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Research Article

THE EFFECT OF ERYTHROPOIETIN DOSE PHASE OF CORRECTION AS DRUG-RELATED PROBLEMS TO TARGET LEVEL OF HEMOGLOBIN IN REGULAR HEMODIALYSIS PATIENTS

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ABSTRACT

Objectives: This research aims to know the effect of drug-related problems (DRPs)-related doses against the target hemoglobin levels in hemodialysis (HD) patients in the regular phase of the correction given the therapy of erythropoietin on H. Adam Malik Medan.

Methods: This research was by the cross-sectional, prospective method, using DRP - Registration Form V7.0 (PCNE) against 50 patients. The data were analyzed statistically using Chi-square test, paired t-test sample, and independent t-test, SPSS version 17.

Results: The target hemoglobin not reaching 30 patients (60%), the level of hemoglobin target exceeded target 1 of the patients (2%). Based on the results of the test t, the value of p=0.038<0.05, then there is a difference in the level of hemoglobin after providing significant erythropoietin therapy between doses and less excess. Test the level of hemoglobin of erythropoietin therapy before and after using a test sample. Paired t-test based on the results, obtained significant value is 0.05, then 0.015< increased hemoglobin level after statistics are given significant therapy of erythropoietin.

Conclusion: The results of this study indicate that there is an effect of DRPs related to excessive dosage; less dose to target hemoglobin level with significant value, so DRPs-associated dose affect the target hemoglobin level.

Keywords: Anemia, Erythropoietin, Drug-related problems, Hemoglobin, Hemodialysis.

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INTRODUCTION

Chronic kidney disease (CKD) is a process of pathological changes in renal function and structure, resulting in a progressive decline in renal function and generally ending with renal failure [1]. According to the World Health Organization, globally, over 500 million people have CKD, approximately 1.5 million people have to live by hemodialysis (HD) [2].

HD is a process used in patients with terminal stage renal disease that requires long-term therapy or permanent therapy [3]. Chronic kidney patients undergoing HD will suffer from anemia [4].

Anemia in renal disease if Hb ≤10 g/dL and Ht ≤30%, anemia will be more severe if renal function becomes worse, anemia that occurs in CKD is usually normokrom normositer type [5]. Anemia is a big enough problem of maintaining the quality of life of chronic kidney patients, increasing morbidity and mortality [6].

Anemia was defined as Hb level <13.0 g/dL for men and <12.0 g/dL for women as per the World Health Organization guidelines. CKD was defined as a reduced excretory function with an estimated long fiber granular (glomerular filtration rate) <60 ml/min/1.73 m^2 as a marker of kidney dysfunction [7].

Anemia in CKD is mainly caused by reducing the production of erythropoietin, a hormone that will stimulate the bone marrow to produce red blood cells [8]. Under normal circumstances, 90% of erythropoietin is produced in the kidneys in the juxtaglomerolus and only 10% is produced in the liver [9].

Erythropoietin is the preferred treatment of anemia in chronic kidney patients with target Hb 11–12 g/dL, hemoglobin levels more than 13 g/dL will increase the risk of thrombosis [10].

Drug-related problems (DRPs) are an event or state of drug therapy that significantly or potentially interferes with the desired outcome of the therapy, recovers from illness, eliminates or reduces symptoms of pain, stops or slows the painful process, and prevents disease or disease symptoms [11]. Identify DRPs criteria including unwanted reaction drugs, drug selection, drug dosage, time, drug interactions, and others [12]. Pharmacists play a key role in identifying and preventing DRPs by conducting interventions with the doctor, patient, and the nurse based on predicted DRPs [13].

Research on DRPs has been largely done on the use of drugs in various cases of illness, including orthopedic open invoice patients [14], in dyspepsia patients [15], in orthopedic post-operative [16]. Based on a search conducted on LITBANG (Research and Development) of RSUP, H. Adam Malik Medan is known that the study of the influence of doses of erythropoietin phase correction as DRPs to target hemoglobin level in the regular HD patient has never been done and the number of cases that occur due to the use of erythropoietin therapy, the importance of the authors to conduct research with the title "The effect of erythropoietin dose phase of correction as DRPs to target level of hemoglobin in regular HD patients."

METHODS

Research design

This research was by the cross-sectional, prospective method, using DRP - registration Form V7.0 (PCNE) against 50 patients [17]. The data were analyzed statistically using Chi-square test, paired t-test sample, and independent t-test, SPSS version 17.

Data source

Sources of research data are secondary data in the form of medical records of regular HD patients who receive erythropoietin therapy, laboratory results, and nurse records.

Place and time of research

The study was conducted at the Hemodialisa Installation of RSUP H. Adam Malik Medan, from August to October 2017.

