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Effect of erythropoietin in treatment of renal anemia in a sample of Iraqi patient

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Abstract: *Background:* Anemia is a common complication of chronic kidney disease and it is associated with a reduce in the quality of life of patients, it contributes an increase in morbidity and mortality and accelerates the rate of progression of chronic kidney disease. *Objective:* The study aims to evaluate effect of erythropoietin in treatment of anemic patients with chronic kidney disease. *Methods:* Two hundred Iraqi patients who were diagnosed as renal anemia from June 2014 to January 2019. They were given erythropoietin for seven months. *Results:* One hundred sixty patients (80%) showed response to treatment, While the other 40 patients (20%) didn't respond to treatment. The two groups were divide din to three sub-groups depending on degree of anemia according to the value of hemoglobinmild (Hemoglobin≥ 10g/dL) , moderate (8 g/dL ≤ Hemoglobin< 10g/dL)and severe (Hemoglobin< 8 g/dL) respectively. In the recombinant human erythropoietin responders results showed increase in hemoglobin (g/dl) and hematocrit (%) levels with decrease in total iron binding capacity (mg/dl) levels during the period of erythropoietin therapy while, in the recombinant human erythropoietin non-responders results showed decrease in hemoglobin (g/dl) andhematocrit % levels and there was no change in total iron binding capacity (mg/dl) levels during the period of erythropoietin therapy. *Conclusion:* Treatment with erythropoietin seems improvement in hemoglobin, hematocrit and total iron binding capacity levels in a large number of anemic patients with chronic kidney disease.
Keywords: Chronic Kidney Disease, Epoetin, Renal Anemia.

Introduction

Anemia is an almost universal complication of chronic kidney disease (CKD). It contributes considerably to reduced quality of life of patients with CKD and has been associated with a number of adverse clinical outcomes [1]. Before the availability of the recombinant human erythropoietin (rhEPO or epoetin), patients frequently require blood transfusion, exposing them to the risks of iron overload, transmission of viral hepatitis and sensitization which reduce the chances of successful transplantation[1-2].

The advent of rhEPO in the late 1980 S changed this situation completely and the ability to correct anemia has shown that its consequences go beyond reduced physical capacity to affect abroad spectrum of physiologic function [3].Thus, there is a strong rationale for managing anemia in CKD patients and yet the optimal treatment strategies are still incompletely defined[1,4-5].

Material and Methods

From June 2014 to January 2019, a total of 200 patients (100 males &100 females) were studied. Those patients were seen in the department of nephrology in Al-Kindy Teaching Hospital, Baghdad / Iraq. The age ranged from 45-75 years, all patients were diagnosed as having renal anemia from history, clinical examination and laboratory investigations. Patients were given epoetinalfa (4000 IU). Subcutaneously once, twice or three times a week, depending on the degree of anemia. All patients received iron supplement, folic acid orally and B^{12} injection (intramuscular) according to the degree of anemia and response. All patients were not on dialysis.

Results

In this study 200 CKD patients with renal anemia were given EPO treatment(4000 IU),

Patients depending on the response to EPO therapy were classified into two groups, rhEPO responders 160 patients (80%) and rhEPO non-responders 40 patients(20%), the two groups were divided in to three sub-groups depending on degree of anemia according to the value of hemoglobin (Hb) mild(Hb≥ 10g/dl) , moderate (8 g/dL ≤ Hb< 10g/dL)and severe (Hb< 8 g/dL) respectively. EPO dose (4000 IU syringe) was as follow:

1. rhEPO responders;
   a. *Mild anemia:* Four times (Month (M) 1-Month5) and two times (M6-M7) per month.
   b. *Moderate anemia:* Four times (M1-M2), eight times (M3-M6) and four times (M7) per month.
   c. *Severe anemia:* Eight times (M2-M6) and four times (M7) per month.
2. rhEPO non- responders;
   a. *Mild anemia:* Four times (M1-M4), eight times (M5-M6) and twelve times (M7) per month.
   b. *Moderate anemia:* Four times (M1-M2), eight times (M3-M5) and twelve times (M6-M7) per month.
   c. *Severe anemia:* Eight times (M1-M4) and twelve times (M5-M7) per month.

In the rhEPO responders results showed increase in Hb (g/dl) and hematocrit (Hct) (%) levels with decrease in total iron binding capacity (mg/dl) levels during the period of EPO therapy.

Table-1: Comparison of Hb between rhEPO responders patients

Groups / Months	Mild (NO:36) Mean ± S.D.	Moderate (NO:62) Mean ± S.D.	Severe (NO:42) Mean ± S.D.
M1	10.18 ± 0.26 BC	8.59 ± 0.45 AC	6.54 ± 0.39 AB
M2	10.57 ± 0.59 ** BC	9.35 ± 0.44 ** AC	8.14 ± 0.91 ** AB
M3	10.91 ± 0.48 ** BC	9.91 ± 0.57 ** AC	8.84 ± 1.03 ** AB
M4	11.45 ± 0.53 ** BC	10.56 ± 0.63 ** AC	9.48 ± 0.98 ** AB
M5	12.00 ± 0.53 ** BC	11.09 ± 0.74 ** AC	10.19 ± 0.88 ** AB
M6	12.56 ± 0.48 ** BC	11.67 ± 0.78 ** AC	10.89 ± 0.88 ** AB
M7	13.29 ± 0.65 ** BC	12.23 ± 0.77 ** AC	11.58 ± 0.93 ** AB

