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Original Research Article

Comparative study of efficacy and safety of erythropoietin and darbepoetin for treatment of anemia in chronic kidney disease patients: a comparative, observational and prospective study

Bikesh K. Shah[1]*, Waseem H. Bhat[1], Jeeva George[2], Balakeshwa Ramaiah[2]

[1]Department of Pharmacy, Karnataka College of Pharmacy, Bangalore, Karnataka, India
[2]Department of Pharmacy Practice, Karnataka College of Pharmacy, Bangalore, Karnataka, India

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***Correspondence:**
Dr. Bikesh K. Shah,
Email: bikeshshah2013@gmail.com

ABSTRACT

Background: Anemia is a common prognosis of chronic kidney disease (CKD). It is predominantly managed with erythropoietin and darbepoetin. The objective of this study was to compare the efficacy and safety of erythropoietin injection versus darbepoetin for treating renal anemia amongst patient with CKD.
Methods: Patients of either gender diagnosed with anemia due to CKD, irrespective of dialysis who had haemoglobin less than 12g/dl were included in the study. Comparison of efficacy and safety of erythropoietin and darbepoetin was done based on the laboratory values of hemoglobin (Hb), red blood cells (RBCs), haematocrit (PCV) and adverse events respectively.
Results: A total of 108 patients met the inclusion criteria; 54 of them were treated with erythropoietin and 54 were treated with darbepoetin. The changes in Hb, RBCs and PCV in the group of patients who were on erythropoietin were 1.16, 0.49 and 3.76 respectively. Similarly, the changes in Hb, RBCs and PCV in the group of patients who were on Darbepoetin were 1.19, 0.42 and 3.52 respectively. The differences in the changes of Hb, RBCs and PCV in the both groups of patients were 0.04, 0.07 and 0.24 respectively. A total of 4 adverse events (HTN, vomiting, headache and joint pain) were reported by 24 (44.44%) patients of erythropoietin group and a total of 1 adverse event (HTN) was reported by 19 (35.19%) patients of darbepoetin group.
Conclusion: Both erythropoietin and darbepoetin were found to be equally effective and safe for the treatment of anemia in CKD patients.

Keywords: Anemia, Chronic kidney disease, Darbepoetin, Erythropoietin

INTRODUCTION

Chronic kidney disease (CKD) is a progressive loss of function over several months to years, characterized by gradual replacement of normal kidney architecture with interstitial fibrosis.[1] CKD is the 16th leading cause of years of life lost worldwide with an incidence rate between 8% to 16%. Appropriate screening, diagnosis and management by primary care clinicians are necessary to prevent adverse CKD-associated outcomes, including cardiovascular disease, end stage kidney disease, anaemia and death.[2,8] anaemia is one of the most common complications of CKD. Anaemia is defined as a reduction in one or more of the major red blood cell measurements; haemoglobin concentration, haematocrit, or red blood cell count.[3]

Traditionally, the only treatment available was to give red blood cell transfusions, but this was time-consuming, expensive, an infection risk, may lead to fluid and iron overload and promotes antibody formation, which may give problems if transplantation is subsequently

attempted.[9] Different types of erythropoiesis-stimulating agents (ESAs) used in anemia due to CKD are as follows.

Erythropoietin (EPO) is a hormone produced by the kidney that promotes the formation of red blood cell by the bone marrow. The kidney cells producing erythropoietin are responsive to decreased oxygen levels in the blood flowing through the kidney. These cells produce and secrete erythropoietin in response to low oxygen levels.

The most common use is in people with anaemia (low blood count) related to kidney dysfunction. When the kidneys are not properly functioning, they produce less than normal amounts of erythropoietin, which can lead to low red blood cell production, or anaemia. Erythropoietin triggers the bone marrow to increase red blood cell production. The resulting rise in red cells increases the oxygen-carrying capacity of the blood.[4,10]

Darbepoetin (DPO) is a novel erythropoiesis-stimulating protein (NESP) that is a recombinant hyperglycosylated analogue of epoetin which stimulates red blood cell production by the same mechanism as the endogenous hormone Produced by recombinant DNA technology. It is a 37 Kda, glycoprotein containing 165 amino acids and five N-linked oligosaccharide chains, whereas endogenous erythropoietin (EPO) and the shorter-acting recombinant human erythropoietin (rHuEPO) contain only three.[6,7]

METHODS

Study type

It was a prospective, observational study.

