EFFECTIVITY OF ERYTHROPOIETIN-ALPHA BETWEEN FIXED-DOSE AND ADJUSTMENT-DOSE IN CHRONIC KIDNEY DISEASE PATIENTS WITH ANEMIA ON HEMODIALYSIS

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ABSTRACT

Anemia is a common complication in chronic kidney disease (CKD) patient with hemodialysis. The cause of anemia is mainly due to erythropoetin deficiency because the kidneys as a erythropoetin producer are damaged. The most appropriate management of anemia in CKD with hemodialysis is the administration of Erythropoietin Stimulating Agent (ESA) or erythropoetin (Epo). The effectiveness of Epo therapy is influenced by the type of Epo used, the dose of Epo given, the route and frequency of Epo administration, as well as several conditions that affect it such as infection or inflammation, absolute and functional iron deficiency, and malnutrition. Therapeutic targets can be achieved if the dose given is in accordance with the needs of the patient, based on the patient's weight The purpose of this study was to determine the differences in the achievement of Epo-alpha fixed-dose administration compared with adjustment-dose in patients with CKD anemia with hemodialysis after administration of Epo-alpha for 4 weeks in outpatient poly hemodialysis units at Bhayangkara H.S Hospital. Samsoeri Mertojoso Surabaya. In this study, there were 20 patients who met the inclusion criteria (15 male and 5 female) divided into 2 groups, 10 patients in the fixed-dose group and 10 patients in the adjustment-dose group. In the fixed-dose group with a adequacy level of 132.25 ± 29.17, the average Hb change achievement was 0.68 ± 0.63 g / dL (p=0.008), whereas in the adjustment-dose group the achievement of the average Hb change the mean was 1.09 ± 0.82 g / dL (p=0.002). For the Hct parameter, the average Hct change in the fixed-dose group was 2.77 ± 2.23% (p=0.004), while in the adjustment-dose group the average Hct change achievement was 4.02 ± 2.63 g / dL (p=0.001). There was no difference in the achievement of the effectiveness of Epo on the two parameters Hb (p=0.224) and Hct (p=0.256) in the fixed-dose group compared with adjustment-dose.

***Keywords**: Epo; erythropoietin; erythropoietin-alpha; foxed-dose; adjustment-dose; CKD with anemia; hemodialysis*

ABSTRAK

Anemia merupakan komplikasi yang sering terjadi pada pasien PGK stadium 5 dengan hemodialisis. Penyebab anemia ini terutama diakibatkan oleh defisiensi eritropoetin karena ginjal sebagai penghasil eritropoetin mengalami kerusakan. Penatalaksaan anemia pada PGK dengan hemodialisis yang paling tepat adalah dengan pemberian Erythropoietin Stimulating Agent (ESA) atau eritropoetin (Epo). Efektivitas terapi Epo dipengaruhi oleh jenis Epo yang digunakan, dosis Epo yang diberikan, rute dan frekuensi pemberian Epo, serta beberapa kondisi yang mempengaruhi seperti infeksi atau inflamasi, defisiensi besi absolut dan fungsional, dan malnutrisi. Target terapi dapat dicapai bila dosis yang diberikan sesuai dengan kebutuhan pasien yaitu berdasarkan berat badan pasien. Tujuan dari penelitian ini adalah untuk mengetahui perbedaan capaian Epo alfa pemberian fixed-dose dibandingkan dengan adjustment-dose pada pasien PGK anemia dengan hemodialisis setelah pemberian Epo alfa selama 4 minggu di poli rawat jalan unit hemodialisis RS Bhayangkara H.S. Samsoeri Mertojoso Surabaya. Pada penelitian ini, terdapat 20 pasien yang memenuhi kriteria inklusi (15 laki-laki dan 5 perempuan) yang terbagi menjadi 2 kelompok, 10 pasien pada kelompok fixed-dose dan 10 pasien pada kelompok adjustment-dose. Pada kelompok fixed-dose dengan tingkat kecukupan dosis 132,25 ± 29,17, capaian perubahan Hb rata-rata adalah 0,68 ± 0,63 g/dL (p=0,008), sedangkan pada kelompok adjustment-dose capaian perubahan Hb rata-rata adalah 1,09 ± 0,82 g/dL (p=0,002). Untuk parameter Hct, rata-rata perubahan Hct pada kelompok fixed-dose adalah 2,77 ± 2,23 % (p=0,004), sedangkan pada kelompok adjustment-dose capaian perubahan Hct rata-rata adalah 4,02 ± 2,63 g/dL (p=0,001). Tidak ada perbedaan capaian efektivitas Epo pada kedua parameter Hb (p=0,224) dan Hct (p= 0,256) pada kelompok fixed-dose dibandingkan dengan adjustment-dose.

