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Analysis of Cost-Effectiveness of Antihypertensive Therapy in Hypertension Patients at A-Ihsan Regional Public Hospital in 2023

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Abstract

Hypertension is a disease that causes an abnormal increase in blood pressure, which causes cardiovascular disease. Long-term hypertension therapy requires large costs. Apart from that, existing antihypertensives are also very varied, so a cost-effectiveness analysis is needed to choose medications that balance costs and advantages. This study aims to determine the most economical antihypertensive medication at Al-Ihsan Regional Public Hospital in Baleendah. Based on patient medical records, this study was carried out retrospectively. Therapy data and treatment costs are the basis for the data collection process. The data is processed descriptively. The reduction in blood pressure that meets the target and the length of stay (LOS) is used to determine how effective the therapy was; the ACER and ICER values are used to determine how cost-effective the procedure was. According to the research findings, the average total cost of group A (ACEI with CCB) is IDR 2,311,000.00, whereas group B (ARB with CCB) is IDR 2,888,823.00. The efficacy of group A (ACEI with CCB) was 83.3%, while group B (ARB with CCB) was 52.4%. The findings showed that among inpatient hypertension patients at Al-Ihsan Regional Public Hospital, group A (ACEI with CCB) was more cost-effective, with an Average Cost Effectiveness Ratio (ACER) value of IDR 27,743,097, than group B (ARB with CCB ACER value of IDR 55,130,209). Based on this study, therapy of group A (ACEI with CCB) offers excellent therapeutic efficacy at a reduced cost. Hospitals are expected to have the ability to handle their spending on hypertension medications appropriately and efficiently

Keywords: Combination of Antihypertensives, Hypertension, Cost-Effectiveness Analysis

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Introduction

Hypertension is a disease characterized by high blood pressure (BP), which can result in problems such as heart failure, stroke, cardiovascular disease, and renal failure.[1] Systolic blood pressure (SBP) of 140–159 mmHg and diastolic blood pressure (DBP) of 90–99 mmHg are the parameters used to characterize hypertension for stage 1, and SBP values of 160–179 mmHg and DBP values of 100–109 mmHg are used to characterize hypertension for stage 2.[2]

According to the West Java Provincial Health Service, the percentage of people receiving health services for hypertension patients based on BP readings, particularly for Bandung regency, is 82.75%, which is higher than the percentage for West Java Province (70.3%).[3] Hypertension therapy takes longer to be treated and requires many costs.[4] Pharmacoeconomics analyzes medical therapy costs. It deals systematically with the meaning, measurement, and comparison of costs.[5]

Antihypertensive therapy is a common practice at Al-Ihsan Regional Public Hospital. It involves the combination of medications such as calcium channel blockers (CCB) and ACEIs (Angiotensin-Converting Enzyme Inhibitors) or ARBs (Angiotensin Receptor Blockers). Varying drug prices are important when making decisions about whether to use drugs for patients. Cost-effectiveness analysis (CEA) is crucial for recommending the best therapy at an effective cost.[6]

Methods

A descriptive analysis combined with an observational study approach was conducted. A total sampling technique was used in 2023 to collect data retroactively. The data taken was divided into 2 groups: A (ACEI with CCB) and B (ARB with CCB). The pharmacoeconomic study used is Cost-Effective Analysis (CEA), using the perspective of hospitals as health service providers. The Incremental Cost Effectiveness Ratio (ICER) and Average Cost Effectiveness Ratio (ACER) values illustrate the CEA technique. The efficacy and total cost comparison is known as ACER. The total cost used is direct medical costs. Based on the two therapy groups, if one group has lower costs but high effectiveness, it does not require ICER calculations. ICER is calculated if the cost of each intervention is more expensive with high effectiveness or cheaper with low effectiveness.[7]

Data was taken from the medical records installation, management information system, and finances at Al-Ihsan Regional Public Hospital. These costs include the costs of hypertension medication, other medications, medical equipment costs, facility costs, diagnostic costs, and examination costs during hospitalization.

The patient's length of stay (LOS) and BP readings upon admission and discharge from the hospital are used to gauge effectiveness. Patients diagnosed with hypertension and older than 18 years old who were randomized to either group A (ACEI with CCB) or group B (ARB with CCB) for antihypertensive medication met the study's inclusion criteria. The exclusion criteria in this study were incomplete data and pregnant or breastfeeding patients.

Results and Discussion

This study was conducted at Al-Ihsan Regional Public Hospital for 4 months for patients who received the combination of antihypertension therapy (ACEI with CCB and ARB with CCB) in 2023. According to the study's results, twenty-seven patients met the requirements. Table 1 shows the patient characteristic data.

