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Original Article

Comparison of Efficacy of Erythropoietin Alpha with Erythropoietin Beta in Treatment of Anemia in Patients of End Stage Renal Disease on Hemodialysis

Bilal Javaid, Muhammad Irfan, Sumaira Hassan, Ijaz Nabi, Fatima Rehman

Allied Hospital, Faisalabad Medical University, Faisalabad

Abstract

Objective: To compare the efficacy of erythropoietin (EPO) alpha with erythropoietin beta in treatment of anemia in patients of end stage renal disease (ESRD) on hemodialysis.

Methods: This Prospective Cohort was carried out in the Department of Nephrology, Allied hospital, Faisalabad from 11/06/2022 to 10/12/2022. 170 patients meeting the selection criteria were enrolled. Group A patients received erythropoietin alpha for 3 months. Group B patients received erythropoietin beta for 3 months. The dosage was administered subcutaneously. Efficacy was assessed after 3 months of treatment as per the operational definition.

Results: Mean age in Group A was 45.79+10.91 and in Group B 44.74+11.28 years. Mean BMI of the patients in Group A was 27.36+2.69 and in Group B 27.42+2.83. Mean duration of dialysis in Group A was 2.91+1.18 years and in Group B 2.87+1.14 years. Efficacy in Group A was 17(20%) and in Group B 38(44.7%).

Conclusion: The study concluded that erythropoietin beta is better than erythropoietin alpha in treatment of anemia in patients of ESRD on hemodialysis.

Keywords: End stage renal disease (ESRD), anemia, erythropoietin alpha, hemodialysis, erythropoietin beta, efficacy.

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Corresponding Author: Dr. Bilal Javaid, **Email:** dr.bilaljavaid160@gmail.com

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Introduction

Anemia is prevalent in individuals with chronic kidney disease (CKD), affecting 15.4% of adults compared to the overall population (7.4%). Anemia affects 8.1% of patients with stage 1 CKD and 53.4% of those with stage 5 CKD, making it more frequent in individuals with more severe renal disease1. Notably, anemia in individuals with CKD is linked to a higher likelihood of experiencing a decline in health-related quality of life, CVD, hospitalization, development of ESRD and death comparing to CKD patients who do not have anemia.[2]

The major cause of anemia in CKD is inadequate synthesis of EPO as a result of renal failure which is an essential growth factor for erythroid progenitor cells. The renal cortex's peritubular interstitial cells are responsible for the synthesis of erythropoietin. That component is hematopoietic.[3] EPO is a vital growth factor necessary for the enrollment, multiplication, and survival of erythroid progenitor cells. This is a hematopoietic factor.[4] Erythropoietin is mostly secreted in response to hypoxia. In patients with ESRD the production of EPO is inadequate due to the deterioration of normal renal microvasculature's ability to detect oxygen, an increase in the required oxygen pressure in the surrounding tubular area for EPO release, the transformation of peri-tubular interstitial cells into fibroblasts that generate matrix, the accumulation of pro-inflammatory cytokines that impede erythropoietin synthesis and dysregulation of the autonomic sympathetic system.[5]

Erythropoiesis-stimulating agents (ESAs) is being utilized for treating anemia associated with CKD since the 1980s.[6] The majority of individuals with ESRD require erythropoietin or blood transfusions in order to reach the desired hemoglobin (Hb) level. Three EPO stimulating drugs may be classified into two main categories: short-acting agents and long-acting medications.[7]

Both erythropoietin alpha and erythropoietin beta are

popular short-acting ESAs used to treat anemia in patients with CKD. Variations in carbohydrate structures of recombinant human erythron-poietins (rHuEPOs) are responsible for disparities in the way these substances are distributed and exert their effects in the body. After an intravenous infusion, EPO-beta had a 20% longer half-life than the EPO-alpha. EPO-beta exhibited slower drug absorption after subcutaneous injection compared to EPO-alpha. Its extended duration of action justifies its utilization particularly during the maintenance phase of renal anemia therapy.[8] According to research, after three months, the effectiveness of EPO-alpha and beta (Hb levels of ≥ 11 g/l after 3 months) was 22.2% and 40% respectively.[5]

Patients receiving hemodialysis due to ESRD often struggle with anemia. This research compared the effectiveness of EPO-beta and alpha in treating anemia in ESRD patients in order to lower related morbidities and mortality.

