

## COMPARISON OF ERYTHROPOIETIN AND DARBEPOETIN IN CHRONIC KIDNEY DISEASE PATIENTS IN A TERTIARY CARE HOSPITAL

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### ABSTRACT

Chronic kidney disease (CKD), is a progressive loss of kidney function over several months to years and cause complications like anaemia. Erythropoiesis stimulating agents (ESAs) such as erythropoietin and darbepoetin are widely used as a first-line treatment for the management of renal anaemia in CKD patients. Treatment of anaemia with ESAs could reduce the need for red blood cell transfusion and improve outcome and quality of life (QOL). As there are not enough studies in Indian literature regarding the comparison of erythropoietin and darbepoetin in chronic kidney disease patients, the present review is undertaken. This review is designed to compare the effect of erythropoietin and darbepoetin by measuring serum Haemoglobin and creatinine in CKD patients. In review articles it is observed that erythropoietin and darbepoetin shows comparable effect in bringing Hb to normal ranges but there observe an increase in creatinine in some patients. Darbepoetin is a unique erythropoietic agent with an approximately threefold longer half-life than erythropoietin, allowing less frequent dosing than erythropoietin.

**KEY WORDS:** Anaemia, Chronic kidney disease, Erythropoietin, Darbepoetin, Haemoglobin, Creatinine.

### INTRODUCTION

Chronic kidney disease (CKD), also known as chronic renal disease, is progressive loss in kidney function characterized by gradual replacement of normal kidney architecture with interstitial fibrosis over a period of months or years. The most common recognized cause of CKD is Diabetes mellitus. Others include hypertension, glomerulonephritis, congenital abnormalities and idiopathic. Swelling, uremia, high BP, drowsiness, fatigue, chest pain, itching etc are common symptoms of CKD.

Anaemia is associated with worsening of cardiovascular morbidity and is an independent predictor of mortality in patients with chronic kidney disease (CKD). Anemia is a condition in which the body has fewer red blood cells than normal. Red blood cells carry oxygen to tissues and organs throughout the body and enable them to use energy from food. With anemia, red blood cells carry less oxygen to tissues and organs—particularly the heart and brain—and those tissues and organs may not function as well as they should. Anemia commonly occurs in people with chronic kidney disease (CKD)—the permanent, partial loss of kidney function. Anemia might begin to develop in the early stages of CKD, when someone has 20

to 50 percent of normal kidney function. Anemia tends to worsen as CKD progresses. Most people who have total loss of kidney function, or kidney failure, have anemia.

Healthy kidneys produce a hormone called erythropoietin (EPO). This hormone is a chemical produced by the body and released into the blood to help trigger or regulate particular body functions. EPO prompts the bone marrow to make red blood cells, which then carry oxygen throughout the body. When kidneys are diseased or damaged, they do not make enough Erythropoietin. As a result, the bone marrow makes fewer red blood cells, causing anemia. When blood has fewer red blood cells, it deprives the body of the oxygen it needs. In anaemic CKD, Haemoglobin (Hb) levels are decreased and if blood tests indicate kidney disease as the most likely cause of anemia, hence treatment with erythropoietin and darbepoetin done to bring it to normal ranges.

These erythropoietin stimulating agents are produced by recombinant DNA technology in cell culture, and include epoetin alfa and darbepoetin alfa has been shown to exert its effects by binding to the erythropoietin receptor (EpoR). EPO is highly glycosylated (40% of total molecular weight), with half-life in blood around five hours. EPO's

half-life may vary between endogenous and various recombinant versions. Additional glycosylation or other alterations of EPO via recombinant technology have led to the increase of EPO's stability in blood (thus requiring less frequent injections).

Patients who receive EPO should have regular blood tests to monitor their hemoglobin so the health care provider can adjust the EPO dose when the level is too high or too low. Health care providers should discuss the benefits and risks of EPO with their patients.

Many people with kidney disease need iron supplements and EPO to raise their red blood cell count to a level that will reduce the need for red blood cell transfusions. In some people, iron supplements and EPO will improve the symptoms of anemia.

Erythropoietin cause hypertension as side effect so requires conventional antihypertensive treatment or a reduction in dose so as to eliminate hypertensive effect.

## REVIEW OF LITERATURES

1. **Jeffrey Patton<sup>1</sup> et al** ;(2004)conducted a study on "Effectiveness of Darbepoetin Alfa Versus Epoetin Alfa in Patients with Chemotherapy Induced Anemia Treated in Clinical Practice" .The objective of this retrospective observational cohort study was to compare the effectiveness of darbepoetin alfa with that of epoetin alfa in patients with chemotherapy-induced anemia using data from non contemporaneous chart audits conducted at a community-based oncology practice.For the first chart audit, data were collected from consecutive patients with nonmyeloid malignancies with diagnoses of chemotherapy-induced anemia and hemoglobin levels  $\leq 10.5$  g/dl who were receiving concurrent chemotherapy and had at least 5 weeks of visits from July-September 2000. After therapeutic substitution of darbepoetin alfa for epoetin alfa for all patients with chemotherapy-induced anemia, data were collected from consecutive darbepoetin alfa-treated patients with diagnoses of chemotherapy-induced anemia and at least 8 weeks of visits from June-October 2002 (darbepoetin alfa was approved in July 2002). The results of the study shows Darbepoetin alfa, 100  $\mu$ g once weekly or 200  $\mu$ g every 2 weeks, appears to be as effective as epoetin alfa, 40,000 U once weekly, for the treatment of chemotherapy-induced

anemia in the clinical practice setting. The mean change in hemoglobin level was 1.1 g/dl for the darbepoetin alfa patient group and 1.0g/dl for the epoetin alfa patient group.

