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ORIGINAL ARTICLE

Analysis of Clinical Oral Manifestation of Patients with Antihypertensive Therapy in South Kalimantan

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ABSTRACT

Background: Hypertension is generally defined as systolic and diastolic pressures of more than 140/90 mmHg. Hypertension can be treated in various ways, either by using traditional herbs or scientific treatment with medicine. Antihypertensive medicine sometimes causes some side effects such as xerostomia and gingival enlargement. **Objective:** The purpose of this research is to analyze the correlation between age, type of medicine, amount of medicine consumption, and duration of treatment with clinical manifestations of the oral cavity in patients with antihypertensive therapy. **Materials and Method:** This research is an observational analytic study with a cross-sectional design. Data were obtained from medical records, anamnesis, and clinical oral examination. **Results:** The research was taken with a purposive sampling technique of 41 samples. It showed that the hypertension patients were mostly in the age of 46-55 years (53.7%), the type of medicine that mainly consumed was calcium channel blocker (34.2%), hypertension patients were found to consume only one type of medicine (75.6%), the duration of treatment was more than one year (85.4%) and the prevalence of oral manifestations presented was 70.7% with the most frequent manifestation of xerostomia (79.3%). The analysis test results showed that there was no correlation in both age and type of medicine with clinical oral manifestations ($p>0.05$), while there was a correlation in the amount of medicine consumption and duration of treatment with clinical oral manifestations in patients with antihypertensive therapy ($p<0.05$). **Conclusions:** There is a correlation in both the amount of medicine consumption and duration of treatment with clinical oral manifestations in patients with antihypertensive therapy.

Key words: hypertension, antihypertensive, clinical oral manifestation

INTRODUCTION

Hypertension is generally defined as systolic and diastolic pressure of more than 140/90 mmHg.[1] World Health Organization (WHO) states that the number of people with hypertension will keep increasing along with the increase in population. It is estimated that around 29% of people in the whole world will experience hypertension. According to WHO, Indonesia is among the 10 countries with the highest prevalence of hypertension. Hypertension prevalence in Indonesia is 31.4% with the highest prevalence is in South Kalimantan (44.1%). According to the 2018 Riskesdas, the city with the highest cases of hypertension in South Kalimantan is Banjarmasin with a total of 46.79% which occupies the fourth rank after Hulu Sungai Tengah, Tabalong, and Barito Kuala.[2]

Hypertension patients often do not aware that they suffer from high blood pressure, therefore this disease is considered as one of the silent killers.[3] Increased blood pressure that occurs over a long period of time are five times more likely to affect the kidneys (kidney failure), six times more likely to affect the heart (coronary heart disease), and 12 times more likely to induce stroke.[4,5]

Various treatments have been suggested for the management of hypertension, whether by using traditional medicine (the use of herbal leaves) or scientific treatment with medicine. The anti-hypertensive medicines are diverse for patients with hypertension, including diuretics such as hydrochlorothiazide, angiotensin-converting enzyme inhibitors (ACEi) such as captopril, beta blockers such as bisoprolol, angiotensin receptor inhibitors (ARB) such as candesartan, and calcium channel

blockers (CCB) such as amlodipine. Use of anti-hypertensive medicines can be prescribed with a single regimen or in combination with other medications if necessary.[6,7,8]

Hypertension medication sometimes causes side effects such as complaints in the oral cavity. Previous researches on patients using anti-hypertensive medication showed that there were some clinical manifestations observed such as xerostomia, gingival enlargement, erythema multiforme, lichenoid medication reaction, salivary gland swelling, and the change of taste sensation.[9-11] Until recently, there has been no research about oral manifestations in hypertensive patients in South Kalimantan, especially in Banjarmasin. Based on that condition, it is needed to determine the clinical oral manifestations in hypertensive patients in Banjarmasin.

MATERIALS AND METHODS

This research has obtained research permission and ethical clearance issued by the Health Research Ethics Commission of the Faculty of Dentistry, Lambung Mangkurat University No. 032 / KEPKG-FKGULM / EC / I / 2020. This research is an observational analytic study with a cross-sectional design. Data were obtained from medical records, history taking, and clinical examination of the oral cavity in hypertensive patients in Banjarmasin.

