



Analysis of the Effectiveness of Antihypertensive Drugs on Blood Pressure Reduction in Patients Receiving Calcium Channel Blocker and Angiotensin Receptor Blocker Therapy

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ABSTRACT

This study aimed to analyze the effectiveness of antihypertensive drugs from the Calcium Channel Blocker (CCB) and Angiotensin Receptor Blocker (ARB) classes in reducing blood pressure among hypertensive patients. The study employed a retrospective observational design using medical record data collected from November 2024 to February 2025 and was conducted in four primary healthcare centers in Banyumas Regency. A total of 70 patients enrolled in the PROLANIS program were selected using purposive sampling. Data were analyzed based on changes in blood pressure and statistically tested using the One-Way ANOVA test. The results showed that the ARB + CCB combination therapy was the most frequently used regimen (50%) and achieved the lowest mean blood pressure value (129.94/77.25 mmHg) among the therapy groups. Statistical analysis indicated a significant difference in systolic and diastolic blood pressure between patients receiving monotherapy and combination therapy ($p < 0.05$). These findings suggest that the ARB + CCB combination therapy was associated with greater blood pressure reduction compared to monotherapy among hypertensive patients in primary healthcare settings.

Keywords: *hypertension; calcium channel blocker; angiotensin receptor blocker; combination therapy; effectiveness*

1. INTRODUCTION

Hypertension is a significant global health problem, as it contributes substantially to premature mortality. According to data from the World Health Organization (WHO), approximately 22% of the world's population suffers from hypertension, and the number of affected individuals is projected to continue increasing, reaching 1.5 billion by 2025. In Indonesia, the burden of this disease remains high, including in Central Java Province, which recorded more than 8.5 million cases in 2023, with Banyumas Regency contributing over 170,000 cases (Cheng *et al.*, 2020; Dinas Kesehatan Jawa Tengah, 2023; Lestari *et al.*, 2020). A surge in poorly managed hypertension prevalence may lead to severe complications such as cardiovascular disease, stroke, and renal disorders (Anshari, 2019; Ayu, 2021; Ulfa Azhar *et al.*, 2019).

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Hypertension control efforts are generally implemented through long-term pharmacological therapy using antihypertensive medications. The choice of therapy is tailored to the patient's clinical response and may involve either monotherapy or combination therapy. Commonly prescribed drug classes include diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), and beta-blockers (Febri Nilansari *et al.*, 2020). Although antihypertensive therapy cannot permanently cure hypertension, effective treatment plays a crucial role in maintaining controlled blood pressure levels and preventing complications (Fauziah *et al.*, 2019).

Recent international guidelines, including the 2017 ACC/AHA and 2018 ESC/ESH hypertension guidelines, recommend early initiation of combination therapy, particularly in patients with stage 2 hypertension or high cardiovascular risk, due to improved blood pressure control and faster achievement of therapeutic targets. These recommendations highlight the growing emphasis on combination regimens in contemporary hypertension management.

A study by (Ristiyorini *et al.*, 2024) demonstrated that CCBs, particularly amlodipine, were the most frequently used agents in monotherapy (84%), while combinations of ARBs and CCBs especially candesartan and amlodipine were the preferred choice in combination therapy (56.3%). Monotherapy was administered to 54% of patients, whereas 46% received combination therapy, predominantly involving two antihypertensive drug classes. However, the effectiveness of monotherapy in achieving target blood pressure remained low, with only 4 out of 146 patients successfully reaching the recommended targets. Statistical analysis revealed significant differences between therapy types in terms of systolic and diastolic blood pressure reduction.

Although previous clinical trials and international guidelines have established the superiority of ARB–CCB combination therapy, limited evidence exists regarding its real-world effectiveness in Indonesian primary healthcare settings, particularly among PROLANIS participants. Most published studies were conducted in controlled environments, which may not fully represent routine clinical practice.

