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Effectiveness of Antihypertensive Monotherapy and Combination Therapy in Managing Blood Pressure Among the Elderly

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ABSTRACT

OBJECTIVE To evaluate the effectiveness of monotherapy versus combination therapy in controlling blood pressure in the elderly population in eastern Indonesia, i.e., Central Sulawesi.

METHODS This study used a cross-sectional design, examining secondary data from the medical records of inpatients with hypertension in a population in eastern Indonesia. The inclusion criteria included patients aged 45 years or older receiving antihypertensive therapy who had complete blood pressure data. Data were analyzed using R 4.3.2. Relationships between variables were tested using inferential analysis. A p-value < 0.05 was set as the statistical significance threshold.

RESULTS Most patients were female (60.0%) and aged 45-59 years (40.0%). Nearly half (48.0%) had been diagnosed with uncomplicated hypertension, while 29.0% also had cardiovascular comorbidities. Patients received either monotherapy or combination therapy, with calcium channel blockers (CCBs) being the most common drug class used. Blood pressure significantly decreased after therapy, with mean systolic pressure reduced from 162 to 135 mmHg and diastolic from 95 to 79 mmHg (p = 0.000). Combination therapy produced a slightly greater reduction than monotherapy, although the difference was not statistically significant. These findings suggest that both monotherapy and combination therapy can effectively reduce blood pressure in elderly patients, with combination therapy offering potential advantages. This study highlights the need for personalized treatment strategies that consider the age, comorbidities, and drug tolerance of all elderly patients based on hypertension therapy guidelines.

CONCLUSION Both combination and monotherapy treatment strategies are similarly effective in lowering blood pressure in elderly patients. Given the presence of comorbidities and the risk of side effects, a personalized approach using combination therapy may offer an effective and safe option for managing hypertension in geriatric patients. These findings support more informed and tailored clinical decision-making in hospital care settings.

KEYWORDS hypertension, eastern Indonesia, middle-aged, antihypertensive therapy, blood pressure

INTRODUCTION

Hypertension is one of the most influential risk factors for the occurrence of heart and blood vessel disease. Hypertension often does not show symptoms, so it may only be recognized when it has caused organ disorders such as heart dysfunction or stroke (1). Risk factors for hypertension are classified into 2 groups, namely those that can be modified, including smoking, obesity, lifestyle, stress, and those that cannot be altered, including age, gender, ethnicity, and hereditary factors (2, 3). The risk of hypertension increases with age, as evidenced by the finding of a tendency for an increased prevalence of hypertension in adults compared to adolescents. Hypertension occurs more often in the age group over 74 years (64.0%), followed by the age group 65-74 years (57.1%), 55-64 years (49.5%), and is lowest in the age group 45-54 years (39.1%) (4). Central Sulawesi Province is included in the 11 regions with the most significant number of hypertension sufferers in Indonesia and is ranked the 2nd highest for hypertension sufferers in eastern Indonesia, with the percentage of the adult population suffering from hypertension reaching 29.1% (4).

The high incidence of hypertension in Central Sulawesi, especially in the city of Palu, is closely related to the lifestyle of the community, which tends to be less physically active, has a low-fiber diet, excessive salt consumption, overweight/obesity, stress, and low compliance with therapy (5). Appropriate antihypertensive drug therapy can reduce morbidity and mortality, especially in the elderly (6).

To date, European (1) and US (7) guidelines mainly recommend starting therapy with one drug but approve starting combination therapy for patients at high risk or with very high blood pressure. In contrast, the NICE guidelines do not recommend this initial strategy even for patients with severe hypertension in the UK (8). Evidence suggests that monotherapy can effectively reduce blood pressure in only a small number of hypertensive patients, and most subjects require a combination of at least two drugs to achieve the target blood pressure (9).

The strategy for selecting antihypertensive therapy, namely whether it should be preceded by monotherapy or combination therapy as the initial approach in hypertension therapy, is still a debate that has not yet been resolved. The presence of comorbidities that often accompany hypertension in the elderly allows for polypharmacy in treatment, so recommendations for selecting monotherapy or combination antihypertensive therapy are important considerations for health workers in hospitals in order to provide and effective treatment for patients. This study aimed to compare the effectiveness of single and combination antihypertensive drugs on blood pressure in elderly patients undergoing hospital treatment.