Methods

This Prospective Cohort was conducted at the Department of Nephrology, Allied hospital, Faisalabad. Duration of the study was six months from 11/06/22 to 10/12/2022. The sample size was estimated using the WHO calculator of at a 5% level of significance, power of the study was 80%, the effectiveness of erythropoietin Alpha as 22.2% and the efficacy of erythropoietin Beta was 40%8. A total of 170 patients, including both males and females, aged between 18 and 70 years, who had ESRD with anemia and had been on hemodialysis for more than 3 months were included in study. Patients with uncontrolled hypertension, anemia other than CKD, chronic liver failure, uncontrolled hyperparathyroidism, heart failure, a history or current blood coagulation disorders, a known allergy to erythropoietin were not included in the study. The enrolled patients were allocated into two groups using a lottery approach. EPO brands were international and dose was as per manufacturer's recommendation. Group A patients received EPO-alpha (6000 IU thrice weekly) for 3 months. Group B patients received EPO-beta (5000 IU twice weekly) for 3 months. The dosage was administered subcutaneously. Efficacy was assessed after 3 months of treatment as per operational definition (increase in Hb>1 gram/dL). All the data was analyzed using SPSS V-25. For comparison of efficacy among both groups chi-square test was applied. P- value ≤0.05 was considered significant.

Results

A total of 170 patients were considered consisting of 138 (81.2%) males and 32 (18.8%) females showing clear domination of males in this study. Further characteristics of patients are shown in Table 1.

Comparison of mean Hb levels of the patients shows 8.51+0.55 in Group A and 8.52+0.55 in Group B, p-value=0.889 whereas these findings after treatment in Group A were 8.94+1.12 and in Group B 9.59+1.34, p-value 0.001.

Table 2: *Hb levels of patients in both groups*

Hb Levels	Group-A		Group-B		P value
	Mean	SD	Mean	SD	
Before treatment	8.51	0.55	8.52	0.55	0.889
After treatment	8.94	1.12	9.59	1.34	0.001

In our study, comparison of efficacy in both groups shows that in Group A 17(20%) and in Group B 38(44.7%), p-value 0.000.

Table 3: *Efficacy of both groups*

Efficacy	Group-A	Group-B	P value
	N (%)	N (%)	
Yes	17(20)	38(44.7)	0.000
No	68(80)	47(55.3)	
Total	**85(100)**	**85(100)**	

Effect modifiers like age, duration of dialysis, BMI, gender, hypertension, and diabetes mellitus was strati-fied (Table 4).

Table 1: *Basic Characteristics of Patients*

		Group-A		Group-B		P Value
		Mean	SD	Mean	SD	
Age(years)		45.79	10.91	44.74	11.28	0.251
Gender	Male	71	83.5%	67	78.8%	0.278
	Female	14	16.5%	18	21.2%	
BMI		27.36	2.69	27.42	2.83	0.364
Duration of dialysis		2.91	1.18	2.87	1.14	0.201
Diabetes Mellitus		52	61.2%	49	57.65	0.377
Hypertension		41	48.2	38	44.7	0.379
Total		85	100.0%	85	100.0%	-

Table 4: *Comparison of efficacy of both groups by demographic and clinical factors*

Factors		Efficacy	Study Groups		Total	P-value
			A	B		
Age	18-50	Yes	10(32.3%)	21(67.7%)	31(100%)	0.021
		No	40(56.3%)	31(43.7%)	71(100%)	
	51-70	Yes	7(29.2%)	17(70.8%)	24(100%)	0.007
		No	28(63.6%)	16(36.4%)	44(100%)	
Gender	Male	Yes	14 (35%)	26 (65%)	40 (100%)	0.011
		No	57 (58.2%)	41 (41.8%)	98 (100%)	
	Female	Yes	3 (20%)	12 (80%)	15 (100%)	0.013
		No	11 (64.7%)	6(35.3%)	17 (100%)	
BMI	Up-to 30	Yes	15 (31.9%)	32 (68.1%)	47 (100%)	0.002
		No	57 (59.4%)	39 (40.6%)	96 (100%)	
	>30	Yes	2 (25%)	6 (75%)	8 (100%)	0.127
		No	11(57.9%)	8 (42.1%)	19 (100%)	
Duration of Dialysis	1-2	Yes	7 (25.9%)	20 (74.1%)	27 (100%)	0.004
		No	34 (59.6%)	23 (40.4%)	57 (100%)	
	>2	Yes	10 (35.7%)	18 (64.3%)	28 (100%)	0.039
		No	34(58.6%)	24 (41.4%)	58 (100%)	
Diabetes Mellitus	Yes	Yes	13(34.2%)	25(65.8)	38(100%)	0.006
		No	39(61.9%)	24(38.1%)	63(100%)	
	No	Yes	4(23.5%)	13(76.5%)	17(100%)	0.020
		No	29(55.8%)	23(44.2%)	52(100%)	
Hypertension	Yes	Yes	11(37.9%)	18(62.1%)	29(100%)	0.048
		No	30 (60%)	30(60%)	50(100%)	
	No	Yes	6 (23.1%)	20 (76.9%)	26(100%)	0.002
		No	38 (58.5%)	27 (41.5%)	65 (100%)	

