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COMPARISON BETWEEN EPOETIN ALPHA AND DARBEPOETIN ALPHA IN MANAGEMENT OF ANEMIA IN PATIENT ON MAINTENANCE HEMODIALYSIS. SINGLE CENTER STUDY IN IRAQ

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ABSTRACT

Introduction: Chronic kidney disease (CKD) stands as a leading cause of global mortality in the 21st century, recent updates as of 2022 indicate that CKD has affected over 800 million people worldwide, with a growing prevalence. (1) In 2023, Iraq recorded a total of 10,721 patients undergoing HD, with an estimated population of 45.5 million, resulting in a prevalence rate of 235.6 patient per million. Anemia is an almost universal complication of chronic kidney disease (CKD). The use of ESAs in the management of renal anemia has been shown to improve survival, reduce cardiovascular morbidity, and enhance quality of life and needs of blood transfusion and its complication. Short half-life Epoetin alfa is a primary choice for treating anemia in patients with CKD. [2]. Darbepoetin alfa, as a second-generation long-acting recombinant erythropoietin preparation, is a new recombinant glycoprotein. ***Methods***: Retrospective study with analytical element was conducted from 1st of November 2023 to 31 of January 2025 in the Iraqi center of hemodialysis at Baghdad teaching hospital. In our center the erythropoietin stimulating agent as treatment for anemia was switched for all patients from erythropoietin alpha (Eprex) to darbepoetin alpha (Aransep) in May of 2025. So, the hemoglobin level for 3 consecutive months between Nov. 2023 to April 2024 were studied in Eprex arm, and from May 2024 to Feb. 2025 for Aransep arm. ***Results:*** A total of 95 patients who met the eligibility criteria were enrolled in this study. The demographic and clinical characteristics of patients were studied. The mean Age of patients was 52.5±15.2 (18-76), 55.8% of patient was male. The main cause of CKD in studied patients was hypertension (HT) 39 (41%) then diabetic nephropathy 20 (21%) is second cause. The hemoglobin level was studied for three consecutive months in the erythropoietin alpha and darbepoetin group. The mean hemoglobin in each group was 10.0±1.4 (6.4-13), 9.8±1.2 (6.4-12.3) respectively with no statically significant p value: 0.180 between two group. The target level (10–12g/dl) of mean hemoglobin was achieved by 47.4% by epoetin alpha compared to 41.1% by darbepoetin with no significant difference between the two drugs in achieving this target Hb range (P value 0.45). ***Conclusion:*** Darbepoetin alpha shows no inferiority for corrected anemia compared to epoetin alpha in hemodialysis patients, with no major side effect that needs discontinuation of drug.

KEYWORDS: Anemia; chronic kidney disease; epoetin alpha; darbepoetin alpha; erythropoietin stimulating agent; Hemodialysis; Iraq; switch.

INTRODUCTION

Chronic kidney disease (CKD) stands as a leading cause of global mortality in the 21st century, with significant risk factors, including diabetes mellitus, hypertension, and obesity. Recent updates as of 2022 indicate that CKD has affected over 800 million people worldwide, with a growing prevalence.[1] In 2023, Iraq recorded a total of 10,721 patients undergoing HD, with an

estimated population of 45.5 million, resulting in a prevalence rate of 235.6 patient per million.[2]

Anemia is an almost universal complication of chronic kidney disease (CKD), untreated anemia has been associated with poor outcomes such as deterioration of cardiac function, decreased cognition, mental acuity, fatigue, and mortality.[3,4]

The mechanisms of anemia in CKD are multifactorial. The progressive reduction of endogenous erythropoietin (EPO) levels has been considered to play an important role. However, other factors have also been described to contribute to anemia in CKD patients, such as an absolute iron deficiency due to blood losses or an impaired iron absorption, an ineffective use of iron stores due to increased hepcidin levels, systemic inflammation due to CKD and associated comorbidities, a reduced bone marrow response to EPO due to uremic toxins, a reduced red cell life span, or vitamin B12 or folic acid deficiencies.[5]