Population and sample

Population

The population in this study was the regular HD patient of RSUP H. Adam Malik Medan.

Sample

The selected sample must meet the inclusion criteria and does not meet the exclusion criteria.

Table 1: Frequency distribution based on gender

Gender	Frequency (%)
Man	31 (62.0)
Women	19 (38.0)
Total	50 (100.0)

Table 2: Frequency distribution by age

Age (year)	Frequency (%)
20–30	11 (22.0)
31–40	7 (14.0)
41–50	6 (12.0)
51–60	16 (32.0)
>60	10 (20.0)
Total	50 (100.0)

Table 3: Frequency distribution based on attendant diagnosis

Attendant diagnosis	Frequency (%)
Valid	
Diabetes mellitus	1 (2.0)
Diabetes nephropathy	3 (6.0)
Chronic glomerulonephritis	5 (10.0)
Hypertension nephropathy	33 (66.0)
HN+CHF	1 (2.0)
Chronic disease obstruksi	6 (12.0)
Systemic lupus erythematosus	1 (2.0)
Total	50 (100.0)

Table 4: Distribution of frequency based on stage

Stage	Frequency (%)
5	50 (100.0)

The inclusion criteria are as follows:

a. Undergo regular HD
b. Anemic patients
c. Get erythropoietin phase correction therapy.

Exclusion criteria are as follows:

a. Not necessarily get erythropoietin therapy
b. Replace the type of erythropoietin
c. The patient is in an unstable state.

Number of samples

The sample size was the number of regular HD patients in RSUP. H. Adam Malik calculated based on the Raosoft program [18], with values:

- The margin of error = 5%
- Confidence level = 95%
- Population size = 100
- Data installation in HD 2017 RSUP H. Adam Malik Medan
- Response distribution (response distribution) = 50%
- Then obtained a large sample of at least 50 people.

Tools and materials

Tools used

a. Syringe 3cc
b. Tube EDTA.

Materials used

a. Blood.

Research steps

The steps of this research are carried out as follows:

a. Requesting the recommendation of the Dean of the Faculty of Pharmacy USU to be able to conduct research in RSUP H. Adam Malik Medan
b. Request approval of the Research Ethics Committee in the medical field of Faculty of Medicine, University of North Sumatra, to be approved by the Director of RSUP H. Adam Malik Medan
c. Contact the Director of RSUP H. Adam Malik Medan to obtain permission to conduct research and data retrieval with a letter of recommendation from the Faculty of Pharmacy USU
d. Data collection of erythropoietin therapy given to regular HD patients based on the RSUP Formulary. H. Adam Malik Medan, the list of JAMKESMAS erythropoietin therapy drugs, and List of Askes Price Places Ceiling (DPHO).
e. Choose patients who meet inclusion criteria
f. Data retrieval
g. Data analysis.

Research procedures

Materials examined were blood taken before and after erythropoietin therapy, examined by clinical pathology laboratory workers at RSUP H. Adam Malik Medan. Measurement of this tool is using Sysmex G 20 engine.

Table 5: Effect of dose-related DRPs less and excess of the target hemoglobin

Cross tabulation	Target hemoglobin level			Total
Count	<0.5 (not achieved)	0.5–1.5 (target achieved)	>1.5 (excess target)	
Dose				
Less	17	10	0	27
Excess	1	1	0	2
Right	12	8	1	21
Total	30	19	1	50
Chi-square tests	Value	df	Asymp. significant (two-sided)	
Pearson Chi-square	1.565[a]	4	0.015	
Likelihood ratio	1.914	4	0.022	
Linear-by-linear association	0.464	1	0.032	
Number of valid cases	50			

Analysis of samples is using whole blood mode. Working procedure of this tool checks the status of LED indicator on tool and sampler under READY condition. Click the Analysis Button sampler on the control menu. Select discrete test. Click Ok. Put the shelf on the loader sampler [19].

The data collected in this research are:

a. Records of data from medical records in the HD room of RSUP. H. Adam Malik Medan includes data on patient demographic characteristics (sex, age, type of erythropoietin, and stage)
b. Patient data related to the inclusion criteria
c. Patient laboratory data, recorded before and after erythropoietin therapy. Assessment/measurement an increase in hemoglobin levels is done by comparing the results of laboratory data before the patient obtains erythropoietin therapy was compared with laboratory results after patients received erythropoietin therapy
d. The captured data are moved to the data collection sheet. The lack of medical record data is supplemented by looking at nurse records, SIRS data, and pharmaceutical depot drug records.

Data analysis

Data were analyzed statistically using Chi-square test, paired t-test sample, and independent t-test, SPSS version 17 program.

