COST-EFFECTIVENESS ANALYSIS OF COMBINATION ANTIHYPERTENSIVE DRUG ON HYPERTENSION OUTPATIENTS AT RSUD KABUPATEN KARANGANYAR 2020

Arayni, WCT.[1], Oetari, RA.[1], Hanifah, IR[1*].
Faculty of Pharmacy, Universitas Setia Budi, Surakarta
inaratul.rh.setiabudi@gmail.com

Abstract

Hypertension is the leading risk factor for myocardial infarction, stroke, acute renal failure, and death. Hypertension is one of the ten most common diseases at the RSUD Kabupaten Karanganyar. Antihypertensive drugs in RSUD Kabupaten Karanganyar that are often used are Herbesser (diltiazem HCl), candesartan, and ramipril. This research aimed to compare cost-effective combination antihypertensive (Herbesser-candesartan and Herbesser-ramipril) for outpatients at RSUD Karanganyar in 2020. The subjects were 84 outpatients who received combination antihypertensive (Herbesser – candesartan and Herbesser – ramipril). Therapeutics outcome saw from normal blood pressure at the next consultation, collected from patient medical records. The medical expenses were calculated from direct medical costs written in billing invoices based on a payer perspective. Cost-effectiveness analysis was performed by calculating the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER). The results showed that the combination of Herbesser – ramipril was more effective (83%) than Herbesser – candesartan (79%). The average direct medical cost of the Herbesser – candesartan was IDR 743,852, and Herbesser – ramipril was IDR 868,855. In addition, the combination drug of Herbesser – candesartan was more cost-effective (ACER IDR 942,213 per percent activity) than Herbesser – ramipril (ACER IDR 1.046.813 per percent activity) with an ICER value of IDR 31,250 per percent activity. In conclusion, the combination Herbesser-candesartan is a cost-effective medication for hypertension outpatients at RSUD Kabupaten Karanganyar in 2020.

Keywords: CEA, hypertension, Herbesser, Candesartan, Ramipril

Introduction

Hypertension is one of the most common diseases found in medical practice, a risk factor for myocardial infarction, stroke, acute kidney failure, and death. Hypertension can cause complications by affecting several target organs such as the heart, brain, kidneys, eyes, and peripheral arteries due to high blood pressure and how long the high blood pressure is not

controlled or not treated. Based on RISKESDAS (Basic Health Research) in 2018 shows that the prevalence of hypertension in Indonesia has increased by 34.1% (Riskesdas, 2018). Hypertension or high blood pressure increases the systolic blood pressure of more than 140 mmHg and diastolic blood pressure of more than 90 mmHg on two measurements with an interval of five minutes in a state of sufficient rest. Increased blood pressure that lasts for a long time can cause damage to the kidneys, heart, and brain if not detected early to get adequate treatment (Yulanda, 2017). Hypertension is included in the ten most significant diseases that are increasing until 2019.

International hypertension guidelines recognize that most patients will require two or more combinations of antihypertensive drugs to achieve the desired blood pressure target. These drugs can be given as separate agents or in combination in a single pill (Riskesdas, 2018). However, every health care institution around the world has limited human resources as experts, time, facilities, and funds in running the health care system, including in handling hypertension. This limitation has prompted the selection of priorities so that the regulation of health services can run efficiently through pharmacoeconomic considerations (Bang, 2012). Pharmacoeconomic studies that consider clinical factors and economic factors can assist in rational drug selection, which can provide highly beneficial effects for patients (KEMENKES RI, 2013). One of the pharmacoeconomic methods used is Cost-Effectiveness Analysis (CEA). CEA is used to measure the cost of using drugs compared to the effectiveness of health services. Using this comparison, clinicians can choose an alternative with a lower cost for each outcome (Andayani, 2013). This study aims to determine which therapy is more cost-effective between the combination drug Herbesser - candesartan and Herbesser - ramipril in outpatient hypertension patients at the RSUD Kabupaten Karanganyar in 2020.

Material and Methods

This study is a non-experimental, descriptive study using secondary patient data in medical records and billing data for hypertension patients undergoing outpatient treatment at the RSUD Kabupaten Karanganyar in 2020. This research was conducted after the researcher passed the "Health Research Ethics Committee Dr. Moewardi General Hospital."

Data collection was carried out using the purposive sampling method to obtain samples according to the desired criteria. The selected criteria consist of inclusion criteria and exclusion criteria. Inclusion criteria were BPJS outpatients with hypertension, use antihypertensive drugs Herbesser - candesartan and Herbesser - ramipril more than three months at RSUD Kabupaten Karanganyar

in 2020. Exclusion criteria were incomplete patient medical record data and incomplete billing data.

