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ORIGINAL ARTICLE

Investigation of the Efficacy of a Biogeneric Recombinant Human Erythropoietin Alfa in the Management of Renal Anemia in Patients on Hemodialysis: A Multi-center Clinical Trial

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SUMMARY

Background: **Recombinant human erythropoietin (rHuEPO) is the cornerstone therapy for anemia associated with chronic kidney disease. However, not all patients with renal anemia receive sufficient doses of rHuEPO due to its high cost. The present trial aimed to evaluate the efficacy of Epolyrec, a biogeneric rHuEPO, in the management of renal anemia in patients on hemodialysis.**

Methods: **Seventy-two patients with end stage renal disease (ESRD) who were receiving hemodialysis were assigned to receive Epolyrec subcutaneously at a dose of 40 - 80 IU/Kg in 2 - 3 divided doses after each dialysis session for 12 weeks. Hemoglobin, hematocrit, and CBC/DIFF together with biomarkers of iron status, renal function, and trace elements were evaluated at baseline and during the course of trial.**

Results: **Hemoglobin concentrations and hematocrit progressively increased from baseline (8.45 ±1.42 mg/dL and 27.05 ±4.64% for hemoglobin and hematocrit, respectively) to the end of trial (10.56 ±1.93 and 34.06 ±6.70) ($p<0.001$). RBC count ($p = 0.026$), reticulocyte count ($p = 0.045$), and MCV ($p<0.001$) were also significantly increased at the end of trial (3.86 ±0.91x10^6/µL, 0.78 ±0.31%, and 93.50 ±10.90 fL for RBC count, reticulocyte count, and MCV, respectively) compared to baseline (0.98 ±3.38, 0.18 ±0.63, and 89.75 ±9.35). Serum iron and ferritin were decreased while creatinine and phosphorous increased by the end of trial. No significant change was observed in WBC count, RDW, MCH, MCHC, BUN, PTH, Na, Ca, K, and Mg ($p>0.05$). The frequencies of evaluated side effects were generally low and <10%.**

Conclusions: **Epolyrec is clinically efficacious in the elevation of hemoglobin and hematocrit in anemic ESRD patients receiving hemodialysis. Future comparative trials are warranted to compare the efficacy and safety of Epolyrec to those of innovator products.**

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KEY WORDS

Recombinant human erythropoietin; anemia; hemodialysis; biogeneric

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INTRODUCTION

Anemia is one of the most prevalent complications of chronic kidney disease. Based on the world health organization (WHO) definition, diagnosis of anemia is made when the hemoglobin level falls below 13 g/dL (in adult men and postmenopausal women) and below 12 g/dL in pre-menopausal women [1]. Prior to the ad-

vent of recombinant human erythropoietin in 1982, about 25% of dialysis patients required blood transfusions and anabolic steroids to maintain their hemoglobin and hematocrit within the acceptable range [2]. To date, several risk factors have been identified for the development of anemia in patients with advanced renal failure including insufficient production and activity of erythropoietin, decreased survival of red blood cells (RBCs), gastrointestinal bleeding secondary to uremia, blood loss from hemodialysis and repeated blood sampling, and iron and folate deficiency [3]. If remained untreated, anemic hemodialysis patients may experience hemoglobin levels as low as 6 - 8 g/dL and complications such as asthenia, reduced exercise tolerance, depression, dyspnea, and cardiovascular outcomes such as left ventricular hypertrophy and angina [4]. On the other hand, treatment of anemia in such patients would eliminate associated complications and improve their quality of life. Although there is no universal consensus on the ideal hemoglobin and hematocrit level in hemodialysis patients, most of the references have suggested an 11.0 - 12.5 g/L range for hemoglobin and a 33 - 36% range for hematocrit [5-7].

After correcting water and electrolyte imbalances, recombinant human erythropoietin - in particular alfa epoetin - is the most effective drug for the treatment of anemia in hemodialysis patients. However, alfa epoetin is expensive and not available for all patients. Besides, a fraction of patients under treatment with this pharmaceutical may encounter some known complications or even develop drug resistance [8,9]. Therefore, introduction of cost-effective and widely-available biogeneric brands of alfa epoetin with proven efficacy and safety would be highly desirable and increase patients' access to treatment. Epolyrec is a biogeneric recombinant human alfa erythropoietin which has been produced by a manufacturer inside the country. The present trial aimed to evaluate the efficacy of this pharmaceutical in the management of renal anemia in patients on hemodialysis.

