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Evaluation of Haematological Parameters in Sudanese Haemodialysis Patients Treated with Recombinant Erythropoietin

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Abstract:

Background: *Administration of recombinant human erythropoietin is an important factor in successful treatment of anaemia in haemodialysis patients. The current study aimed to evaluate haematological parameters in patients with chronic renal failure who received erythropoietin therapy.*

Materials and methods: *This study is a cross-sectional study targeting 148 Sudanese haemodialysis patients. They were classified into three groups based on erythropoietin treatment, group1 included patients who received erythropoietin regularly, group2 included those received erythropoietin irregularly, and group3 included those who didn't received erythropoietin. Blood samples were collected from all patients, haematological parameters were measured using automated haematological analyzer (Sysmex kX-2IN), and data analyzed using statistical package for social sciences (SPSS).*

Results: *All patients were anemic with significant decreased in hemoglobin concentration (Hb), packed cells volume (PCV) and red blood cells (RBCs) count. In 83.1% the anaemia was normocytic normochromic anaemia, 1.4% microcytic hypochromic anaemia, and 15.5 macrocytic normochromic. Mean Hb, PCV, and RBCs count were significantly lower in patients who didn't treated by erythropoietin*

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compared with those treated with erythropoietin, and also in those receiving erythropoietin irregularly compared to those receiving erythropoietin regularly. Iron supplement was found to have a positive effect on anaemia parameters, as patients not receiving iron supplement were had significantly lower Hb, PCV, and RBCs count than those receiving iron supplement.

Conclusion: *Erythropoietin and iron supplement should be accompanied for treatment of anaemia of haemodialysis patients.*

Key words: chronic renal failure; haemodialysis; Erythropoietin; Anaemia

Introduction

Chronic kidney disease (CKD) is becoming a major public health problem worldwide **(**Zhang and Rothenbacher., 2008) **.** The mortality rate among patients with chronic kidney disease is much higher than among those without. As glomerular filtration rate declines and patients approach end-stage renal disease (Perazella., *et al* 2006), In Sudan, according to ministry of health records, the prevalence of renal failure is increasing through the few past years (siddig., *et al* 2008).

Anaemia is a frequent complication of chronic kidney disease. (Mara., 2008; Almukhtar., *et al* 2006). Anaemia severity generally relates to the degree of renal impairment. The dominant mechanism is inadequate production of erythropoietin; other contributory factors in include suppressive effects of uraemia, decrease red blood cell survival, blood loss due to platelet function impairment by uremia, folate loss in dialysis, iron deficiency, vitamin B12 deficiency, haemolysis, chronic infection, inflammation, and aluminum toxicity (Drew provan., *et al* 2006; Stauffer and Fan., 2014).

In patients with chronic kidney disease, normochromic normocytic anaemia mainly develops from decreased renal synthesis of erythropoietin. The anaemia becomes more severe

as the glomerular filtration rate (GFR) progressively decreases, (Stauffer and Fan., 2014). Treatment with recombinant human erythropoietin in pre-dialysis patients corrects anaemia, avoids the requirement for blood transfusions and also improves quality of life and exercise capacity (Linman., 1975; levy., 2009).

In vivo erythropoietin is produced primarily by the kidneys, peritubular cells are the probable site of synthesis in the kidneys. Extra renal organs such as the liver also secrete this substance. Ten to fifteen percent of erythropoietin production occurs in the liver, which is the primary source of erythropoietin in the unborn, this glycoprotein hormone with a molecular weight of 46,000, stimulates erythropoiesis and can cross the placental barrier between the mother and the fetus. Erythropoietin was the first human hematopoietic growth factor to be identified; the gene for erythropoietin is located on chromosomes7 (Turgeon, 2012).

Before erythropoietin was synthesized and made available for injection, many patients with kidney disease had to receive blood transfusions to treat anaemia. Now erythropoietin can be made and people with kidney disease are given this form of erythropoietin to correct anaemia (Edmund., 1991).