Study place

The study was conducted in the department of nephrology, Bangalore Baptist hospital, Bangalore, India.

Study duration

The study period was from June 2023 to November 2023, on chronic kidney disease patients having anaemia.

Inclusion criteria

Patients who were registered in Bangalore baptist hospital, age between 18-97 years of both sexes, having anemia due to CKD and prescribed with either erythropoietin or darbepoetin were included in the study.

Exclusion criteria

Pregnant and lactating females, patients who were on RBC transfusion and those who underwent recent surgeries were excluded from the study.

A total of 108 cases were selected on the basis of inclusion and exclusion criteria, and were divided randomly into two groups based on treatment. Group A (erythropoietin): Erythropoietin 4000 units Subcutaneously twice weekly (n-54) and group B (darbepoetin): darbepoetin 40 mcg subcutaneously once monthly (n-54). Data on the drugs, lab reports of RBCs, PCV and Haemoglobin was recorded. Also, the adverse drug reactions related to the study drugs were also noted. Lab values of RBCs, PCV and haemoglobin were used to evaluate the efficacy of both the drugs. And the ADRs were used to assess the safety of both the drugs. Data were collected and analyzed using z-test.

RESULTS

The study comprised of 108 patients, with 54 patients in each group. Demographic variables were assessed. Maximum number of patients was aged between 58-77 years of age, with male gender predominance. In both the groups, most of the patients were having stage 5 CKD (Table 1).

Table 1: Comparison of demographics data in the study groups.

Parameters		Group EPO		Group DPO	
		No.	**%**	**No.**	**%**
Age group (in years) Mean±SD	18-37	9	16.67	2	3.71
	38-57	20	37.04	18	33.33
	58-77	21	38.89	28	51.85
	78-97	4	7.41	6	11.11
	54.72±16.16			60.74±13.17	
Gender	Male	37	68.52	32	59.26
	Female	17	31.48	22	40.74
Stages of CKD	Acute on CKD	7	12.96	15	27.78
	3	2	3.7	8	14.81
	4	2	3.7	3	5.56
	5	36	66.67	26	48.15
	ESRD	7	12.96	2	3.7
Total		54	100	54	100

Table 2: Comparison of haemoglobin levels in the study groups.

Drugs	Hb before, Mean±SD	Hb after, Mean±SD	Mean change in Hb	P value
Erythropoietin	7.84±1.33	9±1.48	1.16	P<0.0001
Darbepoetin	8.6±1.25	9.79±1.31	1.19	P<0.0001

Table 3: Comparison of RBCs levels in the study groups.

Drugs	RBC before, Mean±SD	RBC after, Mean±SD	Mean change in RBC	P value
Erythropoietin	2.78±0.54	3.27±0.58	0.49	P<0.0001
Darbepoetin	3.08±0.65	3.5±0.63	0.42	P<0.0001

Table 4: Comparison of PCV levels in the study groups.

Drugs	PCV before, Mean±SD	PCV after, Mean±SD	Mean change in PCV	P value
Erythropoietin	24.06±4.22	27.83±4.65	3.77	P<0.0001
Darbepoetin	26.25±4	29.77±4.03	3.52	P<0.0001

Table 5: Shows the adverse events reported by patients on erythropoietin.

Adverse events	No. of patients	%
HTN	21	38.89
Headache	1	1.85
joint pain	1	1.85
Vomiting	1	1.85

Table 6: Shows the adverse events reported by patients on darbepoetin.

Adverse events	No. of patients	%
HTN	19	35.19

Efficacy assessment

Improvement in the haemoglobin, RBCs and PCV were evaluated after treatment. Before treatment, the mean±SD of haemoglobin level in group A and group B were 7.84±1.33 and 8.6±1.25 respectively. Similarly, after treatment, the mean±SD of haemoglobin level in group A and group B were 9±1.48 and 9.79±1.31 respectively.