Based on these conditions, this study aims to analyze the effectiveness of antihypertensive therapy, particularly calcium channel blockers and angiotensin receptor blockers, in reducing blood pressure among hypertensive patients in several primary healthcare centers (Puskesmas) in Banyumas Regency. The study was conducted at Cilongok I, Rawalo, Sokaraja II, and Wangon I Primary Healthcare Centers, which were selected based on geographical representation to provide a more comprehensive overview. Therefore, this study aims to provide contextual real-world evidence to bridge the gap between guideline recommendations and daily primary care implementation.

2. METHODS

This study employed a retrospective observational design using medical record data collected over a four-month period from November 2024 to February 2025. Although blood pressure measurements were obtained from repeated visits, the analysis was conducted cross-sectionally by comparing antihypertensive therapy groups based on aggregated blood pressure outcomes. The study was conducted in February 2025 at four primary healthcare centers (Puskesmas) in Banyumas Regency, namely Sokaraja II, Cilongok I, Wangon I, and Rawalo.

The study population consisted of all hypertensive patients enrolled in the Chronic Disease Management Program (Program Pengelolaan Penyakit Kronis/PROLANIS) who underwent routine examinations during the study period. Sample selection was carried out using a purposive sampling method based on predefined inclusion and exclusion criteria, resulting in a total of 70 respondents. Data were collected by recording patients' blood pressure measurements from November 2024 to February 2025, as well as the types of antihypertensive therapy used, based on entries in the PROLANIS health monitoring records.

Blood pressure control was defined according to guideline-recommended thresholds (<140/90 mmHg). Partial reduction was defined as a decrease of ≥ 10 mmHg in systolic blood pressure without

reaching the target level, while no reduction referred to the absence of meaningful systolic blood pressure improvement.

Statistical analysis was performed using the One-Way ANOVA test to compare differences in systolic and diastolic blood pressure between antihypertensive therapy groups. Prior to ANOVA testing, normality was assessed using the Shapiro–Wilk test and homogeneity of variance was evaluated using Levene’s test.

Ethical approval for this study was obtained from the Institutional Ethics Committee of Harapan Bangsa University (Approval No: B.LPPM-UHB/465/05/2025). All patient data were anonymized to ensure confidentiality and privacy.

3. RESULTS AND DISCUSSION

Based on the study results, a total of 70 patients were classified according to the antihypertensive drug classes used, either as monotherapy or combination therapy.

Table 1. Antihypertensive Profile of Hypertensive PROLANIS Patients

Antihypertensive Therapy	Frequency	(%)
ARB	4	5,71
CCB	23	32,86
ARB + CCB	35	50
ACEI + CCB	8	11,43

The most frequently prescribed antihypertensive monotherapy was the calcium channel blocker (CCB) class, used by 23 patients (32.86%). Meanwhile, the combination of angiotensin receptor blockers (ARBs) and CCBs was the most commonly used combination therapy, administered to 35 patients (approximately 50%). These findings are consistent with previous studies reporting that CCBs were the predominant class used in monotherapy (35.7%), while the ARB–CCB combination was the most frequently prescribed regimen in combination therapy (28%) ([Hastuti, 2022](#)).

CCBs are recommended as first-line therapy for hypertension according to the JNC VIII guidelines, as they inhibit the influx of calcium ions through calcium channels in the membranes of cardiac and vascular smooth muscle cells, leading to vasodilation and a subsequent reduction in blood pressure. Clinically, CCBs have been shown to effectively lower blood pressure in various specific conditions, including hypertension during pregnancy and hypertension in the elderly population ([Chobanian et al., 2003](#)).

The combination of ARBs and CCBs is widely used because it produces synergistic effects on vascular and cardiac function, as well as on the sympathetic nervous system and the renin–angiotensin system. This combination accelerates blood pressure reduction in elderly patients with hypertension and also provides cardioprotective effects, thereby potentially reducing morbidity and mortality associated with cardiovascular complications ([Hadidi et al., 2019](#); [Indrajaya, 2017](#)).

Overview of the Effectiveness of Monotherapy and Combination Antihypertensive Therapy on Patients’ Blood Pressure

The effectiveness of antihypertensive therapy was evaluated based on changes in the mean systolic and diastolic blood pressure values and their standard deviations over the last four months. The data were analyzed by classifying patients according to therapeutic outcome categories, namely patients who achieved target blood pressure reduction, those who experienced blood pressure reduction but did not reach the target, and those who showed no reduction.

