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The Effect of Oral N-Acetyl Cysteine Administration on Acute Kidney Injury Patients at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

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ABSTRACT

Background: Acute kidney injury (AKI) is a clinical condition characterized by a rapid decline in kidney function that includes structural damage (injury) or malfunction (impairment). AKI is a common complication that occurs in 5-10% of patients due to various underlying etiologies. One of the underlying pathophysiology of AKI is the role of discharge reactive oxygen species (ROS), which causes injury to kidney cells. From various studies, it has been reported that N-acetylcysteine (NAC) has anti-inflammatory and antioxidant effects and has an effect on reducing serum creatinine values. **Methods:** This research is an open randomized clinical trial without control involving 30 patients at Dr. Mohammad Hoesin General Hospital, Palembang, who were all given intervention in the form of NAC 1200 mg/day, starting in September – October 2023. This study aimed to determine the role of NAC in reducing serum creatinine values in patients with acute kidney injury at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. Data analysis was carried out using SPSS 21 univariate and bivariate. **Results:** From the research results, it was found that the average age of patients was 53.9 years, involving 21 males (70%, N=30) and 9 females (30%, N=30). The most common causes were prerenal and then renal (53.3% and 46.7%). The initial serum creatinine level was found to be 2.12 ± 0.79 mg/dL (n = 30 samples), and after administration of the intervention, the mean serum creatinine level was 1.28 ± 0.63 mg/dL (n = 30 samples). By using a paired t-test, there was a decrease in serum creatinine levels significant (p=0,012). **Conclusion:** NAC administration to patients with acute kidney injury of pre-renal or post-renal causes has a statistical effect on reducing serum creatinine values in patients with acute kidney injury at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

1. Introduction

Acute kidney injury (AKI) is a common complication that can occur in 5-10% of critically ill patients due to various underlying etiologies characterized by a sudden decrease in kidney function. Renal function assessment modalities include increasing serum creatinine and decreasing production urine output (UO). This modality is also used as the basis for determining the severity of AKI globally. The kidneys play a role in maintaining the body's homeostasis.

Decreased kidney function causes homeostasis failure in AKI patients, increasing mortality and morbidity, and is associated with high hospital care costs.¹⁻⁴

So far, the pathophysiology that often underlies AKI in hospitals is ischemia, mostly caused by transplant surgery, prolonged resuscitation, shock, and sepsis. Ischemia is described as a disruption in the supply of blood and nutrients to kidney cells, causing tissue hypoxia and cellular injury. Restoration of blood flow will minimize hypoxic insults, but excessive

reoxygenation exacerbates tissue damage with an intense inflammatory response, including the production of reactive oxygen species (ROS), reactive nitrogen species (RNS), superoxide anion (O_2^-), and hydroxyl radicals (OH). Both ROS and RNS reduce antioxidant capacity and cause injury to kidney cells by the processes of protein oxidation, lipid peroxidation, and DNA damage. This imbalance results in cell dysfunction, which, in severe cases, can progress to cell death through apoptosis or necrosis.⁵⁻⁹

N-acetylcysteine (NAC) is an antioxidant that can regenerate glutathione and is mainly used for acetaminophen overdose. However, N-acetylcysteine (NAC) has also been tested in the prevention of acute kidney injury (AKI), such as postoperative AKI and contrast-induced AKI (CI-AKI) with mixed results, mainly using changes in serum creatinine levels before and after NAC treatment as a result. Nevertheless, considering its low cost and lack of side effects, NAC has been recommended for use by the guidelines of kidney disease improvement global outcomes (KDIGO) in the context of CI-AKI, although NAC is generally recommended for patients with chronic kidney disease (CKD), with eGFR <60 ml/min/ 1.73 m² in clinical practice, supporting evidence is insufficient. A recent systematic review from the Agency for Healthcare Research and Quality (AHRQ) also supports its use for the prevention of AKI or preservation of residual kidney function. Therefore, a large number of studies are ongoing, and the results of these large trials can quantitatively prove the effectiveness of NAC in preventing AKI.¹⁰⁻¹³ This study aimed to determine the role of NAC in reducing serum creatinine values in patients with acute kidney injury at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

2. Methods

This research is an experimental study through an open, randomized clinical trial without control. This research was conducted in the inpatient installation and internal medicine polyclinic at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia, from

September 2023 - October 2023. A total of 30 research subjects participated in this study, where the research subjects met the inclusion criteria. The inclusion criteria for this study were all patients with a diagnosis of acute kidney injury based on KDIGO 2012, and the patient was willing to take part in the study by signing informed consent. This study has received approval from the medical and health research ethics committee of Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia (No.DP.04.03/D/XVIII.6.8/ETIK/168/2023).

