The Effects of Subtotal Nephrectomy Method on Urea and Creatinine Serum in Hypertension Animal Model

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Abstract. Chronic kidney failure is a disease that causes a decrease in kidney function in cleaning the blood of toxic materials, which causes accumulation of metabolic waste in the blood. Renal failure can cause severe azotemia and uremia. Subtotal nephrectomy is a method to induce hypertension and renal failure. This research is a laboratory experiment study using serum from 30 rats that have been treated. The positive control group was (one kidney was removed and giving 3% NaCl solution), 5/6 subtotal nephrectomy group (kidney was removed 5/6), the negative control group was (Shame operated). Urea and Creatinine levels will be checked using spectrophotometry. The data analysis used a one way ANOVA test. The average urea level (mg/dl) in the negative control group was 20.39 ± 2.59, while the positive control group obtained an average of 31.78 ± 6.15, and the 5/6 nephrectomy group obtained an average urea level of 33.17 ± 7.34. For creatinine levels (mg/dl), the mean of the negative control group was 1.12 ± 0.41; the positive control group was 1.64 ± 0.24 and in the 5/6 nephrectomy group 1.63 ± 0.17. A P-value of urea and creatinine levels was $p < 0.05$, which means that there are differences in urea and creatinine levels in experimental animal models of hypertension with the 5/6 sub nephrectomy method. In conclusion, there are significant differences in urea and serum creatinine between sub nephrectomy method and control groups.

Keywords: Hypertension · Urea · Creatinine

1 Introduction

The prevalence of blood pressure is high even though the awareness and therapy of the disease are still very deficient [1]. Blood pressure is affected by several factors including neural, vascular, and hormonal factors [2]. Neural factors such as stress, sympathetic nervous activity, and diurnal variations vascular factors such as endothelial function, and hormonal factors are influenced by the Renin Angiotensin Aldosterone (RAA) system. These three factors can affect blood pressure [3]. Stress that occurs in the hypertensive patient can be followed by increased cortisol levels [4]. Kidney disease, including renal

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Table 1. Ureum and Creatinine Level

	Average Value		
	Negative Control	**Positive Control**	**5/6 Subtotal Nephrectomy**
Ureum Level	20.39 ± 2.59	31.78 ± 6.15	33.17 ± 7.34
Creatinine Level	1,12 ± 0.41	1,64 ± 0.24	1,63 ± 0.17

arterial stenosis (RAS), is a major cause of secondary hypertension. Chronic kidney failure is a disease that causes a decrease in kidney function in cleaning the blood of toxic materials, which causes the accumulation of metabolic waste in the blood [5]. Renal failure can cause severe azotemia and uremia. Azotemia is an abnormal increase in residual nitrogenous materials in the blood such as urea, uric acid, and creatinine [6].

2 Method

The research was a laboratory experimental study using serum from 30 rats that have been treated for 30 days. The subjects in this study use male Wistar rats (Rattus norvegicus), aged 2–3 months with a weight of 100–200 g. The number of rats used as subjects was in accordance with the World Health Organization (WHO) criteria, which is a minimum of ten (10) rats based on Federer's formula. The groups consist of 3 groups: group 1 was sham-operated group (same operation without kidney removal) with ketamine anesthesia, group 2 was a control group/hypertension model (surgery by removing 1 kidney and giving 3% NaCl solution) with ketamine anesthesia, and group 3 was the 5/6 nephrectomy treatment group (surgery with 5/6 kidney removal) with ketamine anesthesia.