MATERIALS AND METHODS

Study design

Included patients had end stage renal disease (ESRD) who were receiving hemodialysis and had a glomerular filtration rate (GFR) <14 mL/min/1.73 m^2 together with a hematocrit <30% or hemoglobin <10 g/dL. Presence of adequate iron stores (serum ferritin >100 mg/L and transferrin saturation >20%) was also among the inclusion criteria. Patients who were diagnosed with iron deficiency were given intravenous iron in order to achieve acceptable iron status prior to inclusion into the trial. None of the patients were contraindicated for erythropoietin therapy. Exclusion criteria were C-reactive protein (CRP) concentrations >10 mg/dL, uncontrolled hypertension, symptomatic ischemic heart disease, history of cerebrovascular events, graft rejection, polycystic kidney disease, myeloma and other malignancies.

This study was a multi-center prospective clinical trial investigating the efficacy of Epolyrec (a biogeneric Iranian made recombinant erythropoietin alfa; Recpharma, Tehran, Iran) in the elevation of hemoglobin level and hematocrit in anemic ESRD patients who were receiving hemodialysis. Patients (n = 72; mean age: 52.6 ±13.3 years; females/male: 44/28) were recruited from among out-patients refered to the dialysis units at Milad (n = 19 ~ 26.4%), Shahid Chamran (n = 10 ~ 13.9%), Baqiyatallah (n = 8 ~ 11.1%), Shahid Fayazbakhsh (n = 15 ~ 20.8%), and Shahid Labafinejad (n = 20 ~ 27.8%) Hospitals in Tehran, Iran. Epolyrec was administered subcutaneously at a dose of 40 - 80 IU/Kg in 2 - 3 divided doses after each dialysis session for 12 weeks. The study was approved by the institutional Ethics Committee and written informed consent was obtained from participants.

Laboratory assessments

Primary efficacy measures included changes in serum hemoglobin, hematocrit, and complete blood count with differential (CBC/DIFF) from baseline to the end of trial (week 12). These examinations were carried out biweekly. Other efficacy measures (evaluated monthly) were changes in serum levels of iron, ferritin, transferring, and total iron binding capacity (TIBC), trace elements including Na, K, Ca, and P, renal function biomarkers including creatinine, blood urea nitrogen (BUN) and uric acid, serum parathyroid hormone (PTH), and albumin.

Assessment of adverse events

Patients were asked daily (via telephone or direct interview) about the incidence of typical adverse effects during the course of trial. The type, severity, and duration of each adverse event was recorded in a separate form. Evaluated side effects included headache, hypertension, nausea, weakness, arthralgia, edema, vomiting, dizziness, fatigue, chest pain, thrombosis, rashes, diarrhea, and rare reactions (hypersensitivity, myocardial infarction, and stroke).

Statistical analysis

Statistical analyses were performed using SPSS software (version 16). Data were presented as mean ±SD (for numerical variables) or number and percentage (for categorical variables). Comparison of biochemical parameters between different time points were carried out using one-way analysis of variance (ANOVA) with Bonferroni post-hoc test. Non-parametric variables were evaluated using Friedman and Wilcoxon signed ranks tests. Repeated measures ANOVA and Pearson correlation coefficient were used to assess the impact of age and gender on hemoglobin and hematocrit values. A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

Demographic characteristics

Among the participants included, 67 were being dialyzed 3 times per week while others had 2 dialysis sessions during the week. Demographic characteristics of patients including age, gender, marital status, educational level, insurance, weight, height, body mass index (BMI), systolic and diastolic blood pressures are summarized in Table 1.

