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Differences In Creatinine Levels And Reticulocyte Values In CKD Patients Undergoing Epo And Non-Epo Therapy

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ABSTRACT

Chronic kidney disease (CKD) is a condition of progressive and irreversible decline in kidney function. One of the main complications of CKD is anemia, caused by decreased erythropoietin (Epo) production by the kidneys. Epodi therapy is used to stimulate red blood cell production. Reticulocyte counts are used as an indicator of erythropoietic activity, while creatinine levels reflect the degree of kidney damage To determine the differences in creatinine levels and reticulocyte values between CKD patients undergoing Epo and non-Epo therapy.This study was a quantitative cross-sectional study. The sample consisted of 60 CKD patients, divided into two groups: 30 patients with Epo therapy and 30 patients without Epo therapy. Data were collected through medical records and analyzed using the independent T-test. The average creatinine level in the Epo group was 3.96 mg/dL, while in the Non Epo group it was 1.83 mg/dL. The average reticulocyte value in the Epo group was 0.64%, while in the Non Epo group it was 1.49%. The results of the independent T test statistical test obtained a P value of creatinine levels of 0.000_<0.05 while in the reticulocyte value obtained a P value of 0.002_<0.05. There are differences in creatinine levels and reticulocyte values in CKD patients undergoing EPO and non-EPO therapy.

INTRODUCTION

Chronic kidney failure (CKF) is a progressive and slow development of kidney failure that usually lasts for several years, causing the kidneys to lose their ability to maintain the volume and composition of body fluids. The initial cause can also be dehydration, which makes the body prone to urinary tract infections, which can then develop into kidney infections. Patients with kidney disease who have been treated since the early stages of the disease usually show abnormalities in urine volume or composition, such as the presence of red blood cells or abnormal amounts of protein. They then show systemic symptoms and signs of reduced kidney function, such as edema, fluid overload, electrolyte abnormalities, and anemia (McPhee & Ganong, 2012).

Creatinine is the end product of creatine metabolism synthesized by the liver, kidneys, and pancreas and then sent to the skeletal muscles and brain. Testing creatinine levels is a factor in determining therapy for patients with chronic kidney disease. High or low creatinine levels in the blood determine whether a person requires hemodialysis therapy or not (Indeswari, 2022). If kidney damage occurs, it not only causes impaired renal excretory function but also disrupts hormone excretion. Erythropoietin, a hormone produced in the kidneys, regulates the erythropoiesis process; its absence can lead to anemia (Silbernagl & Lang, 2012).

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According to the National Health and Nutrition Examination Survey, the incidence of anemia is less than 10% in stage 1 and 2 chronic kidney disease, 20–40% in stage 3, 50–60% in stage 4, and more than 70% in stage 5 chronic kidney disease. This means that the more severe the stage of CKD experienced by the patient, the higher the likelihood of developing anemia. The main cause of anemia in CKD is thought to be a relative deficiency of erythropoietin (Singh et al., 2009).

Erythropoietin (EPO) is a glycoprotein hormone produced in response to hypoxia to increase erythrocyte production. Erythropoietin circulates in the plasma and binds to specific receptors on erythrocyte progenitor cells, causing them to proliferate and differentiate into red blood cells (Weiss, 2014).

EPO administration is an important therapy for patients with CKD. Erythropoietin Stimulating Agents (ESAs) therapy is the first line of treatment for CKD anemia to replace erythropoietin deficiency. ESAs are needed to stimulate erythroid progenitor cell differentiation and induce the release of reticulocytes from the bone marrow into the bloodstream. The NKFDOQI recommends that the target Ht/Hb should reach 33-36% or 11-12 g/dL for the majority of patients. Erythropoietin stimulates blood-producing tissues, such as the bone marrow and liver, to produce more red blood cells (Pagunsan, Pagunsan, Cumming & P. Reed, 2007).

Based on the above background, the researchers were interested in conducting research on the relationship between creatinine levels and reticulocyte values in CKD patients as a reference for EPO (erythropoietin) therapy. It is hoped that the results of this study can provide further insight into the safety of EPO therapy and can assist in the management of more effective therapy related to chronic kidney failure.