Discussion

One of the most common complications that individuals with chronic renal failure experience is anemia. Additionally, renal anemia contributes to cardiovascular problems.[9,10] This study was conducted to evaluate the better treatment strategy for improvement of anemia in patients of ESRD on hemodialysis so that associated morbidities can be reduced.

In our study, mean age in Group A was 45.79+10.91 and in Group B 44.74+11.28 years, mean BMI of the patients in Group A was 27.36+2.69 and in Group B 27.42+2.83. Mean duration of dialysis in Group A was 2.91+1.18 years and in Group B 2.87+1.14 years. Mean Hb levels was 8.51+0.55 in Group A and 8.52+0.55 in Group B at baseline and after treatment in Group A were 8.94+1.12 and in Group B 9.59+1.34, p-value 0.001. The results of a study showed that after 3 months, mean Hb was 10.9±0.86 in EPO-alpha and 10.4±0.94 in EPO-beta8. Comparable results were found in two different RCTs from Iran, Bosnia and Herzegovina[11,12] and a brief report from UK[13]. Comparison of efficacy in both groups shows that in Group A 17(20%) and in Group B 38(44.7%), p-value 0.000.

In a previous study, efficacy of EPO-alpha and EPO-beta in treatment of anemia in patients of ESRD on hemodialysis after 3 months was 22.2% and 40% respectively.[2] These findings correspond to our results. Several papers conducted a comparative analysis of the therapeutic effectiveness of epoetin alpha and epoetin beta in keeping Hb level within a specified range of 10-12 g/dl throughout a treatment duration of 3-4 months. Various studies done in this context found no statistically significant difference in hematocrit levels among individuals treated with both epoetin alpha and epoetin beta for the treatment of anemia caused by chronic renal disease.[14,15] Azmandian et al conducted research that found a difference in EPO-alpha and EPO-beta in their ability to sustain hemoglobin levels of 11 g/dl. This study provides evidence in favor of epoetin beta.[14] No significant difference was detected between the two medications in terms of sustaining hemoglobin levels equal to or greater than 11 g/dl. However, there

was a reduced frequency of obtaining hemoglobin levels of 13 g/dl with Cinnapoetin. Different research done in a similar manner observed a significant rise in hemoglobin levels when individuals with CKD were treated with EPO-beta as compared to those treated with EPO-alpha.[15]

Our research findings indicate that EPO-beta exhibited superior efficacy compared to EPO-alpha. While the first observation lasted just three months, it is necessary to conduct a further randomized controlled trial to validate these findings over a longer length, ensuring both external and internal validity. Despite its brief duration of three months, the research spanned the whole three-month period. Furthermore, it would have the capability to identify the factors present in our community with renal sickness that contribute to a substantial reaction to different forms of erythropoietin, resulting in a noteworthy advantage.

Conclusion

We concluded that erythropoietin beta is better than erythropoietin alpha in treatment of anemia in patients of end stage renal disease on hemodialysis.

Ethical Approval: The IRB/EC approved this study via letter no 48.ERC/FMU/2021-22/256 dated March 17, 2023.

Conflict of Interest: None

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Authors' Contribution

BJ: Conceptualization of the project

MI, FR: Design of the work.

SH, IN: Data acquisition, analysis, or interpretation.

MI, SH, IN: Draft the work.

BJ, FR: Critical review critically of important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

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