Hemoglobin

Hemoglobin concentrations progressively increased from baseline to the end of trial ($p<0.001$). Hemoglobin values were significantly higher than baseline (8.45 ±1.42 mg/dL) at all assessed intervals i.d. weeks 2 (9.49 ±1.87 mg/dL), 4 (9.91 ±2.12 mg/dL), 6 (10.01 ±2.03 mg/dL), 8 (10.32 ±1.89 mg/dL), 10 (10.24 ±1.79 mg/dL), and 12 (10.56 ±1.93 mg/dL) ($p<0.001$) (Figure 1). Overall, mean hemoglobin elevation during the course of trial (from baseline to week 12) was found to be 2.18 ±1.87 mg/dL which is equivalent to ~ 26% increase. At the end of the 12th week, hemoglobin levels of 52 patients (78.8%) increased by >1 g/dL while 14 patients (21.2%) experienced <1 g/dL elevation.

Hematocrit

Hematocrit concentrations progressively increased from baseline to the end of trial ($p<0.001$). Hematocrit values were significantly higher than baseline (27.05 ±4.64%) at all assessed intervals i.d. weeks 2 (30.26 ±5.79%), 4 (31.91 ±6.5%), 6 (31.94 ±6.01%), 8 (33.14 ±6.03%), 10 (33.05 ±6.22%) and 12 (34.06 ±6.70%) ($p<0.001$) (Figure 2). Overall, mean hematocrit elevation during the course of trial (from baseline to week 12) was found to be 7.22 ±6.50% which is equivalent to ~ 27% in-crease. At the end of the 12th week, hemoglobin levels of 68.2% of patients increased by >5% while 31.8% of patients experienced <5% elevation.

Effect of age and gender on hemoglobin and hematocrit changes

A secondary analysis was performed to evaluate the effect of age and gender on hemoglobin and hematocrit response to Epolyrec. The magnitude of change in hemoglobin concentration from baseline to week 12 was found to be significantly greater in males (2.91 ±2.02 mg/dL) than in females (1.67 ±1.59 mg/dL) ($p = 0.007$). However, comparison of hematocrit changes did not reveal any significant difference between the genders (8.86 ±7.55% in males and 6.13 ±5.52% in females; $p>0.05$) in spite of the greater increase in males. Both hemoglobin ($r = -0.35$, $p = 0.004$) and hematocrit ($r = -0.30$, $p = 0.015$) changes were negatively and significantly correlated with age.

To assess the impact of age and gender on the hemoglobin and hematocrit changes, these variables were entered as confounding factors into the repeated measures ANCOVA model. After excluding age and gender effect, post-trial hemoglobin and hematocrit were still significantly higher than baseline values ($p<0.001$). This indicates that epoetin therapy with Epolyrec is capable of increasing hemoglobin and hematocrit levels regardless of the patient's age and gender.

CBC/DIFF

Overall, there was an increasing trend in the RBC count ($p<0.001$), reticulocyte count ($p<0.001$), and mean corpuscular volume (MCV) ($p = 0.047$) from baseline ($3.38 \pm 0.98 \times 10^6/\mu L$, 0.63 ±0.18%, and 89.75 ±9.35 fL for RBC count, reticulocyte count, and MCV, respecttively) to the end of trial ($3.86 \pm 0.91 \times 10^6/\mu L$, 0.78 ±0.31%, and 93.50 ±10.90 fL). RBC count was found to be significantly higher at weeks 8 ($3.76 \pm 0.81 \times 10^6/\mu L$; $p = 0.048$), and 12 ($3.86 \pm 0.91 \times 10^6/\mu L$; $p = 0.026$) compared to baseline. At baseline, 86.1% of patients had RBC count below normal range while this rate decreased to 62.1% at the end of trial ($p<0.001$). Regarding MCV, values were significantly higher at weeks 2 (91.66 ±9.10 fL; $p<0.001$), 4 (92.37 ±9.36 fL; $p<0.001$), and 12 (93.50 ±10.90 Fl; $p<0.001$) compared to baseline. Reticulocyte count was significantly higher compared to baseline only at week 12 (14.66 ±2.11%; $p = 0.045$). Abnormally low reticulocyte count was present in 9.1% of patients at baseline, while decreasing to 1.9% at the end of trial. A decreasing trend was observed in the platelet count during the course of trial ($p = 0.001$). There were significant reductions in platelet count at weeks 2 ($160.94 \pm 50.06 \times 10^3/\mu L$; $p = 0.003$) and 10 ($159.66 \pm 52.15 \times 10^3/\mu L$; $p = 0.028$) compared to baseline ($178.56 \pm 57.28 \times 10^3/\mu L$). As for the white blood cell (WBC) count, red cell distribution width (RDW), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), the overall pattern of changes during the course of trial was not found to be statistically significant ($p>0.05$) (Table 2).