3 Result and Discussion

The research showed that there were differences in the levels of urea and creatinine in each group. The results of the examination of urea levels and creatinine levels for each group are as follows (Fig. 1):

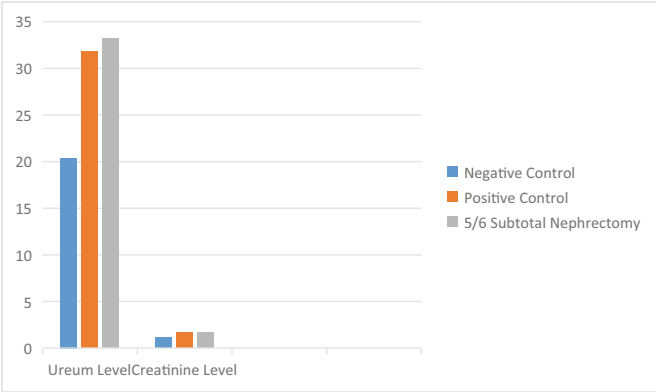

Fig. 1. Ureum and Creatinine Level

4 Discussion

4.1 5/6 Subtotal Nephrectomy

The 5/6 subtotal nephrectomy model was obtained by performing a unilateral nephrectomy followed by a nephrectomy of 2/3 of the kidney on the other side, resulting in a total reduction of 5/6 of the kidney. Under these conditions, the remaining healthy nephrons will experience a prolonged increase in their filtration rate, failing of their excretory function due to fibrosis and loss of structure of healthy nephrons [7]. Furthermore, experimental animals will experience glomerular and systemic hypertension syndrome [8], proteinuria and matrix expansion [9], and will experience glomerulosclerosis and interstitial fibrosis in nephrons that were previously still intact and healthy [10].

4.2 Urea

Examination of urea levels in the blood determines the presence of abnormalities or damage to kidney function. Urea is the major excretory product of protein metabolism. After being synthesized in the liver, urea is carried into the blood to the kidneys and filtered by the glomerulus, urea is reabsorbed in the proximal tubule. Decreased kidney function can cause an increase in urea levels because the excretion of urea in the urine decreases [6]. The results of the measurement of urea levels can be seen in Table 1. In the negative control group, the average urea level was 20.39 ± 2.59 mg/dl. In contrast in the positive control group, the average was 31.78 ± 6.15 mg/dl, and the 5/6 nephrectomy group obtained an average urea level of 33.17 ± 7.34 mg/dl.

The normal level of urea in Wistar rats is 15–21 mg/dl. The urea level in the positive control group and the 5/6 subtotal nephrectomy group experienced an increase, while the average urea level in the negative control group was normal. It happened because in the positive control group and the 5/6 subtotal nephrectomy group, the rat kidney was damaged. Meanwhile in the negative control group the urea level was normal because the rats were not treated, so the kidneys were not damaged. These results were then

analyzed to obtain a significant value of 0.000 where $p < 0.05$. Urea will not make failure in renal except in high concentration [11].

The increase in blood urea can be caused by several conditions, including the increased tissue protein catabolism accompanied by a negative nitrogen balance, the excessive breakdown of blood proteins, the reduced urea excretion due to decreased glomerular filtration rate, and the influence of toxic chemicals [12].

4.3 Creatinine

Creatinine is a product of the body's metabolism which is constantly produced, filtered by the kidneys, not reabsorbed, and secreted by the proximal tubule [13]. Metabolically, creatinine is an inactive component that then diffuses into the plasma and is excreted in the urine. Increased levels of creatinine in blood and urine can describe the glomerular filtration rate [12]. In this study, the results of measuring creatinine levels are presented in Table 1. The table shows that the average creatinine level in the negative control is 1.12mg/dl; the positive control group is 1.64 mg/dl, and the 5/6 nephrectomy group is 1.63 mg/dl. This result shows that in the positive control and 5/6 nephrectomy group, creatinine levels increased where the average value of Wistar rats was 0.578–1.128 mg/dl. The results of the analysis obtained a significant value of 0.001 where $p < 0.05$.

Factors that can affect creatinine levels are gender, hunger conditions, and the size of muscle tissue. The increase in creatinine levels in the blood can also be caused by several conditions, including tissue hypoxia, decreased glomerular filtration rate [14], certain metabolic diseases, toxic chemicals, temperature, and aging [15]. Several studies have shown different creatinine levels in Wistar rats based on the treatment given.

5 Conclusion

The research obtained a significant value of urea and creatinine levels $p < 0.05$, which means that there are differences in urea and creatinine levels in experimental animal models of hypertension with the 5/6 subtotal nephrectomy method.

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