



*Research Article*

## Evaluation of variations in the response of hypertensive patients in the outpatient installation of the UPT Puskesmas, Babat Lamongan District

Primanitha Ria Utami<sup>[1]\*</sup>, Riana Prastiwi Handayani<sup>[1]</sup>, Sheila Sheila<sup>[2]</sup>

<sup>1</sup> Program Studi S1 Farmasi, Fakultas Ilmu Kesehatan, Universitas Muhammadiyah Lamongan, Lamongan, East Java, Indonesia

<sup>2</sup> Program Studi D3 Farmasi, Fakultas Ilmu Kesehatan, Universitas Muhammadiyah Lamongan, Lamongan, East Java, Indonesia

\* Corresponding Author's Email: [prima.nitha@yahoo.co.id](mailto:prima.nitha@yahoo.co.id)

### ARTICLE INFO

#### Article History

Received August 8, 2020

Revised August 22, 2020

Accepted August 29, 2020

Published October 6, 2020

#### Keywords

Hypertension

Variation of response

Antihypertensives

Blood pressure

#### Doi

10.22219/farmasains.v5i1.13956

### ABSTRACT

Hypertension has long been a health problem that can have severe impacts on society. Measurement of blood pressure is one of the determinants of antihypertensive treatment's success, which can be seen from the reduction in the patient's blood pressure towards achieving the target blood pressure. Less than optimal blood pressure control is the most common risk factor for CVD and cerebrovascular disease. The role of the selection of antihypertensive therapy in each patient's condition is individual. Each patient will vary in response to various types of antihypertensive treatment. The research design carried out was retrospective descriptive with the observation of variations in answer to the use of antihypertensives in outpatient hypertension patients at the Babat Health Center with an examination period from January to December 2019. The study was divided into two groups, namely the positive and negative response groups. Patient characteristics data (age, sex, and treatment regimen) were statistically tested with the chi-square test to see whether there was a difference in eating or not between the two groups. It is said a positive response if the patient's blood pressure has decreased after three months of using antihypertensives. Harmful if after three months of antihypertensive use, there is no change in blood pressure or increased blood pressure. The evaluation was carried out on patients with negative responses, what factors were the causes. The results of patient characteristics,  $p > 0.05$ , were not significant differences between the two groups. There are variations in the negative response caused by the therapy regimen that is not optimal, lifestyle, and metabolism of antihypertensive drugs that are different for each individual.

## 1. INTRODUCTION

Hypertension has long been a health problem that can have severe impacts on society. The condition of hypertension is characterized by an increase in blood pressure that exceeds normal limits, namely systolic blood pressure (SBP)  $> 140$  mmHg and diastolic blood pressure (DBP)  $> 90$  mmHg on two measurements with a time interval of five minutes in a sitting position. In patients aged  $> 60$  years, according to the Joint National Committee (JNC 8) guidelines blood pressure is said to be uncontrolled if it is  $> 150/90$  mmHg (James et al.,

2014). Hypertension is a significant risk factor for cardiovascular diseases (CVD) such as stroke and coronary heart disease. Hypertension is also often referred to as the silent killer because blood pressure tends to be high for a long time, causing complications in other organs. This is supported by the JNC 8 guideline, which states that an increase in SBP by 20 mmHg or an increase in DBP 10 mmHg in hypertensive patients can increase the risk of cardiovascular events (About 45% of the causes of death are due to heart disease and 51% from a stroke) (Parati, Ochoa, Lombardi & Bilo, 2013) The prevalence of hypertension is susceptible to attacking adults over 25 years of age, and the data is from the population of Singapore, where about 40% have an increase in blood pressure (BP) which can cause 7.5 million deaths annually worldwide (Setia, Subramaniam, Tay & Teo, 2017).

Blood pressure clinical data is one of the critical indicators of successful antihypertensive treatment can be seen from the decrease in the patient's blood pressure towards achieving the target blood pressure. The target blood pressure is adjusted for the patient's comorbid disease. Based on the American College of Cardiology guidelines, the target blood pressure achievement in patients with comorbid DM, CVD, CKD is less than 130/80 mmHg (Carey & Whelton, 2018). This is also supported by Aronow & Shamliyan (2018) research in adult patients with diabetes and arterial hypertension, to reduce the risk of stroke, left ventricular hypertrophy and ECG abnormalities, macroalbuminuria, intensive monitoring of daily blood pressure fluctuations, blood pressure 120-130/80 mmHg is accompanied by modification of a healthy lifestyle, monitoring side effects in the form of orthostatic hypotension, and other drug-related hazards. A single RCT study from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) showed that adult patients with diabetes and high arterial blood pressure (SBP 130-190 mmHg) performed good blood pressure and glycemic control intensively reduced their risk. diabetes-related death, fatal or nonfatal stroke (Margolis et al., 2014).

