THE EVALUATION OF INCREASED SERUM CREATININE DUE TO THE USE OF ACEI THERAPY ON HYPERTENSION PATIENTS IN UNDATA HOSPITAL, PALU, CENTRAL SULAWESI PROVINCE

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ABSTRACT

Objective: This study aims to determine the mean baseline value and the evaluation of serum creatinine in hypertensive patients after receiving angiotensin-converting enzyme inhibitor (ACEi) antihypertensive therapy for the first time in a span.

Methods: This study used a cross-sectional design with a prospective approach by carrying out laboratory tests of serum creatinine using the Jaffe method using the patient's blood at the beginning as the baseline value and a month after treated with (ACEi) antihypertensive therapy as the evaluation value. The results of this research were analyzed using the SPSS statistical paired test to observe the occurrence of increased serum creatinine as the aftereffect of ACEi antihypertensive treatment. The total of samples which met the inclusion and exclusion criteria was 30 patients.

Results: The findings showed an increase of serum creatinine value, where statistics displayed the significant value of **P below 0.05 with the mean baseline value of 0.98 and an average evaluation value of 1.14. When examined clinically, despite the increase of serum creatinine, the patient's kidney function is still within a normal range.

Conclusion: The study concluded that the increase of serum creatinine value can become one's indicators of decreasing kidney function.

Keywords: Angiotensin-converting enzyme inhibitor, Antihypertensive, Hypertension, Creatinine serum.

INTRODUCTION

Hypertension is defined as a continuous increase in arterial blood pressure. The blood pressure is the result of cardiac output multiplied with the total peripheral resistance. Hypertension is one of the most significant factors of cardiovascular disease. More than 90% of individuals suffer from essential hypertension and <10% undergo secondary hypertension which can be caused by a specific disease or drug use [1].

The prevalence of hypertension in Indonesia is based on the doctor's diagnosis. Or those who are currently taking medicine with the age of more than or equivalent to 18 years old is 8.8%. On the other hand, based on the populations' characteristics of age, the older the patient is, the more increase incidents of hypertension will occur, in which the ages of 18–24 years old are of 13.2%, 25–34 years old are of 20.1%, 35–44 are of 31.6%, 45–43 years old of 45.3%, 55–64 years old of 55.2%, 65–74 years old of 63.2%, and ages over 75 years amounted to 69% [2].

The use of angiotensin-converting enzyme inhibitor (ACEi) such as captopril, lisinopril, and angiotensin receptor blocker (ARB), for instance, valsartan, losartan, and calcium channel blockers (CCB) such as amlodipine and felodipine is the first-line agents for most hypertensive patients and can reduce the incidence of cardiovascular disease [1].

Based on JNC 8, the use of ACEi or ARB will usually increase the serum creatinine and can produce other metabolic effects such as hyperkalemia, although the increase in creatinine or potassium levels does not always need adjustments [3].

This study aims to determine the mean baseline value and the evaluation of serum creatinine in hypertensive patients after receiving ACEi antihypertensive therapy for the first time in a 1-month span.

METHODS

This research was conducted based on the approval of the code of ethics Number: 4809/UN 28.1.30/KL/2019 which was carried out prospectively using a cross-sectional study focusing on observational research (non-experimental). The data were collected on hypertensive patients in Undata Hospital Palu, who had their first time receiving ACEi therapy. They were over than 18 years of age and were willing to participate in the research aiming to investigate on the serum creatinine values. This was done by taking initial serum creatinine data based on the results of the reports' complete laboratory examinations on the patient's status during the therapy. The examination was conducted for a month concurrently with the ACEi therapy the patients have received. The data collection consisting of directly taking blood samples at Undata Hospital Palu.

Creatinine examination method

Kinetic test without deproteinization as adapted of the Jaffe method by the use of Erba XL 300 chemical analyzer. The principle is that creatinine forms an orange-red complex in a picrate base solution. The difference in absorbance in a certain time during conversion is proportional to the creatinine concentration in the sample.

