to December 2022 as shown in table 1, where the female sex numbered 37 patients (57.81%) more than the male numbering 27 patients (42,18%). Patient characteristics based on age group in this study obtained data as shown in table 1, namely in the 18-44 age group there were 9 (14.06%), in the 45-60 age group there were 30 (46.87%) while the age group >60 as many as 25 (39.06%). There were 3 (4.68%) diagnosed with hypertension without comorbidities and of these there were 61 (95.31%) diagnosed with hypertension with comorbidities. Diabetes mellitus is the disease that most often accompanies hypertension, namely 26 patients with a percentage of 40.62%.

Treatment of hypertension in hypertensive outpatients at the Internal Medicine Polyclinic at Hospital X in Wajo Regency from July to December 2022, as shown in table 2, shows that the most widely used antihypertensive combination is Calcium Channel Blocker (CCB) with Angiotensin II Receptor Blocker (ARB) of 25 39.05%) with a combination of 10 mg amlodipine and 8 mg candesartan were 18 (28.12%) and a combination of 5 mg amlodipine and 8 mg candesartan were 7 (10.93).

The recommended blood pressure target is based on the Joint National Commission (JNC) VIII, namely patients <60 years <140/90 mmHg and patients >60 years <150/90. Based on the data in figure 3, the most effective drug combination in lowering blood pressure was the combination of CCB and ARB of 68%, followed by the combination of BB and ARB of 50%, CCB and BB of 50%, ARB and diuretics of 33.33 % and CCB and Diuretics by 25%. So it can be concluded that the most effective combination of two antihypertensive drugs in reducing blood pressure is the combination of Calcium Channel Blocker (CCB) and Angiotensin II Receptor Blocker (ARB) with a percentage of 71.42%.

The cost components in this study were direct medical costs which included the cost of antihypertensive drugs and administrative costs including the cost of routine checks obtained from the Outpatient Pharmacy Installation and the BPJS section at Hospital X in Wajo Regency. Based on the calculations obtained, the lowest two-drug combination treatment was ARB and Diuretics of IDR 196,700 followed by CCB and ARB of IDR 203,735, CCB and Diuretics of IDR 207,440, CCB and BB of IDR IDR 225,170. So it can be concluded that the combination therapy of two antihypertensive drugs with the lowest therapeutic cost is a combination of Angiotensin II Receptor Blocker (ARB) and Diuretics with a value of IDR 196,700.

The cost-effectiveness of therapy is calculated using the ACER (Avarage Cost-Effectiveness Ratio) formula which aims to compare the average total cost of various patterns of using a combination of two antihypertensive drugs with the effectiveness of therapy that reaches the expected target. Based on the results obtained as shown in figure 5, the lowest ACER value was owned by the combination of CCB and ARB with a value of IDR 2,996, followed by the combination of CCB and BB of IDR 4,345, BB and ARB of IDR 4,503, ARB and Diuretics of IDR 5,901 as well as CCB and Diuretics of IDR 8,297.

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Discussion

Women and men have the same potential to experience hypertension in adulthood, but at geriatric age women experience an increased risk of hypertension compared to men due to hormonal factors. The prevalence of hypertension in women is caused by hormonal changes, one of which is the occurrence of menopause which is experienced around the age of 50 years or more. Women who have not experienced menopause have the hormone estrogen as a protector, this hormone encourages an increase in HDL (High Density Lipoprotein) which functions to prevent narrowing of blood vessels. If estrogen production decreases, the body cannot maintain vasodilation which can control the increase in blood pressure, this increasing the risk of hypertension. In addition, the use of hormonal contraceptives can cause hypertension because they contain the hormones estrogen and progesterone which can affect blood pressure [8]. As a person ages, the capacity of the body's organs decreases, including the cardiovascular system, in this case the heart and blood vessels. Blood vessels narrow and the walls of blood vessels become stiff, causing blood pressure to rise. This is because in old age, large blood vessels lose their elasticity and become very stiff so that blood is forced through blood vessels that are narrower than usual, causing an increase in blood pressure [9].

The comorbid disease that most patients with hypertension suffers from is diabetes mellitus. Hypertension and diabetes mellitus are two diseases that have a linear relationship. In diabetes mellitus patients, high insulin levels will cause an increase in stress hormones produced by the kidneys. Increased levels of this hormone will cause neurological stress which will cause blood to clot in the arteries [8].

The Calcium Channel Blocker (CCB) class works by limiting the influx of transmembrane calcium into the smooth muscle of blood vessels and cardiac muscle. The CCB acts as a peripheral arterial vasodilator, directly reducing vascular resistance, thereby lowering blood pressure, while the myocardium acts to slow the heart rate. The next working effect of CCB is to widen the coronary arteries thereby increasing blood flow to the heart [10]. With this mechanism of action, this CCB class is the first line in hypertension therapy. The benefits of using CCB in the treatment of hypertension include consuming it once a day, this increases patient compliance in taking medication and allows blood pressure control for 24 hours. In addition, it can minimize the risk of side effects if consumed at night. CCB can minimize the risk of atherosclerosis by preventing damage to the lipid layer on the vascular membrane. Many benefits are obtained from the use of CCB in stroke patients. This is because the CCB class, especially the dihydropyridine class, is often used to treat patients with high blood pressure that is not effectively controlled with ACEI/ARB [11]. In addition, CCB is not affected by the amount of salt consumed, so it is beneficial for people who do not follow a salt diet. The use of amlodipine is sometimes limited by its side effects which can cause peripheral edema and headache. Concern over the potential for these side effects may prevent doctors from prescribing amlodipine to eligible patients, despite its proven benefits. The CCB group has the lowest cost, therefore combined with other drug classes that are not related to other diseases, the cost of therapy remains the lowest [12].

