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Evaluation of Hemoglobin, Erythrocyte Sedimentation Rate and C-Reactive Protein Parameters as Predictors for Resistance to Erythropoietin Therapy in Sudanese Chronic Hemodialysis Patients

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Abstract

Background: Chronic renal failure (CRF) is a major health problem and greatly affects the economic and social status of affected patients worldwide. In Sudan, according to Ministry of Health records, the prevalence rate of renal failure had increased during the few past years, whereby the number of hemodialysis Sudanese patients had reached 2,858 patients. Most of the researchers focused on the effect of renal failure on hematological parameters, but few Sudanese literature was available highlighting the evaluation of haemoglobin (Hb), C - reactive protein (CRP), and erythrocyte sedimentation rate (ESR) in patients with CRF receiving erythropoietin (Epo) whether responsive or nonresponsive for treatment.

Objective: To evaluate the Hb, ESR, and CRP parameters as predictors for resistance to erythropoietin therapy in Sudanese chronic hemodialysis patients.

Materials and methods: This was across-sectional study targeting 60 Sudanese chronic hemodialysis patients, classified into two groups based on their responsiveness for erythropoietin treatment. Group one: included patients responded to at least 3 months regular Epo therapy. Group two: included patients not responding to at least 3 months regular Epo therapy. Blood specimens were collected from all patients. Hb was measured by the automated (Biosystem CC13y-SA3.0), CRP was measured by the (KAYNE NS KT15030115 Mispa12) and ESR was measured by the (Westegren's method).

Results: In the 60 hemodialysis patients, the means were: Hb (9.07 ± SD 2.0), ESR (95.4 ± SD43.3), and CRP (45.0 ± SD 43.3). 50% of the total cases were found in group one, and the other 50% were in group two. The means in group one were: Hb (11.3±SD 0.98), ESR (57± SD 19.6), and CRP (13.9 ± SD 3.8). While, the means in group two were: Hb (6.7 ± SD 0.9), ESR (133.8 ± SD 19.8), and CRP (76.1 ± SD 18.9). The findings of these parameters showed a significant association with Epo therapy (p = 0.000, p = 0.000, and p = 0.000 for Hb, ESR, and CRP respectively).

Conclusion: The haemotological parameters CRP and ESR are useful predictors for resistance to erythropoietin therapy in patients undergoing chronic hemodialysis.

Keywords: Hb, ESR, CRP, Sudanese chronic haemodialysis patients, Erythropoietin therapy.

Introduction

Anemia is defined as reduction in the haemoglobin concentration of the blood. Although normal values can vary between laboratories typical values would be less than 13.5g/dl in adult males and less than 11.5g/dl in females. From the age of 2 years to puberty, less than 11.0 g/dl indicates anemia. Anemia is not a disease per se, but a reflection of some other problem. It occurs when the balance between the normal rates of blood loss and blood production is disturbed. There are three basic mechanisms by which this occurs: (a) blood loss, (b) excessive destruction of red blood cells (hemolysis), and (c) abnormally low production of red blood cells by the bone marrow. In a persons with normal renal function[1].

In CRF, anemia is almost always present, and can be a result of any of the mechanisms listed above. However, the typical "anemia of chronic renal insufficiency" is a result of a decreased production of red blood cells by the bone marrow. This defect in red blood cell production is largely explained by the inability of the failing kidneys to secrete the hormone erythropoietin. This hormone is a necessary stimulus for normal bone marrow to produce red blood cells. In addition, other factors associated with renal failure such as inflammation[1].

Inflammation is one of the major causes of unresponsiveness to erythropoietin treatment. The definition of responsiveness for Epo is that the patient is receiving Epo regularly for at least 3 months and his Hb is more than 10 g/dl. On the other hand, unresponsiveness is defined as the patient is receiving Epo regularly for at least 3 months and his Hb is less than 10 g/dl[1].

External organs such as the liver also secrete Epo. 10-15% of erythropoietin production occurs in the liver, which is the primary source erythropoietin in the newborn. This glycoprotein hormone with a molecular weight of 46,000 stimulates erythropoiesis and can cross the placental barrier between the mother and his fetus. Erythropoietin was the first human hematopoietic growth factor to be identified. The gene for erythropoietin is located on the chromosome 7. C-reactive protein (CRP) is a substance secreted by the liver and inflammation causes a rapid increase in its serum concentration. CRP is a long-term predictor of cardiovascular risk and mortality in the general population and in chronic renal failure patients[2].

About one-third of patients with CRF have serum CRP concentration more than 10 mg/l. In dialysis patients, high CRP levels are associated with low Hb levels and/or Epo resistance. Renal failure describes a medical condition in which the kidneys fail to adequately filter toxins and waste products from the blood. Before Epo was synthesized and made available for injection, many patients with kidney disease had to receive blood transfusions to treat anemia. Now that Epo can be made, people with kidney disease can be given this form of Epo to correct anemia. The injectable form is called recombinant human erythropoietin and is almost identical to what a normal kidney makes[3].

The present study aimed to evaluate Hb, ESR, and CRP in chronic hemodialysis Sudanese patients receiving erythropoietin therapy.

Materials and methods

This was a descriptive, cross-sectional, hospital based study conducted in chronic haemodialysis patients attending Bahry Dialysis Center (Sudan) during the period from August 2017 to February 2018. Ethical approval was received from Al Neelain University Ethical Board and from the Sudan Ministry of Health Research and Ethical Committee. Permission to collect the specimens was granted by the authorities of Bahry Dialysis Center. A signed, informed consent was obtained from all participants before specimens collection; and a detailed explanation of the study objectives was given to them. High ethical standards were maintained throughout the entire duration of this study. Clinical and laboratory data was collected by a structured interview questionnaire and analyzed by the Statistical Package for Social Sciences (SPSS) program. The means of Hb, ESR, and CRP were determined, and p-value was calculated between the two study groups. Pearson correlation was performed between Hb on one side, and ESR and CRP on the other side.