***Kata kunci**: Epo; eritropoetin; eritropoetin alfa; foxed-dose; adjustment-dose; PGK dengan anemia; hemodialisis*

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pISSN:2355-8393 ● eISSN: 2599-056x ● doi: http://dx.doi.org/10.20473/fmi.v55i4.17334
● Fol Med Indones (2019;55:306-310 ● Received 13 Jul 2017 ● Accepted 25 Jan 2018

INTRODUCTION

Kidney is an important organ that has a variety of functions for the body, of water and solutes, acid - base balance, including regulating blood pressure and hemodynamic intra-glomerular, transport produce erythropoietin, eliminate the drug and its metabolites. Damage can occur in kidney caused by various factors, so they can appear various complications. Complications caused due to kidney damage include abnormalities of water and electrolyte balance, hypertension, acidosis, and anemia.

Anemia is a frequent complication in patients with chronic kidney disease (CKD), which began to appear at stage 3 to 5 of CKD. The primary cause in patients with CKD is insufficient production of erythropoietin (EPO) by the diseased kidneys. Additional factors include iron deficiency, acute and chronic inflammation with impaired iron utilization ("anemia of chronic disease"), severe hyperparathyroidism with consequent bone marrow fibrosis, and shortened red cell survival in the uremic environment. Less common causes include folate and vitamin B12 deficiency and aluminum toxicity (Bargman 2010).

Based on the primary caused of anemia in CKD, Epo is the first choice for therapy of anemia in CKD. Adequate bone marrow iron stores should be available before treatment with EPO is initiated. Iron supplementation is usually essential to ensure an adequate response to EPO in patients with CKD because the demand for iron by the marrow frequently exceeds the amount of iron that is immediately available for erythropoiesis (measured by percent transferrin saturation), as well as the amount in iron stores (measured by serum ferritin) (Bargman 2010).

The aim of this study was to analyze the performance difference in hemoglobin levels after administration of erythropoietin alpha-dose and fixed-dose adjustment in patients with CKD-anemic hemodialysis based on data Hb and Hct.

The success of EPO therapy is influenced by various factors, including the dose of EPO, iron sufficiency status which can be seen from Saturation value of Transferin (ST) and Ferritin Serum (FS), route of EPO administration, presence or absence of bleeding, etc.

MATERIALS AND METHODS

A prospective observasional study was conducted in outpatient setting at Hemodialysis Unit of Bhayangkara Hospital during April-August 2016. Patient selection based on inclusion and exclusion criteria.

All sample was devided in two groups, one group received fixed-dose therapy with 3000 IU subcutaneus erythropoietin twice a week every after dialysis, and the other group received the adjustment-dose of 40 IU/kg/weight. Blood sampel was taken in pre-treatment and post-treatment after 4 weeks of erythropoetin therapy. The measurement parameter were haemoglobin and haematocrit level.

RESULTS

There were 20 patients in this study (10 patients in the fixed-dose group and 10 patients in the dose-adjustment) (Tabel 1). After the treatment, the mean of haemoglobin level for fixed-dose group was 0.69 ± 0.63 g/dL (p=0.008), and the adjustment-dose group was 1.09 ± 0.82 g/dL (p=0.002) (Tabel 2). The mean of haematocrit level for fixed-dose group was 23.2 ± 2.72 g/dL (p=0.004), and the adjustment-dose group was 4.02 ± 2.63 g/dL (p=0.001) (Tabel 3). The result showed that 70% patient performed increase of Hb level on fixed-dose group and 90% patient on adjustment group. The fixed-dose group showed the increase of haematocrit level for about 60% patient and 80% patient on adjustment group.

