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ORIGINAL ARTICLE

Evaluation of Anemia Management in Maintenance Hemodialysis Patients in Two Dialysis Centers in Khartoum State

[1]Safaa Yahia,[2]Somia Babeker , [3]Asma Magboul , [4]Azza Salih ,[5]Hagir Hassan , [6,7] Somia Mustafa Elagib , [8]Salma Ahmed Ali Babiker ,[9]Reem Falah Alshammari *[10,11] Halima Mustafa Elagib
[1] College of Pharmacy, Department of Clinical Pharmacy, Omdurman Islamic University / Sudan
[2,3,4,5] College of Pharmacy, 5th Year Students,Omdurman Islamic University / Sudan
[6]College of Science and Art, Biology Department, Almikhwa, Al- Baha University, Saudi Arabia
[7]Faculty of Teachers. Science Department. Nile Valley University, Edammer, Sudan
[8]Family Physician, Family Medicine, Ha,il University Clinics, University of Ha'il / Saudi Arabia
[9]College of Medicine, Department of Family and Community Medicine, University of Ha'il / Saudi Arabia
[*10]College of Medicine, Department of Pharmacology, University of Ha'il / Saudi Arabia
[*11]College of Pharmacy, Department of Pharmacology, Omdurman Islamic University, Sudan
Corresponding Author: Dr. Halima Mustafa Elagib
Email: halimaelagibwork@gmail.com, Mobile: 00966534528906

ABSTRACT
Anemia is a common and serious complication of end stage renal disease that leads to increase hospitalization rate, decrease quality of life and increase cardiovascular disease risk. The main treatment of anemia is erythropoiesis-stimulating agent along with iron supplementation. The aim of the study to evaluate the anemia management in renal hemodialysis patients. Study was conducted in two dialysis centers in Khartoum state in Sudan. Data extracted retrospectively and prospectively in the period from January to June 2016. All patients over 18 years of age with CKD undergoing maintenance hemodialysis for three months or more were included, Patients excluded if they had cancer or receiving chemotherapy, radiotherapy or having any other diseases that cause anemia, hepatitis or HIV infection. Patients for whom hemoglobin levels were not documented during the study period were not included in this study. Data analyzed by statistical package for social sciences (SPSS) version 16 and Microsoft excel 2013.The study included 160 patients, 57.5% male and 42.5% female. 55.6% of patients had hemoglobin level less than 10 g/dl and 18.7% more than 14 g/dl, the mean hemoglobin level 9.9±2.2 g/dl. Regarding drug therapy 90.6% of patients received erythropoietin therapy with a mean weekly dose of 8082.8 ± 1450.5 U/week, 51% of patients received iron intravenously, 6.2% orally, 7.5% by both route. Regarding iron indices ferritin level available only for 57 patients and there is no documentation for Serum transferrin saturation. The study concluded that management of anemia of end stage renal disease require further evaluation as erythropoietin and iron doses need to be individualized for each patient according to their hemoglobin level.
KEYWORDS: *Chronic, Kidney, Failure, Evaluation, Anemia, Hemodialysis*

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INTRODUCTION

Anemia related to chronic kidney disease (CKD) is a serious complication requiring expenditure of huge medical efforts and resources [1] and leading to development of left ventricular hypertrophy, angina, and congestive heart failure, it contributes to the progression of CKD. It considers as one of the factors that responsible for high morbidity and mortality in patients with chronic renal failure, reduced their survival rate [2]and increase hospitalization rate [3]. The prevalence of anemia of CKD is proportionally related to increase in severity of kidney impairment that range from 1% in stage2 to nearly 100% in end stage renal disease (ESRD) [4]. There are several factors that may be responsible for anemia in CKD including blood loss, vitamins deficiencies, iron deficiency, infection, inflammation, and erythropoietin (EPO) deficiency