Table-2: Comparison of Hct between rh EPO responders patients

Groups / Months	Mild (NO:36) Mean ± S.D.	Moderate (NO:62) Mean ± S.D.	Severe (NO:42) Mean ± S.D.
M1	32.56 ± 0.84 BC	27.84 ± 1.36 BC	21.57 ± 1.23 AB
M2	33.78 ± 1.89 ** BC	30.11 ± 1.34 ** BC	26.47 ± 2.69 ** AB
M3	34.78 ± 1.42 ** BC	31.81 ± 1.74 ** BC	28.62 ± 3.09 ** AB
M4	36.44 ± 1.59 ** BC	33.74 ± 1.90 ** BC	30.48 ± 2.91 ** AB
M5	38.00 ± 1.51 ** BC	35.32 ± 2.23 ** BC	32.67 ± 2.66 ** AB
M6	39.78 ± 1.46 ** BC	37.09 ± 2.32 ** BC	34.71 ± 2.69 ** AB
M7	41.83 ± 1.92 ** BC	38.74 ± 2.35 ** BC	36.76 ± 2.88 ** AB

Table-3: Comparison of TIBC between rhEPO responder patients			
Groups / Months	Mild (NO:36) Mean ± S.D.	Moderate (NO:62) Mean ± S.D.	Severe (NO:42) Mean ± S.D.
M1	278.14 ± 39.15 C	292.63 ± 40.02	300.03 ± 37.12 A
M2	273.69 ± 37.94 B	290.44 ± 41.08 A	290.72 ± 37.45
M3	269.83 ± 37.12 B	284.73 ± 41.09 A	282.39 ± 36.79 *
M4	269.56 ± 36.80 B	278.94 ± 41.90 A	275.00 ± 35.57 **
M5	269.37 ± 36.65	275.63 ± 41.80	274.28 ± 34.70**
M6	268.71 ± 35.35	273.42 ± 40.10	274.18 ± 35.15**
M7	268.65 ± 33.98	273.00 ± 40.16	274.11 ± 36.89**

In the rhEPO non-responders results showed decrease in Hb (g/dl) andHct % levels. There was no change in TIBC (mg/dl) levels during the period of EPO therapy.

Table-4: Comparison of Hb between rhEPO non-responder patients			
Groups / Months	Mild (NO:8) Mean ± S.D.	Moderate (NO:26) Mean ± S.D.	Severe (NO:26) Mean ± S.D.
M1	10.89 ± 0.87 BC	8.86 ± 0.51 AC	6.46 ± 0.56 AB
M2	11.41 ± 1.16 BC	9.39 ± 0.66 ** AC	7.96 ± 0.62 ** AB
M3	9.90 ± 1.07 C	9.47 ± 1.07 * C	8.36 ± 1.41 ** AB
M4	10.45 ± 1.48 C	9.66 ± 1.43 *	8.89 ± 1.80 ** A
M5	9.95 ± 1.17 BC	8.64 ± 1.48 A	8.21 ± 1.76 ** A
M6	9.08 ± 1.36 ** C	8.05 ± 1.10 **	7.36 ± 1.53 ** A
M7	8.01 ± 0.95 ** C	6.61 ± 1.42 ** C	5.67 ± 1.27** AB

Table-5: Comparison of Hct between rhEPO non-responder patients			
Groups / Months	Mild (NO:8) Mean ± S.D.	Moderate (NO:26) Mean ± S.D.	Severe (NO:26) Mean ± S.D.
M1	32.13 ± 5.19 BC	28.31 ± 1.38 AC	21.96 ± 0.99 AB
M2	34.75 ± 3.41 BC	30.04 ± 2.03 ** AC	25.46 ± 2.04 ** AB
M3	31.75 ± 3.88 C	30.31 ± 2.98 ** C	29.25 ± 3.86 ** AB
M4	33.00 ± 4.44 C	30.92 ± 4.39 **	29.04 ± 4.94 ** A
M5	31.50 ± 4.04 C	28.00 ± 4.55	26.81 ± 5.28 ** A
M6	28.63 ± 3.70 C	25.96 ± 3.12 *	24.12 ± 4.60 *A
M7	25.38 ± 2.62 ** C	23.46 ± 2.76 ** C	19.00 ± 4.55** AB

*: Significant at level $P < 0.05$ / **: Highly Significant at level $P < 0.01$/ A: Significant mild group with other groups at level $P < 0.05$ /B:Significant moderate group with other groups at level $P < 0.05$ / C: Significant severe group with other groups at level $P < 0.05$.

Discussion

In the present study Hb was higher in rhEPO responder patients than rhEPO non-responder patients. Also Hb is strongly correlated with increased rhEPO doses. This finding supports other similar studies [6-9] which demonstrated that the essential role for the treatment of rhEPO in improving anemia and quality of life in CKD both in patients on dialysis and those who are not on dialysis .Thus,rhEPO therapy maintains red blood cell mass and increasing Hb by promoting the survival ,proliferation and differentiation of erythrocytic progenitors [10].

Goda [11]showed that, Hb became higher in EPO therapy groups compared to that of non-EPO therapy groups form 7.00 ± 0.52 to 9.25 ±0.47 ($p< 0.05$) for 3 months. Romina and Geraldo [12] concluded that, epoetinalfa was effective in significantly increasing Hb in CKD patients with anemia. The drug is also safe and well tolerated, with no incident case of pure red cell aplasia (PRCA).Forty patients showed poor response to rhEPOdespite compliance and adherence to iron, vitamin B12 and folate need to be studied for anti-EPO antibodies causing Pure red cell aplasia (PRCA).

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