Less than optimal blood pressure control is the most common risk factor for CVD and cerebrovascular disease. The role of the selection of antihypertensive therapy in each patient's condition is individual. Each patient will vary in response to various types of anti-hypertensive therapy. According to previous research, there is a decrease in systolic blood pressure of 120-139 mmHg and diastolic 80-89 mmHg in stage II hypertensive patients after being treated with antihypertensive drugs for three months (Ulfa et al., 2018). In another study, it was stated that the Calcium Channel Block (CCB) class of antihypertensive therapy effectively reduced blood pressure to 16.9-21.15 mmHg from the initial blood pressure of 230/110 mmHg after three months of treatment.

Based on research variability in blood pressure is closely related to target organ damage, cardiovascular events, and mortality in hypertensive patients. This is influenced by increased blood pressure fluctuations that cause left ventricular hypertrophy, stiffness of blood vessels, and kidney lesions. Therefore, the monitoring of Blood Pressure Variability (BPV) can be used as a support for antihypertensive treatment accompanied by cardiovascular disease (Höcht, 2013). Another study by Stevens et al (2016), stated that the variation in blood pressure response with SD (standard deviation) values in systolic blood pressure of 7mmHg could be considered an 18% greater risk of cardiovascular disease than patients with stable SD blood pressure shows 2 mmHg. The meta-analysis study also showed that each class of antihypertensive therapy had different blood pressure reduction potentials. The influence of variation in response to antihypertensive therapy regimens reduced blood pressure control, resulting in increased variability in blood pressure results and an increased risk of CVD (Webb et al., 2010). Therefore, this study aims to see variations in hypertensive patients' responses in terms of the therapy regimen and blood pressure.

## 2. MATERIALS AND METHODS

The research design carried out was a retrospective descriptive with the observation of variations in response to the use of antihypertensives in outpatient hypertension patients at the Babat Public Health Center with the examination period from January to December 2019. The material used was a data collection sheet according to the data taken. The data taken were age, gender, therapy regimen, and blood pressure from the first month to the third month-therapeutic regimen in the form of hypertension pharmacological therapy, dosage, and usage rules.

The sample used in this study were patients who met the inclusion criteria and passed the screening from the exclusion criteria with a minimum sample size of 44 patients. The calculation is done with the following formula.

$$n = \frac{N \cdot Z^2 \cdot p \cdot q}{d^2 \cdot (N - 1) + Z^2 \cdot p \cdot q}$$

$$= \frac{50 \times 1.96 \times 0.5 \times 0.5}{(0.05 \times (50 - 1)) + (1.96 \times 0.5 \times 0.5)}$$

$$= 44.1 = 44 \text{ patients}$$

Information:

n = estimated sample size

N = estimated population size

z = normal standard value for  $\alpha = 0.05$  (1.96)

p = estimated proportion, if unknown is assumed to be 50%

q = 1 - p (100% - p)

d = selected error rate (d = 0.05)

The inclusion criteria in this study were routine control outpatients between January-December 2019 with a diagnosis of stage 1 hypertension (both without and with comorbidities), patients over 18 years old, and patients with single or combination antihypertensive therapy. Patients with incomplete data and patients with pregnant conditions. The study was divided into two groups, namely the positive and negative response groups. It is said that a positive response if the patient's blood pressure has decreased after three months of using antihypertensives. Harmful if after three months of antihypertensive use, there is no change in blood pressure or increased blood pressure.

Evaluation is carried out on patients with a negative response, any factors that cause it. Then for statistical analysis using SPSS was carried out on patient characteristic data (age, sex, and therapy regimen), which aims to see whether the characteristics of these patients are significant differences or not between the positive and negative response groups. The SPSS test used was the chi-Square test with parameters if the p-value <0.05, there was a significant difference, whereas if p > 0.05 the difference was not significant.