A total of 60 CRF patients undergoing hemodialysis were classified into two groups based on their responsiveness for erythropoietin treatment. Group one: included patients responded to at least 3 months regular Epo therapy. Group two: included patients not responding to at least 3 months regular Epo therapy. Patients under 20 years or treated with blood transfusion during last 3 months were excluded from study. 2 ml venous blood specimen was collected in Ethylene Diamine Tetra Acetic Acid (EDTA) blood containers for analysis of Hb by the (Biosystem CC13Y-SA3.0); and ESR was analyzed by Westegren's method. Another 2 ml venous blood specimen were collected in plain blood containers for analysis of CRP) by the (KAYNE NS KT 15030115 Mispa12) system.

Results

In the 60 hemodialysis patients, means were: Hb (9.07 ± SD 2.0), ESR (95.4 ± SD43.3), and CRP (45.0 ± SD 43.3). 50% of total cases were found in group one, and other 50% in group two.

In group one:

* Mean of Hb was 11.3 ± SD 0.98 (maximum value was 12.9 g/dl, minimum value was 10.0 g/dl, and median value was 11.30 g/dl).
* Mean of ESR was 57± SD 19.6 mm/1hr (maximum value was 89.0 mm/1hr, minimum value was 20.0 mm/1hr, and median value was 59,0 mm/1hr).
* The mean of CRP was 13.9 ± SD 3.8 mg/dl (maximum value was 20.0 mg/dl, minimum value was 8.0 mg/dl, and median value was 13,50 mg/dl).

In group two:

* Mean of Hb was 6.7± SD 0.9 g/dl (maximum value was 8.50 g/dl, minimum value was 5.0 g/dl, and median value was 6.80g/dl).
* Mean of ESR was 133.8 ± SD19.8 mm/1hr (maximum value was 178.0 mm/1hr, minimum value was 101.0 mm/1hr, and median value was 130 mm/1hr)
* Mean of CRP was 76.1± SD18.9 mg/dl (maximum value was 101.0 mg/dl, minimum value was 38.0mg/dl, and median value was 79.5 mg/dl).

These findings showed a significant association with Epo therapy ($p = 0.000$, $p = 0.000$, and $p = 0.000$ for Hb, ESR, and CRP respectively).

As shown in Table (1), in group one there was an inverse correlation (-.150) between Hb and ESR and between Hb and CRP (-.50). As regard group two there was a positive correlation (0.289) between Hb and ESR and between Hb and CRP (0.062).

Table (1): Pearson correlation between Hb, ESR, and CRP in the study groups

Groups	Hb	ESR	CRP
Group one Pearson correlation Sig. (2-tailed)	1	-.150 .427	-.50 .772
N	30	30	30
Group two Pearson correlation Sig. (2-tailed)	1	.289 .122	.062 .745
N	30	30	30

Discussion

The present study aimed to evaluate Hb, ESR, and CRP in hemodialysis Sudanese patients receiving erythropoietin. This study revealed that all group one patients were responding for erythropoietin treatment and levels of Hb, ESR, and CRP were normal. All group two patients were not responding for erythropoietin treatment and levels of ESR and CRP were high, but the level of Hb was low. The high level of ESR and CRP in group two may be related to an inflammation status, where the inflammatory cytokines suppress the bone marrow erythropoiesis. The Pearson correlation gave a strong inverse correlation between Hb and CRP in group one, and intermediate correlation between Hb and ESR. In group two, there was an intermediate direct correlation between Hb and ESR and a very weak direct correlation between Hb and CRP. These findings were in concordance by Peter Barany and his colleagues (1997)[4] who divided their patients into two groups depending on responsiveness for Epo therapy, and the mean of Hb in their first group was (10.16 ± SD 0.7 g/dl) and the Hb mean in their second group was (7.2 ± SD 1.01 g/dl): p = 0.001. The mean of CRP in their first group was (10.6 ± SD 4.3 mg/dl); and the mean of CRP in their second group was (55.6 ± SD 30.9 mg/dl): p = 0.002. They concluded that the level of CRP is a strong predictor for resistance to Epo therapy in patients undergoing chronic hemodialysis.

In another study, Peter Barany and his colleagues (2001)[5] investigated serum C-reactive protein, erythropoietin resistance, and inflammation. They concluded that in patients with chronic renal failure, inflammation is associated with resistance to Epo. In treatment of patients with mild to moderate inflammation, the dose of Epo should be increased. Serial measurements of serum CRP are the best way to monitor the acute-phase response in clinical practice.

In the study of Bradbury and his co-workers (2009)[6] they discussed the impact of elevated CRP on erythropoiesis stimulating agent (ESA) and the dose and responsiveness in hemodialysis patients. They concluded that measurement of inflammation by an elevated CRP level appears to be an independent predictor of greater ESA dose requirements. Patients with the highest ESA doses can achieve comparable Hb levels even after controlling potential confounding variables[6].
Recommendation: From this study it may be recommended that CRP and ESR tests should be used to evaluate hemodialysis patients under Epo therapy.
Conclusion: The haemotological parameters CRP and ESR are useful predictors for resistance to erythropoietin therapy in patients undergoing chronic hemodialysis.

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