METHODS

Participants and study design

This study used a cross-sectional design with retrospective data collection. Data were obtained from the medical records of hypertensive patients hospitalized in the Undata Regional General Hospital, Palu City, Eastern Indonesia, during 2020. The required minimum sample size was calculated using the Slovin formula. The subjects' data met the inclusion criteria: over 45 years of age, diagnosed with hypertension, having received antihypertensive therapy, and having blood pressure measurement data at the beginning and after treatment. Exclusion criteria were subjects with incomplete medical record data and those discharged from the hospital at their own request. The collected data included demographic information, clinical details, and therapy profiles.

Data analysis

Data analysis was carried out using R 4.3.2 software. The Wilcoxon signed-rank test was used for paired data, while the Mann-Whitney U test was used for unpaired data analysis. Results are presented as percentage proportions and significance values. *P*-values < 0.05 are considered statistically significant.

RESULTS

This study successfully collected the medical records of 40 elderly hypertensive patients who had been hospitalized. The personal characteristics data collected included gender and age. The hypertensive patients were primarily women (60.0% vs. 40.0%), with the largest age group being middle-aged, i.e., 45-59 years (40.0%) (Figure 1A and 1B). As many as 48.0% of the patients

had received treatment following a diagnosis of hypertension without complications, while 29.0% of the hypertensive patients also had other cardiovascular comorbidities, which are categorized as HT with other cardiovascular diseases (Figure 1C).

All patients had received antihypertensive therapy either singly or in combination. A total of 40.0% of the patients were treated with a single type of antihypertensive drug. In comparison, 52.0% of patients received a combination therapy regimen of two antihypertensive drugs, 3.0% received a combination of three antihypertensive medications, and 5.0% received a combination of four antihypertensive drugs (Figure 2A). The most frequently used anti-hypertensive medications were in the calcium channel blockers (CCB) class, either singly (39.0%) or in one of three combinations (26.0%, 11.0%, and 8.0%). The CCB class was often combined with antihypertensives from the angiotensin receptor blocker (ARB) class (26.0%) and the beta blocker class (11.0%) (Figure 2B).

Anti-hypertensive therapy regimens have been shown to significantly reduce mean blood pressure, both systolic and diastolic. In this study, the most frequent blood pressure classification of patients before therapy was stage 2 hypertension, while after therapy the average blood pressure of most of the patients was classified as prehyper-