Creatinine + Picric acid→Creatinine picrate complex

Data analysis

Data analysis was performed in a quantitative-descriptive technique. Descriptive analysis is done by describing the data obtained from medical records, including the demographic and clinical characteristics of patients and the profiles of drugs used during the treatment processes. Quantitative analysis was carried out on the results of serum creatinine laboratory values in hypertensive patients as an analyst of the relationship between the independent variables and the dependent

Table 1: The data of patients' age and gender for those treated with ACEi class therapy in Undata Hospital Palu

Data	Amount (n=30)	Percentage
Gender		
Male	16	53.33
Female	14	46.67
Age		
18–30	2	6.67
31–50	6	20
51–64	15	50
≥65	7	23.33

ACEi: Angiotensin-converting enzyme inhibitor

Table 2: Complications and comorbidities of patients treated with ACEi class therapy in Undata Hospital Palu

Complications and comorbidities	Amount of patients with complications (n=30)	Percentage
HHD	17	56.67
CAD	17	56.67
APS	8	26.67
CHF	6	20
DM Type II	4	13.33
OA	2	6.67
ADHF	1	3.33
Acute transdermal myocardial infarction	1	3.33
Coronary artery aneurysm	1	3.33
Diastolic dysfunction	1	3.33
Dyspepsia	1	3.33
CHF	1	3.33
Febris	1	3.33
Unspecified fever	1	3.33
ASD	1	3.33
Constipation	1	3.33
Vertigo	1	3.33
Bronchitis	1	3.33
Pharyngitis	1	3.33
ADHF	1	3.33

ADHF: Acute decompensated heart failure, HHD: Hypotension heart disease, CAD: Coronary artery disease, APS: Antiphospholipid antibody syndrome, CHF: Congestive heart failure, OA: Osteoarthritis, ASD: Autism spectrum disorder, ADHF: Acute decompensated heart failure, DM: Diabetes mellitus

variables with a statistical correlated t-test (paired test) for the incidence of increased serum creatinine values due to the use of ACEi drugs.

RESULTS

After collecting laboratory data on serum creatinine values before and after receiving ACEi drug therapy, it was obtained that there was an increase in the average value of serum creatinine on patients after receiving therapy for a month.

DISCUSSION

Based on the results of Table 1, the number of patients with a history of hypertension is a majority of men, though it was not much different from women. Men took the percentage of 53.33%, while women were 46.67%. This result is almost similar to a study conducted [4], in which the number of patients with hypertension between men and women is not significantly different, with the total sample of 29 people consisting of 15 (52%) women and 14 (48%) men. This study is also aligned with the research produced [5], where cases of hypertension are more common in men than women. The activity of plasma renin (prorenin and renin levels) in men is usually higher than women, which eventually affects the synthesis of AT-II in the angiotensin renin system. Testosterone can directly stimulate sodium reabsorption through the proximal tubule of the kidney. Androgen receptors localized to the renal proximal tubules can impact on the synthesis of the Renin-Angiotensin system component, thereby increasing the production of AT-II in the kidneys and hence affecting blood pressure.

Findings also discovered that the most dominant age group was of the 51–64 years old group consisting of 15 patients. A similar study carried out [6] resulted that the majority of patients suffering from hypertension was of the age group of 56–61 years old consisting of 51 people (55.44%), followed by the age group of 46–55 years old consisting of 23 patients (25%), then the age group of 36–45 years old consisting of 10 patients (10.87%), continued by the age group of 26–35 years old consisting of 5 patients (5.43%), followed by those of the age group of 18–25 years old consisting of 3 patients (3.26%). Hypertension is a multifactorial disorder caused by various factors. As one's age added, so would the blood pressure level. After the age of 45 years old, the artery walls would experience thickening due to the accumulation of collagen in the muscle layer. As a result, the blood vessels would gradually narrow and became stiff. Systolic blood pressure would then increase due to the decreasing flexibility of large blood vessels [7].

As shown on Table 2, the results of the study showed the most complications and comorbidities of hypertensive patients in Undata Hospital, Palu, namely HHD and CAD, with the same amount of patients, each consisting of 17 patients (56.67%). Uncontrolled hypertension can cause complications of other diseases. Hypertension has a strong correlation with one's incidence of cardiovascular morbidity and mortality.

The occurrence of hypertension may lead to the risk of stroke, myocardial infarction, angina, heart failure, kidney failure, and even premature deaths caused directly by increased blood pressure levels. Blood pressure levels ranging from 115 mm Hg systolic and/or 75 mmHg diastolic as a risk of cardiovascular disease and it multiplies with each increase of 20 mmHg systolic and/or 10 mm Hg diastolic. Patients with blood pressure in the position of prehypertension also have a risk of suffering from cardiovascular disorders [8].

The results of the study displayed on Table 3 found the combination of two antihypertensives had a higher percentage. A therapy combining two antihypertensives agents is needed for most hypertensive patients to reach the targeted blood pressure levels [8]. The class of drugs used in a single therapy is ACEi, then in a combination of two antihypertensives therapy mostly used the combination of ACEi and CCB. This study is in line with the research done [9], where antihypertensive pharmacological management is mostly given in combination and the drug class, which is most widely used, is ACEi. For the treatments of 22 patients in combining two antihypertensive drugs, the most used drugs are ACEi and CCB. The combination treatments are given by JNC 8, where the combination is done using a combination from different classes of drugs.