### 3. RESULTS AND DISCUSSIONS

Results of research data on each patient characteristic (age, sex, and treatment regimen) show a p value > 0.05 (**Table 1**), which means there is no significant difference between positive and negative responses to patient characteristics. The number of patients who showed a positive response was 95 patients, while the negative response was 11 patients (**Table 2**). Characteristics of the patient, the dominant gender are female. Women are prone to experiencing menopause, which causes a decrease in hormone estrogen and progesterone, which can regulate blood pressure. Besides, obesity and the disruption of lipid profile (increased total cholesterol, low HDL) tend to cause systolic blood pressure in women to be higher than men (**Ong, Tso, Lam & Cheung, 2008**). Further patient characteristics in terms of age indicate that most hypertensive patients are planting (45-59 years old). Entering the elderly, there will be changes in the structure of blood vessels, decreased elasticity of blood vessels, which triggers an increase in blood pressure (**Lionakis, Mendrinis, Sanidas, Favatas & Georgopoulou, 2012**). Most of the antihypertensive regimens in this study were administered singly. Based on the JNC 8 guidelines, antihypertensive drugs begin with the use of a single drug. If the target blood pressure is not reached within one month of treatment, an increase in the initial drug dose or addition of other drug classes derived from first and second-line therapy can be done. A two-drug combination is recommended for patients whose blood pressure is more than 20/10 mmHg above the target blood pressure. Suppose systolic blood pressure is 140-159 mmHg, and diastolic is 90-99 mmHg. In that case, mono-therapy antihypertensives need to be given, and if systolic blood pressure > 160 mmHg and diastolic > 100 mmHg, a combination of two

**Table 1.** Patient characteristics

Patient Characteristics	Response		Total	p (Value)
	Positive	Negative		
<b>Gender</b>				
Male	36	3	39	0.743
Women	59	8	67	
Total	95	11	106	
<b>Age</b>				
40-50	20	4	24	0.675
51-60	45	4	49	
61-70	24	2	25	
71-80	6	1	7	
Total	95	11	106	
<b>Therapeutic Regimen</b>				
Single	80	10	90	1
Combination	15	1	16	
Total	95	11	106	

**Table 2.** Antihypertensive response

	Positive Response (patient)	Negative Response (patient)	Total
Number of Patients	95 (87%)	11 (13%)	106 (100%)

**Table 3.** Description of the negative response to antihypertension

No. Patient	Therapeutic Regimen	Pre-Systolic BP (mmHg)	Pre-Diastolic BP (mmHg)	Post-Systolic BP (mmHg)	Post-Diastolic BP (mmHg)	Increased Systolic BP	Increase in Diastolic BP
16	candesartan 8 mg 1x1	149	88	152	92	3	4
34	amlodipine 5 mg 1x1	137	88	144	92	7	4
55	amlodipine 5 mg 1x1	139	86	144	91	5	5
56	amlodipine 5 mg 1x1	137	88	142	90	5	2
67	amlodipine 5 mg 1x1	147	90	150	92	3	2
68	amlodipine 10 mg 1x1	152	95	160	99	8	4
78	amlodipine 10 mg 1x1	154	92	154	93	0	1
80	amlodipine 10 mg 1x1	158	94	158	95	0	1
103	candesartan 8mg 1x1, amlodipine 5 mg 1x1	151	90	152	90	1	0
104	amlodipine 10 mg 1x1	150	99	150	99	0	0
106	amlodipine 10 mg 1x1	159	97	159	97	0	0
Average ± SD		148 ± 7.44	92 ± 4.01	151 ± 5.91	94 ± 3.20	3 ± 2.84	2 ± 1.78

types of drugs is necessary (James et al., 2014).

The existence of various factors in the antihypertensive therapy regimen and the patient's blood pressure, namely experiencing an increase in blood pressure after being observed for three months of retrospective therapy (Table 3), caused variations in the negative response to the success of antihypertensive treatment as is the case in research that the achievement of blood pressure reduction in hypertensive patients after three months of therapy showed effective results marked by a decrease in the average pre blood pressure of 149/93 mmHg and the average post blood pressure to 130/82 mmHg (Ulfa et al., 2018). Whereas in the data of this study, 11 patients showed variations in negative responses to antihypertensive treatment. It can be analyzed from the factor of the accuracy of selecting antihypertensives, which should be adjusted to the condition of patients with comorbid or non-comorbid patients. Of the 11 patients who showed a variety of negative responses, some had a comorbid cardiovascular disease such as CHD, stroke, diabetes mellitus (DM), and kidney disease (CKD). Comorbid risk factors will influence the selection of appropriate antihypertensive therapy and its treatment regimen singly or combined (Webb et al., 2010). There is still the inaccuracy of selecting a single therapy given to patients who have comorbid, causing variations in the negative response, which is also seen from the increase in blood pressure generated for three months.

Factors affecting treatment targets can include treatment risks (e.g., hypotension, side effects), comorbidities, vascular complications, and patient adherence behavior during the treatment period (particularly elderly patients receiving polypharmacy). Lifestyle modification by losing weight, implementing the DASH diet, increasing physical activity, reducing alcohol consumption, can support blood pressure reduction and increase the effectiveness of antihypertensive therapy (de Boer et al., 2017). Another factor that also plays an essential role in the variation of individual responses to antihypertensive treatment is the patient's pharmacogenomics (Bhardwaj et al., 2015).