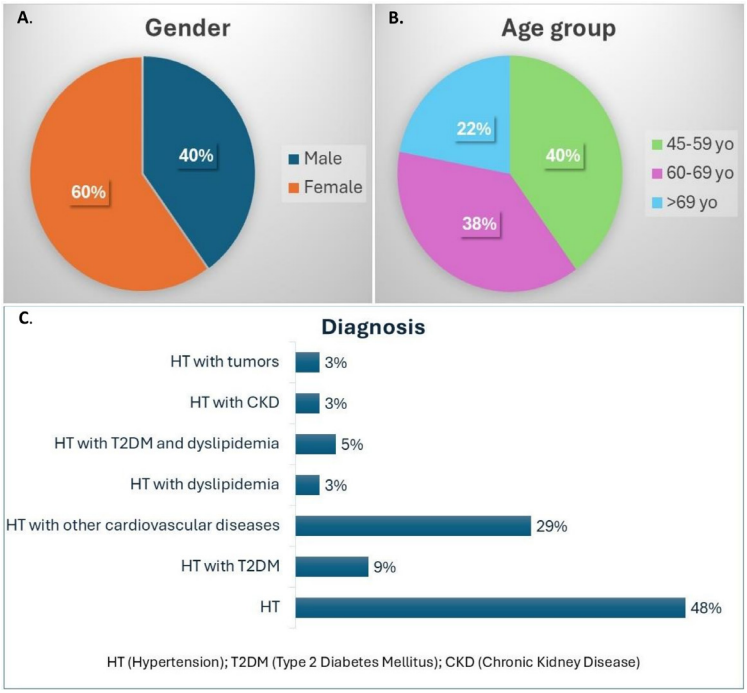


Figure 1. Patient characteristics profile and diagnosis

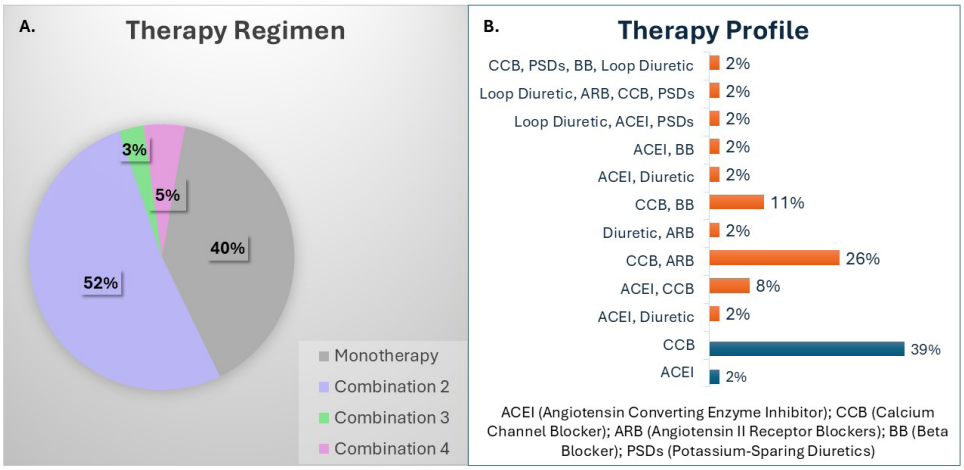


Figure 2. Regimens and profile of therapies for elderly hypertensive patients

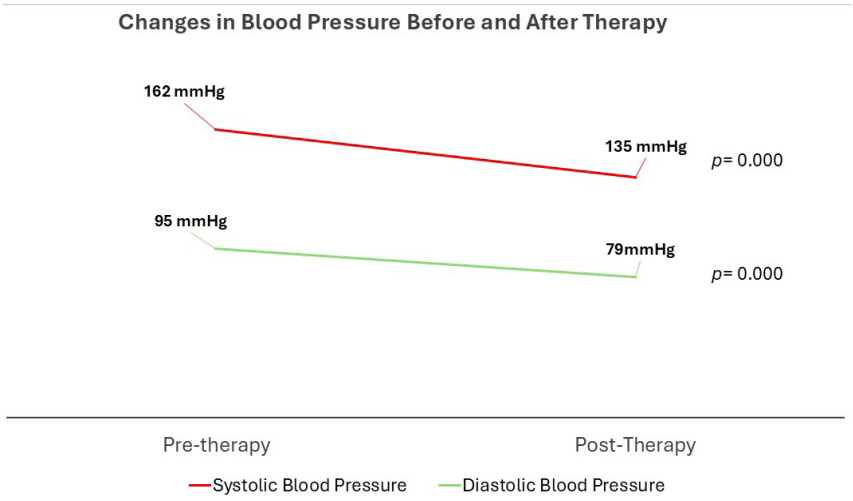


Figure 3. Effect of antihypertensive drugs on blood pressure in elderly hypertensive patients

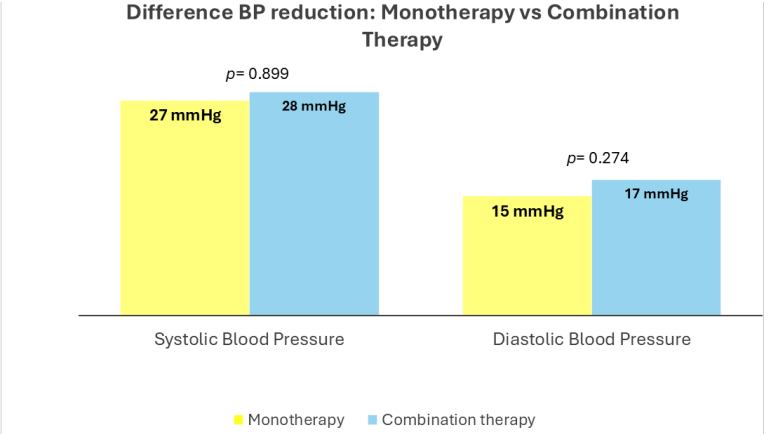


Figure 4. Differences in blood pressure reduction based on hypertension therapy regimen in elderly patients

tension. Overall, average systolic blood pressure decreased from 162 mmHg before therapy to 135 mmHg (p = 0.000) after therapy, as did diastolic blood pressure, which decreased from 95 mmHg before therapy to 79 mmHg (p = 0.000) (Figure 3).

Figure 4 shows the difference in blood pressure reduction based on the therapy regimen of elderly patients. The combination therapy group showed a greater reduction in systolic and diastolic blood pressure compared to the group receiving monotherapy.

The average reduction in systolic blood pressure reduction was 27 mmHg in the 16 patients receiving antihypertensive monotherapy, while in the 24 patients receiving combination therapy, the average decrease was 28 mmHg. The difference in average diastolic blood pressure reduction in the monotherapy group was 15 mmHg, whereas the combination therapy group showed a greater average reduction of 17 mmHg. Although the difference in blood pressure reduction in the combination group was greater than in the monotherapy group, the difference between the two groups was not statistically significant ($p > 0.05$).