Erythropoietin (EPO) is an erythropoiesis-stimulating glycoprotein(30.4 kDa) consists of 165 amino acid which are arranged in four connected alpha helices acids with three N-linked and one O-linked carbohydrate chains (6,7) , It has been known since the 1950s that the kidney plays a crucial role in erythropoiesis through the amount of circulating erythropoietin, whose production is regulated by the body's oxygen supply and demand, its produced by fibroblast-like interstitial peritubular cells of the kidneys, and in a much lesser proportion, by the perisinusoidal cells in the liver. Hepatic erythropoietin production during fetal and early postnatal life but does not compensate for loss of kidney production in adults.[4,5,8]

EPO binds to erythroid progenitor cells receptors mainly in the bone marrow and serves as a key stimulus for red cell survival, proliferation and differentiation. EPO is produced predominantly by the response to changes in tissue oxygen tension. Erythropoietin is normally present in the circulation in low concentrations (0.01to 0.03 U/mL) under basal conditions, but the concentration increases 100-fold to 1000-fold in response to hypoxia and anemia (7), in a process regulated by hypoxia The production of EPO is controlled at the level of the EPO gene transcription. One of the most important factors that regulates its expression is the hypoxia-inducible factor (HIF) system, whose activity depends on the tissue oxygen levels.[5]

In CKD patients, EPO levels are inadequately low with respect to the degree of anemia. EPO deficiency starts early in the course of CKD, but it appears that when eGFR falls below 30 ml/min per 1.73 m2 this deficiency becomes more severe (5). This absolute EPO deficiency can be caused by a decrease in the EPO production and/or by errors in EPO-sensing. Even in kidney failure, the production of EPO capacity can remain significant, but the main problem appears to failure of EPO production to increase in response to chronically reduced hemoglobin concentration (Functional EPO deficiency or resistance) .[4,5]

For many years, Epo was thought to act exclusively on erythroid progenitor cells. Thus, this hormone is actually used to treat anemia like in patients with renal failure or in patients with cancer. However, although kidney and liver are the two major sources of Epo synthesis, Epo mRNA expression has also been found in some other tissues, such as brain (neurons and glial cells), retina, heart, bone marrow, spleen, and others. In these tissues EPO is released in response to "tissue injury" and appears to have protective functions.[6,9,10] In vitro and in vivo experimental studies as well as small interventional clinical studies suggest a potential beneficial effect of externally administered EPO in other clinical condition other than anemia like early diabetic retinopathy and diabetic macular oedema (6), prophylactically from Dox-induced cardiotoxicity via reducing apoptosis and cardiomyopathy[11] as neuroprotective effect against neurological disorders like Alzheimer's disease, Parkinson's disease, neuroinflammation and epilepsy.[12]

Erythropoiesis-stimulating agents (ESAs) have been available for almost three decades and remain the central strategy for the treatment for anemia in patients with CKD, in addition to iron replacement. The use of ESAs in the management of renal anemia has been shown to improve survival, reduce cardiovascular morbidity, and enhance quality of life and needs of blood transfusion and its complication.[4,13]

Erythropoiesis-stimulating agents (ESAs) are a group of medications made of recombinant EPO and its synthetic derivatives (epoetin alfa, epoetin beta, darbepoetin alfa, methoxy polyethylene glycol-epoetin beta) .[14]

Recombinant epoetins, first introduced in 1986, are available as epoetins alpha, beta, delta and omega each differing from the endogenous protein, and from each other, by the presence of individual sugar and sialic acid residues.

Darbepoetin alfa, as a second-generation long-acting recombinant erythropoietin preparation, is a new recombinant glycoprotein that is introduced in two N-linked glycosylation sites by replacing five amino acid residues in 165 amino acid residues of epoetin alfa a recombinant epoetin produced for extra stability and consequent less frequent dosage,[15] was approved by the FDA and European Medicines Agency (EMA) in 2001 for the treatment of anemia resulting from renal failure and immunotherapy.

Four epoetin's are currently approved by the FDA for use in end-stage renal disease

- epoetin alpha (Epogen®; Procrit®; Eprex®; Erypo®).