Iron status biomarkers

Serum iron ($p = 0.063$) and ferritin ($p<0.001$) were progressively decreased during the course of study. Decreased iron level reached statistical significance at the end of month 3 (81.04 ±111.83 µg/dL) compared to baseline (102.25 ±105.70 µg/dL) ($p = 0.013$). As for ferritin, concentrations were found to be lower than baseline (669.94 ±339.89 ng/mL) at all assessed time points i.d. months 1 (581.31 ±292.40 ng/mL; $p = 0.009$), 2 (591.31 ±292.24 ng/mL; $p = 0.047$), and 3 (515.40 ±252.52 ng/mL; $p = 0.002$). In contrast, transferrin and TIBC remained statistically unchanged during the study (Table 3).

Table 1. Demographic characteristics of the study population.

Parameter		
Age (years)		52.6 ±13.3
Gender	Male	28 (38.9)
	Female	44 (66.1)
Dialysis frequency (no/week)	2	5 (7.0)
	3	67 (93.0)
Marital status	Single	10 (13.9)
	Married	54 (75.0)
	Widowed or divorced	8 (11.1)
Educational level	Less than diploma	54 (75.0)
	Diploma and higher	18 (25.0)
Insurance	Yes	70 (97.2)
	No	2 (2.8)
Weight (kg)		64.0 ±12.1
Height (cm)		163.2 ±7.9
BMI (kg/m^2)		24.3 ±4.2
Systolic blood pressure (mmHg)		133.5 ±24.3
Diastolic blood pressure (mmHg)		80.8 ± 9.2

Values are expressed as mean ±SD or number (%). BMI: body mass index.

Table 2. Changes in CBC/DIFF parameters during the course of trial.

Parameter	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12
RBC (×10^6/µL)	3.38 ±0.98	3.39 ±0.83	3.60 ±0.87	3.62 ±0.82	3.76 ±0.81	3.75 ±0.87	3.86††† ±0.91
p-value*	-	>0.05	>0.05	>0.05	0.048	>0.05	0.026
WBC (× 10^3/µL)	6.23 ±1.94	6.25 ±2.03	6.43 ±2.46	6.01 ±1.88	6.025 ±1.71	6.18 ±1.63	6.30 ±2.07
p-value	-	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
Plt (× 10^3/µL)	178.56 ±57.28	160.94 ±50.06	178.92 ±65.46	170.65 ±52.02	170.42 ±49.28	159.66 ±52.15	165.82 ±58.69††
p-value	-	0.003	>0.05	>0.05	>0.05	0.028	>0.05
Reticulocyte (%)	0.63 ±0.18	0.65 ±0.17	0.65 ±0.15	0.72 ±0.28	0.66 ±0.17	0.66 ±0.18	0.78†† ±0.31
p-value	-	>0.05	>0.05	>0.05	>0.05	>0.05	0.045
MCV (fL)	89.75 ±9.35	91.66 ±9.10	92.37 ±9.36	91.39 ±11.32	91.23 ±9.94	91.61 ±14.83	93.50 ±10.90†
p-value	-	0.001	0.001	>0.05	>0.05	>0.05	0.003
MCH (pg)	27.64 ±4.26	28.63 ±3.04	28.53 ±3.08	28.65 ±4.36	28.26 ±3.04	28.73 ±3.11	28.65 ±3.36
p-value	-	>0.05	>0.05	0.009	>0.05	>0.05	>0.05
MCHC (%)	31.20 ±1.42	31.14 ±1.82	30.63 ±2.10	31.46 ±1.73	31.01 ±1.57	31.20 ±1.68	31.03 ±2.13
p-value	-	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05
RDW (%)	14.67 ±1.91	14.57 ±1.35	15.01 ±1.88	14.64 ±1.60	15.02 ±1.84	14.83 ±1.66	14.66 ±2.11
p-value	-	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

RBC: red blood cell; WBC: white blood cell; Plt: platelet; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width. *Comparison with baseline; Comparison of values during the course of trial using one-way ANOVA: $^†p = 0.047$; $^{††}p = 0.001$; $^{†††}p<0.001$.