DISCUSSION

The erythropoietin was given by a subcutaneous administration, eventhough the intravenous administration more comfortable for the patients. This administration was choosed because the subcutaneous administraton would give a longer elimination half life and makes a longer duration of effects.

Target for this therapy is increase of haemoglobin level about 0.5 - 1.5 g/dL in 4 weeks (not to exceed 12 g/dL). Table 2 shows mean increased haemoglobin level on fixed-dose group as much as 0.68 ± 0.63 g/dl (p=0.008), and 1.09 ± 0.82 g/dl on adjustment-dose group (p=0.002). This therapy should be increase the haematocrit level about 2 - 4 % in 4 weeks (Lydia 2011). Table 3 shows shows mean increased haematocrit level on fixed-dose group as much as 2.77 ± 2.23 % (p=0.004), and about 4.02 ± 2.63 % (p=0.256) for adjustment-dose group.

Both fixed-dose and adjustment-dose gave good outcomes to increase haemoglobin level, but there is no significant difference between two groups both on haemoglobin increased (0.224) and haematocrit level (p=0.224). Nevertheless, adjustment-dose more recommended than fixed-dose.

Table 1. Characteristics of patients

Characteristics	Samples (n=20)		Mean ± SD	
	Fixed-dose (n=10) Total (n)/%	Adjustment-dose (n=10) Total (n)/%	Fixed-dose	Adjustment-dose
Age (year)*				
<35	2/20	1/10	48.50 ± 13.15	46.10 ± 12.43
35-44	1/10	4/40		
45-54	4/40	2/20		
55-64	2/20	3/30		
>64	1/10	-		
Gender				
Male	7/70	8/80	-	-
Female	3/30	2/20		
Weight(kg)*				
<50	1/10	-		
50-60	6/60	7/70	60.60 ± 10.84	58.35 ± 8.29
>60	3/30	3/30		
HD schedule				
Once a week	1/10	-	-	-
Twice a week	9/90	9/90		
3 times a week	-	1/10		
Ethiology**				
Hipertention	7/70	7/70	-	-
Diabetes Mellitus	3/30	2/20		
Kidney Infection	3/30	2/20		
Hb level (g/dl)*				
7.0 - 7.9	5/50	3/30		
8.0 - 8.9	4/40	6/60	7.97 ± 0.73	8.12 ± 0.63
9.0 - 9.9	1/10	1/10		
Hct Level (%)*				
10 - 20	1/10	-	-	-
21 - 30	9/90	100		
Complaint				
Headache	-	1/10	-	-
Nausea	2/20	-		
Vomiting	-	-		
Serum Iron (µg/dl)*				
<65	4/40	4/40	92.50 ± 51.76	81.40 ± 39.8
65-175	5/50	6/60		
>175	1/10	-		
Total Iron Binding Capacity (µg/dl)*				
<250	9/90	10/100		
250 - 425	1/10	-	210.60 ± 38.26	213.2 ± 45.03
>425	-	-		
Transferrin Saturation (%)*				
<20	-	-	41.61 ± 21.86	39.78 ±17.84
20 - 40	8/80	70		
>40	2/20	30		
Ferritin Serum (ng/mL)*				
<100				
100 - 500	-	-	657.39 ± 420.62	645.79 ± 415.53
>500	3/30	4/40		
	7/70	6/60		