- methoxy polyethylene glycol-epoetin beta (Mircera®) (not currently available because of patient issues).
- darbepoetin alpha (Aranesp®)
- peginesatide (Omontys®), approved in March 2012, is an EPO receptor-binding synthetic pegylated peptide, MW 45 kDa, with no amino acid sequence homology to EPO. In February 2013, the FDA, and the drug companies involved, announced that Omontys® had been recalled 'as a result of new post-marketing reports regarding serious hypersensitivity reactions, including potentially life-threatening anaphylaxis, which can be or fatal'.(16)

ESAs are generally indicated for patients with impaired red blood cell production conditions. The FDA-approved indications for ESA administration are[17]

1) anemia secondary to chronic kidney disease (CKD). suggestion initiation of ESA therapy when the Hb concentration is ≤9.0–10.0 g/dl (90–100 g/l), recommend targeting a Hb level below 11.5 g/dl (115 g/l).(19)
2) chemotherapy-induced anemia in patients with cancer. ESAs may be prescribed to patients when cancer treatment is not expected to be curative, and the hemoglobin is <10 g/dL.[19], The FDA approved using epoetin (1993) and darbepoetin (2002) for patients with chemotherapy-induced anemia.
3) Anemia associated with HIV infection in patients receiving ≤ 4200 mg/week of zidovudine, with endogenous serum EPO levels ≤ 500 units/mL.[17]
4) Reduction of allogeneic RBC transfusions in high-risk patients with a perioperative hemoglobin of 10-13 g/dL(17).
5) patients with anemia undergoing elective surgery (pre-op and post-op).
6) anemia in preterm infants.

Epoetin alfa (recombinant human erythropoietin, rHuEPO) is a kind of erythropoiesis stimulating agent (ESAs) that is a primary choice for treating anemia in patients with CKD. 2 However, due to its short half-life(has a half-life of 6 hours after intravenous administration and 24 hours after subcutaneous administration) (17), its optimal administration route and dose remain controversial.

Darbepoetin alfa, as a second-generation long-acting recombinant erythropoietin preparation, is a new recombinant glycoprotein, Compared with endogenous erythropoietin and epoetin alfa (rHuEPO), darbepoetin alfa has the characteristics of a prolonged half-life in the blood (The average terminal half-life of darbepoetin in adults after subcutaneous administration (t1/2 = 48.4 h) exceeds that of intravenous (t1/2 = 25.3 h))(17), and increased biological activity in vivo.

Clinical studies have shown that darbepoetin alfa with a reduced dose frequency (once a week or biweekly) for treating anemia in CKD patients has similar efficacy and safety as epoetin alfa (15), benefiting both patients and health care staff.

Table (1): Dosing of erythropoietin-stimulating agents (ESAs)[18]

ESA agent	Initial dose	Dose adjustment
Epoetin alfa and beta	***CKD not receiving dialysis:*** 4,000 or 10,000 units weekly or every 2 Weeks ***CKD G5D***: 50-100 units/kg, 3 times weekly (may round to convenient dose in units)	***CKD not receiving dialysis:*** Increase or decrease dose and/or dosing frequency as needed (generally not given more than once per week) ***CKD G5D***: Increase by 25 units/kg/dose if Hb rise is <1.0 g/dl (<10 g/l) after 4 weeks. Reduce by 10–25 units/dose if Hb rise is >2 g/dl (20 g/l) in 4 weeks.
Darbepoetin	***CKD not receiving dialysis:*** 40-100 µg every 2–4 weeks ***CKD G5D:*** 0.45 µg/kg weekly or 0.75 µg/kg every 2 weeks (may round to convenient dose: 25, 40, 60,100, 150, or 200 µg (300 µg and 500 mcg also available)	***CKD not receiving dialysis***: Increase or decrease dose and/or dosing frequency as needed (generally not given more than once per week) ***CKD G5D:*** Increase by 25% if Hb rise is <1.0 g/dl (<10 g/l) after 4 weeks. Decrease dose by 25% if Hb rise is >2 g/dl (20 g/l) in 4 weeks.

Aim of study

This study aimed to verify that the efficacy and safety of darbepoetin alfa compare to epoetin alfa in maintaining Hb levels within the target range (10.0–12.0 g/dL) for the treatment of renal anemia in hemodialysis patients. (15).

Patients and methods

Design: Retrospective study with analytical element was conducted from 1st of November 2023 to 31 of January 2025 in the Iraqi center of hemodialysis at Baghdad Teaching Hospital.