The material used was secondary patient data, consisting of medical records and billing data for hypertension patients at RSUD Kabupaten Karanganyar from January to December 2020. The data obtained were analyzed for the effectiveness of therapy, total cost, average cost, ACER, and ICER values.

The effectiveness of therapy was seen from the decreased blood pressure until it reached the appropriate target after taking antihypertensive drugs. The targeted treatment was 140/90 mmHg for hypertensive patients aged less than 60 years and 150/90 mmHg for hypertensive patients aged more than 60 years old (Houle, 2014).

The results of CEA are described as a ratio, either by ACER (Average Cost-Effectiveness Ratio) or ICER (Incremental Cost-Effectiveness Ratio).

$$\text{ACER} = \frac{Cost\ (Rp)}{Effectiveness\ (\%)}$$

$$\text{ICER} = \frac{Cost\ A - Cost\ B\ (Rp)}{Effectiveness\ A - Effectiveness\ B\ (\%)}$$

ACER is intended to obtain differences from each alternative therapy and comparison. The smaller the value, the more cost-effective treatment is considered. The ICER method is used to determine the increase in therapy costs by adding or replacing treatment which may increase the cost of therapy, but with an increase in costs to the patient, it will have a better effect on the drug (Andayani, 2013).

Result And Discussion

There were 1219 cases of hypertension patients, with 2001 visits from January to December 2020. In addition, 84 hypertension patients received combination therapy of Herbesser – candesartan and Herbesser – ramipril with complete medical records and billing data.

Table 1. Distribution of outpatient hypertension patients by age at RSUD Kabupaten Karanganyar in 2020.

Age	Group A (Patients)	Percentage (%)	Group B (Patients)	Percentage (%)	Total number of patients
<60	9	47,37	30	46,15	39
≥60	10	52,63	35	53,85	45
	19	100	65	100	84

Source: Processed raw data
Group A = Herbesser-Candesartan, Group B = Herbesser-Ramipril

Increasing age greatly affects blood pressure because the work of organs, one of which is the heart and cardiovascular system, decreases with age. Thus, aging has a substantial effect on the cardiovascular system. Under these conditions, thickening of the arterial wall and reduced permeability of the blood vessel wall resulting in increased lipoprotein transport into the arterial wall, increased proliferation of smooth muscle cells, and the synthesis of extracellular matrix molecules (Adrian, 2019). In addition, hypertension is also influenced by the female hormone estrogen, which also plays a role in maintaining the quality of blood vessels.

Table 2. Distribution of outpatient hypertension patients by gender in RSUD Kabupaten Karanganyar in 2020.

Gender	Group A (Patienst)	Percentage (%)	Group B (Patienst)	Percentage (%)	Total number of patients
Male	7	36,84	26	40	33
Female	12	63,16	39	60	51
	19	100	65	100	84

Source: Processed raw data
Group A = Herbesser-Candesartan, Group B = Herbesser-Ramipril

The hormone estrogen can protect blood vessels from oxidative reactions and prevent blood vessels from experiencing inflammation (Poorojal, 2016). During premenopause, women will gradually experience a decrease in estrogen levels. This process will continue to occur where the quantity of the hormone estrogen will naturally decrease, which generally occurs at the age of 45 to 55 years (Nuraini, 2015).

Table 3. The effectiveness of Antihipertensive Combination Drug at RSUD Kabupaten Karanganyar in 2020

Antihipertensive Drug	Number of patients	Total patient who reached the target	Percentage (%)
Group A	19	15	79
Group B	65	54	83
	84	69	

Source: Processed raw data
Group A = Herbesser-Candesartan, Group B = Herbesser-Ramipril

The effectiveness of therapy in this study was seen from the decrease in the patient's blood pressure until it reached the appropriate target after taking antihypertensive drugs. The effectiveness of therapy was measured by reducing blood pressure to 140/90 mmHg for hypertensive patients aged less than 60 years and decreasing blood pressure to 150/90 mmHg for hypertensive patients aged 60 years or older (Skarayadi, 2017).

Herbesser works by inhibiting the entry of calcium into arterial blood vessel cells, thereby causing dilation of the coronary arteries and peripheral arteries, thereby causing relaxation of the heart and smooth muscles. Relaxation of vascular smooth muscle will cause vasodilation associated with a reduction in blood pressure. Candesartan works by blocking the binding of angiotensin II to its receptors, while ramipril prevents the conversion of angiotensin I to angiotensin II (KEMENKES RI, 2013).