That the combination of ACEi/ARB with CCB is much better to be used. ACEi/ARB is included in the renin-angiotensin-aldosterone system (RAAS) and the antihypertensive group of CCB is sensitive toward RAAS, which can help in increasing renin levels, and hence would increase the antihypertensive effects of ACEi/ARB [10]. In addition to that, this combination can also be given to patients with other complications and can protect the kidneys of patients with chronic kidney failure.

Based on the research results displayed in Table 4, the ACEi-class drug most commonly prescribed to patients is ramipril, where there were 30 patients with the details of those who received ramipril was 21 patients (70%), lisinopril was 8 patients (26.67%), and imidapril was 1 patient (3.33%). Ramipril is most widely prescribed as when compared with other ACEi drugs, it is a drug with the least chronic heart failure effects [11].

As displayed on Table 5, the results showed that after a month, patients who were treated with ACEi therapy experienced changes in their

Table 3: Distribution of various medicines for antihypertensives patients with hypertension at RSUD Undata Palu

Therapeutic regimen	Class	Medicines	Amount (n=30)	Percentage
Single	ACEi	Ramipril	4	13.33
		Imidapril	1	3.33
		Lisinopril	3	10
Combination of 2	ACEi + Diuretic	Lisinopril + Furosemide	1	3.33
		Ramipril + Furosemide	6	20
	ACEi + CCB	Ramipril + Amlodipine	7	23.33
		Lisinopril + Amlodipine	4	13.33
Combination of 3	ACEi + Diuretic + CCB	Ramipril + Furosemide + Amlodipine	4	13.33

ACEi: Angiotensin-converting enzyme inhibitor, CCB: Calcium channel blocker

Table 4: Treatment therapy given to hypertensive patients at RSUD Undata Palu

Class of medicines	Medicines	Number of patients (n=30)	Percentage
ACEi	Ramipril	21	70
	Lisinopril	8	26.67
	Imidapril	1	3.33

ACEi: Angiotensin-converting enzyme inhibitor

Table 5: Scores of mean baseline and evaluation of serum creatinine

Evaluation parameters	Mean (n=30)		Average deviation SCr	p-value
	Baseline	Evaluation		
Serum creatinine	0.98 mg/dl	1.14 mg/dl	0.147	0.000

*p<0.05= significantly different

serum creatinine values. Based on the results of the statistical test paired sample t-test, there was a significant difference between the baseline value and the serum creatinine evaluation of patients who had been undergoing ACEi therapy for a month. The significance value is *p<0.05 which indicates a significant difference between the baseline value and serum creatinine evaluation based on statistical results. When reviewed clinically, an increase in the value of serum creatinine can affect the patient's kidney function, where an increase in the value of serum creatinine can result in a decrease in the patient's kidney function. The results of this study are aligned to studies conducted [12], who showed that there were differences in the values of after and before implementing captopril and ramipril therapies against serum creatinine values where *p=0.000 stating that there was a significant relationship toward the values of serum creatinine after the treatment within 1 month.

The treatment of ACEi can reduce the GFR values due to the inhibition of angiotensin II vasoconstriction in efferent arterioles. ACEi administration can increase the concentration of creatinine, but the increased level is low (below 1 mg/dl), so it does not guarantee as a therapy replacement. Discontinuation of therapy or decrease in dosage is done if the increased level is high enough [8]. Indonesian cardiologists association stated that there is an urgent need to reexamine the patient's kidney function 1–2 weeks after having the ACEi therapy. A checkup on the serum creatinine values must immediately be conducted to identify any signs of abnormalities before serious complications occur [13].

That only 10% of patients treated with ACEi received recommendations to monitor their kidney functions, and only 20% of patients experienced an increase in serum creatinine of 30% or more which stopped their ACEi therapy [14].

CONCLUSION

The result of the evaluation of serum creatinine increase due to the implementation of ACEi therapy on hypertensive patients in RSUD Undata Palu can be concluded that the mean value obtained at the initial examination (baseline) is 0.98 and the mean value of the post-test (evaluation) is 1.14. Therefore, the treatment of antihypertensive ACEi groups toward the incidence of an increase in serum creatinine gives a significant value, which is 0.000. At last, it can be concluded that the increase in serum creatinine value can become one's indicators of decreasing kidney function.

AUTHORS' CONTRIBUTIONS

Amelia Rumi: Concept, design, interpretation of data, drafting a final report, revising of article, and approval of the article to be published. Nurhalima: Concept, design, collection of data, interpretation of data, drafting a final report, and revising of the article.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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