Blood pressure control was defined according to guideline-recommended thresholds (<140/90 mmHg). Partial reduction was defined as a decrease of ≥ 10 mmHg in systolic blood pressure without reaching the target level, while no reduction referred to the absence of meaningful systolic blood pressure improvement.

Table 2. Effectiveness of Monotherapy and Combination Antihypertensive Therapy

Drug Class	Achieved Target Reduction	Reduction Not Achieving Target	No Reduction
ARB	3	1	0
CCB	15	4	4
ARB + CCB	17	8	10
ACEI + CCB	6	2	0

Of the 27 patients receiving monotherapy, 23 were treated with calcium channel blockers (CCBs) and the remaining 4 patients received angiotensin receptor blockers (ARBs). Among the 23 patients treated with CCBs, 15 achieved blood pressure reduction in accordance with the therapeutic target, 4 patients experienced a reduction in blood pressure that did not reach the target, and the remaining 4 patients showed no reduction in blood pressure. Of the 4 patients receiving ARB monotherapy, 3 achieved blood pressure reduction in line with the therapeutic target, while 1 patient experienced a reduction that did not meet the target.

Combination therapy with ARB + CCB was administered to 35 of the 43 patients receiving combination treatment, while ACE inhibitor (ACEI) + CCB combination therapy was given to 8 patients. Among the 35 patients treated with ARB + CCB combination therapy, 17 achieved blood pressure reduction consistent with the target, 8 experienced blood pressure reduction that did not meet the target, and 10 showed no reduction. Six of the eight patients receiving ACEI + CCB combination therapy achieved target blood pressure reduction, whereas the remaining two patients experienced a reduction that did not reach the therapeutic target.

Table 3. Mean Blood Pressure of Hypertensive PROLANIS Patients

Criteria	Group	Average Monthly Blood Pressure (mmHg)				Mean BP	SD
		November	December	January	February		
Achieved Target Reduction	ARB	134,66/80	123/76,66	125/71	121,66/75	126,08/75,67	5,09/3,24
	CCB	142,86/79,06	136/79,06	136,8/81,53	127,66/76,13	135,83/78,95	5,41/1,91
Did Not Achieve Target Reduction	ARB	154/89	149/90	130/90	140/70	143,25/84,75	9,15/8,53
	CCB	157,5/86,75	162,25/82,25	156/79,25	150,75/71,25	156,63/79,88	4,10/5,65
No Reduction	CCB	141,5/79,5	146,75/80,5	149,25/89,75	157,75/78,75	148,81/82,13	5,89/4,45
Achieved Target Reduction	ARB + CCB	132,76/77,82	130,94/76,29	130,41/77,94	125,64/76,94	129,94/77,25	2,63/0,78
	ACEI + CCB	142,5/82,83	141,16/77,5	131,83/75,5	122,5/75,5	134,5/77,83	8,054/2,99
Did Not Achieve Target Reduction	ARB + CCB	163,875/94	158,5/93	155/88,125	146,25/88,75	155,91/90,97	6,41/2,57
	ACEI + CCB	153/77,5	150/81,5	146/89,5	142/80,5	147,75/82,25	4,15/4,44
No Reduction	ARB + CCB	150,6/87,8	152,6/87,6	156,2/89,7	161,1/86,4	155,13/87,88	3,99/1,18

Based on the mean blood pressure values of hypertensive PROLANIS patients, the combination therapy of angiotensin receptor blockers (ARBs) and calcium channel blockers (CCBs) demonstrated the greatest reduction in blood pressure compared to other therapeutic regimens, with an average blood pressure of 129.94/77.25 mmHg. This finding indicates that, clinically, the ARB–CCB combination was the most effective therapy in reducing blood pressure among patients in this study.

However, as this study employed a retrospective observational design, these findings indicate an association rather than a definitive casual relationship between therapy type and blood pressure reduction.