#### 4. CONCLUSIONS

There is a variation/variability in response to antihypertensives' use, namely, positive and negative responses with more positive response patients. Patients with a negative response can be caused by several factors, including the therapy regimen is not optimal, lifestyle, metabolism of antihypertensive drugs that are different for each individual, pharmacogenomics.

#### 5. REFERENCES

- Aronow, W. S., & Shamliyan, T. A. (2018). Blood pressure targets for hypertension in patients with type 2 diabetes. *Annals of translational medicine*, 6(11). Doi:10.21037/atm.2018.04.36
- Bhardwaj, S., Balgir, P. P., & Goel, R. K. (2015). Pharmacogenomics and personalized management of hypertension. *Journal of Critical Reviews*, 2(2), 1-6.

- Carey, R. M., & Whelton, P. K. (2018). Prevention, detection, evaluation, and management of high blood pressure in adults: synopsis of the 2017 American College of Cardiology/American Heart Association Hypertension Guideline. *Annals of internal medicine*, 168(5), 351-358. Doi:10.7326/M17-3203
- De Boer, I. H., Bangalore, S., Benetos, A., Davis, A. M., Michos, E. D., Muntner, P., ... & Bakris, G. (2017). Diabetes and hypertension: a position statement by the American Diabetes Association. *Diabetes Care*, 40(9), 1273-1284. doi:10.2337/dci17-0026
- Höcht, C. (2013). Blood pressure variability: prognostic value and therapeutic implications. *International Scholarly Research Notices*, 2013, i398485. Doi:10.5402/2013/398485
- James, P. A., Oparil, S., Carter, B. L., Cushman, W. C., Dennison-Himmelfarb, C., Handler, J., ... & Smith, S. C. (2014). 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *Jama*, 311(5), 507-520. Doi:10.1001/jama.2013.284427
- Lionakis, N., Mendrinos, D., Sanidas, E., Favatas, G., & Georgopoulou, M. (2012). Hypertension in the elderly. *World journal of cardiology*, 4(5), 135-147. doi:10.4330/wjc.v4.i5.135
- Margolis, K. L., O'Connor, P. J., Morgan, T. M., Buse, J. B., Cohen, R. M., Cushman, W. C., ... & Lipkin, E. W. (2014). Outcomes of combined cardiovascular risk factor management strategies in type 2 diabetes: the ACCORD randomized trial. *Diabetes care*, 37(6), 1721-1728. doi:10.2337/dc13-2334
- Ong, K. L., Tso, A. W., Lam, K. S., & Cheung, B. M. (2008). Gender difference in blood pressure control and cardiovascular risk factors in Americans with diagnosed hypertension. *Hypertension*, 51(4), 1142-1148. Doi:10.1161/HYPERTENSIONAHA.107.105205
- Parati, G., Ochoa, J. E., Lombardi, C., & Bilo, G. (2013). Assessment and management of blood-pressure variability. *Nature Reviews Cardiology*, 10(3), 143. Doi:10.1038/nrcardio.2013.1
- Setia, S., Subramaniam, K., Tay, J. C., & Teo, B. W. (2017). Hypertension and blood pressure variability management practices among physicians in Singapore. *Vascular Health and Risk Management*, 13, 275. Doi:10.2147/VHRM.S138694
- Stevens, S. L., Wood, S., Koshiaris, C., Law, K., Glasziou, P., Stevens, R. J., & McManus, R. J. (2016). Blood pressure variability and cardiovascular disease: systematic review and meta-analysis. *bmj*, 354, i4098. doi:10.1136/bmj.i4098
- Ulfa, N. M., Prasetya, R. A., & Adelia, L. (2018). Profil Penurunan Tekanan Darah pada Terapi Obat Antihipertensi Golongan CCB Dihidropiridin Antara Amlodipin Dibandingkan Nifedipin Oral Osmotik (Studi Dilakukan di Poli Penyakit Dalam RS Bhayangkara Porong). *Journal of Pharmacy and Science*, 3(1), 34-39.
- Webb, A. J., Fischer, U., Mehta, Z., & Rothwell, P. M. (2010). Effects of antihypertensive-drug class on interindividual variation in blood pressure and risk of stroke: a systematic review and meta-analysis. *The Lancet*, 375(9718), 906-915. Doi:10.1016/S0140-6736(10)60235-8