Patients: Patients: Total 96 patients who were on regular hemodialysis for more than one year who were switched from epoietin alpha (Eprex®) to darbepoetin alpha (Aranesp®).

Inclusion criteria

- Chronic kidney disease patient on regular hemodialysis for more than one year.
- Age ≥ 18yrs.
- Patients who received epoietin alpha and darbepoetin for more than 3months to each drug.

Exclusion criteria

- Chronic blood loss.
- Serum Ferritin <200mg/dl.
- Frequent blood transfusion.
- MCV more than 100.
- Malignancy.

In our center the erythropoietin stimulating agent as treatment for anemia was switched for all patients from epoietin alpha (Eprex®) to darbepoetin alpha (Aransep®) at May of 2025.

So, we designed this study to evaluate the difference between epoietin alpha (Eprex®) and darbepoetin (Aransep®) in achieving targeted hemoglobin, correction of anemia and also studied the complication of darbepoetin alpha in our patient.

Th hemoglobin level for 3 consecutive months between Nov. 2023 to April 2024 were studied in Eprex arm, and from May 2024 to Feb. 2025 for Aransep arm. During this month's patients did not need any blood transfusion, history of blood loss or history of surgical operation. All patients received IV iron to maintain serum ferritin between 200–500 mg/dL.

The clinical and laboratory data related to CKD management were collected from patients by direct questioner, monthly laboratory results and dialysis session records.

Statistical analysis

The collected data were coded, entered, presented, and analyzed by computer using the available data base software program statistical package of IBM SPSS-29 (IBM Statistical Packages for Social Sciences- version 29, Chicago, IL, USA). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different means (quantitative data) was tested using Paired-t-test for difference of paired observations (or two dependent means). The significance of difference of different percentages (qualitative data) was tested using Pearson Chi-square test (□2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05..[20-24]

Sample size

All eligible patients filled out the consent form and completed the research tool in a written format. The sample size was calculated using the following formula: Where ***n*** is the sample size, α is the first type, Z is the table-based normal distribution index that is considered at 5% type-one error (P<0.05), σ represents the small variable variance, and d shows the accuracy of quantitative variable estimation. In this study, a first type error, z, σ, and d equal to 0.05, 96.3, 7.38, and 0.99, respectively. After adjusting for the non-response of 10%, 100 were considered as the sample size, and 95 were included in the data analysis.[25,26]

RESULTS

A total of 95 patients who met the eligibility criteria were enrolled in this study. The demographic and clinical characteristics of patients included in analysis are shown in Table {2}. The mean Age of patients was 52.5±15.2 (18-76), 55.8 of patient was male. Approximately more than three quarters 81 (85.3%) of patients had hypertension at time of collected data diagnosed either before 54(67%), after 5(6%) or a time of started hemodialysis22(27%). More than a quarter of 27 patients (28.4%) had diabetes (DM) about 20(74%) of them the DM is cause of CKD. And about one third of patients had cardiovascular disease, either coronary vascular disease, heart failure or pulmonary hypertension.

The main cause of CKD in studied patients was hypertension (HT) 39 (41%) then diabetic nephropathy 20 (21%) is second cause.

Noticed more than half of patients 51 (63.7%) had history of blood transfusion, and about one third of them 15(29.4%) received three unit and more.

The mean duration of hemodialysis (HD) was 4.8±2.6 (1-12), and the majority of patients 89 (93.7%) used arteriovenous fistula as vascular access to hemodialysis. About 7 (7.4%) of patients had history of renal transplantation. Most of the patients 78 (82.1%) complained to ESA.

Table (2): Demographic and clinical characteristics of patients.