Table 3. Changes in iron status biomarkers during the course of trial.

Parameter	Baseline	Month 1	Month 2	Month 3
Serum iron (µg/dL)	102.25 ±105.70	90.86 ±74.31	96.26 ±103.19	81.04 ±111.83
p-value*	-	>0.05	>0.05	0.013
Ferritin (ng/mL)	669.94 ±339.89	581.31 ±292.40	591.31 ±292.24	515.40 ±252.52
p-value	-	0.009	0.047	0.002
Transferrin (mg/dL)	107.61 ±80.39	100.58 ±81.03	110.67 ±135.48	97.68 ±75.67
p-value	-	>0.05	>0.05	>0.05
TIBC (µg/dL)	236.79 ±77.94	230.39 ±77.64	225.30 ±54.32	227.62 ±57.59
p-value	-	>0.05	>0.05	>0.05

TIBC: total iron binding capacity; *Comparison with baseline.

Table 4. Changes in renal function biomarkers and PTH during the course of trial.

Parameter	Baseline	Month 1	Month 2	Month 3
Uric acid (mg/dL)	6.54 ±1.24	6.36 ±1.39	6.70 ±1.36	6.73 ±1.30
p-value*	-	> 0.05	> 0.05	>0.05
BUN (mg/dL)	94.17 ±56.31	89.36 ±39.02	90.41 ±44.27	97.25 ±48.98
p-value	-	>0.05	>0.05	>0.05
Craetinine (mg/dL)	9.15 ±3.19	9.16 ±2.75	8.95 ±2.78	10.26 ±2.87†††
p-value	-	>0.05	>0.05	0.002
PTH (pg/mL)	381.25 ±423.47	337.13 ±350.33	376.00 ±410.05	421.06 ±414.60
p-value	-	>0.05	>0.05	>0.05

BUN: blood urea nitrogen; PTH: parathyroid hormone. *Comparison with baseline; Comparison of values during the course of trial using one-way ANOVA: †††*p*<0.001.

Table 5. Changes in trace elements during the course of trial.

Parameter	Baseline	Month 1	Month 2	Month 3
Calcium (mg/dL)	8.93 ±1.09	9.04 ±0.92	8.68 ±1.47	9.01 ±1.25
p-value*	-	>0.05	> 0.05	>0.05
Potassium (mg/dL)	5.35 ±0.95	5.32 ±0.76	5.24 ±0.79	5.40 ±0.80
p-value	-	>0.05	> 0.05	>0.05
Phosphorus (mg/dL)	6.05 ±1.60	6.10 ±1.98	6.16 ±1.61	6.74 ±2.14††
p-value	-	>0.05	>0.05	0.049
Sodium (meq/L)	139.99 ±6.60	138.42 ±5.70	139.38 ±5.26	138.84 ±4.89
p-value	-	>0.05	>0.05	>0.05
Albumin (meq/L)	4.09 ±0.73	3.93 ±0.57	3.98 ±0.43	4.02 ±0.63
p-value	-	>0.05	>0.05	>0.05

***Comparison with baseline; Comparison of values during the course of trial using one-way ANOVA: ††*p* = 0.009.**

Table 6. Incidence of evaluated side effects during the course of trial.