DISCUSSION

The findings of this study highlight essential patterns in blood pressure control among elderly patients with hypertension. Both monotherapy and combination therapy demonstrated effectiveness in lowering systolic and diastolic blood pressure, with combination therapy producing a slightly greater mean reduction, although the difference was not statistically significant. These findings suggest that both therapeutic strategies can be effective in clinical practice, depending on individual characteristics, comorbidities, and cardiovascular risk factors.

Gender and age are two critical determinants of the epidemiology of hypertension. This study found that more older women than older men suffer from hypertension (60.0% vs. 40.0%). This

difference can be attributed to physiological changes in women during the aging process, particularly when transitioning into perimenopause and menopause. Estrogen, the primary sex hormone in women, has a protective effect on the cardiovascular system. Estrogen protects the blood vessel wall by increasing vasodilation by releasing nitric oxide and inhibiting inflammation and atherosclerosis (10). When levels of this hormone decrease during the transition to perimenopause and menopause, this protection is reduced, leading to increased arterial stiffness and increased risk of hypertension (11).

Regardless of hormonal status, the aging process causes structural changes in blood vessels, such as a loss of elasticity in large arteries, which contributes to an increase in systolic blood pressure. This process continues as estrogen levels naturally decline in women aged 45-55 (12). Based on World Health Organization (WHO) criteria, the elderly are categorized as middle-aged (45-59 years), elderly (60-74 years), old (75-90 years), and very old (over 90 years) (13). In middle age, large arteries begin to stiffen, forcing blood through narrower vessels and raising pressure (12, 14, 15). Consequently, hypertension prevalence increases markedly with age, especially in postmenopausal women, and contributes to cardiovascular comorbidities such as arrhythmias and coronary heart disease (CHD) (11, 16).

Untreated hypertension can cause structural and functional changes in the heart, such as left ventricular hypertrophy, which increases the risk of arrhythmias (17). In addition, hypertension can also contribute to the development of atherosclerosis, namely the accumulation of plaque on the walls of the arteries, which is the leading cause of CHD. High blood pressure can damage the arterial endothelium, facilitating the accumulation of lipids and the formation of plaques. This plaque accumulation can narrow the coronary arteries, reduce blood flow to the heart muscle, and increase the risk of a heart attack (15). Severe atherosclerosis can narrow the lumen of the coronary arteries, reduce oxygen supply to the myocardium, and trigger acute myocardial ischemia or infarction. The combination of comorbidities of hypertension with other cardiovascular diseases can increase the likelihood of an elderly person being hospitalized.

Comorbidity with metabolic diseases such as diabetes mellitus, dyslipidemia, and obesity further worsens the prognosis of elderly hypertensive patients. Type 2 diabetes mellitus, for example, contributes to endothelial dysfunction and increased insulin resistance, both of which accelerate the progression of hypertension (19). Hypertension and diabetes are also often accompanied by increased low-density lipoprotein (LDL) cholesterol levels, synergistically increasing cardiovascular risk. Studies have shown that the combination of diabetes and hypertension results in a more significant LDL-increasing effect than when both occur separately (20).

Hypertension therapy guidelines from various health organizations have recommended a combination-based approach as an initial strategy, especially for patients at moderate to high risk. In 2021, the Pharmaceutical Service Guidelines for Hypertension were updated from the ESC/ESH Guidelines for Managing Arterial Hypertension, stating that initial hypertension therapy should begin with two medications, i.e., an angiotensin-converting enzyme inhibitor (ACEI) or ARB group combined with a CCB or diuretic. At the same time, monotherapy should be given to patients with low-risk grade 1 hypertension, very old patients (≥ 80 years) and frailer patients. The second therapeutic strategy involves using a triple combination, such as an ACEI or ARB combined with a CCB and diuretics. The third therapeutic strategy can be augmented with spironolactone or other diuretics, alpha blockers, or beta blockers (1, 21).

Some guidelines recommend low-dose combination therapy as the preferred initial treatment for most hypertensive patients because it provides a more rapid and substantial reduction in blood pressure through the synergistic action of two different mechanisms (6). Although monotherapy may be considered for patients with low-risk stage 1 hypertension or the very elderly and the frail, a major clinical challenge is avoiding failure to achieve blood pressure targets promptly, which often necessitates the addition of a second medication. Low-dose combination therapy, particularly in the form of fixed-dose combinations (FDCs), is increasingly supported for its proven ability to improve adherence by simplifying treatment into a single pill and reducing clinical iner-

tia (22, 23). Initiating therapy with FDCs results in faster and more sustained blood pressure control compared with stepwise monotherapy escalation.

