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COST EFFECTIVENESS ANALYSIS OF CAPTOPRIL AND AMLODIPINE IN HYPERTENSION WITH DIABETES MELLITUS IN MAGELANG REGENCY HEALTH CENTER

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ABSTRACT

Backgrounds: Hypertension and Diabetes Mellitus are interrelated diseases and have a strong predisposition to the occurrence of cardiovascular disease and atherosclerosis. BPJS Kesehatan states that the cost of hypertension services has increased every year, indicating the need to control costs through pharmacoeconomic studies. One method that can be used is cost-effectiveness analysis. Find out the effective drugs in terms of cost and therapy. **Aim**: To determine the cost-effectiveness of Captopril and Amlodipine for hypertensive patients with co-morbidities of diabetes mellitus at the Magelang District Health Center. **Methods:** This study was conducted retrospectively with medical record data for 2019-2020. The sample in this study was 35 with 15 groups of 10 mg/day amlodipine and 20 groups of 25 mg/day captopril. The outcome assessed was the number of patients who achieved the therapeutic target for 1 month using the drug. **Results:** The percentage of therapeutic effectiveness of amlodipine 10 mg/day was 86,7% while captopril 25 mg was 60%. The average direct medical cost of the amlodipine 10 mg/day is Rp10.429,30 greater than captopril 25 mg/day, which is Rp7.298,80. The ACER value of amlodipine 10 mg/day was Rp. 12.023,00 and captopril 25 mg/day was Rp. 12.164,00. Calculation of ICER value of the average direct medical cost of the 10 mg/day amlodipine group is Rp10.423,93 greater than captopril 25 mg/day, which is Rp7.298,80. **Conclusion** : Amlodipine is more cost-effective than captopril with an ACER value of RP. 12.023,00.

***Keywords**: Cost Effectiveness Analysis, Antihypertensive, Hypertension, Diabetes Mellitus*

INTRODUCTION

Hypertension was defined as a systolic blood pressure value of 140 mmHg and a diastolic blood pressure of 90 mmHg.[1] Riskesdas 2018 states that the prevalence of hypertension based on the results of blood pressure measurements in people aged >18 years is 34.1%. Hypertension and Diabetes Mellitus are interrelated diseases and have a strong predisposition to cardiovascular disease and atherosclerosis. This is why hypertension and diabetes mellitus must be recognized and treated early and aggressively.[2] Captopril and Amlodipine are drugs that can overcome these diseases. Amlodipine is a calcium channel blocker (CCB) and captopril is an angiotensin converting enzyme inhibitor (ACEI) which is rapidly absorbed but has a short duration of action.[3]

Data from Badan Penyelenggara Jaminan Sosial (BPJS) Kesehatan states that the cost of hypertension services has increased every year, namely in 2016 of 2.8 trillion rupiah, in 2017 and 2018 of 3 trillion rupiah. The high cost of treatment for hypertension indicates the need to control costs through pharmacoeconomic studies. One method that can be used to conduct pharmacoeconomic research is cost-effectiveness analysis. In general, cost-effectiveness analysis is defined as analytical and mathematical procedures used to assist in selecting an action to be taken from various alternative approaches. These cost-effectiveness results can help determine clinical treatment in choosing the best cost-effective treatment.[4]

Based on this explanation, this research is needed to find out which hypertension drug is the best in terms of cost and therapeutic effect. So that the cost of drugs for hypertensive patients with co-morbidities of diabetes mellitus can be controlled.

METHODS

This study is an analytic observational study with a cross-sectional design. This study was conducted retrospectively with the assessed outcome being a decrease in blood pressure reaching the therapeutic target after 1 month of using the antihypertensive Captopril 25 mg/day or Amlodipine 10 mg/day. The sample of this study were outpatients with a diagnosis of hypertension with comorbid diabetes mellitus who received therapy with

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Captopril 25 mg/day or Amlodipine 10 mg/day at the Bandongan Health Center, Tempuran Health Center and Mertoyudan II Health Center in Magelang Regency for the period January 2019 – December 2020. The sample was used in this study were 35 patients consisting of Amlodipine 10 mg/day (15 patients) and Captopril 25 mg/day (20 patients).

This study uses secondary data in the form of medical records. The data obtained were then analyzed for the description of the research subjects which included gender, age, hypertension staging, average reduction in blood pressure, and patterns of use of antihypertensives and other drugs. The blood pressure reduction data obtained were then analyzed whether the decrease had reached the therapeutic target. The number of patients who reached the therapeutic target was analyzed for % effectiveness by means of the number of patients who achieved the therapeutic target divided by the number of patients multiplied by 100%.