Side effect	No. assessed patients	No. observed events	Percent
Headache	72	**7 (9.7)**	**9.7**
Hypertension	72	**5 (6.9)**	**6.9**
Nausea	72	**5 (6.9)**	**6.9**
Weakness	72	**5 (6.9)**	**6.9**
Arthralgia	72	**5 (6.9)**	**6.9**
Edema	72	**4 (5.6)**	**5.6**
Vomiting	72	**4 (5.6)**	**5.6**
Dizziness	72	**3 (4.2)**	**4.2**
Fatigue	72	**3 (4.2)**	**4.2**
Chest Pain	72	**2 (2.8)**	**2.8**
Thrombosis	72	**2 (2.8)**	**2.8**
Hypersensitive Reaction	72	**2 (2.8)**	**2.8**
Rush	72	**1 (1.4)**	**1.4**
Diarrhea	72	**1 (1.4)**	**1.4**
MI	72	**0 (0.0)**	**0.0**
Stroke	72	**0 (0.0)**	**0.0**

MI: myocardial infarction.

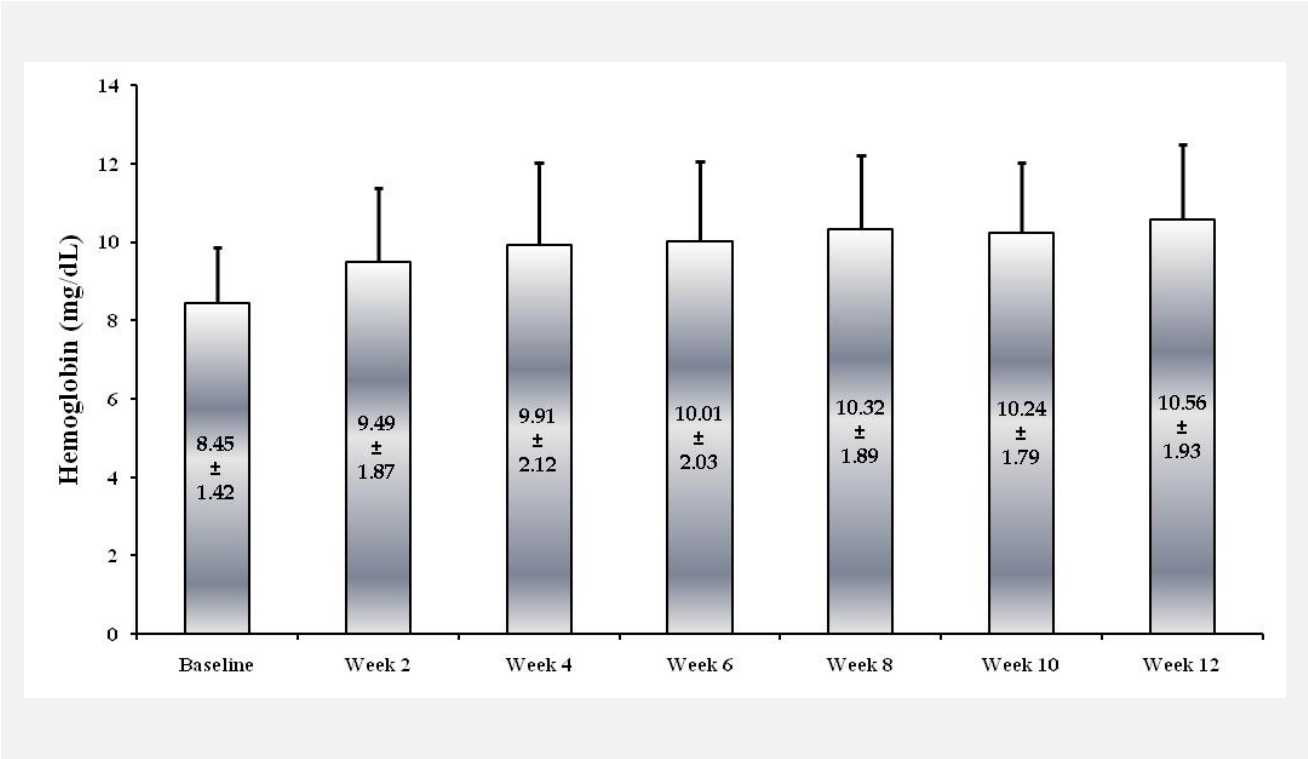

Figure 1. Changes in hemoglobin concentration during the course of trial. Comparison with baseline value: ***p<0.001.