Table 1. Features of the Patient According to Age and Gender

Characteristics	Number (n)	(%)
Gender:		
Male	16	59.26
Female	11	40.74
Total	27	100
Age		
>18-40	1	3.70
>40-60	10	37
>60	16	59.3
Total	27	100

Hypertension patients treated at Al-Ihsan Regional Public Hospital in 2023 who used antihypertensive combination therapy were 16 males (59.26%) and 11 females (40.74%). The number of men who experience hypertension is greater than that of women. Men are more likely to experience BP increases; however, hormonal considerations cause women probably going to develop hypertension after menopause. Therefore, women are more at greater risk than men to experience hypertension during that time.[8]

Based on age, most patients who experienced hypertension were >60 years old (16 patients; 59.3%), >40-60 years old (10 patients;37%), and >18-40 years old (1 patient; 3.7%). The arteries lose their elasticity as people age, which causes structural and functional changes in the blood artery system that raise SBP. This increases the risk of hypertension in people aged 60 to 74.[9] Increasing age causes physiological changes, such as increased sympathetic nerve activity in the elderly.[10] Renal blood flow and glomerular filtration rate are lowered due to impaired renal function and baroreceptor reflex sensitivity. Peripheral vascular resistance rises due to decreased blood vessel flexibility, raising BP.[11]

JNC VIII recommends ACEI, ARB, low-dose thiazide diuretics, or CCB for non-black patients with hypertension. The recommended initial therapy for blacks is low-dose thiazide diuretics, or CCB.[12] ACE inhibitors inhibit ACE from converting angiotensin I to angiotensin II.[13] The decreased angiotensin II production causes increased natriuretic, so BP decreases, and cardiac smooth muscle remodeling is prevented. A decrease in arterial and venous pressure causes a decrease in preload and afterload.[14]

ACE inhibitors can also catalyze the degradation of bradykinin, which provides vasodilation, anti-inflammatory, and anti-fibrinolysis effects.[15] ACE inhibitors do not cause angiotensin I to become angiotensin II. The adrenal medulla releases catecholamines, pre-capillary arterioles, and post-capillary venules constrict, aldosterone is produced and released, cardiac myositis and vascular smooth muscle cells are stimulated to hypertrophy, and norepinephrine reuptake is inhibited.[16]

The pituitary and adrenal cortex produce antidiuretic hormone and aldosterone in response to angiotensin II. Aldosterone activates internal mineralocorticoid receptors, which results in the reabsorption

of salt and water from the atmosphere.[17] The antidiuretic hormone stimulates the creation of aquaporin-2 channels in the collecting duct, leading to selective air reabsorption. The effects of aldosterone and angiotensin II cause adverse cardiac remodeling. Aldosterone and angiotensin-II are lowered by ACE inhibitors, preventing detrimental cardiac remodeling.[18]

Angiotensin II receptor antagonists, also known as ARBs, prevent angiotensin II from acting at particular receptors, especially the AT1 receptors in tissues such as the adrenal gland and smooth muscle. The body's renin-angiotensin-aldosterone system (RAAS) regulates BP and fluid balance. Angiotensin II is a potent hormone that narrows blood vessels. Angiotensin II receptors come in two varieties: AT1 and AT2. Angiotensin II-induced AT1 receptor activation has several effects, including muscle cell proliferation, sodium reabsorption in the kidneys, water retention, and vasoconstriction.[18]

On the other hand, stimulation of the AT2 receptor results in vasodilation and anti-proliferative effects. ARBs inhibit angiotensin II's vasoconstrictive and aldosterone-secreting effects by specifically inhibiting AT1 receptors in organs such as blood vessels and the adrenal gland, all without appreciably changing heart rate. Renin and angiotensin II levels rise in response to AT1 receptor blockade, which increases AT2 receptor stimulation. Unlike ACE inhibitors, ARBs do not inhibit the enzyme that breaks down bradykinin, which promotes vasodilation; hence, they do not affect its levels.[19]

It is believed that ARBs work by lowering adverse effects and potentially improving therapeutic efficacy. By opposing angiotensin II-induced vasoconstriction, water intake, aldosterone release, catecholamine release, and arginine vasopressin release, ARBs displace angiotensin II from angiotensin I receptors and reduce BP.[20] Moreover, ARBs prevent fluid reabsorption.[13] The ARBs exhibit similar clinical characteristics, although variances in their pharmacokinetic profiles may result in discrepancies in efficacy.

