

Drug Utilization Evaluation of Antihypertensives in Elderly HHD Patients at the Polyclinic of RSUP Dr. Mohammad Hoesin Palembang

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ABSTRACT

Hypertensive heart disease is a significant cause of morbidity and mortality globally that tends to increase with age. The high prevalence of uncontrolled blood pressure leads to an increase in the occurrence of HHD, so the optimal use of antihypertensive drugs is essential in preventing and controlling HHD. This study aims to determine the drug utilization evaluation of antihypertensives in elderly hypertensive heart disease patients at the polyclinic of RSUP Dr. Mohammad Hoesin Palembang. Period of January - June 2023. This research is a descriptive study in the form of a drug utilization evaluation, with a sample of 157 patients. Data were collected using the total sampling technique, using secondary data from patient medical records. The most common therapeutic regimen was a combination of 2 antihypertensive drugs (42.7%), with the most frequent drug class combination being CCB + ARB (21.7%). Based on the PERHI 2021 recommendations, 97.3% of drugs were at the appropriate dose, and 88.8% were administered at the appropriate frequency of administration. Most drug combinations, dosages, and frequencies of antihypertensives administered to patients were appropriate, with the most common combination being two drugs: CCB and ARB.

INTRODUCTION

The proportion of the world's population aged 60 years or older is expected to almost double from 2015 to 2050, from 12% to 22% (World Health Organization, 2015). Following WHO predictions, Indonesia is currently entering a period of an aging population where life expectancy is increasing along with the increasing number of elderly. The elderly population in Indonesia has increased from 18 million (7.56%) in 2010 to 25.9 million individuals (9.7%) in 2019 (Ministry of Health Republic Indonesia, 2019).

The aging process is often associated with the incidence of NCDs. The highest non-communicable disease in the elderly group is hypertension, with a prevalence of 32.5%

(Pangribowo, 2022). Hypertension has complications that can affect several target organs, including the kidneys, heart, brain, eyes, and peripheral arteries (Muhadi, 2016). In the heart, uncontrolled hypertension can cause complications in the form of hypertensive heart disease (Dai et al., 2021).

Hypertensive heart disease is the leading cause of morbidity and mortality globally. There has been a 137.91% increase in the prevalence of HHD over the last 3 decades, from 7.82 million cases in 1990 to 19.60 million cases in 2019 (Lu & Lan, 2022). The incidence and mortality rates of HHD tend to increase in line with increasing age in both sexes (Dai et al., 2021).

HHD is a heart condition that includes impaired function and structure of the left

atrium, left ventricle, and coronary arteries due to chronically high blood pressure (Masenga & Kirabo, 2023). HHD may be manifested by systolic and diastolic dysfunction, left ventricular hypertrophy (LVH), various forms of adaptation of the heart and its blood vessels, and HHD with heart failure (Georgiopoulou et al., 2010; Lu & Lan, 2022).

The high prevalence of uncontrolled blood pressure leads to an increase in the occurrence of HHD, so appropriate use of antihypertensive drugs is essential in preventing and controlling HHD (Dai et al., 2021; Georgiopoulou et al., 2010). LVH represents one of the initial manifestations of HHD and is believed to be a compensatory response due to chronic hypertension. However, if hypertension remains untreated, LVH may progress to complications such as arrhythmias, heart failure, sudden cardiac arrest, and mortality (Masenga & Kirabo, 2023). To prevent complications and induce LVH regression, all individuals with left ventricular hypertrophy are recommended to receive antihypertensive treatment (PERKI, 2015).

The JNC-8 guidelines recommend 4 classes of initial therapy for hypertension in the non-black population, including calcium channel blockers (CCB), thiazide diuretics, angiotensin-converting enzyme inhibitors (ACEI), or angiotensin II receptor blockers (ARB), in contrast to the JNC-7 guidelines which also recommend β -blockers, which are currently only used in hypertension with a history of other cardiovascular diseases such as heart failure, angina, post-IMA, and atrial fibrillation (Bell et al., 2015; PERHI, 2021). Antihypertensive drugs that have been proven to induce LVH regression include CCBs, ACEIs, and ARBs (PERKI, 2015). A study conducted at RSUD Undata, Palu, Central Sulawesi, reported that two-drug antihypertensive combinations were the most commonly prescribed regimen among hospitalized patients with HHD (35.08%), with ACEIs and CCBs being the most frequently used drug classes (Olive, 2019).