The mean change in haemoglobin concentration before and after treatment were 1.16 and 1.19 in group A and group B respectively.

The mean improvement in haemoglobin concentration in both the groups were significantly same (Table 2 and Figure 1). Before treatment, the mean±SD of RBCs level in group A and group B were 2.78±0.54 and 3.08±0.65 respectively. Similarly, after treatment, the mean±SD of RBCs level in group A and group B were 3.27±0.58 and 3.5±0.63 respectively. The mean change in RBCs concentration before and after treatment were 0.49 and 0.42 in group A and group B respectively.

The mean improvement in RBCs concentration in both the groups were significantly same (Table 3 and Figure 2). Before treatment, the mean±SD of PCV level in group A and group B were 24.06±4.22 and 26.25±4 respectively. Similarly, after treatment, the mean±SD of PCV level in group A and group B were 27.83±4.65 and 29.77±4.03 respectively. The mean change in PCV level before and after treatment were 3.77 and 3.52 in group A and group B respectively. The mean improvement in PCV level in both the groups were significantly same (Table 4 and figure 3).

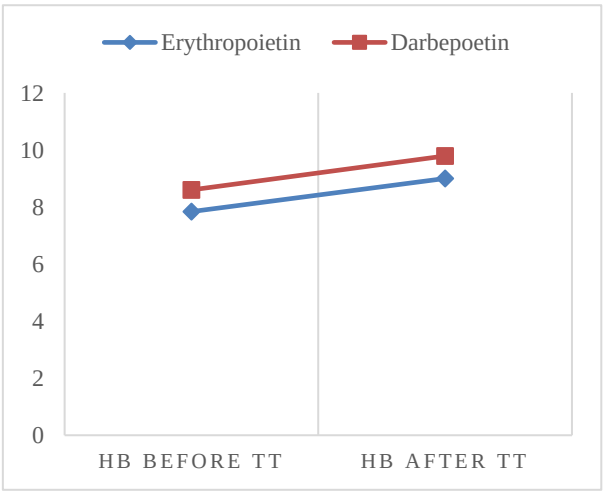

Figure 1: Comparison of haemoglobin changes in both the study groups.

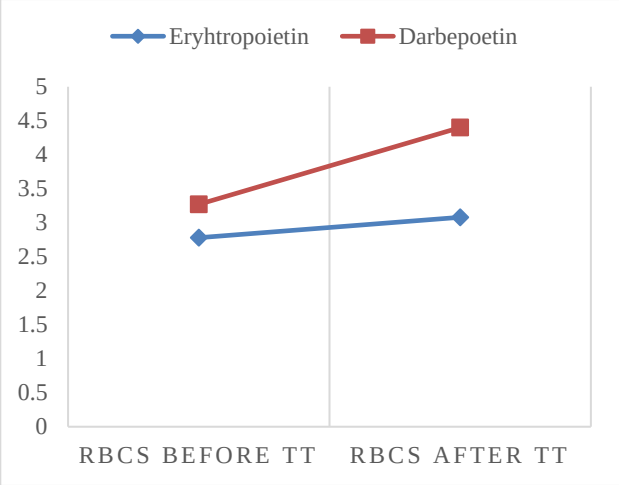

Figure 2: Comparison of RBCs changes in both the study groups.

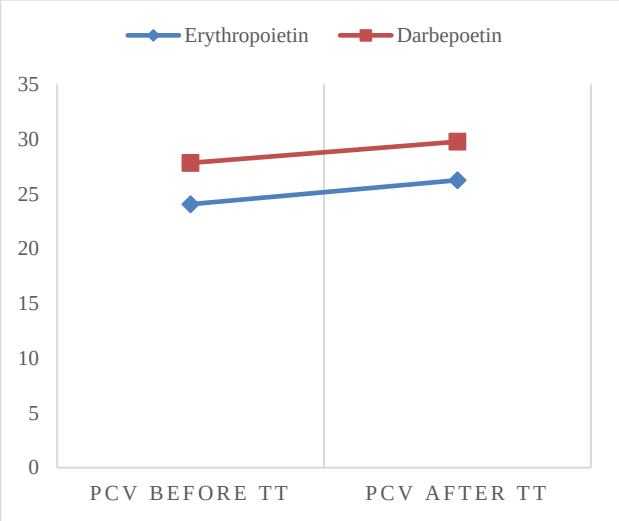

Figure 3: Comparison of PCV changes in both the study groups.