ARBs are effective in reducing blood pressure and reducing cardiovascular events, namely Left Ventricular Hypertrophy (LVH) in patients with kidney failure [13]. ARB class drugs are effective in lowering blood pressure in patients who have high renin levels. ARB does not affect heart rate, sudden stop and does not cause hypertension [6]. Several studies have shown that candesartan is a drug with high benefits when given to hypertensive patients with complications from kidney problems because this drug has been shown to reduce albuminuria levels in patients [14]. Candesartan has a favorable renal hemodynamic effect by increasing renal blood flow and maintaining or increasing the glomerular filtration rate while decreasing renal vascular resistance and filtration fraction. Candesartan reduces urinary protein excretion in hypertensive patients with microalbuminuria or nephropathy of certain etiologies and has no adverse effect on blood glucose or lipid profile. Calcium Channel Blocker (CCB) class of drugs is the most appropriate choice to be combined with Angiotensin Receptor Blocker (ARB) because CCB has a strong ability to lower blood pressure in a short time and side effects can be suppressed [15].

Conclusions

Based on the research that has been done, it can be concluded as follows:

1. Combination therapy of two antihypertensive drugs in hypertensive outpatients at Hospital X in Wajo Regency for the period July-December 2022 which is the most effective in reducing blood pressure is a combination of Calcium Channel Blocker (CCB) and Angiotensin II Receptor Blocker (ARB) with a percentage of 68%.
2. Combination therapy of two antihypertensive drugs with the lowest therapeutic cost is a

combination of Angiotensin II Receptor Blocker (ARB) and Diuretics with a value of IDR 196,700. 3. The combination of two antihypertensive drugs Calcium Channel Blocker (CCB) and Angiotensin II Receptor Blocker (ARB) with an ACER value of IDR 2,996 is the most cost-effective compared to other combination groups.

Ethical Considerations

There was no ethical consideration to be consider in this research.

Conflict of Interest

The authors declared no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not for profit sectors

Tables

Table 1 - Patient characteristics

Characteristics	Total	Percentage (%)
Gender		
Male	27	42,18
Female	37	57,81
Age (Years)		
18 - 44	9	14,06
45 - 60	30	46,87
>60	25	39,06
Hypertension Diagnosis		
Uncomplicated hypertension	3	4,68
Hypertension with comorbidities	61	95,31
Concomitant Diseases		
Diabetes melitus	26	40,62
Dyspepsia	8	12,5
Hyperlipidemia	2	3,12
Vertigo	2	3,12
DM + CKD	4	6,25
DM + CHF	4	6,25
DM + CAD	4	6,25
HHD + CAD	10	15,62
HHD + Gout	2	3,12
Hypertiroid + CAD	2	3,12

Note: CKD (Chronic Kidney Disease), CHF (Congestive Heart Failure), CAD (Coronary Artery Disease), HHD (Hypertensive Heart Disease).

Table 2 - An overview of patterns of use of antihypertensive drugs

Drug Class	Drug Type	Total	Percentage (%)
ARB + Diuretic	Candesartan 8 mg + Furosemide 40 mg	9	14,06
BB + ARB	Bisoprolol 5 mg + Candesartan 8 mg	8	12,5
CCB + ARB	Amlodipin 10 mg + Candesartan 8 mg	18	28,12
	Amlodipin 5 mg + Candesartan 8 mg	7	10,93
CCB + BB	Amlodipin 5 mg + Bisoprolol 5 mg	6	9,37
	Amlodipin 10 mg + Propanolol 40 mg	4	6,25
CCB + Diuretic	Amlodipin 10 mg + Furosemide 40 mg	12	18,75
Total		64	100%

Note: CCB = Calcium Channel Blocker, BB = Beta Blocker, ARB = Angiotensin II Reseptor Blocker.

Table 3 - Effectiveness of antihypertensive drug therapy

Therapeutic Patterns	Number of Patients	Blood Pressure Reached	Effectiveness (%)
ARB + Diuretic	9	3	33,33
BB + ARB	8	4	50
CCB + ARB	25	17	68
CCB + BB	10	5	50
CCB + Diuretic	12	3	25

Table 4 - Cost of antihypertensive drug therapy

Antihypertensive group	Average Cost (IDR)		Total Average Cost (Rp)
	Drug	Administration	
ARB + Diuretik	13.200	183.500	196.700
BB + ARB	41.670	183.500	225.170
CCB + ARB	20.235	183.500	203.735
CCB + BB	33.750	183.500	217.250
CCB + Diuretik	23.940	183.500	207.440

Table 5 - Calculation of the cost effectiveness of therapy

Therapeutic Patterns	Cost (IDR)	Effectiveness (%)	ACER (IDR)
ARB + Diuretik	196.700	33,33	5.901
BB + ARB	225.170	50	4.503
CCB + ARB	203.735	68	2.996
CCB + BB	217.250	50	4.345
CCB + Diuretik	207.440	25	8.297

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