which is considered as the major cause [5] given that kidney is the main source of EPO[6]. Other secondary factors contributing to the development of anemia including hemoglobinopathies, aluminum toxicity, and hypothyroidism that lead to poor response to EPO reduced proliferative activity of erythroid precursors in bone marrow and erythrophagocytosis. In addition, the reduced life span of red blood cells (RBCs) secondary to oxidative damage of the membrane of red blood cells (RBCs) in chronic hemolysis patients may worsen anemia [7],folic acid deficiency, hyperparathyroidism and uremic environment are also contributing factors [4]. Erythropoiesis stimulating agents (ESAs) are the main treatment for patients with anemia of CKD that correct and maintain hemoglobin (Hgb) levels, reduce the requirement for blood transfusions [8],improvement in energy and physical function and improvement in quality of life [9].Intravenous (IV) iron supplementation is other important therapy along with EPO therapy [4]. The[10]guidelines for stage 5 patients, suggest that to initiate ESA therapy when the hemoglobin is between 9.0–10.0 g/dl (90–100 g/l), to avoid having the Hgb concentration fall below 9.0 g/dl (90 g/l). In addition to that, initial ESA dose is determined using the patient's Hgb concentration, body weight, and clinical Circumstances and Re-evaluate ESA dose if the patient suffers from an ESA related adverse effects or at an acute or progressive illness that may cause ESA hypo responsiveness. For long use the ESA therapy, suggest that ESAs not to be used to maintain Hgb concentration above 11.5 g/dl [10]In study done in Riyadh, Saudi Arabia on 87 patients collected from two-hemodialysis centers show that the mean Hgb value was 11.16 ± 0.97 g/dl. 39 patients had mean Hgb values between 11.0 and 12.0 g/dl, which is, target range recommended by [10]. 26 patients had mean Hgb values between 10.0 to 11.0 g/dl. Nine patients had mean Hgb values less than 10 g/dl while 30 patients exceed the recommended range (>12 g/dl). Also this study show that the mean weekly erythropoietin dose was 8099 ± 5946 IU/Week (135 ± 99 IU/kg/Week) which is given by IV route at end of session of dialysis and the erythropoietin dose decreased with increase of Hgb concentration[11]. Multicenter prospective observational Cohort study carried out in Korea in 10 clinic centers in period between September 2006 to September 2011 on 362 patients revealed that,33.1% of these patients had hemoglobin level less than 10 g/dl , 60.3% of the, patients had hemoglobin level 10-12 g/dl and 6.4 with hemoglobin level ≥ 12 g/dl[3]. To evaluate the anemia management in hemodialysis patients.

MATERIAL AND METHODS

Our study was retrospective and prospective cross sectional descriptive, that done on 160 patients in two dialysis centers in Khartoum state, Association specialized hospital dialysis center and Academic teaching hospital dialysis center. All patients over 18 years of age with CKD undergoing maintenance hemodialysis for three months or more were included, Patients were excluded if they have cancer or were receiving chemotherapy, radiotherapy or having any other diseases that cause anemia, hepatitis or HIV infection. Patients for whom hemoglobin levels not documented during the study period were not included. Data regarding patient's demographics, medical conditions, laboratory investigations and drug therapy in the period from January to June 2016 extracted retrospectively and prospectively. For patients with incomplete files demographic data and medical history obtained by direct questioning of patients. Data analyzed by statistical package for social sciences (SPSS) version 16 and Microsoft excel 2013. Discrete variables expressed as counts and percentages. Continuous variables expressed as mean ± SD for normally distributed. A chi-square test used to test for differences between discrete variables while one way Anova used to compare means for continuous.

RESULT:

As shown in table 1.

Table 1: Patient's demographics data

Patients characteristics	Total %
Gender ,number of patients (N)=160	
Male	57.5
Female	42.5
Age ,N = 157	
18-39	25.5
40-49	20.4
50-59	21
60-69	19.7
70-79	10.2

>80	3.2
Causes of CKD N = 156	
Hypertension	48.1
Diabetes mellitus	3.8
Glomerulonephritis	3.8
Obstructive uropathy	4.5
Drugs induce	2.6
Gouty arthritis	1.3
Others / unknown	19.6
Onset of hemodialysis ,N = 153	
3-11 months	22.2
1-5 years	67.3
5-10 years	7.8
>10 years	2.6
Frequency of hemodialysis ,N = 159	
Once weekly	1.9
Twice weekly	86.8
3 times weekly	11.3