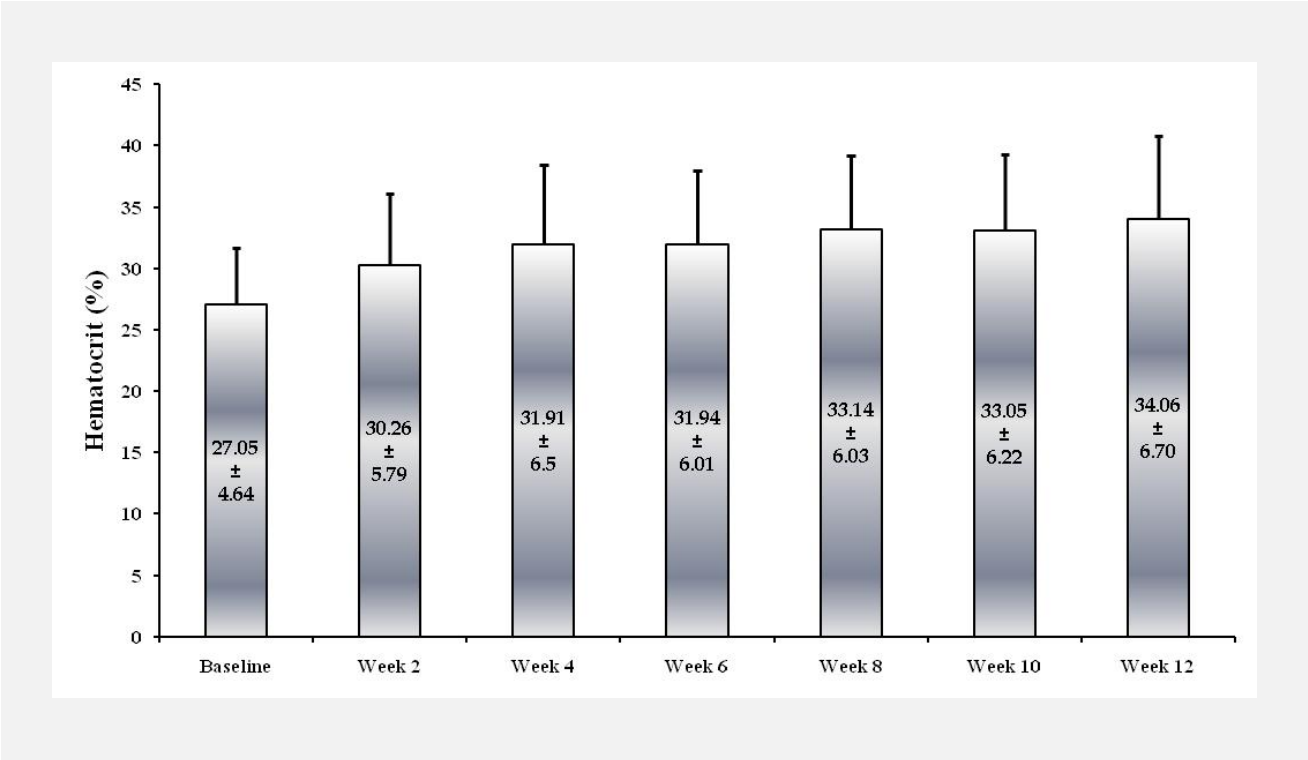

Figure 2. Changes in hematocrit during the course of trial. Comparison with baseline value: ***p<0.001.

Renal function biomarkers and PTH

There was no significant alteration in BUN, uric acid, albumin- and PTH levels by the end of trial ($p>0.05$). In contrast, serum creatinine was found to be significantly elevated at month 3 (10.26 ±2.87 mg/dL) compared to baseline level (9.15 ±3.19 mg/dL) ($p = 0.002$) (Table 4).

Trace elements

No significant change was observed in calcium, sodium, and potassium concentrations during the trial. However, serum phosphorus levels significantly increased by the end of trial ($p = 0.009$) as noted in month 3 (6.74 ±2.14 mg/dL) compared to baseline (6.05 ±1.60 mg/dL) ($p = 0.049$) (Table 5).