Patient demographics	***n:95 %***
Age (years)	
Mean±SD (Range)	52.5±15.2 (18-76)
Gender	
Male	53 (55.8%)
Female	42 (44.2%)
History of blood transfusion	
No	44(46.3%)
Yes	51(63.7%)
one unit	*25(49%)*
Two unit	*11(21.6%)*
Three and more	*15(29.4%)*
Clinical characteristics:	
Comorbidities:	
Hypertension	81(85.3%)
Diabetes	27(28.4%)
Coronary artery disease	15(15.8%)
Heart failure	13(13.7%)
Stroke (CVA)	5 (5.3%)
Others	4 (4.2%)
Patient compliance	
Compliance	78 (82.1%)
Noncompliance	17(17.9%)

HD duration (years)	
Mean±SD (Range)	4.8±2.6 (1-12)
Etiology of CKD	
Hypertension	39(41%)
Diabetes	20 (21%)
Analgesic nephropathy	8 (8%)
Solitary kidney	6 (6.3%)
Obstructive uropathy	4 (4.2%)
Hereditary disease; polycystic kidney, oxalosis	6 (6.3%)
Acute kidney injury; sepsis, COVID 19	4 (4.2%)
Vesicoureteral reflex	1 (1%)
Unknown	12(13%)
Hemodialysis access	
Permeant venous catheter	4 (4.2%)
Arteriovenous fistula	89 (93.7%)
Arteriovenous Graft	2 (2.1%)
Prior renal transplantation	
0	88(92.6%)
1	5 (5.3%)
2	2 (2.1%)

The hemoglobin level was studied for three consecutive months in the epoietin alpha and darbepoetin group, as shown in Table [3]. The mean hemoglobin in each group was 10.0±1.4 (6.4-13), 9.8±1.2 (6.4-12.3) respectively with no statically significant p value: 0.180 between two group.

Table [3]: Hemoglobin level in epoetin alpha and darbepoetin group.

	Hb >10 g/dl	Hb 10-12 g/dl	Hb< 12g/dl	Hb level
	n (%)	n (%)	n (%)	Mean±SD (Range)
Epoeten alpha				
Month 1	38(40%)	44(46%)	13(13.7%)	10.3±1.6 (6.8-13.4)
Month 2	45 (47.4%)	45(47.4%)	5(5.3%)	9.9±1.6 (6.5-12.9)
Month 3	52 (54.7%)	34(35.8%)	9 (9.5%)	9.7±1.6 (5.4-12.8)
Mean Hb of 3months	45 (47.4%)	45 (47.4%)	5 (5.3%)	10.0±1.4 (6.4-13)
Darbepoetin				
Month 1	58(61.1.%)	35(36.8%)	2(2.1%)	9.6±1.2 (6.5-12.1)
Month 2	50 (52.6%)	42 (44.2%)	3(3.2%)	9.9±1.3 (6.8-13.6)
Month 3	33 (34.7%)	56 (58.9%)	6 (6.3%)	10.2±1.3 (6.7-13.5)
Mean Hb of 3months	53 (55.8%)	39 (41.1%)	3 (3.2%)	9.8±1.2 (6.4-12.3)

The target level (10–12g/dl) of mean hemoglobin was achieved by 47.4% by epoetin alpha compared to 41.1% by darbepoetin with no significant difference between the two drugs in achieving this target Hb range (P value 0.45). Detailed percentages of Hb levels within different ranges are provided in Table.[4]

Table [4]: Comparison between mean hemoglobin level in three months.

Hb level (n, %)	**epoetin alpha**	**darbepoetin**	**p value**
Low (< 10 g/dl)	45(47.4%)	53 (55%)	0.454
Target (10–12 g/dl)	45(47.4%)	39(41.1%)	
High (> 12 g/dl)	5(5.3%)	3(3.2%)	
Mean Hb	10.0±1.4 (6.4-13)	9.8±1.2 (6.4-12.3)	0.180
Significant difference between two dependent means using Paired-t-test at 0.05 level			

The mean dose of epoetin alpha(4000unit) and darbepoetin(40mg/dose) were 12.3±6.2 (3-24, 3.6±0.9 (2-6) respectively. Approximately 13 doses for epoetin alpha and 4 dose for darbepoetin, and majority of patients had no change in dose during this three month as see in table [5].

Table [5] the mean dose of ESA.