Safety assessment

Besides assessing efficacy of both the drugs, their adverse effects were also studied. It was found that patients suffered from more episodes of hypertension, 38.89 % and 35.19 % in group A and group B respectively which was found to be significantly same for both the drugs. Other adverse effects were headache, joint pain and vomiting (Table 5 and 6).

DISCUSSION

The present study was conducted to assess and compare the efficacy and safety of erythropoietin 4000 units and darbepoetin 40 mcg in the treatment of anaemia due to CKD patients. Demographic variables like age, gender and stages of CKD were evaluated and found to be comparable in both the groups. The improvement in haemoglobin, RBCs and PCV were evaluated before and after using erythropoietin and darbepoetin using the lab values. Erythropoietin and darbepoetin are erythropoiesis-stimulating agents (ESAs).[11] Erythropoietin acts directly on kidney to produce erythrocytes (RBCs) by binding to EPO receptors present on Colony forming unit (CFU), proerythroblast and basophilic erythroblast and activating them to convert into polychromatophilic erythroblast.[4,12]

Darbepoetin binds to erythropoietin receptor monomers resulting receptor dimerization and Janus kinase-2 (JAK-2) intracellular signal transduction pathway activation which leads to proliferation, differentiation, maturation and inhibition of apoptosis of RBCs.[4,6] They increase the RBCs, haemoglobin and PCV concentrations.

It was found that both the drugs significantly increase the haemoglobin, RBCs and PCV concentrations and the mean improvement in all the concentrations were same in both the groups so, both were found to be equally effective.

In the study conducted by Sinha et al, the mean change in haemoglobin in the group of patients on erythropoietin and darbepoetin were 1.85 and 1.84 respectively. The difference in the mean change in Hb levels amongst the two groups was 0.01g/dl. The difference was not statistically significant. So, the results of this study demonstrated that efficacy of Darbepoetin is similar to Erythropoietin for treating patient having anemia due to CKD.[5]

In current study, a total of 108 patients (54 on EPO and 54 on DPO) were enrolled in the study, out of which 21(38.89%) patients from EPO group and 19 (35.19%) patients from DPO group reported increase in Blood pressure (HTN), 1(1.85%) patient reported headache, 1(1.85%) patient reported joint pain, 1 (1.85%) patient reported vomiting from EPO group. As the numbers of adverse effects reported by both the groups of patients were similar so, erythropoietin and darbepoetin was found to be equally safe.

In the study conducted by Sinha et al, in the Darbepoetin group out of 63 patients, 25 (39.7%) patients and 32 (50.8%) patients out of 63 in erythropoietin group experienced at least one TEAE (Treatment emergent Adverse events).

Patients mostly reported TEAEs of mild to moderately severe in nature except one (1.58%) from EPO group who experienced severe TEAE. None from DPO group reported any TEAE related to the study drug; whereas, 4 patients from the EPO group reported 5 AE related to the study drug. In the EPO group, 4 patients reported 5AEs that were related to the study drug.[5]

The commonly reported events in both the treatment groups were pyrexia (DPO vs EPO 9.5% vs 7.9%), joint pain (9.5%vs.15.9%), vomiting (4.8%vs.6.3%), There was no statistical difference between the two groups in terms of TEAEs. Altogether, DPO had a similar safety profile to that of EPO and no antibody formation was identified.[5]

CONCLUSION

As there was not much difference between the mean change in hemoglobin, red blood cells and haematocrit levels between groups of patients on Erythropoietin and Darbepoetin so, both the drugs were found to be equally effective for patients having anemia due to CKD. Adverse events reported by the patients on Erythropoietin are more than that of Darbepoetin but statistically significant adverse effects were same for both the groups so, both the drugs were equally safe for the patients having anemia due to CKD.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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