Cost analysis using direct medical costs includes the cost of antihypertensives and other drug costs. The data on the average total direct medical costs and drug effectiveness obtained were analyzed for cost effectiveness. The results of the analysis are expressed as Average cost effectiveness ratio (ACER) or as Incremental cost effectiveness ratio (ICER).

ACER shows the average total direct medical cost of a therapy divided by clinical results in the form of % effectiveness.[5] A drug is more cost-effective if the ACER value of a drug is the lowest of the drugs being compared. The incremental cost effectiveness ratio (ICER) determines how much additional costs and therapeutic effectiveness are obtained when alternative therapies are given to other treatments that not only increase medical costs but can also increase the effects, benefits, and outcomes.[6]

RESULTS AND DISCUSSION

Patient Characteristics

Table 1 Patient Characteristc of Hypertensive Patients with Diabetes Mellitus

	Captopril	Amlodipine
Gender		
Male	20%	66,7%
Female	80%	33,7%
Age		
<45	0	0
45-64	35%	46,7%
55-64	65%	53,3%
Hypertension Category		
Stage 1	40%	26,7%
Stage 2	60%	73,3%
Treatment	57,15%	42,85%
Average drop in blood pressure	31,10/9 mmHg	35,53/10,20 mmHg

a. Gender

The results showed that there were 10 (66,7%) male and 5 (33,3%) female with amlodipine therapy. While in the captopril group there were 16 (80%) female and 4 (20%) male .The cause of hypertension in female may be due to several things, such as menopause, contraceptive pills and the activity of the Renin Angiotension System (RAS).[7,8] Hypertension by gender is also influenced by psychological factors. Male are more related to work such as feeling less comfortable with work, unemployment, and unhealthy behaviors such as smoking and alcohol consumption.[9]

b. Age

Based on the demographic data of the patient's age, it was found that the most hypertensive patients with comorbid diabetes mellitus were aged 55-64 years in both groups. Increasing age will cause a decrease in the function of the body's organs so that the heart has to work extra to pump blood in order to move the body's burden which causes high blood pressure.[10]

c. Hypertension Category

The results showed that hypertensive patients with comorbid diabetes mellitus in both groups, there was more stage 2 in hypertension. There were 40% in stage 1 and 60% in stage 2 with captopril therapy. While in amlodipine therapy there were 26,7% in stage 1 and 73,3% in stage 2.

d. Treatment

Patients who received amlodipine 10 mg were 15 patients with a percentage of 42,85% and who received Captopril 25 mg were 20 patients with a percentage of 57,15%. Research results indicate the pattern of use of drugs other than antihypertensives given to patients. The results showed that 11 patients were given the antidiabetic metformin, 1 patient was given glimepiride, 2 patients were taking glibenclamide and 13 patients were given a combination of metformin and glimepiride. Therapies other than antidiabetic are 4 Vitamin B 12, Antalgin 1, Paracetamol 1, Mefenamic Acid 1, Ibuprofen 1, Comvit t , Hemafort 1.

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Patients are given analgesics and vitamins are expected to overcome the complaints experienced by patients due to hypertension and diabetes mellitus. Common complaints experienced by hypertensive patients include headache, restlessness, blurred vision and chest pain.[9] Diabetic Peripheral Neuropathy (NPD) is one of the most common chronic complications of diabetes mellitus. Complaints that are often felt by patients include pain, burning, paraesthesia (tingling and stinging). The decrease in neuropathy symptoms can be overcome by giving neurotrophic vitamins such as vitamins B1, B6, and B12.[11]

e. Average drop in blood pressure

The study showed that the average decrease in blood pressure in patients taking amlodipine 10 mg/day was 35.53/10.20 mmHg higher than captopril 25 mg/day, which was 31.10/9 mmHg.

Therapeutic Effectiveness

Table 2. Therapeutic Effectiveness of Hypertensive Patients with Diabetes Mellitus

Therapy	Number of patients	Achieve therapeutic goals	Percentage
Amlodipine	15	13	86,7%
Captopril	20	12	60%

The results showed that the effectiveness of amlodipine 10 mg/day therapy was 87,5% higher than captopril 25 mg/day (60%). The effectiveness of amlodipine is higher because amlodipine has a higher bioavailability of around 64-90%, and is not affected by food. Binding to plasma proteins is about 93%. While the bioavailability of captopril is 70-75% and can be influenced by food. Food can reduce the bioavailability of drugs by about 24-30%.[5] However, this study has limitations, such as the small number of samples, medication adherence and drug side effects that could affect the effectiveness of therapy.

Cost Analysis

The costs analyzed in this study are direct medical costs including antihypertensive costs and other drug costs.