From the data that has been stated above, such as the increasing elderly population, the prevalence and mortality of HHD which increases with age, variation of antihypertensive prescribing patterns, and the absence of data related to the drug utilization evaluation of antihypertensive in elderly hypertensive heart

disease patients in Palembang City to date, the researchers are interested in conducting research on drug utilization evaluation of antihypertensive drugs in elderly HHD patients at the Polyclinic of Dr. Mohammad Hoesin Hospital Palembang for the period January - June 2023.

METHODS

Types of Research

This research is a descriptive study in the form of a drug utilization evaluation using secondary data, which is medical record data of elderly hypertensive heart disease patients who received antihypertensive drugs for the period January - June 2023 at the Outpatient Installation of RSUP Dr. Mohammad Hoesin Palembang.

Population and Sample

The population of this study was all medical records of elderly hypertensive heart disease patients who received treatment at the Outpatient Installation of RSUP Dr. Mohammad Hoesin Palembang from January to June 2023 and who met the inclusion criteria and did not meet the exclusion criteria, in which the entire population (157 patients) was included as the sample. There was no minimum sample size because this study used a total sampling technique.

Data Collection Technique

Data was taken using a total sampling technique, where all population units were taken as sample units. The inclusion criteria in this study were the medical records of patients aged ≥ 60 years who were diagnosed with hypertensive heart disease with or without comorbidities for the period January - June 2023 and received antihypertensive drug therapy. Meanwhile, the exclusion criteria for this study were incomplete medical records of the variables needed. The variables studied included patient characteristics (age, gender, blood pressure control status, chief complaint, comorbidities), drug class, drug type, and appropriateness of antihypertensive drugs. Blood pressure control status was determined according to the 2018 ESC/ESH Guidelines, with controlled blood pressure defined as $<140/90$ mmHg and uncontrolled blood pressure as

≥140/90 mmHg (Astuti et al., 2021; Williams et al., 2018). The chief complaint was defined as the primary symptom or condition that prompted patients with HHD to seek treatment. The appropriateness of antihypertensive therapy, including drug dosage and frequency of administration, was evaluated according to the PERHI 2021 Guidelines.

Data Analysis

Data were processed using the SPSS application. All collected data is analyzed using univariate analysis and presented in tables accompanied by descriptive explanations of the research variables that have been determined.

RESULT AND DISCUSSION

Based on table 1, patients were predominantly from the 60-69 years age group, with a total of 93 people. This study aligns with the research conducted by (Prakoso, 2019), which found that patients suffering from HHD are mainly in the age group of 60-69 years (70%). Aging is related to degenerative processes involving arterial thickening and stiffness due to increased collagen deposition and decreased elastin fibers. Arterial stiffness that increases with age is closely related to the increased occurrence of hypertension (Hernandorena et al., 2019). In addition, there is increased sympathetic nerve activity, increased plasma catecholamine concentrations, and decreased baroreceptor reflex sensitivity in elderly patients (Hernandorena et al., 2019). Uncontrolled and prolonged hypertension can lead to hypertensive heart disease (HHD) (González et al., 2018). Globally, the prevalence of HHD tends to increase with age. However, in this study, there was a decrease in the incidence of HHD in the age group of 70-79 years and ≥80 years. It may reflect the high mortality associated with the disease, which could result in fewer surviving patients in this age group.

There were more male than female patients, as shown in Table 1, with a slight difference of 51% (80 people) in males and 49% (77 people) in females. This study is similar to the research conducted by Yang et al. in 2023, which found that the prevalence of HHD is higher in men than in women (Yang et al., 2023). Compared to women, men tend to have lower health

awareness, lower compliance, and unhealthy lifestyles such as smoking, alcohol consumption, and poor diet, which can increase the risk of HHD (Roth et al., 2020)