2. **Kiyoto koibuchi<sup>2</sup> et al**;(2015)conducted a study on "Comparing the efficacy of continuous erythropoietin receptor activator and darbepoetin Alfa treatments in Japanese patients with chronic kidney disease during the predialysis period:A propensity-matched analysis". In this study, compared the efficacy of continuous erythropoietin receptor activator (CERA) and darbepoetin alfa (DA) in patients with chronic kidney disease (CKD) over 6 months prior to initiation of dialysis. This was a retrospective study ,74 pairs of patients (one in each group) were included and results showed that CERA may be more effective than DA for management of anaemia during the predialysis period in CKD patients.

3. **Wanic Kossowska<sup>3</sup>M.et al**; (2010) conducted a study on "Results of anemia treatment with darbepoetin alfa and erythropoietin beta in patients with chronic kidney disease". The aim of study was to analyze the results of anemia treatment with darbepoetin alfa and erythropoietin beta in patients with chronic kidney disease (3,5stage of CKD) in predialysis period. In the study were analyzed 35 and 20 patients during 11 months,and also measured blood pressure.During 11 months of observation blood pressure was not changed but a creatinine serum level was stable in females and increased in males. Erythropoietin beta was well tolerated and injection pain was smaller compared to darbepoetin alfa.

4. **John Glaspy<sup>4</sup> et al**;(2006)conducted a study on "Randomized Comparison of Every-2-Week Darbepoetin Alfa and Weekly Epoetin Alfa for the Treatment of Chemotherapy-Induced Anemia". This non inferiority study systematically compares efficacy and safety of DA and EA using common doses and schedules used in clinical practice.Of 1,220 patients randomly assigned, 1,209 received greater than or equal to one dose of the study drug.Patients were randomly assigned 1:1 to DA 200 micro gram every two weeks (Q2W) or EA 40,000 units every week (QW) for up to 16 weeks with identical dose adjustment rules. This large, phase III study demonstrates comparable efficacy of DA Q2W and EA

QW. Less frequent dosing offers potential benefits for patients, caregivers and health care providers.

5. **Can C<sup>5</sup> et al;**(2013)conducted a study on “Comparison of recombinant human erythropoietin and darbepoetin alpha in children”. The aim was to compare the clinical efficacy of recombinant human erythropoietin(rHuEPO) and darbepoetin alpha (DA) in the treatment of anemia in children with chronic kidney disease (CKD). Thirty four(13 female, 21 male) CKD patients were enrolled in the study. Mean age was  $11.42 \pm 4.05$  years. Nine patients were on hemodialysis, 18 were on peritoneal dialysis and seven patients were in CKD stage 4. Seventeen patients received rHuEPO and the remaining 17 patients received DA. Hemoglobin (Hb) was not significantly different between the two groups during monthly follow up and at the end of 6 months ( $P > 0.05$ ), but there was a significant increase within each group at the end of 6 months ( $P = 0.01$  for rHuEPO;  $P = 0.02$  for DA). Hb was not different between the patients on and not on dialysis in both groups at the end of the study ( $P > 0.05$ ). The efficacy of the s.c. and i.v.routes was similar within each group ( $P > 0.05$ ). Systolic hypertension was observed in only one patient in the DA group, no other adverse effect was observed in either groups. Result shows that DA is a reasonable alternative to rHuEPO in the treatment of anemia in pediatric CKD patients, due to its clinical efficacy, convenience of use, patient compliance and tolerability.

6. **Voils A<sup>6</sup> et al;**(2007) conducted a study on “Comparison of darbepoetin alfa and epoetin alfa in the management of anemia of critical illness”.It was a retrospective, descriptive study conducted on intensive care unit with seventy-two patients who spent at least 3 days in the cardio-thoracic, medical, or surgery-trauma intensive care units and received at least one weekly dose of epoetin alfa 40,000 units (33 patients) or darbepoetin alfa 100  $\mu\text{g}$  (39 patients). Number of epoetin alfa and darbepoetin alfa doses, hemoglobin concentrations, and cumulative number of transfusions were recorded for up to 28 days after the first dose was given, and the data were statistically analyzed. Patients receiving darbepoetin alfa 100 micro  $\mu\text{g}/\text{week}$  and those receiving epoetin alfa 40,000 units/week for anemia of critical illness achieved similar rates of transfusion independence and increases

in hemoglobin concentrations from baseline at 28 days. Compared with previously published studies, erythropoietic agents were administered late in the course of critical illness in response to low hemoglobin concentrations.

## CONCLUSION

From the above survey of information it can be well known that the erythropoietin and darbepoetin exhibit comparable efficacy in bringing Hb back to normal ranges in CKD patients with anaemia. So, it is important to take into consideration about this studies regarding the comparison of erythropoietin and darbepoetin in CKD patients in a tertiary care hospital which is helpful in determining the most effective medicine which can be treated anaemic condition in CKD patients .

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