Antihypertensive Cost

Antihypertensive costs are costs incurred to treat hypertension. Antihypertensive costs are calculated by means of the number of drugs consumed by the patient for one month multiplied by the price of each drug. The results showed that the cost of antihypertensive Amlodipine 10 mg/day was more expensive than Captopril 25 mg/day. This may be due to the price of the drug Amlodipine 10 mg/day is more expensive than Captopril 25 mg/day. Based on the data, the price of Amlodipine 10 mg was Rp. 143,00 while the price of Captopril 25 mg/day was Rp. 88,00. The calculation of the antihypertensive cost obtained was then analyzed using the Mann-Whitney non-parametric test. The result is p = 0.000, so it is concluded that there is a significant difference between the two groups in antihypertensive costs.

Table 3. Cost of Antihypertensive, Other Drug, and Direct Medical Cost

Cost	Amlodipin (Rp)	Captopril (Rp)	P
Averege of anti-hypertensive cost	4.290,00	2.816,00	0,000*
Averege of other drug cost	6.133,93	4.482,80	0,036*
Averege of total medical cost	10.423,93	7.298,80	0,000*

*) significant

Other Drug Costs

Cost of other drugs that are calculated includes the cost of antidiabetic drugs, painkillers and vitamins. The total of other drug cost analyze by independent t-test, and p value showed 0.000. This study concluded there is a significant difference between the two groups in other drug costs. Antidiabetic costs were calculated in this study because hypertension is associated with diabetes mellitus. In accordance with previous research regarding a history of Diabetes Mellitus (DM) with the incidence of hypertension at the Janti Health Center, it was stated that there was a significant relationship between the history of DM and the incidence of hypertension at the Janti Health Center. Ten People who have a history of DM will tend to have high blood pressure.[12]

Direct Medical Cost

Direct medical costs are costs that are most often measured, are inputs that are used directly to

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provide therapy. For example treatment, therapy monitoring, therapy administration, patient consultation and counseling, diagnostic tests, hospitalization.[13] Direct medical costs analyzed in this study include antihypertensive costs and other drug costs. The results showed that the average direct medical cost of the Amlodipine group was Rp. 10.423,93 and Captopril was Rp. 7.298,80. Based on the analysis of the independent t-test, the direct medical costs were obtained at 0.000 ($p < 0.05$). It can be concluded that there is a significant difference in costs between the two groups in direct medical costs.

Cost Effectiveness Analysis

Cost effectiveness analysis was carried out by finding the ACER value in each group. The results showed that the ACER value of Amlodipine 10 mg/day was Rp. 12.023,00 and Captopril 25 mg/day was Rp. 12.164,00 per therapy effectiveness. The effectiveness of Amlodipine 10 mg/day is high but the costs are also high, it is necessary to calculate the ICER value. It was found that the ICER value Rp. 11.704,60, which means that an additional fee of Rp. 11.704,60 is needed to increase the 1% effectiveness of amlodipine.

Table 4. Cost Effectiveness of Hypertensive Patients with Diabetes Mellitus

Therapy	Total direct medical costs (Rp)	ACER (Rp)	ICER (Rp)
Captopril	7.298,80	12.164,00	11.704,6
Amlodipine	10.423,93	12.023,00	

Some the limitations of the study, such as the number of samples, medication adherence and drug side effects, which were not studied, Amlodipine 10 mg/day therapy is not necessarily more cost-effective than Captopril 25 mg/day even though the ACER value of Amlodipine 10 mg/day is lower than Captopril 25 mg/day. The difference between the ACER values of the two drugs is also not too far. So that the choice of therapy between Amlodipine 10 mg/day and Captopril 25 mg/day for policy holders can be done with various considerations such as the availability of drugs at the puskesmas and the patient's condition.

CONCLUSION

The cost effectiveness of Amlodipine 10 mg/day with an ACER value is Rp. 12.023,00 while the ACER value of Captopril is Rp. 12.164,00. The effectiveness of Amlodipine is high but the costs are also high, it is necessary to calculate the ICER value. The ICER value of Amlodipine is Rp. 11.704,60, so an additional fee of Rp. 11.704,60 is needed to increase 1% of the effectiveness of therapy.

ETHICAL APPROVAL

Ethical approval was obtained form the Health Research Ethics Commmite of Faculty Medicine Diponegoro University. The ethical clearance of this research was No.30/EC/KEPK/FK-UNDIP/II/2021.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, M.I.B., E.A., and I.R.E.D; methodology M.I.B., E.A., and I.R.E.D; formal analysis, M.I.B; resources, writing—original draft preparation, M.I.B. and E.A.; writing—review and editing E.A., project administration, M.I.B funding acquisition M.I.B, etc.

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