The present study aimed to evaluate haematological parameters in patients with chronic renal failure who received recombinant human erythropoietin.

Materials and methods

This is a descriptive cross- sectional study, conducted at dialysis centers in Khartoum state hospitals, in the period from February to May 2014.

Study population

A total of 148 patients with chronic renal failure undergoing haemodialysis were enrolled in this study; they were classified into three groups, group1 received regular erythropoietin therapy with iron supplement, gruop2 received irregular erythropoietin therapy and iron supplement, group3 didn't not receive erythropoietin therapy. Patients who treated with blood transfusion in the last three months were excluded from the study.

Sample collection and analysis

Two milliliter (ml) of whole blood was collected in ethylene diamine tetra acetic acid (EDTA) blood container from each subject and complete blood count (CBC) was performed using automated hematology analyzer (SYSMEX KX-2I N, JAPAN). Blood film was prepared from each sample, stained with Leishman stain, and red cell morphology examined using X100 lense.

Data collection and analysis

Data was collected by structured interview questionnaire and analyzed by statistical package for social sciences (SPSS).

Ethical Considerations

This study was approved by faculty of medical laboratory sciences, Al Neelain University, and informed consent was obtained from all participants before sample collection.

Results

A total of 148 patients with end stage renal failure on maintenance haemodialysis for at least 1year were enrolled in this study. 88 (59.5%) of them were males and 60 (40.5%), were females; the age of the patients was ranged from 16 -89 years (Mean±SD:46.3±15.1). 50 (33.8%) were treated with regular

erythropoietin (twice per week), 48 (32.4%) were also treated with erythropoietin but irregularly, while 50 (33.8) were not treated with erythropoietin. 93(62.8%) patients were receiving iron therapy.

The results showed that, all patients were anemic; the anaemia was sever in 23(15.5%) patients, moderate in 83(56.1%), and mild in 42(28.4%) patients.

Of the patients, 121(83.1%) had normocytic normochromic anaemia, 2(1.4%) had microcytic hypochromic anaemia, and 23(15.5%) had macrocytic normochromic anaemia (Table1).

Table (1): Haematological parameters in study subjects

Parameters	**Results**			
	Minimum	**Maximum**	**Mean**	**Stander deviation**
Hb (g/dl)	4.80	13.80	9.12	1.95
PCV (%)	14.50	38.10	28.35	7.87
RBCs ($X10^6/\mu l$)	1.49	4.70	2.92	0.63
MCV (fl)	28.30	120.90	94.77	10.77
MCH (pg)	18.90	40.50	31.40	3.10
MCHC (g/dl)	15.2	38.1	32.4	31.2

Hb: Hemoglobin concentration; **PCV:** Packed cell volume; **RBCs**: Red blood cell count; **MCV:** Mean cell volume; **MCH:** Mean cell hemoglobin; **MCHC:** Mean cell hemoglobin concentration

Mean hemoglobin concentration, haematocrit, and red blood cells count were significantly lower in patient not treated with erythropoietin compared with those treated with erythropoietin, and also in those receiving erythropoietin regularly compared to those receiving erythropoietin irregularly (Table2).

Table (2): Comparison of anaemia parameters according to erythropoietin therapy

Parameter	Erythropoietin therapy						*P. value*
	Regular		Irregular		Not received		
	Mean	SD	Mean	SD	Mean	SD	
HB (g/dl)	10.60	1.55	9.48	1.16	7.20	1.10	0.00
PCV (%)	32.3	5.6	29.2	5.37	22.38	3.6	0.00
RBCs ($X10^6$/µl)	3.30	1.05	2.98	0.43	2.37	0.40	0.00
MCV (fl)	97.58	9.29	95.40	6.34	92.69	11.07	0.23
MCH (pg)	31.87	2.69	32.87	7.65	30.67	3.25	0.09
MCHC (g/dl)	31.87	2.69	32.87	7.65	30.67	3.25	0.30

Hb: Hemoglobin concentration; **PCV:** Packed cell volume; **RBCs**: Red blood cell count; **MCV:** Mean cell volume; **MCH:** Mean cell hemoglobin; **MCHC:** Mean cell hemoglobin concentration

Iron therapy was found to have a positive effect on anaemia parameters , as patients not receiving iron therapy were had significantly lower mean hemoglobin concentration , packed cell volume and RBCs count than those receiving iron therapy (Table3).