The more contemporary ARB medications, like candesartan, olmesartan, telmisartan, and irbesartan. Irbesartan offers longer half-lives and durations of action than its older counterparts, losartan and valsartan. Given their longer duration of action, the newer drugs may make it easier to control BP for the entire day. Valsartan and losartan might necessitate twice-daily dosing, whereas ARBs with longer durations of action do not provide additional benefits when administered more frequently than once daily.[21] As ACE inhibitors and ARBs are examples of typical RAAS pathway inhibitors that function differently from CCBs, combining them should produce complementary or synergistic effects rather than using two drugs that target the same route.[22]

Calcium channel blockers obstruct particular cell membrane channels that allow extracellular calcium to pass through. Although there are several kinds of calcium channels, L-type channels in humans are the primary target of the CCBs that are now in use. CCBs relax the vascular smooth muscle cells, which lowers BP and causes vasodilation by preventing the inward flow of calcium. CCB is divided into two classes, namely non-dihydropyridine and dihydropyridine. Both are based on their physiological effects.

Non-dihydropyridine CCBs in cardiac muscle will reduce contractility and slow down the activity of the sinus pacemaker, namely sinoatrial (SA) and atrioventricular (AV) node conduction velocities.[23]

Table 2. Blood Pressure and Average Total Cost of Therapy for Group A (ACEI with CCB)

Respondent Number	Age	BP at Admission (mmHg)	BP at Discharge (mmHg)	Reached The Target/ No	Total Cost (IDR)
1	52	166/94	127/80	✓	7.330.377
2	40	164/77	145/79	X	781.458
3	68	171/100	128/76	✓	1.453.220
4	62	210/139	144/94	✓	1.548.656
5	70	130/88	124/80	✓	1.824.303
6	49	174/86	125/75	✓	928.207
Total= 6 patients				✓= 5 X= 1	Average= 2.311.000

Table 3. Blood Pressure and Average Total Cost of Therapy for Group B (ARB with CCB)

Respondent Number	Age	BP at Admission (mmHg)	BP at Discharge (mmHg)	Reached The Target/ No	Total Cost (IDR)
1	64	199/80	131/85	✓	884.721
2	69	147/90	122/70	✓	6.246.877
3	59	225/128	147/96	X	2.858.090
4	80	187/78	121/81	✓	10.653.440
5	46	170/100	142/72	X	1.975.258
6	65	203/124	158/82	X	1.766.226
7	49	240/110	178/103	X	2.649.147
8	55	195/60	125/67	✓	1.613.178
9	51	188/103	134/79	✓	1.087.905
10	64	207/80	186/108	X	2.017.599
11	81	163/106	135/83	✓	2.000.628
12	69	159/92	123/70	✓	674.285
13	52	170/85	110/70	✓	1.328.026
14	70	183/91	151/74	X	2.304.844
15	76	172/102	155/108	X	2.398.884
16	47	170/100	122/72	✓	1.456.032
17	73	180/130	120/80	✓	746.163
18	65	230/138	148/84	X	1.836.273
19	54	209/99	184/95	X	2.164.801
20	81	168/91	171/86	X	10.156.113
21	71	161/83	132/81	✓	3.867.798
Total= 21 patients				✓= 11 X= 10	Average= 2.888.823

Table 4. Effectiveness of Hypertension Treatment to Reach Therapeutic Targets

Therapeutic Effectiveness	ACE I with CCB		ARB with CCB	
	Total	%	Total	%
Reached the target	5	83,3	11	52,4
Not reached the target	1	16,7	10	47,6
Total	**6**	**100**	**21**	**100**

Table 5. Distribution of Hypertensive Patients Based on Length of Stay Group A (ACEI with CCB)

Length of Stay	Number (n)	Targeted	Untargeted	%
1-2 days	2	1	1	16.7
3-4 days	4	4	0	66.7
5-6 days	-	-	-	-
≥7 days	-	-	-	-
Total	6	5	1	-
%	-	83.3	16,7	100

Table 6. Distribution of Hypertensive Patients Based on Length of Stay Group B (ARB with CCB)

Length of Stay	Number (n)	Targeted	Untargeted	%
1-2 days	7	6	1	86
3-4 days	11	3	8	27
5-6 days	2	2	0	100
≥7 days	1	0	1	0
Total	21	11	10	-
%	-	52	48	100

Table 7. Overview of ACER Calculations for Antihypertensive Drugs

	Group A	Group B
Average Total Cost (IDR)	2.311.000	2.888.823
Therapeutic Effectiveness (%)	83,3	52,4
ACER (IDR)	27.743,0972	55.130,2099

*ACER = Average Total Cost / Therapeutic Effectiveness

The agents are verapamil and diltiazem. Dihidropiridin CCBs work as peripheral arterial vasodilators, reducing vascular resistance and lowering BP. The agents are amlodipine and nifedipine. A second line from a different class is initiated if monotherapy fails to reach BP targets.[24]

Combining ACEI with CCB or ARB with CCB is considered more effective in controlling BP. In individuals with severe systolic hypertension, benazepril and amlodipine combination therapy was considerably more effective than monotherapy in decreasing SBP and pulse pressure.[22] Some patients cannot take ACEI due to coughing side effects; therefore, ARB is used.[25]

Nearly no hypertensive patient at Al-Ihsan Regional Public Hospital receives monotherapy because their BP doesn't meet the target; instead, a combination of antihypertensives is used as a treatment option. Combinations of ACEI with CCB (group A) and ARB with CCB (group B) were the types of combination therapy used in this investigation.