Table 1. Characteristics of elderly HHD patients

Characteristics	n	%
Age		
60-69 years old	93	59.2
70-79 years old	51	32.5
80 years old	13	8.3
Sex		
Male	80	51
Female	77	49
Blood Pressure		
Controlled	107	68.2
Uncontrolled	50	31.8
Chief Complaints		
Shortness of breath	28	17.8
Chest pain	22	14
Leg swelling	9	5.7
Palpitations	1	0.6
Headache	5	3.2
Other complaints	37	23.6
No complaints	55	35
Comorbidities		
Present	140	89.8
None	17	10.2

Table 1 showed that 68.2% of HHD patients had controlled blood pressure. This is in line with Tamburian et al.'s research in 2015, which found that as many as 55% of hypertensive patients had controlled blood pressure (Tamburian et al., 2016). Controlled blood pressure is influenced by the patient's high awareness and understanding of the importance of maintaining normal blood pressure, as they are aware of the dangers that can arise, including the onset of complications such as stroke, kidney failure, heart failure, and death (Akri et al., 2022; Naryati & Priyono, 2022). In this study, 31.8% patients had uncontrolled blood pressure. Uncontrolled blood pressure can be caused by non-compliance in taking medication due to the elderly who tend to forget and get tired of constantly taking antihypertensive drugs, have never taken medication before, the drugs given are not adequate, or have a poor lifestyle, so that the target blood pressure is not achieved (Darussalam & Warseno, 2019; Tamburian et al., 2016).

The most common chief complaint was no complaint (35%), as shown in Table 1. HHD patients with left ventricular hypertrophy are asymptomatic but can also cause chest pain due to increased oxygen demand due to hypertrophied myocardium (Tackling & Borhade, 2019). This could also be due to the patient's controlled blood pressure, preventing complications and symptoms.

Patients with comorbidities accounted for 89.8%, while those without accounted for 10.2%, as shown in Table 1. It may be because the elderly have physiological changes and decreased physical and mental capacity, thus increasing the risk of disease (World Health Organization, 2022). In addition, hypertension has complications involving various target organs, including the kidneys, heart, brain, eyes, and peripheral arteries (Muhadi, 2016).

Table 2 shows that the most common comorbidity in this study was CAD (25.5%). The results of this study align with research conducted by (Yunita, 2023), indicating that CAD is the most common comorbidity in HHD patients, affecting 45 out of 98 patients. Hypertension is a significant risk factor for CAD, with its mechanism involving the effect of elevated blood pressure on the development of atherosclerotic plaques through endothelial dysfunction. The presence of atherosclerotic plaques narrows the lumen of blood vessels, disrupting oxygen delivery and leading to CAD (Weber et al., 2016).

Table 2. Comorbidity distribution of elderly HHD patients

Comorbidities	n	%
Coronary Artery Disease	40	25.5
Diabetes Mellitus type 2	39	24.8
Dyslipidemia	27	17.2
Osteoarthritis	20	12.7
Osteoporosis	17	10.8
Heart Failure	16	10.2
Dyspepsia	14	8.9
BPH	11	7.0
Acute Kidney Injury	9	5.7
Neuropathy	9	5.7
COPD	8	5.1

Based on the research that has been done, as shown in Table 3, the most common drug use is 2 drug combinations, as much as 42.7%, and the

least is a combination of 4 drugs, as much as 12.1%. The results of this study are similar to research conducted by Olive et al. in 2019, which showed that in HHD patients, the use of 2 combinations of antihypertensive drugs (35.08%) was the most widely used (Olive, 2019). Most patients require two or more antihypertensive drugs to achieve blood pressure targets. Suppose the target blood pressure is not achieved within one month of taking antihypertensive drugs. In that case, it is possible to increase the dose of the first drug or add a second drug from one of the recommended antihypertensive classes, such as ARBs or ACEIs, CCBs, and thiazide diuretics. Combination therapy of 2 drugs with different classes can be used as initial therapy in patients with stage 2 hypertension or when SBP >20 mmHg and or DBP >10 mmHg above the target blood pressure. If the combination of two drugs is not able to achieve the target blood pressure, then a third drug can be added (Bell et al., 2015). A combination of 4 antihypertensive drugs was the least used regimen (12.1%). Using an excessive number of medications can lead to non-compliance, increased expenses, adverse side effects, and drug interactions, thereby reducing the quality of life of elderly patients (Assalwa et al., 2021; Fauziah et al., 2020).