The population in this research were male patients suffering from hypertension at RSUD Dr. H. Mochammad Ansari Saleh Banjarmasin from January to March 2020. The sample in this research was taken with a purposive sampling technique of 41 samples. The sample in this research was hypertension patients who were treated at Cardiology Polyclinic RSUD Dr. H. Mochammad Ansari Saleh Banjarmasin who met the inclusion and exclusion criteria. Dependent variable of this study was the clinical oral manifestations. Independent variables of this study were age, type of medicine, amount of medicine consumption, and duration of treatment in patients with antihypertensive therapy. This research was conducted at the Cardiology Center of RSUD Dr. H. Mochammad Ansari Saleh Banjarmasin. Prior to the research, the researchers gave an explanation to the respondents about the benefits and the research procedures that was going to be carried out. After the respondents agreed to participate, the respondents were required to sign an informed consent as a sign of approval to participate as research respondents. Later on, anamnesis was recorded and the clinical oral examinations based on medical record of oral medicine department were performed using a dental mirror. The intraoral examination was performed to observe if there were some clinical manifestations of anti-hypertensive medication's effect such as xerostomia, gingival enlargement, erythema multiforme, lichenoid medication reaction, salivary gland swelling, and the change of taste sensation.

The results of the data were analyzed using the chi-square test to determine the correlation of age, type of medicine, amount of medicine consumption, and length of treatment with clinical manifestations of the oral cavity. But if it did not meet the requirements for the 2x2 table, data were analyzed using the Fisher's exact test and for table 2*k use the Kolmogorov-Smirnov test.

RESULTS

The results were obtained from 41 hypertension patients in Cardiology Polyclinic RSUD Dr. H. Mochammad Ansari Saleh Banjarmasin. Each sample was differentiated based on age, type, and amount of medicine consumption and duration of antihypertensive treatment. The frequency distribution of respondents with antihypertensive therapy based on age can be seen in Table 1.

Table 1. Characteristics of research respondents based on age

Age	Quantity (n)	Percentage (%)
Late Adulthood (36–45 years)	4	9.8%
Early Elderly (46-55 years)	22	53.7%
Late Elderly (56-65 years)	15	36.5%
Total	**41**	**100%**

Table 1 shows that hypertension was mostly suffered by respondents between the age of 46-55 years old (53%) and the least at the age of 36-45 years old (9.8%). The frequency distribution of respondents with antihypertensive therapy based on the type of medicine consumed can be seen in Table 2.

Table 2. Characteristics of research respondents based on the type of medicine.

Type of Medicine	Quantity (n)	Percentage (%)
Angiotensin Converting Enzyme inhibitor (ACEi)	6	14.6%
Angiotensin Receptor Blocker (ARB)	11	26.8%
Calcium Channel Blocker (CCB)	14	34.2%
ARB dan *Beta Blocker*	7	17.1%
ARB, *Beta Blocker* dan CCB	3	7.3%
Total	**41**	**100%**

Table 2 shows the type of medicine that is most consumed by respondents is CCB (34.2%). The frequency distribution of respondents with antihypertensive therapy based on the amount of medicine consumed can be seen in Table 3.

Table 3. Characteristics of research respondents based on the amount of medicine consumed.

Total Consumption	Quantity	Percentage
1 Type of Medicine	31	75.6%
>1 Type of Medicine	10	24.4%
Total	**41**	**100%**

Table 3 shows that respondents with antihypertensive therapy only consume one type of antihypertensive medicine (75.6%). The frequency distribution of respondents with antihypertensive therapy based on the duration of treatment can be seen in Table 4.

Table 4. Characteristics of research respondents based on the treatment of duration.

Treatment of duration	Quantity (n)	Percentage (%)
<1 Year	6	14.6%
>1 Year	35	85.4%
Total	**41**	**100%**

Table 4 shows that respondents with antihypertensive therapy were found to have been taking antihypertensive medication for more than one year (85.4%). The frequency distribution of respondents with antihypertensive therapy based on the number of clinical oral manifestations can be seen in Table 5.

Table 5. Percentage of the presence of clinical oral manifestations of anti-hypertensive medication's effect in respondents with antihypertensive therapy.

Manifestation of the oral cavity	Quantity (n)	Percentage (%)
Have no Manifestation	12	29.3%
Have Manifestation	29	70.7%
Total	**41**	**100%**

It can be seen from Table 5 that the number of respondents with antihypertensive therapy is 29 people (70.7%) who presented with clinical oral manifestations. The variance of clinical oral manifestations of respondents with antihypertensive therapy can be seen in Table 6.

Table 6. Variance of clinical oral manifestations of respondents with antihypertensive therapy.

Types of Manifestation	Quantity (n)	Percentage (%)
Xerostomia	23	79.3%
Xerostomia dan *Gingival Enlargement*	6	20.7%
Total	**29**	**100%**

Table 6 shows that the clinical oral manifestations were xerostomia (79.3%) and *xerostomia* with *gingival enlargement* (20.7%). The results of the data were analyzed to determine the correlation of age, type of medicine, amount of medicine consumption, and length of treatment with clinical oral manifestations.