	1st month	2nd month	3rd month	Mean dose/3months	Dose increase	No change	Dose Increase
Eprex (4000u /dose)	12.5±6 (2-24)	12.1±6.2 (3-24)	12.2±6.4 (2-24)	12.3±6.2 (3-24)	20 (21.1%)	62 (65.3%)	13 (13.%)
Aransep (40mg /dose)	3.6±1.0 (2-6)	3.7±1 (2-6)	3.7±1.1 (1-6)	3.6±0.9 (2-6)	20 (21.1)%	50 (52.6%)	25 (26%)

Regarding the darbepoetin during the 6-month study period, about 7(7.4%) patients reported a direct side effect related to darbepoetin injection inform of pain at site injection(5patients) and one patient reported knee pain and other patient reported multiple ecchymosis at same day of injection.

As seen in table [6] 11 from 95 patients had history of venous thrombosis, 7 of them had history of AV fistula thrombosis 3 of them on time of epoetin alpha, 3 was on darbepoetin and one of them, and one patient had recurrent Av fistula thrombosis on epoetin and darbepoetin time.

Table [6]: History of thrombosis events in studied patients.

Venous thrombosis n 11	Epoetin alpha	Darbepoetin
AV fistula thrombosis 7*	4	4
DVT	2	0
Central vein thrombosis	1	0
Intracardiac thrombus	1	0
*one patient had two thrombosis event.		

DISCUSSION

This study was a comparative retrospective study aimed to evaluate and compare the efficacy of short-acting erythropoietin (Eprex®) versus long-acting erythropoietin (Aranesp®) in treating renal anemia among patients with ESRD undergoing hemodialysis. Both Aranesp® and Eprex® are the most extensively utilized ESAs under governmental health insurance in Iraq to correct anemia in CKD patients.

The main cause of CKD in our patients is hypertension (41%) and diabetes (21%), this result is similar to many Iraqi studies, where diabetes was between (25.4% to 38.6%) [2,27,28,29,30,31,32], and hypertension [23.4% to 40%].[2,27,28] but there were studies found glomerulonephritis is one of main causes (15.2%,50%).[30,31]

When analyzed hemoglobin level during randomized three consecutive months(at which no history of surgery, bleeding , blood transfusion) in epoetin alpha and darbepoetin group the mean hemoglobin was 10.0±1.4 (6.4-13), 9.8±1.2 (6.4-12.3); the average Hb concentration difference about 0.2±0.2 with no statically significant, so darbepoetin is no inferior to epoetin alpha in control of anemia in hemodialysis patient, and this consistent with randomized prospective studies in China[33] and Qatar[34], also with retrospective multicenter study in Spain.[35] The recent Iraqi multicenter prospective study in Anbar 2025[36] found that Darbepoetin led to significantly higher mean hemoglobin levels at six months (9.44 ± 0.99) compared to Epoetin (8.90 ± 1.05). However, the median change in hemoglobin from baseline [8.84 ± 0.79), (8.41 ± 1.08) respectively] did not differ significantly between the groups. The prospective Egyptian studies[37,38] revealed darbepoetin alpha is more effective in achieving targeted hemoglobin comparable to epoetin alpha.

About 53% of patient in epoetin alpha had HB ≥10g/dl and in darbepoetin group was 45% with no statistical difference. Noticing the corrected anemia was increased with time in darbepoetin group from 35% in 1st month to 65% in 3rd month in contrast to epoetin alpha group. Treatment with darbepoetin alfa Q weekly is more efficient than epoetin alfa in achieving target hemoglobin, with lower time.[38] The Egyptian study Over 6-month study period, found both DA and Epoetin demonstrated significant increases in Hb levels from baseline. However, with its extended intervals, Aranesp effectively stabilized patients' Hb levels within the desired target range(63%) and exhibited a more substantial correction effect on anemia compared to Eprex (50%), Notably, the Aranesp group showed a significantly greater efficacy with a mean Hb difference of 1.2 g/dl between the first and sixth months, in contrast to the 0.7 g/dl difference observed in the Eprex group ($P < 0.001$).[37]

The Iraqi studies on erythropoietin stimulating agent show correction of anemia between (20-60%).[32,39,40,41] for epoetin alpha and reach 68% when used mircera .[32]