N-acetylcysteine is given as 600mg orally every 12 hours for 48 hours. Acute kidney injury is a sudden decrease in kidney function as assessed based on KDIGO 2012, where serum creatinine levels are assessed as a marker of acute kidney injury. The data obtained in this research is presented in the form of tables, diagrams, and narratives. Data is processed with a program called statistical package for social science (SPSS) version 25. The statistical analysis design used is univariate analysis and bivariate analysis. Univariate analysis was carried out to obtain an overview of the research variables. The results of the analysis are presented in the form of tables and narratives. Bivariate analysis aims to determine the relationship between n-acetylcysteine administration and serum creatinine in AKI patients. The analysis will be carried out using paired t-tests. After the analysis is carried out, a p-value will be obtained with a degree of significance $\alpha = 0.05$. The p-value is then compared with the α value. If the value of $p \leq \alpha$ (p-value ≤ 0.05), then the hypothesis is accepted. If the p-value $> \alpha$ (p-value > 0.05), then the hypothesis is rejected. Apart from that, the correlation coefficient (r) is also looked at to see how strong the relationship is between the research variables.

3. Results

Table 1 describes the general characteristics of patients with acute renal failure in the internal medicine department of Dr. Mohammad Hoesin General Hospital, Palembang.

Table 1. General characteristics of research subjects.

	Total (n=30)	Percentage (%)
Age	53,9 (35 – 70)	
Gender		
Male	21	70,0
Female	9	30,0
Etiology		
Pre-renal	16	53,3
Renal	14	46,7

In this study, it was found that the average age of patients in the research sample was 53.9 (35 - 70) years. The research subjects were dominated by 21 males (70%), while 9 people (30%) were females. Based on the cause, the etiology of acute kidney injury was prerenal (n = 16, 53.3%) more often than renal (n = 14, 46.7%).

The Shapiro-Wilk normality test was carried out to see whether the research data was normally distributed. A p-value > 0.05 was obtained for all data, so the data was concluded to be normally distributed. Analysis was carried out to assess the relationship

between mean serum creatinine levels before and after administration of N-Acetylcysteine. The initial mean serum creatinine level was 2.12 ± 0.79 mg/dL (n = 30 samples). After administering the intervention, the mean serum creatinine level was 1.28 ± 0.63 mg/dL (n = 30 samples). Test carried out paired *t-test* in both groups to assess whether there was a statistically significant decrease in serum creatinine levels. Based on the tests carried out, the p-value = 0.012 was obtained. The p-value <0.05 indicates that the decrease is statistically significant. The test results are shown in Table 2.

Table 2. Relationship between serum creatinine levels before and after administration of N-Acetylcysteine.

	Administration of N-Acetylcysteine		P
	Before (mg/dL)	After (mg/dL)	
Serum creatinine levels	2,12 ± 0,79	1,28 ± 0,63	0,012

4. Discussion

The results of the study found that there was a decrease in the initial mean serum creatinine level (2.12 ± 0.79 mg/dL) to the final mean serum creatinine level (1.28 ± 0.63 mg/dL) after oral administration of N-acetylcysteine. This mean was found to be statistically significant. N-acetylcysteine has been used to reduce the risk of acute kidney injury in patients who experience nephropathy due to contrast use. N-acetylcysteine can reduce the risk of contrast-induced nephropathy by reducing serum creatinine, although it is not associated with the need for dialysis and mortality in patients. However, several studies did not find a relationship between the use of N-acetylcysteine and acute kidney injuries due to the risk of bias and heterogeneity in the study samples.¹⁵

The use of N-acetylcysteine in patients receiving intravenous contrast is not associated with acute renal impairment, mortality, or length of hospital stay.¹⁴⁻¹⁶ A systematic review conducted found a statistically significant reduction in serum creatinine with the non-Jaffe method (3.24 mmol/l [95% CI, 6.29 to 0.18]; P = 0.04) compared with the Jaffe method (0.51 mmol/l [95% CI, 7.56 to 6.53]; P = 0.89). This decrease occurred after administering N-acetylcysteine to the patient. The greater decrease in serum creatinine with the i.v. NAC (31.10 mmol/l [95% CI, 58.37 to 3.83]; P = 0.03) compared with oral NAC (2.5 mmol/l [95% CI, 5.32 to 0, 32] P = 0.08). This systematic review involved 6 studies, 4 of which examined serum creatinine 48 hours after the last NAC administration.¹⁷⁻²⁰

There were several limitations found in this research. The first thing is that there is no comparison group for the intervention carried out, so it cannot assess the greater effectiveness of the use of N-acetylcysteine in patients with acute kidney injury. The absence of randomization is related to the research method used, so it has no effect on the research results. However, to obtain statistically stronger results, randomization can reduce the risk of bias in the final results of the study. Various other variables can also be added in similar types of research, for example, related to the patient's ultrasound results, the patient's urine production, or autoimmune diseases that manifest in the kidneys. Additional research variables will contribute to more results. Finally, this research can be carried out using a larger scale and a longer observation time so that the data obtained can be a picture of the population in general.

5. Conclusion

There is a relationship between the effect of oral N-acetylcysteine administration and decreased levels of serum creatinine in patients with acute kidney disease at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

6. References

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