Cost is an economical expenditure that is calculated to estimate resources in a production or service (Alifiar, 2019). In this study, a cost analysis of hypertension was carried out in outpatients at RSUD Kabupaten Karanganyar based on the payer perspective. The direct costs of outpatient hypertension patients at the RSUD Kabupaten Karanganyar in 2020 consist of the cost of antihypertensive drugs, the cost of other drugs, and the cost of examinations. An average cost will be obtained from these costs, which can later be used as material for analysis to consider which therapy is the most cost-effective.

Table 4. Direct medical costs of outpatient hypertension patients at RSUD Kabupaten Karanganyar in 2020

Antihipertensive Drug	Total biaya rata-rata (IDR)
Group A	743.852
Group B	868.855

Source: Processed raw data
Group A = Herbesser-Candesartan, Group B = Herbesser-Ramipril

The average cost includes the cost of hypertension medication, accompanying drugs, and the cost of a doctor's examination. The average cost of therapy for hypertensive patients in Table 5 shows that patients using group B hypertension drugs spend more than the average therapy costs for hypertensive patients using group A hypertension drugs. The total average cost for each group is IDR. 868,885. The total average cost of the combination B group and the average total cost of Group A is IDR 743,852.

Table 5. The results of ACER value of Antihypertensive Combination Drug in outpatient hypertension patients at RSUD Kabupaten Karanganyar in 2020

Antihipertensive Drug	Effectiveness (%)	Average costs	ACER
Group A	79	743.852	942.213
Group B	83	868.855	1.046.813

Source: Processed raw data

Group A = Herbesser-Candesartan, Group B = Herbesser-Ramipril

The average cost-effectiveness ratio or ACER is the ratio of the costs to benefit from an intervention. It is obtained without reference to comparators, in this case, without reference to other combination therapies (Kodera, 2017). In these circumstances, the calculation of the ACER ratio is used and compares the results obtained between several treatment groups directly (Gauverau, 2012).

Table 5 shows the value of effectiveness, the average total cost, the number of patients using the therapy, and the ACER value of the combination therapy of Herbesser – candesartan and Herbesser – ramipril. The ACER value for group A combination therapy was IDR. 942,213, and the ACER value for group B combination therapy is IDR. 1,046,813. A therapy group can be said to be cost-effective if it has a smaller ACER value compared to other therapy groups. In this study, it was found that the ACER value of the combination therapy group A was lower than the other combination therapy groups so that the therapy that was considered the most cost-effective was the Herbesser-candesartan combination therapy.

Table 6. The results of the calculation of the ICER value of Antihipertensive Combination Drug in outpatient hypertension patients at RSUD Kabupaten Karanganyar in 2020

Antihipertensive Drug	Average costs (IDR)	Effectiveness (%)	ΔC (IDR)	ΔE (%)	ICER
Group A	743.852	79	125.003	4	IDR. 31.250
Group B	868.855	83			

Source: Processed raw data
Group A = Herbesser-Candesartan, Group B = Herbesser-Ramipril

ICER is a ratio of additional costs by considering the benefits of two competing interventions so that it will be known how much additional costs need to be incurred to increase the effectiveness of therapy (Boghi, 2013). In table 6 it can be seen that the ICER value in patients using the combination therapy Herbesser - ramipril against the combination Herbesser - candesartan, which is IDR. 31,250 per activity percentage, meaning that if the Herbesser-ramipril therapy is used in hypertensive patients, an additional cost of IDR. 31,250 per percentage of effectiveness to get an increase in healing in patients.

Table 7. Sensitivity analysis of the use of Herbesser-candesartan combination therapy in hypertensive patients at RSUD Kabupaten Karanganyar in 2020

	Cost Component (IDR)		
	Cost of Drugs	**Cost of Diagnostic**	**Total cost**
Herbesser-Candesartan	713.852	30.000	743.852

+25%	892.315	37.500	929.815
-25%	535.389	22.500	557.889
Difference	356926	15.000	409.426

Source: Processed raw data

Sensitivity analysis is used to make it possible to determine how the results of the analysis will change when there is a change in value by using a reasonable range of values so that it can assist researchers in examining the impact of changes in these assumptions (Rascati, 2013).

From table 7, there are components of the cost of outpatient hypertension patients, including therapy costs and examination costs. In this study, it was found that the most cost effective therapy group was the Herbesser-candesartan combination group with an average total cost of IDR. 743,852. From the table, it can be seen that the most influential cost is the cost of therapy, while the examination cost component has no effect on the overall cost component.