And percentage of erythropoietin resistant about (44-54.5%) for epoetin alpha[40,41], many factors can influence response levels in patients with CKD undergoing hemodialysis (age, body mass index (BMI), number of diseases, serum phosphorus, serum iron, and transferrin saturation).[40] Lower BMI and transferrin saturation, younger age, lower albumin concentration, and a higher baseline IV iron dose were identified as strongly associated with ESA hyporesponsiveness. Additional predictors of ESA hypo responsiveness included female sex, history of heart failure and longer dialysis vintage.[42] The ESA resistance index decreased from 15.1 (8.5) IU/kg/week/g/dL with epoetin to 8.1 (3.9) (first year) and 7.9 (4.0) (second year) with darbepoetin.[35]

The mean dose of epoetin alpha(4000unit) and darbepoetin(40mg/dose) were 12.3±6.2 (3-24), 3.6±0.9 (2-6) per month respectively. Approximately 13 doses for epoetin alpha and 4 doses for darbepoetin, and majority of patients had no change in dose during these three month and about 13% increase in epoetin and 26% in DA group. In Chinese study in 2022 for 28 weeks, the times of dose adjustments in the darbepoetin alfa group and epoetin alfa group were 5.16 ± 2.8 (0-13) and 13.02 ± 9.85(0-33), respectively (Table 4). During the evaluation period, 5%–15% of patients did not need medication for maintenance in the darbepoetin alfa group, and the number of patients maintained with doses ≥30 μg shrank by approximately 30% after switching from epoetin alfa to darbepoetin alfa, targeted Hb about 82% and 81% in epoetin and darbepoetin group respectively.[33] And according to Spain 2014 study after conversion, the erythropoiesis-stimulating agent (ESA) dose decreased significantly, with an annual mean of 174.7 (88.7) international units (IU)/kg/week for epoetin versus 95.7 (43.4) (first year) and 91.4 (42.7) IU/kg/week (second year) for darbepoetin (65% and 64% reduction, respectively). Patients were on target levels (10–12 g/dL) for a mean (SD) of 4 (3) months with epoetin alfa and 8 (5) months with darbepoetin alfa, which represents 42.6% (25.2) and 44.2% (21.0) of the time, respectively The ESA resistance index decreased from 15.1 (8.5) IU/kg/week/g/dL with epoetin to 8.1 (3.9) (first year) and 7.9 (4.0) (second year) with darbepoetin.[35] The conversion rate was 354:1 in patients requiring high (>200 IU/kg/week) doses of epoetin and 291:1 in patients requiring low doses.

Regarding the darbepoetin uses during the 6-months study period, about 7(7.4%) patients reported a direct side effect related to darbepoetin injection inform of pain at site injection(5patients) and one patient reported knee pain and other patient reported multiple ecchymosis at same day of injection. and 11 from 95 patients had history of venous thrombosis, 7 of them had history of AV fistula thrombosis 3 of them on time of epoetin alpha, 3 was on darbepoetin and one of them, and one patient had recurrent Av fistula thrombosis on epoetin and darbepoetin time. Other studies reported pain at the site of the injection, headache, vomiting, nausea, diarrhea, edema, hypertension, hyperkalemia, cerebral hemorrhage, myocardial infarction, muscle spasm as adverse effect.[33,37] There were no discontinuations of darbepoetin alfa due to adverse reactions during the follow-up period.[35]

From the US Renal Data System analysis found darbepoeten DPO and epoetin EPO possess approximately similar safety profiles, at least within the hemodialysis setting, with regard to cardiovascular and mortality outcomes, although small excess risks from DPO cannot be ruled out.[44] The overall efficacy and safety of darbepoetin alfa for the treatment of Chinese renal anemia patients undergoing hemodialysis are consistent with those of epoetin alfa.[33]

This study shows no inferiority of Darbepoetin to epoetin alpha in correction of anemia in hemodialysis patients. With targeting HB about 40% but noticed this percent from first (35%) to third month (53%) is increase. May need to increase the time of study to get accurate results. And the maximum dose of darbepoetin is about 6 doses per month, other study reaches 13 dose/m[33], so need to increase the dose of darbepoetin to increase the target Hb, AL-Shamway et al study 2022 recommended routinely measured CRP where patients with higher CRP require high ESA doses.[38]

CONCLUSION

Darbepoetin alpha shows no inferiority for corrected anemia compared to epoetin alpha in hemodialysis patient, with no major side effect that need discontinuation of drug.

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