Table 7. The correlation between age and clinical oral manifestations in patients on antihypertensive therapy.

Variable of Age	Manifestation of Oral Cavity		Total	Sig.
	Yes	No		
Adulthood (36–45 years)	1 (25 %)	3 (75 %)	4 (100%)	0.068
Early + Early Elderly (46-65 years)	28 (75.7 %)	9 (24.3 %)	27 (100%)	
Total	**29**	**12**	**41**	

Analysis of the correlation between age and clinical oral manifestations in patients with antihypertensive therapy using Fisher's exact test showed that there was no correlation between age and clinical oral manifestations in patients with antihypertensive therapy. The correlation between types of medicines with clinical oral manifestations in patients with antihypertensive therapy can be seen in Table 8.

Table 8. The correlation between types of medicine and clinical oral manifestations in patients on antihypertensive therapy.

Variable Type of Medicine	Manifestation of Oral Cavity		Total	Sig.
	Yes	No		
ACE-i	4 (66.7 %)	2 (33.3 %)	6 (100 %)	0.265
ARB	6 (54.5 %)	5 (45.4 %)	11 (100 %)	
CCB	9 (64.3 %)	5 (35.7 %)	14 (100 %)	
ARB and *Beta Blocker*	7 (100 %)	0 (0 %)	7 (100 %)	
ARB, *Beta Blocker*, and CCB	3 (100 %)	0 (0 %)	3 (100 %)	
Total	**29**	**12**	**41**	

Analysis of the correlation between types of medicines with clinical oral manifestations in patients with antihypertensive therapy was performed using the Kolmogorov-Smirnov test and showed that there was no correlation between the types of medicines with clinical oral manifestations in patients with antihypertensive therapy. The correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy can be seen in Table 9.

Table 9. The correlation between the amount of medicine consumption and clinical oral manifestations in patients on antihypertensive therapy.

Amount of consumption	Manifestation of Oral Cavity		Total	Sig.
	Yes	No		
1 type of medicine	19 (61.3 %)	12 (38.7 %)	31 (100 %)	
>1 type of medicine	10 (100 %)	0 (0 %)	10 (100 %)	0.021
Total	**29**	**12**	**41**	

Analysis of the correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy using Fisher's exact test shows that there was a correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy. The correlation between duration of treatment with clinical oral manifestations in patients with antihypertensive therapy can be seen in Table 10.

Table 10. The correlation between duration of treatment with clinical oral manifestations in patients on antihypertensive therapy.

Treatment of duration	Manifestation of Oral Cavity		Total	Sig.
	Yes	No		
<1 Year	1 (16.7 %)	5 (83.3 %)	6 (100%)	0.005
>1 Year	28 (80%)	7 (20%)	35 (100%)	
Total	**29**	**12**	**41**	

Analysis of the correlation between the duration of treatment with clinical oral manifestations of the patients with antihypertensive therapy was performed using the Fisher's exact test and showed that there was a correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy.

DISCUSSION

Table 1 shows that hypertension was mostly suffered by the respondent aged of 46-55 years old (53%). Pathologic changes after the age of 45 years old, the body's immunity and organ function such as heart and blood vessels will experience decreased work function. This will occur as a result of arterial wall thickening due to collagen substance accumulation on the muscle layer to the blood vessel that will continually tighten and stiffen the artery, resulting in hypertension.[12,13] Based on this research, it is known that age of 56-65 years old group is more likely to receive treatment in the hospital because they tend to experience more complex conditions due to their disease.[13]

Table 2 shows that the type of medicine that is often consumed by respondents is CCB (34.2%). CCB is a type of medicine that is effective in reducing blood pressure because it is quite efficient (drug administration is only once a day), in addition to its capability in inducing relaxation. Absorption of CCB in the body is also perfect, especially in elderly patients, and is the first line of treatment for hypertension.[9,14,15]

Table 3 shows that respondents with antihypertensive therapy only consume one type of antihypertensive medication because the combination with second and third medicine from different types of medication will only be proposed when the goal of reducing blood pressure has not been achieved, in addition to avoid other complications in patients with hypertension.[7,13,14]

Table 4 shows that respondents with antihypertensive therapy were found to have been taking antihypertensive medication for more than one year (85.4%). It is because hypertension is a chronic disease with unstable blood pressure characteristics (increase and decrease) so it requires long-term treatment for life and, if not treated for a long time, will increase the risk of other complications such as kidney failure or coronary heart disease-causing stroke.[4,5,16]