Table (3): Effect of iron therapy on anaemia parameters

Parameter	Iron therapy				*P. value*
	Yes		No		
	Mean	SD	Mean	SD	
Hb (g / dl)	10.1	1.5	7.4	1.2	0.00
PCV (%)	31.0	5.6	22.8	3.8	0.00
RBCs ($x10^6$/µ1)	3.2	0.77	2.3	0.51	0.00
MCV (fl)	96.6	8.1	92.9	10.7	0.019
MCH (pg)	32.4	5.8	30.7	3.2	0.059
MCHC (g / dl)	32.4	5.8	30.8	3.2	0.059

Hb: Hemoglobin concentration; **PCV:** Packed cell volume; **RBCs**: Red blood cell count; **MCV:** Mean cell volume; **MCH:** Mean cell hemoglobin; **MCHC:** Mean cell hemoglobin concentration

No statistically significant correlations was found between morphological type of anaemia and erythropoietin therapy (*P.value*: 0.092) or iron therapy (*P.value*: 0.178).

Anaemia was mild to moderate in most (97.8 %) of the patients who receiving iron therapy, while it was moderate to severe in most (96 %) of those not receiving iron therapy.

Discussion

The present study aimed to evaluate haematological parameters in Sudanese haemodialysis patients treated with recombinant erythropoietin.

The present study revealed that all patients were anaemic, the anaemia was severe in 23 patients (15.5%), moderate in 83 patients (56.1%), and mild in 42 patients (28.4%). This finding was consistent with previous studies found that most patients with chronic kidney disease eventually become anemic (*Nurko*., 2006; Almukhtar *et al*., 2006 ; Hala *et al*., 2014)

In this study, 123(83.1%) patients found to have normocytic normochromic anaemia, two (1.4%) patients had microcytic hypochromic anaemia, and 23(15.5%) had macrocytic normochromic anaemia. To some extent this was consistent with previous studies stated that most haemodialysis patients have normocytic normochromic anaemia, and few patients have microcytic hypochromic anaemia (Arun *et al* 2012; Badreldin and Ali 2013; Bradea 2013).

To study the effect of erythropoietin therapy on anaemia parameters patients were divided into 3 groups, group1 included patients who received erythropoietin regularly, grooup2 included those who received erythropoietin irregularly, and group3 included those who didn't received erythropoietin therapy. The results showed that Hb concentration, PCV and RBCs count were significantly lower in group3 patients than group1 and group2 and in group2 patients compared to group1.

This agree with previous studies reported similar findings (Almukhtar., 2006;Suresh., *et al*, 2012 ; Nurko., 2006).

Iron therapy was found to have a positive effect on anaemia of haemodialysis patients; patients who received iron therapy were found to have higher Hb concentration, PCV and RBCs count compared to those who were not treated with iron therapy. This finding was supported by studies concluded that intravenous iron supplementation is very effective in correcting a poor response to erythropoietin in haemodialysis patients (Ayesh *et al*., 2013)

In the present study, no statistically significant correlation was found between morphological type of anaemia and erythropoietin therapy (*P.value:* 0.092) or iron therapy (*P.value*: 0.178). This may be because the anaemia of chronic renal failure is multi-factorial and this can results variable morphological variations.

The present study showed that, anaemia mild to moderate in most patients who receiving iron therapy, while it was moderate to severe about in patients not receiving iron therapy. This agree with previous study reported that degree types of anaemia different according to iron supplement (Arun *et al.,* 2012; Badreldin and Ali., 2013).

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