According to Table 3, the most widely used drug class in the 2-drug combination was the combination of CCBs with ARBs (21.7%). This is in line with research conducted by Wulandari et al. in 2021, which states that CCBs and ARBs are the most widely used combination for patients with high blood pressure, namely 44.1%, and can achieve blood pressure targets (Wulandari, 2022). The findings of this study align with the recommendations from PERKI (2015), which state that ARBs and CCBs are proven to induce regression of left ventricular hypertrophy, so it is recommended that all individuals with LVH receive this antihypertensive therapy (PERKI, 2015). The combination of CCBs with ARBs is more effective than monotherapy because the side effects of CCBs, namely peripheral edema caused by arteriolar vasodilation, can be overcome by ARBs using venous vasodilation, resulting in simultaneous arterial and venous vasodilation, which not only causes a decrease in blood pressure but also suppresses side effects (Gradman et al., 2011).

In this study, a non-recommended antihypertensive combination according to the 2017 ACC/AHA Guideline was identified in 3.2% of cases (5 patients), consisting of a nondihydropyridine CCB (diltiazem) + β -blocker (bisoprolol, carvedilol). This combination should be avoided as it has an additive effect on cardiac suppression, including decreasing heart rate, atrioventricular conduction, and cardiac contractility that can lead to severe bradycardia, hypotension, and AV block especially with the routine concomitant use (Saedder et al., 2019; Whelton et al., 2018). In addition, one patient (0.6%) received a combination of dihydropyridine CCB (DHP) with nondihydropyridine CCB (NDHP) as shown in

Table 3. The evidence supporting this combination is weak, primarily based on non-randomized studies, with only a few randomized clinical trials. Dual CCB therapy should be considered only as a secondary treatment option due to the lack of additional definitive treatment information. Patients who are potential candidates for dual CCB therapy are those with inadequate blood pressure control when taking other antihypertensive agents. Also, in patients with a partial response to the maximum tolerated dose of a single CCB, which has relative contraindications to other drug classes (Alharthi et al., 2017).

Table 3. Distribution of elderly HHD patients based on antihypertensive class

Therapeutic Regimen	Antihypertensive Class	n	%
Monotherapy	CCB	11	7
	ACEI	1	0.6
	ARB	13	8.3
	B-blocker	2	1.3
	Diuretic	1	0.6
Total		28	17.8
2-Drug Combination	CCB + ARB	34	21.7
	CCB + B-blocker	4	2.5
	CCB + Diuretic	1	0.6
	ARB + B-blocker	15	9.6
	ARB + Diuretic	9	5.7
	ACEI + Diuretic	1	0.6
	B-blocker + Diuretic	2	1.3
	Potassium-Sparing Diuretic + Loop Diuretic	1	0.6
Total		67	42.7
3-Drug Combination	CCB + ARB + B-blocker	10	6.4
	CCB + ARB + Diuretic	5	3.2
	CCB + Potassium-Sparing Diuretic + Loop Diuretic	1	0.6
	Dihydropyridine CCB + Non-dihydropyridine CCB + ARB	1	0.6
	ARB + B-blocker + Diuretic	8	5.1
	ARB + Potassium-Sparing Diuretic + Loop Diuretic	9	5.7
	ACEI + B-blocker + Diuretic	2	1.3
	B-blocker + Potassium-Sparing Diuretic + Loop Diuretic	7	4.5
Total		43	27.4
4-Drug Combination	CCB + ARB + B-blocker + Diuretic	7	4.5
	CCB + ARB + Potassium-Sparing Diuretic + Loop Diuretic	2	1.3
	CCB + ACEI + Potassium-Sparing Diuretic + Loop Diuretic	1	0.6
	ARB + B-blocker + Potassium-Sparing Diuretic + Loop Diuretic	9	5.7
Total		19	12.1

Table 4 shows that the type of drug most widely used in HHD patients is candesartan, as much as 31.1%, followed by bisoprolol (16.3%)

and amlodipine (13.9%). This study's results align with research conducted by Boentara et al. (2022), which found that the most widely used

ARB is candesartan, accounting for approximately 94% (Boentara et al., 2022). The results of this study are also similar to Hastuti's research in 2022, which found that in patients with high blood pressure, the most widely used β -blocker is bisoprolol (20.2%), while the most widely used CCB is amlodipine (35.7%) (Hastuti, 2022). Candesartan is probably widely used due to its more affordable price than other ARBs. Also, the incidence of ARB side effects is low and well-tolerated (Hill & Vaidya, 2020).