Conclusion

1. The percentages of effectiveness of combination therapy using Herbesser - candesartan and Herbesser - ramipril were 79% and 83%, respectively, in outpatient hypertension patients at RSUD Kabupaten Karanganyar.
2. The average direct medical costs of the combination therapies using Herbesser-candesartan and Herbesser – ramipril were IDR. 743,852 and IDR 868,855, respectively.
3. The obtained ACER values of combination therapy of Herbesser – candesartan and Herbesser – ramipril were IDR 942,213 and IDR 1,045,844, respectively. So that the Herbesser – candesartan combination therapy group was found more cost-effective than the Herbesser – ramipril combination therapy group with an ICER value of IDR 31,250 per percent activity

Reference

Adrian, SJ., & Tommy. 2019. Hipertensi Esensial : Diagnosis dan Tatalaksana Terbaru pada Dewasa. *Cermin Dunia Kedokteran* 46(3), 172–178.

Alifiar, I., & Idacahyati, K. 2019. Kajian Farmakoekonomi Penggunaan Obat Antihipertensi pada Pasien Hipertensi yang Dirawat di RSUD Kota Tasikmalaya. *Jurnal Pharmascience*, *5*(2), 126–133. https://doi.org/10.20527/jps.v5i2.5794

Andayani, T. 2013. *Farmakoekonomi : Prinsip dan Metodologi.* (Cetakan 1). Bursa Ilmu Karangkajen. Jakarta.

Bang, H., Zhao, H. 2012. Average Cost-Effectiveness Ratio With Sensored Data. *Journal of Biopharmaceutical Statistics*, 22(2): 401–415. doi:10.1080/10543406.2010.544437.

Borghi, C., Ambrosioni S., Omboni. 2013. Cost-effectiveness Of Zofenopril In Patients With Left Ventricular Systolic Dysfunction After Acute Myocardial Infarction: A post hoc analysis of SMILE-4. *ClinicoEconomics and Outcomes Research*, *5*(1), 317–325. https://doi.org/10.2147/CEOR.S43138

Gauvreau, C. L., Ungar, W. J., KÖhler, J. C., & Zlotkin, S. 2012. The use of cost-effectiveness analysis for pediatric immunization in developing countries. *Milbank Quarterly*, *90*(4), 762–790. https://doi.org/10.1111/j.1468-0009.2012.00682.x

Houle, S. K. D., Padwal, R., Poirier, L., Tsuyuki, R. T. 2014. The 2014 Canadian Hypertension Education Program (CHEP) guidelines for pharmacists: An update. *Canadian Pharmacists Journal*, *147*(4), 203–208. https://doi.org/10.1177/1715163514535341

Kemenkes RI. 2013. *Pedoman Teknis Penemuan dan Tatalaksana Hipertensi*. Direktorat Pengendalian Penyakit Tidak Menular, Subdit Pengendalian Penyakit Jantung dan Pembuluh Darah. Jakarta

Kodera, S., Kiyosue A., Ando J. 2017. Cost-effectiveness analysis of cardiovascular disease treatment in Japan. *International Heart Journal*, *58*(6), 847–852. https://doi.org/10.1536/ihj.17-365

Nuraini, B. 2015. Risk Factors of Hypertension. *J Majority*, *4*(5), 10–19.

Poorolajal, J., Farbakhsh, F., Mahjub, H., Bidarafsh, A., & Babaee, E. 2016. How much excess body weight, blood sugar, or age can double the risk of hypertension? *Public Health*, *133*, 14–18. https://doi.org/10.1016/j.puhe.2015.10.014

Rascati, K. L. 2013. *Essentials of pharmacoeconomics: Second edition*. Texas

Riskesdas. *Hasil Utama Riset Kesehatan Dasar Laporan Nasional 2018*. Badan Penelitian dan Pengembangan Kesehatan Republik Indonesia. Jakarta

Skarayadi, O., Sutarna, T. H., & Ambarsundari, A. 2017. Efektivitas Biaya Terapi Antihipertensi Pada Pasien Rawat Jalan Di Upt Puskesmas Puter. *Kartika Jurnal Ilmiah Farmasi*, *5*(1), 21–23. https://doi.org/10.26874/kjif.v5i1.84

Yulanda, G., & Lisiswanti, R. 2017. Penatalaksanaan Hipertensi Primer. *Majority*, *6*(1), 25–33.