RESULTS AND DISCUSSION

RESULTS

The study was conducted on 50 patients with chronic renal HD at a HD hospital in Haji Adam Malik General Hospital Medan. Began in August 2017 after obtaining approval from the Research Ethics Commission of Health Division, Faculty of Medicine, University of North Sumatra.

The results of the study are presented in the form of percentage table consisting of data of patient demographic characteristics, observed variable data, and variable data that mutually influenced or allegedly influenced each other.

DISCUSSION

From Table 1, it can be seen that 50 patients with chronic kidney patients undergoing regular HD have fulfilled inclusion; male patients as many as 31 people (62%) and women as many as 19 people (38%). From the data obtained, it is known that the number of patients with chronic renal disease regular hemodialysis that is more male than female. One of the factors is due to the smoking lifestyle of men. Smoking behavior can increase the risk of CKD 2.2 times greater than individuals who do not smoke [20].

From Table 2, it can be seen that the age between 20 and 30 years as many as 11 patients (22%), age between 31 and 40 years as many as 7 patients (14%), age 41–50 years is 6 patients (12%), age between 51 and 60 years as many as 16 patients (32%), and age above 60 years, that is, 10 patients (20%). This indicates that the increasing age, kidney function and blood flow to the kidney is reduced, resulting in a 30% decrease in glomerular filtration rate compared to younger people [21].

From Table 3, it can be seen that diabetes mellitus as many as 1 patients (2%), diabetes nephropathy as many as 3 patients (6%), chronic glomerulonephritis as many as 5 patients (10%), hypertension nephropathy as many as 33 patients (66%), HN + CHF as many as 1 patients (2%), chronic disease obstruksi as many as 6 patients (12%), and systemic lupus erythematosus as many as 1 patients (2%).

From Table 4, it can be seen that patients with chronic renal disease regular HD 50 people (100%), i.e. stage 5.

This can happen because in general the symptoms or clinical manifestations of CKD appear suddenly or gradually, and some do not cause clear early symptoms so that the decline in kidney function is often not felt even neglected by the patient and only detected after

Table 6: Differences in hemoglobin levels after being given erythropoietin therapy between the dose of less and excess.

Group statistics					
	Dose	**N**	**Mean**	**SD**	**Standard error mean**
Hemoglobin post terapi erythropoietin	Less	27	8.7296	0.89992	0.17319
	Excess	2	8.9500	0.49497	0.35000

Independent samples test									
	Levene's test for equality of variances		**t-test for equality of means**					**95% confidence interval of the difference**	
	F	**Significant**	**t**	**df**	**Significant (two-tailed)**	**Mean difference**	**Standard error difference**	**Lower**	**Upper**
Hemoglobin post terapi erythropoietin									
Equal variances assumed	2.193	0.150	−3.339	27	0.038	−0.22037	0.65091	−1.55593	1.11519
Equal variances not assumed			−3.564	1.546	0.043	−0.22037	0.39051	−2.47427	2.03353

SD: Standard deviation

Table 7: Hemoglobin levels before and after erythropoietin therapy using test sample test

Paired samples test								
	Paired differences					t	df	Significant (two-tailed)
	Mean	Standard deviation	Standard error mean	95% confidence interval of the difference				
				Lower	Upper			
Pair 1								
Pre-post EPO	−0.01000	0.89994	0.12727	−0.26576	0.24576	−3.079	49	0.003

the condition of the kidney progressively deteriorate and the clinical manifestations are getting worse in the late stages.

Anemia in CKD is typically normocytic, normochromic, and hypoproliferative. The demonstration of a circulating factor responsible for stimulating erythropoiesis and the EPO deficiency is a predominant cause of anemia in CKD.

From Table 5, it can be seen that the effect of dose-related DRPs less and excess of the target hemoglobin. Based on the results of Chi-square test, obtained p=0.015 <0.05, then concluded there is a significant relationship between the dose of less and excessive to the target hemoglobin level.

From Table 6, it can be seen that differences in hemoglobin levels after being given erythropoietin therapy between the dose of less and excess. Based on t-test result, p=0.038 <0.05, there is a difference of hemoglobin level after giving erythropoietin therapy significant between dose less and excess.

From Table 7, it can be seen that hemoglobin levels before and after erythropoietin therapy using a test sample test. Based on paired t-test results, obtained significant value is 0.015<0.05, then the statistical increase in hemoglobin levels after being given significant erythropoietin therapy [22].

CONCLUSION

Based on the description, it can be concluded that there is an effect of DRPs related to excessive dosage; less dose to target hemoglobin level with significance value, so DRPs-associated dose affect the target hemoglobin level.

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