Adverse events

The incidence of evaluated adverse events (headache, hypertension, nausea, weakness, arthralgia, edema, vomiting, dizziness, fatigue, chest pain, thrombosis, hypersensitivity reactions, rashes, diarrhea, myocardial infarction- and stroke) were generally low and not exceeding 10% for any given complication (Table 6).

DISCUSSION

Introduction of recombinant human erythropoietin (rHuEPO) has substantially eliminated the need for blood transfusions and androgen therapy in chronic kidney disease (CKD)-induced anemic patients. These conventional treatments were generally associated with several side effects such as infection, immune reactions, iron overload (in case of transfusion) [10], virilization, acne, priapism- and hepatotoxicity (in case of androgen therapy) [11].

Erythropoietin stimulating drugs consume a considerable fraction of healthcare budgets in different countries. These products have been estimated to constitute about 11% of all Medicare ESRD costs and therefore represent the largest single Medicare drug expenditure in the US (~ $1.75 billion in 2005) [12]. The high cost of epoetin is indeed an important concern which limits patients' access to this medication, particularly in developing countries [13,14]. For instance, in an investigation among Tunisian hemodialysis patients only 10.8% of patients were on erythropoietin while 38% of patients required blood transfusions [14]. This rate of epoetin use in developing world reveals a vast gap compared to developed countries in which statistics indicate administration of epoetin for about 83 - 94% of hemodialysis patients [15].

The expiry of first-generation epoetin patents has allowed pharmaceutical companies to manufacture biogeneric follow-on products. Such pharmaceuticals with established safety and efficacy, low price, and wide availability are of urgent demand for anemic patients who are receiving hemodialysis or those who have undergone kidney transplantation surgery. Epolyrec is a recently introduced biogeneric epoetin alfa that has been manufactured inside the country.

The present study produced results which corroborate the findings of a great deal of the previous work on the efficacy of rHuEPO therapy in ESRD patients receiving hemodialysis [16-18]. As mentioned above, the unique feature of the current investigation is the administration of a newly manufactured biogeneric rHuEPO named Epolyrec. The findings revealed a significant rise in both hemoglobin (~ 25%) and hematocrit (~ 26%) which started as early as week 2 and reached a peak at week 12. Previous cohort [19] as well as prospective [20] studies have reported an inverse association between higher hematocrit levels and mortality rates among anemic ESRD patients.

As expected, mean serum iron and ferritin concentrations decreased with Epolyrec therapy during the course of trial (21.74% and 23.07% for serum iron and ferritin, respectively). This is due to the enhanced incorporation of iron into newly synthesized hemoglobin and red blood cells. Iron deficiency is a frequent problem among ESRD patients receiving hemodialysis [21]. This condition has a profound impact on the responsiveness to the treatment and may add to the dose and thereby cost of rHuEPO [22]. Besides, iron deficiency has been listed among the pathomechanisms of erythropoietin resistance [23]. As mentioned earlier, patients included had a ferritin level above 100 ng/mL and transferrin saturation >20%.

In conclusion, the evidence from this multicenter study favors the efficacy of Epolyrec - as a biosimilar rHuEPO - in the elevation of hemoglobin and hematocrit in anemic ESRD patients receiving hemodialysis. However, recent guidelines suggest that the clinical efficacy of such biopharmaceuticals should be confirmed by at least 2 studies [24]. A limitation of the current study was its single arm and non-placebo controlled design which makes the findings indicative rather than conclusive. Hence, further work needs to be done to establish whether the observed effects can be confirmed in comparison with a placebo control arm. With respect to the efficacy, longer term studies with appropriate follow-up and careful post-marketing surveillance are warranted particularly for the detection of rare side effects such as pure red cell aplasia and other immunologic reactions [25]. Upon establishment of safety and efficacy of Epolyrec, this biopharmaceutical could serve as a readily available and cheap medication for patients with renal anemia as well as those who develop resistance or adverse reactions to the original product. Finally, comparative trials are greatly recommended to compare the efficacy and safety of Epolyrec to those of innovator products.

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Declaration of Interest:
None.

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