According to the NICE therapeutic algorithm, the first step in antihypertensive therapy for patients over 55 years of age typically begins with a single CCB. In step 2, a CCB can be combined with an ACEI, ARB, or thiazide-like diuretic, while step 3 involves a triple combination of ACEI or ARB with a CCB and a thiazide-like diuretic (8). This stepwise approach is tailored according to each patient's clinical response and comorbidities.

The present study showed that a combination of two classes of drugs was most often used in elderly patients, with CCBs the dominant choice. CCBs inhibit the entry of calcium ions into smooth arterial muscle cells, causing vasodilation and lowering blood pressure (24). CCBs are effective in elderly patients, patients at high risk of coronary artery disease, and patients with diabetes. The combination of CCB and ARB also shows synergy in lowering blood pressure while protecting against kidney complications in patients with diabetes mellitus. ARBs work by inhibiting the effects of angiotensin II, which causes vasoconstriction and sodium retention, while CCBs improve peripheral blood flow. This combination is considered effective and safe for geriatric patients (25, 26).

Furthermore, the clinical outcomes in this study suggest that the presence of comorbidities, particularly cardiovascular comorbidities and metabolic disorders such as diabetes mellitus, may affect the overall therapeutic response to antihypertensive treatment. Patients with these comorbidities often exhibit reduced vascular compliance and impaired endothelial function, which can diminish the blood pressure-lowering effect of monotherapy. This highlights the need for a more comprehensive pharmacological approach. In our findings, although the difference between monotherapy and combination therapy in blood pressure reduction was not statistically significant, the combination regimen showed a clinically greater decrease in both systolic and diastolic pressures. This trend aligns with previous evidence indicating that combination therapy offers enhanced control and faster achievement of target blood pressure, especially in patients with multiple comorbid conditions. Therefore, adopting a combination therapy approach may provide additional clinical benefits for elderly hypertensive patients with cardiovascular or metabolic comorbidities, in line with the recommendations of the ESC/ESH and JNC 8 hypertension management guidelines (1, 27).

Although this study did not calculate hazard ratios, the greater blood pressure reduction with combination therapy may represent a clinically relevant benefit. Even modest decreases in systolic pressure are associated with a 20.0-25.0% reduction in cardiovascular risk, suggesting potential long-term advantages of combination therapy (7, 28). The main goal of hypertension management is to prevent target organ damage and reduce morbidity and mortality. Evidence shows that controlling blood pressure below 140/90 mmHg significantly lowers cardiovascular risk (7, 8).

In the studies analyzed, combination therapy regimens statistically significantly reduced blood pressure ($p < 0.05$) and achieved the recommended blood pressure target in the elderly. This shows that the combination therapy approach is highly effective in clinical practice. Guidelines such as JNC 8 and NICE recommend adding a second drug when monotherapy fails, especially if blood pressure exceeds 20/10 mmHg above target (8, 27). However, dose and drug selection must consider risks like orthostatic hypotension in the elderly (29). Lifestyle factors such as sodium intake (30) and adherence to pharmacotherapy (23) is critically important.

This analytical study has limitations, namely, it only involves one population in Indonesia with a limited number of participants; therefore, generalization of the results to other ethnic or regional populations must be done with caution. However, these findings do provide an important basis for evaluating the effectiveness of therapeutic regimens in the elderly group and open up opportunities for broader research in more diverse populations.

CONCLUSIONS

Based on this study, it can be concluded that single and combination antihypertensive therapies have the same strength in lowering blood pressure in the elderly. However, considering the potential side effects and comorbid conditions of the elderly, individually adjusted combination therapy has proven to be an effective and safe strategy in controlling blood pressure.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

AUTHOR CONTRIBUTIONS

I.F.: conceptualization, methodology, analysis, writing — review & editing; C.H.S.: data curation, writing — original draft preparation; Y: visualization, investigation; R.H.: software, validation.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

INSTITUTIONAL REVIEW BOARD STATEMENT

The study was conducted in accordance with the Declaration of Helsinki and approved by the Human Research Ethics Committee of the Faculty of Medicine, Tadulako University (No. 7916/UN28.1.30/KL/2020, approved 20 November 2020).

INFORMED CONSENT STATEMENT

Written informed consent was obtained from all subjects involved in the study.

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