Table 6 shows that the oral manifestations were xerostomia (79.3%) and xerostomia with gingival enlargement (20.7%). The appearance of oral manifestations due to the use of antihypertensive medication can affect the rate of salivary flow through the mechanism of action of neurohormonal displacement patterns in parasympathetic nerve. It is similar to the mechanism that occurred in sympathetic nerves in which the interference of salivary flow in salivary glands is getting affected which induces the decrease of salivary flow rate so as to cause xerostomia.[9,17]

Pathologically, the mechanism of gingival enlargement due to the use of antihypertensive medication is still unclear, but it is believed that the occurrence of gingival enlargement is due to changes in collagen metabolism. The antihypertensive medication prevents calcium action between cells and stimulates the proliferation of gingival fibroblasts or initiated changes in size and cell duplication resulting in the enlargement of gingiva.[18-20]

Analysis of the correlation between age and clinical oral manifestations in patients with antihypertensive therapy showed that there was no correlation between age and clinical oral manifestations in patients with antihypertensive therapy. In previous studies, the occurrence of oral manifestations is generally caused by the use of antihypertensive medication.[9,11,18] However, in Table 7, it is showed that oral manifestations are more likely to be found at the age of 46-65 years by 75.7% compared to age 36-45 years which is only 25%. This is consistent with the theory that states, pathologically along with increasing age, there will be an aging process that will result in the deterioration of salivary glands function as well as the disappearance of parenchymal glands which are being replaced by fatty and connective tissue. Other than that, atrophy of the intermediate duct cell lining reduces the amount of saliva production. [6,21,22]

Analysis of the correlation between types of medicines with clinical oral manifestations in patients with antihypertensive therapy showed that there was no correlation between the types of medicines with clinical oral manifestations in patients with antihypertensive therapy. It is due to the types of medicines that often cause manifestations clinical oral manifestations are ACEi (66.7%) and CCB (64.3%), whereas more than 50% of all types of antihypertensive medicines caused the oral manifestations. This is supported by previous research which states that various kinds of antihypertensive medicines often cause oral manifestations. [9,11,23]

The mechanism of CCB class medicines that cause oral manifestations is by preventing the action of calcium between cells so that it stimulates the proliferation of fibroblasts. When calcium influx in blood vessel muscles is inhibited, this condition will indirectly affect the salivary flow rate.[6,18] The mechanism of ACEi and ARB medicines is almost the same. ACEi medicines act by inhibiting angiotensin I to angiotensin II, while the ARB group blocks angiotensin II receptors so that there is a decrease in aldosterone and vasodilation secretion. This also indirectly affects the flow of saliva by changing its electrolyte fluid balance. The mechanism of Beta Blocker medicines works by blocking the sympathetic nervous system that inhibits the action of endogenous catecholamines at adrenergic receptors, thus affecting the salivary glands. Overall, the mechanism of action of antihypertensive medicines in causing oral manifestations is established as the consequence of its function in autonomic nerves which affects the salivary glands so that saliva is reduced and therefore results in oral manifestations.[5,6,24]

Analysis of the correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy showed that there was a correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy. Table 9 also shows that respondents who consumed more than one type of medicine will cause more oral manifestations (100%) than those who only consume one type of medicine (61.3%). This is supported by the statement of Tambuwun (2015) which stated that the synergistic effect of using a combination of two or three different types of antihypertensive medicines can increase the occurrence of oral manifestations.[9]

Analysis of the correlation between the duration of treatment with clinical oral manifestations in patients with antihypertensive therapy was performed using Fisher's exact test and showed that there was a correlation between the amount of medicine consumption with clinical oral manifestations in patients with antihypertensive therapy. Table 10 also shows that people who take antihypertensive medicines for more than one year cause more oral manifestations (80%) than those who take antihypertensive medicines for less than one year (16.7%). This is supported by research conducted by

Wotulo (2018) which states that the duration of medicine use greatly influences the decrease in salivary flow rate. Mechanically, longer use of antihypertensive medicines will cause pharmacodynamics of medicines that result in myocardial contractility and decreased heart rate. So the cardiac output and the volume of plasma decrease, and the rate of salivary flow also decreases. Decreased salivary production causes increased masticatory activity, thereby stimulating salivary production in some active salivary glands which increases and this can cause exacerbation and decreased ability to speak due to reduced lubrication function.[6,9,17]

CONCLUSION

Based on this research, it can be concluded that there is no correlation in both age and type of medicine consumed with clinical oral manifestations in patients with antihypertensive therapy and there is a correlation between the amount of medicine consumption and duration of treatment with clinical oral manifestations in patients with antihypertensive therapy.

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CONFLICT OF INTEREST

The authors report no conflict of interest.

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