Erythropoiesis stimulating agents

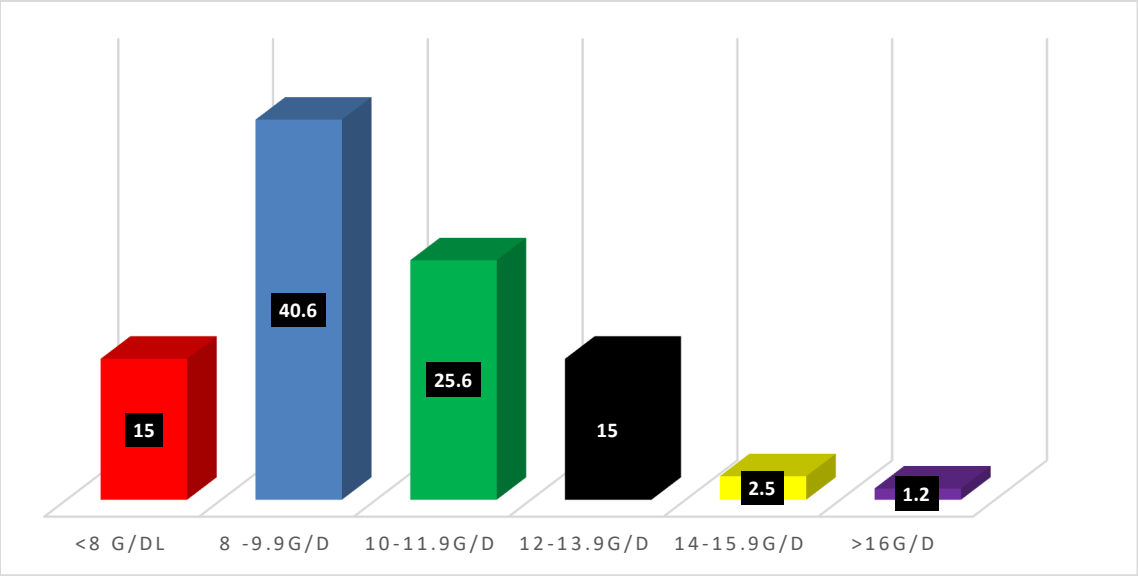

Figure1: Hemoglobin levels distribution among patients.
Values were expressed as frequency percentages P < 0.05* significant difference among patients

Hemoglobin level

The mean Hgb concentration among patients was 9.9±2.2 g/dl. 55.6% of the patients has hemoglobin value less than 10 g/dl as shown in figure 1.

About 90.6% of the patients (145 patients) received erythropoietin therapy subcutaneously, 86.9% of them received it twice weekly after dialysis session. The mean weekly erythropoietin dose was 8082.8 ± 1450.5Unit.

Iron status

Regarding iron therapy 51.9% of the patients received iron therapy intravenously, 6.2 % orally and7.5 % both orally and intravenously. The mean weekly IV iron dose was 162.11 ± 58.671 mg.

Regarding iron indices ferritin level was available only for 57 patients, from them there were17 patients had ferritin level more than 1000 ng/dl with hemoglobin level less than 10 g/dl. No documentation for serum transferrin saturation.

Others

71.2% of all patients received folic acid therapy in dose 1mg per day. The parathyroid hormone recorded for only 44 patients.

Association between hemoglobin levels and patients demographics data:
Factors evaluated such as age, gender and dialysis onset, and all of them show no significant difference, with P value 0 .354, 0.566, 0.122 respectively as shown in table 2.
Association between hemoglobin levels and different variables

Table 2: Association between different Hgb levels with mean EPO dose, and with mean IV iron dose

Hemoglobin levels	Mean erythropoietin dose	Mean intravenous iron dose
>8 g/dl	8545.5 ± 1405	143 ± 51.4
8 – 9.9 g/dl	8070.2 ± 1771.4	164 ± 54.3
10 – 11.9 g/dl	8205.1 ± 893.8	160 ± 64.5
12 – 13.9 g/dl	7428.6 ± 1434.3	171 ± 61.1
14 -15.9 g/dl	8000	225 ± 50.0
≥ 16 g/dl	8000	---
Number of patients	145	93

In addition, other factors such as use of ACEIs, ARBs and high phosphate level with hemoglobin levels evaluated and show no significance with P value 0.143 and 0.347 respectively.