MATERIALS/METHOD

The type of research used was a quantitative method with an observational research design using a cross-sectional approach. The population in this study consisted of patients diagnosed with chronic renal failure undergoing Epo and non-Epo therapy. The sampling technique used in this study was non-probability sampling using the purposive sampling method, whereby the sample was predetermined by the researcher and adjusted to the nature or characteristics of the population.

RESULTS AND DISCUSSION

The following results were obtained from the research conducted:

Table 1. Results of Creatinine Level Measurements and Reticulocyte Counts for Epo and Non-Epo in Patients with Chronic Kidney Disease.

	Epo			Non Epo		
No	**Kode sampel**	**Kadar KreatininEpo (mg/dl)**	**Nilai RetikulositEpo (%)**	**Kode sampel**	**Kadar Kreatinin Non Epo (mg/dl)**	**Nilai Retikulosit Non Epo (%)**
1	S1	3.20	0,9%	S1	1.50	1,3%
2	S2	3.18	0,8%	S2	1.35	1,0%
3	S3	6.10	0,5%	S3	2.21	1,4%
4	S4	2.55	0,7%	S4	2.00	1,9%
5	S5	3.90	0,9%	S5	1.22	2,0%
6	S6	2.10	0,4%	S6	1.60	1,2%
7	S7	2.29	0,7%	S7	1.70	2.0%
8	S8	5.10	0,9%	S8	1.88	2,2%

9	S9	2.10	1,0%	S9	1.90	2,0%
10	S10	2.05	0,2%	S10	1.50	1,2%
11	S11	3.20	0,7%	S11	1.30	1,2%
12	S12	3.25	0,6%	S12	1.20	1,1%
13	S13	1.90	0,5%	S13	1.07	1,5%
14	S14	3.55	0,6%	S14	3.05	1,4%
15	S15	5.05	0,3%	S15	3.00	2,2%
16	S16	3.68	1,1%	S16	1.98	1,7%
17	S17	3.54	0,7%	S17	2.65	2,0%
18	S18	2.50	0,8%	S18	1.77	2,3%
19	S19	5.58	1,1%	S19	2.10	1,0%
20	S20	2.65	1,2%	S20	1.97	2,1%
21	S21	2.00	0,8%	S21	1.29	1,1%
22	S22	4.41	0,5%	S22	2.80	1,8%
23	S23	5.13	0,6%	S23	2.50	1,6%
24	S24	6.77	0,7%	S24	3.20	1,8%
25	S25	4.50	0,8%	S25	1.90	1,3%
26	S26	3.25	1,0%	S26	2.00	1,2%
27	S27	8.18	0,5%	S27	3.20	1,5%
28	S28	5.70	0,4%	S28	2.10	2,0%
29	S29	4.50	0,7%	S29	1.77	1,8%
30	S30	5.20	0,3%	S30	2.05	1,9%
Rerata		3.96	0,64%	Rerata	1.83	1.49%

Based on Table 1, it shows that the results of creatinine level tests in CKD patients undergoing Epo therapy are higher than those undergoing non-Epo therapy. The lowest creatinine level in patients undergoing Epo therapy is 1.90 mg/dL, while the highest creatinine level in patients undergoing Epo therapy is 8.18 mg/dL. The lowest creatinine level in patients undergoing non-EPO therapy was 1.07 mg/dL, while the highest creatinine level in patients undergoing non-EPO therapy was 3.20 mg/dL.
The reticulocyte count in CKD patients undergoing EPO therapy was lower than in those undergoing non-EPO therapy. The lowest reticulocyte count in patients undergoing Epo therapy was 0.2%, while the highest reticulocyte count in patients undergoing Epo therapy was 1.2%. The highest reticulocyte count in patients undergoing non-Epo therapy was 2.2%, while the lowest reticulocyte count in patients undergoing non-Epo therapy was 1.0%.