These results are consistent with a study conducted at Karanganyar Regional Public Hospital, which reported a target achievement rate of 92.3% for ARB + CCB combination therapy (Wulandari & Cahyaningtyas, 2021).

The ARB + CCB combination exerts its antihypertensive effects through two primary mechanisms of action. ARBs block angiotensin II type 1 receptors, resulting in vasodilation and a reduction in excessive vasoconstriction, while CCBs inhibit calcium ion influx into arterial and cardiac smooth muscle cells, thereby decreasing peripheral vascular resistance. In addition, ARBs may mitigate peripheral edema, a common adverse effect associated with CCB therapy, making this combination optimal for maintaining blood pressure stability (Baroroh & Sari, 2017; Mancina *et al.*, 2016).

Comparison of Blood Pressure between Monotherapy and Combination Antihypertensive Therapy

To determine the association between the use of monotherapy and combination therapy on blood pressure, data were analyzed using the One-Way ANOVA test. Prior to conducting the ANOVA, homogeneity and normality tests were performed using the Shapiro–Wilk test to assess whether the data were normally distributed.

When statistically significant differences were identified, post-hoc analysis using Tukey’s HSD test was performed to determine pairwise differences between therapy groups. Effect size (η^2) was calculated to evaluate the magnitude of the observed differences.

Table 4. Results of the Normality Test

Therapy			<i>p</i>	Remarks
CCB	Systolic	pre	0,201	Normally distributed
		post	0,345	
	Diastolic	pre	0,971	
		post	0,962	
ARB	Systolic	pre	0,76	
		post	0,297	
	Diastolic	pre	0,345	
		post	0,444	
CCB + ACEI	Systolic	pre	0,552	
		post	0,266	
	Diastolic	pre	0,262	
		post	0,857	
ARB + CCB	Systolic	pre	0,579	
		post	0,373	
	Diastolic	pre	0,842	
		post	0,192	

The results of the normality test using the Shapiro–Wilk test showed that both the monotherapy and combination therapy groups had *p*-values greater than 0.05, indicating that the data were normally distributed.

Table 5. Homogeneity Test Results

	<i>p</i>	Remarks
Systolic	0,320	Data are homogeneous
Diastolic	0,102	

The results of the homogeneity test using Levene's test showed that both the monotherapy and combination therapy groups had p-values greater than 0.05, indicating that the data were homogeneous.

Table 6. Comparison of Blood Pressure by Antihypertensive Therapy

	<i>p</i>	Remarks
Systolic	0,000	Significant difference observed
Diastolic	0,002	

A significant difference in blood pressure was observed between patients receiving monotherapy and those undergoing combination therapy, as indicated by the One-Way ANOVA results with a p-value < 0.05. This finding is consistent with the study by (Ristiyorini *et al.*, 2024), which reported differences in blood pressure outcomes between monotherapy and combination antihypertensive therapy.

CONCLUSION

This study demonstrates that combination therapy with antihypertensive agents from the angiotensin receptor blocker (ARB) and calcium channel blocker (CCB) classes was associated with greater blood pressure reduction compared to monotherapy among hypertensive patients. The ARB + CCB combination resulted in a more substantial reduction in blood pressure and achieved the lowest mean blood pressure value of 129.94/77.25 mmHg. Statistical analysis further revealed a significant difference between monotherapy and combination therapy in terms of both systolic and diastolic blood pressure reduction ($p < 0.05$).

These findings suggest that the ARB and CCB combination may represent a potentially favorable therapeutic option for hypertension management in primary healthcare settings. However, further prospective and randomized studies are required to confirm these results.

ADVISE

Future studies are recommended to involve a larger sample size and include a greater number of primary healthcare centers or different regions in order to enhance external validity and improve the generalizability of the findings.

Additionally, prospective study designs with longer follow-up periods are suggested to better evaluate the long-term effectiveness and clinical outcomes of antihypertensive combination therapy. Incorporating additional variables such as medication adherence, comorbidities, and lifestyle factors may also provide a more comprehensive understanding of treatment effectiveness

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