Table 2. Distribution of increasing haemoglobin level

Fixed-dose						Adjustment-dose					
Patient Code	Weight (kg)	Doage of Epo (IU)	Hb pre-treatment (g/dL)	Hb post-treatment (g/dL)	Δ Hb	Patient Code	Weight (kg)	Dosage of Epo (IU)	Hb Pre-treatment (g/dL)	Hb post-treatment (g/dL)	Δ Hb
1A	37	3000	7.2	8.7	1.5	1B	52	2080	8.0	9.7	1.7
2A	55	3000	8.5	9.7	1.2	2B	52	2080	8.1	9.1	1.0
3A	55	3000	7.0	7.6	0.6	3B	52	2080	9.4	10.2	0.8
4A	55	3000	7.2	7.3	0.1	4B	53	2120	8.6	9.4	0.8
5A	56	3000	7.5	8.3	0.8	5B	54	2160	8.2	10.4	2.2
6A	57	3000	8.8	9.0	0.2	6B	56	2240	7.6	8.3	0.7
7A	58	3000	7.8	7.2	-0.6	7B	57.5	2300	8.4	7.9	-0.5
8A	65	3000	8.4	9.2	0.8	8B	61	2440	7.6	8.7	1.1
9A	67	3000	9.1	10.2	1.1	9B	71	2840	7.1	7.9	0.8
10A	88	3000	8.2	9.3	1.1	10B	75	3000	8.2	10.5	2.3
Mean ± SD	60.60 ± 10.84	3000 ± 0	7.97 ± 0.73	8.65 ± 1.02	0.68 ± 0.63	Mean ± SD	58.35 ± 8.29	2334. ± 331.74	8.12 ± 0.63	9.21 ± 0.99	1.09 ± 0.82
Span	37 - 88	3000	7.2 - 9.1	7.2 - 10.2	-0.6 - 1.5	Span	52 - 75	2080 - 3000	7.1 - 9.4	7.9 - 10.4	-0.5 - 2.3
P=0.008						P=0.002					
P=0.224											

Table 3. Distribution of increasing haematocrit level

Fixed-dose						Adjustment-dose					
Patient Code	Weight (kg)	Doage of Epo (IU)	Hct pre-treatment (g/dL)	Hct post-treatment (g/dL)	Δ Hct	Patient Code	Weight (kg)	Dosage of Epo (IU)	Hct Pre-treatment (g/dL)	Hct post-treatment (g/dL)	Δ Hct
1A	37	3000(202)	18.9	26.2	7.6	1B	52	2080	24.1	30.8	6.7
2A	55	3000(137)	24.8	28.1	3.3	2B	52	2080	21.9	27	5.1
3A	55	3000(137)	21.1	22.7	1.6	3B	52	2080	27.6	31.0	3.4
4A	55	3000(137)	21.9	22.0	0.1	4B	53	2120	27.7	29.3	1.6
5A	56	3000(134)	22.1	24.2	2.1	5B	54	2160	23.6	29.5	5.9
6A	57	3000(132)	25.1	26.2	1.1	6B	56	2240	22.2	26.9	4.7
7A	58	3000(129)	22.7	23.8	1.1	7B	57.5	2300	25.7	24.6	-1.1
8A	65	3000(115)	21.4	27.2	5.8	8B	61	2440	21.8	25.7	3.9
9A	67	3000(112)	25.9	28.5	2.6	9B	71	2840	21.8	24.0	2.2
10A	88	3000(87.5)	28.1	30.5	2.4	10B	75	3000	23.3	31.1	7.8
Mean ± SD	60.60 ± 10.84	3000 ± 0	23.2 ± 2.72	25.94 ± 2.73	2.77 ± 2.23	Mean ± SD	58.35 ± 8.29	2334. ± 331.74	23.97 ± 2.29	27.99 ± 2.69	4.02 ± 2.63
Span	37 - 88	3000	18.9 - 28.1	22.0 - 30.5	0.1 - 7.6	Span	52 - 75	2080 - 3000	21.8 - 27.7	24.0 - 31.1	-1.1 - 6.7
P=0.004						P=0.001					
P=0.256											

CONCLUSION

There were no differences in Hb (p=0.224) and Hct (p=0.256) targets after 4 weeks of erythropoietin-alpha therapy between fixed-dose and adjustment-dose in this study.

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