The patient's BP dropped in accordance with the objective, indicating the efficacy of the treatment. The JNC VII target BP value for hypertensive patients ≥ 60 years of age with no diabetes comorbidities is <150/90 mmHg and <140/90 mmHg for those <60 years of age.[12] The number of patients in group A is shown in Table 2, while Table 3 shows the number of patients in group B.

Based on the study, patients who reached the most therapeutic targets were in Group A (5 patients; 83.3%), while Group B had 11 patients (52.4%) (Table 4). ACEI and CCB use two distinct but complementary functioning mechanisms. Thus, they work well together to lower BP. As a result of peripheral vasodilation, CCB reduces BP. Through elevated renin activity and the synthesis of angiotensin II, CCB also concurrently activates the sympathetic nervous system (SNS). This will impact how well CCB lowers BP.[26] The addition of ACEI offsets the effect of CCB's RAS activation.

Furthermore, the negative sodium balance brought on by CCB amplifies the antihypertensive effects of ACEI. Peripheral edema is the most common side effect associated with CCB. Because venous circulation is less than arterial dilatation, there is a larger transcapillary gradient and capillary leak, which results in this effect. Due to ACEI's ability to dilate veins and arteries and restore normal transcapillary pressure, this impact may be mitigated. As a result, the peripheral edema brought on by CCB decreases.[27]

The combination of ACEI with CCB can more effectively lower cardiovascular mortality and overall mortality than the atenolol/thiazide combination, according to the study of a randomized controlled trial of the prevention of chronic heart disease and other vascular events by blood pressure and cholesterol-lowering in a factorial study design. This study also found that combining ACEI with CCB can quickly and strongly reduce BP in patients with blood pressure above 160 mmHg.[28]

The effectiveness of therapy can also be seen in LOS (Length of Stay). Table 5 shows that group A had treatment with a shorter duration, namely 1-4 days (only 4 days), with a LOS of 3-4 days (66.7%). Meanwhile, in group B (Table 6), there was a treatment duration of 5-6 days for 2 patients and 7 days for 1 patient, with a LOS of 3-4 days (27%). Overall target achievement for group A was 83.3% (Table 5), while group B was 52% (Table 6).

The LOS can be influenced by two factors, namely sociodemographic factors and the

patient's clinical history.[29] To prevent the severity of hypertension, choosing appropriate and effective treatment is very influential. The drug's ability to decrease blood pressure and the patient's improved condition following therapy both affect how long a patient stays in the hospital.[11]

To analyze cost-effectiveness, table 7 shows that the average total cost of group B is greater (IDR 2,888,823) than group A (IDR 2,311,000). This is affected by the price differential between group A and group B antihypertensive drugs. Group A antihypertensive medications have an average cost of IDR 4,765, but group B has IDR 7,952. The total costs are the costs of hypertension medication, other drugs, medical equipment, facility, diagnostic, and examination costs while the patient is being treated at Al-Ihsan Regional Public Hospital.

Table 7 presents the findings of the CEA of antihypertensive medication, utilizing the ACER value. Group A has the cheapest average total cost (IDR 2,311,000) with a higher percentage of therapy effectiveness (83.3%) than group B. These findings are consistent with previous research, which found that ACEI and CCB have an antihypertensive impact that lowers BP and protects against target organ damage with relatively cheap drug costs.[30]

The ACER value (Table 7) obtained based on the reduction in BP in group A was lower (IDR. 27,743.0972) than group B (IDR. 55,130.2099). So, based on the calculation of the ACER value based on the reduction in BP, it can be stated that therapy group A is more cost-effective than group B.

Based on the two therapy groups, group A has lower costs and high effectiveness, so it does not require ICER calculations. ICER calculations can be calculated if the cost of the tap intervention is more expensive with high effectiveness or cheaper with low effectiveness.[7]

Conclusion

Group A's therapy (ACEI with CCB) has good therapeutic effectiveness and lower costs, according to research findings analyzing the cost-efficiency of antihypertensive therapy in inpatients at Al-Ihsan Regional Public Hospital in 2023. These outcomes were attained by contrasting the average overall cost of treatment with its efficacy. Group A's (ACEI with CCB) average total cost is IDR 2,311,000.00 and group B's (ARB with CCB) average total cost is IDR 2,888,823.00.

Group A's therapy was found to be 83.3% successful, while group B's was 52.4%. The outcomes demonstrated that group A was more economical, with an ACER value of IDR 27,743,097 as opposed to IDR 55,130,209 for group B.

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Conflict of Interest

None declare

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