Table 4. Distribution of antihypertensive drug types of elderly HHD patients

Drug Class	Drug Type	n	%
CCB	Amlodipine	51	13.9
	Nifedipine GITS	5	1.4
	Diltiazem	22	6
ARB	Candesartan	114	31.1
	Valsartan	5	1.4
	Telmisartan	2	0.5
	Irbesartan	1	0.3
ACEI B-blocker	Ramipril	5	1.4
	Bisoprolol	60	16.3
	Propranolol	1	0.3
	Nebivolol	2	0.5
	Carvedilol	3	0.8
Diuretic	Hydrochlorothiazide	5	1.4
	Spironolactone	50	13.6
	Furosemide	41	11.2
Total		367	100

ARBs and ACEIs exhibit distinct pharmacological differences, notably that ARBs do not inhibit bradykinin degradation. This

explains why ARBs do not cause dry cough, making ARBs preferable to ACEIs (Hitner et al., 2021; Katzung, 2017). The use of β -blockers such as bisoprolol is an option in the management of hypertension concomitant with cardiac disorders, such as heart failure, angina, post-IMA, and atrial fibrillation (PERHI, 2021). Amlodipine is a class of CCBs that act on the plasma membrane of smooth muscle by blocking calcium ion channels, which relaxes vascular smooth muscle, resulting in vasodilation. The vasodilating effect of CCBs can reduce peripheral vascular resistance, leading to a decrease in blood pressure due to vascular stiffness, as seen in the elderly (Stevens & Brenner, 2016).

Based on the 2021 PERHI recommendations, of the 363 antihypertensive drugs given, 97.3% were in the appropriate dose (Table 5). Giving an excessively high dose will increase the risk of drug-related side effects, while if it is too low, it does not guarantee that the therapeutic effect of a drug can be achieved; in this case, blood pressure either fails to normalize or the target blood pressure is not achieved. Therefore, it is necessary to give the appropriate dose of drugs (Ministry of Health Republic Indonesia, 2011). In this study, the appropriate frequency of drug administration is 88.8%. The frequency of drug administration must be adjusted to the half-life of a drug. Drugs with a long half-life are sufficient to be used once a day. Meanwhile, drugs with a short half-life can be used several times a day at regular intervals (Katzung, 2017). Some drugs may not be administered at the appropriate dose and frequency if the doctor considers other factors, such as comorbidities or other treatment guidelines.

Table 5. Distribution of drug suitability based on PERHI 2021 guidelines

Drug appropriateness	n		Percentage (%)	
	Appropriate	Inappropriate	Appropriate	Inappropriate
Dose	357	10	97.3	2.7
Frequency of Administration	326	41	88.8	11.2
Total	367		100	

This study has several limitations that should be considered when interpreting the findings. Although incomplete medical records were excluded, the study relied on retrospectively collected data, limiting the analysis to variables that had been routinely documented in the medical records. Due to its retrospective design

and reliance on medical records, patient compliance with antihypertensive therapy could not be assessed. Lastly, clinical outcomes such as blood pressure control over time, hospitalization, cardiovascular events, and mortality were not evaluated. Therefore, the impact of the observed prescribing patterns on

patient outcomes could not be determined. Despite these limitations, this study provides valuable information regarding antihypertensive utilization patterns and the appropriateness of dosing and administration frequency among patients with HHD.

CONCLUSIONS

Most drug combinations, dosages, and frequencies of antihypertensives administered to patients were appropriate, with the most common combination being two drugs: CCB and ARB.

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AUTHORS' CONTRIBUTIONS

All authors made significant contributions to the research.

CONFLICT OF INTERESTS

This publication does not have any competing interests.

ETHICAL CONSIDERATION

This study gained ethical approval from Medical and Health Research Ethics Committee with protocol number 309-2023.

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