DISCUSSION
Our study carried out over 5 month and involved 160 patients, it differs from the study of [11]that involved 87 patients in 7 months, of them males represent 44% compared to 56.9% in our study. Our findings revealed that main cause of end stage renal failure was hypertension compare to diabetic nephropathy as the main cause in study of [11]. The mean Hgb level in current study was 9.9±2.2 g/dl and 55.6% of patients had hemoglobin level less than 10 g/dl in contrast to mean hemoglobin level of 11.16 g/dl with only 10% of patients had hemoglobin level less than 10g/dl in [11] study and 33.1% in [3]. Lower Hgb levels in our study may be attributed to lower doses of EPO therapy for patients' groups with low Hgb level or resistance to erythropoiesis stimulating agent therapy, also irregular use of erythropoiesis stimulating agent by patients for economic reason could be a contributing factor. Moreover this in harmony with the study of [12] found that among the patients who included in the final analysis, 307 (57.5%) were males and the mean age was 48.7±16.1 years. All the analyzed patients were anemic (hemoglobin level<12 g/dL), 67% had a hemoglobin level <10 g/dL. The dosing of EPO in current study is 4000U for all patients that administered after each session; this is not with accordance to [10], which recommended that dosing of EPO therapy based on body weight, Hgb level and other patient's factors [10]. When we compared the mean EPO dosing with different hemoglobin level of patients, we found that there was no significant difference between them with mean weekly EPO dose of 8082.8 ± 1450.5 U .But we observed that patients with higher hemoglobin level still use EPO therapy and according to [10]. The EPO should not be used when hemoglobin level is more than 11.5 g/dl to avoid cardiovascular disease risk. Furthermore, patients with lower hemoglobin level used nearly same weekly dose to that of patients with higher hemoglobin level this may indicate inappropriate management. Variation in response to EPO therapy, iron and vitamins deficiency or no adherence to EPO therapy may also be contributing to observe lower Hgb levels in this subset of patients. KDIGO guideline recommended that iron and folic acid should be assessed and corrected before initiation of erythropoietin therapy [10]. In this study 65.6 % of patients used iron therapy, 51.9% of patients used it by IV route, 6.2 % by oral route and 7.5% by both route in contrast to [11] study in which 81.6 % of patients used iron therapy and all of them used it by IV route. When we compared different hemoglobin levels with mean weekly IV dose of iron we found that patients with lower hemoglobin level (less than 10 g/dl) with mean weekly iron dose of 156 mg/dl in compare to mean weakly dose of about 225 mg/dl for patients with hemoglobin level more than 14 g/dl this indicate inappropriate treatment. Tests used for assessment of iron status are ferritin and TSAT. In this study ferritin values were available only for 57 of patients while TSAT was not recorded, in difference to 48 of patients had ferritin level and 52 of patients had TSAT out of 87 patients in [11] study. Unfortunately, accurate determination of iron status by using serum ferritin alone is a difficult task. It should be combined with TSAT as 10.6 % of patients (17) with hemoglobin level less than 10 g/dl had high ferritin level (more than 1000 ng/dl) these may indicate that there are other factors may responsible for increment of ferritin level like inflammation or infection. To determine other factors that may responsible for lower hemoglobin level we analyzed some patients demographics (age, gender and dialysis onset) along with different hemoglobin levels but we found that there is no significant

difference in contradiction with study done by [11] which found significant difference with female (P value =.04). In addition, other factors that responsible for hypo responsiveness to EPO therapy such as high phosphate level and use of ACEIs or ARBs by the patients analyzed in this study but no significant difference found. Other causes that may contribute to hypo responsiveness to erythropoietin therapy include inflammation, infection, vitamin B12 deficiency and hyperparathyroidism not evaluated in this study as the patients require further assessment of the status of these factors which are not found in the two-dialysis centers and this is considers as one of limitation of this study. Furthermore the data collection period and over all study duration is short to evaluate the anemia management; as other studies done in longer duration range from several months to several years for data collection only. In addition, most of the data collected in our study depend on manually recorded patient's medical record. But we found that this method has numbers of limitations as some important information about treatments of patients and about degree of responsiveness to prescribed medication not documented, some of them had medical record but not contain any information and other had not medicals record at all. Other information that is consider important for such study like blood transfusion and bleeding tendency (by measurement of international normalized ratio (INR) and activated partial thromboplastin time) are not analyzed in our study and this is attribute to poor documentation.

CONCLUSION

Management of anemia of end stage renal disease require further evaluation as erythropoietin and iron doses need to be individualized for each patient according to their hemoglobin level, and assess the factors that may responsible for hypo responsiveness of EPO therapy.

Informed consent

Informed consent was obtained from all participants included in the study.

Ethical Consideration

Before beginning data collection, the study received ethical approval from Khartoum State Ministry of Health Research Department, and permission to the patients' hospital files from the hospital authorities. A written consent was obtained from the patients

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Author Contributions

All the authors contributed evenly with regards to data collecting, analysis, drafting and proofreading the final draft.

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Conflict of Interest

There are no conflicts of interest.

Data and materials availability

All data associated with this study are present in the paper.

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