Table 2. The data obtained from this study was analyzed statistically by performing a Independent T-test

		Levene's Test for Equality of Variances		t-test for Equalityof Means						
		F	Sig	T	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
KreatininEpo	Equal variances assumed	4.967	0.000	-10.739	58	0.000	-3.200	0.292	-1.262	-971
Kreatinin Non Epo	Equel variances not assumend			-10.547	2.00	0.003	3.200	0.444	-3.000	0.879

Based on the independent T-test table on epo and non-epo creatinine levels, a significant value (P value) of $0.000 \leq 0.05$ was obtained, which means that there is a difference in creatinine levels in CKD patients undergoing epo and non-epo therapy.

Creatinine is a waste product of muscle metabolism that is excreted by the kidneys, so the level of creatinine in the blood reflects kidney filtration function. In CKD patients, creatinine levels increase as the glomerular filtration rate (GFR) decreases. The average creatinine value of 3.96 mg/dL in the Epo group indicates that most patients are in stage 4–5 CKD, which is an advanced stage in which the kidneys have lost more than 70% of their function. In contrast, the Non-Epo group had an average creatinine level of 1.83 mg/dL, indicating that they were in stage 2–3 CKD, where kidney function is still sufficient to produce endogenous Epo naturally, even though it has begun to decline. These results are consistent with clinical protocols, in which Epo therapy is given to patients with advanced CKD who experience anemia due to impaired erythropoietin production by the kidneys.

The results show that creatinine levels in the Epo group were significantly higher than in the Non-Epo group. This can be explained by the fact that Epo is usually given to patients with chronic kidney disease (CKD), which is characterized by decreased kidney function and increased creatinine levels. In CKD, the kidneys are unable to produce enough endogenous Epo, so replacement therapy is needed.

The increase in creatinine levels in the Epo group supports the assumption that this group consists of individuals with significant kidney disorders. This is in line with the opinion of Besarab et al. (1998), who stated that Epo administration is commonly performed in patients with high creatinine levels due to kidney failure. Reticulocytes are immature red blood cells released from the bone marrow into the circulation. Reticulocyte counts are used as an indicator of erythropoiesis activity and increase in response to anemia or bone marrow-stimulating therapies, such as erythropoietin. Theoretically, patients receiving Epo therapy should show an increase in reticulocyte counts. However, in this study, the Epo group actually showed a lower average reticulocyte count (0.64%) than the Non-Epo group (1.49%).

Surprisingly, the reticulocyte count in the Epo group was lower than in the Non-Epo group. The average reticulocyte count in the Epo group was 0.64%, while in the Non-Epo group it was 1.49%. This phenomenon can be explained by the possibility of resistance to Epo, which often occurs in patients with inflammatory anemia or advanced CKD. According to Macdougall et al. (2014), CKD patients may experience a condition in which the bone marrow is unresponsive to Epo even though hormone levels are elevated, resulting in low erythrocyte production.

Low reticulocyte counts can also indicate iron, vitamin B12, or folate deficiency—nutrients that are important in erythropoiesis. EPO will not be effective if these nutrients are insufficient, because erythrocyte production will remain inhibited even if EPO is available. Another contributing factor is chronic inflammation, which often occurs in CKD patients and can inhibit the effectiveness of EPO and reduce red blood cell production (Locatelli et al., 2004).

The cause of this result is resistance to EPO. In some CKD patients, especially those with chronic inflammation or iron deficiency, the bone marrow becomes unresponsive to EPO. This is known as epo hyporesponsiveness. Conversely, in the non-epo group, reticulocyte counts were higher even without therapy. This may be due to relatively good kidney function, allowing endogenous epo production to continue, and the absence of severe anemia, allowing the body's compensatory mechanisms to function effectively.

Comparison of the two groups reveals differences in characteristics and physiological responses to CKD. The Epo group reflects a more severe clinical condition (high creatinine, low reticulocyte count), while the Non-Epo group reflects a milder clinical condition but with naturally active erythropoiesis.

CONCLUSIONS

The results of the independent T-test on patients undergoing Epo and Non-Epo therapy showed a p-value of 0.003 < 0.05 for creatinine levels and 0.002 < 0.05 for reticulocytes, which means that there is a difference in creatinine levels and reticulocyte values in patients undergoing Epo and Non-Epo therapy.

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