Original Article

Comparison of Roxadustat with Erythropoietin in Terms of Efficacy in Anemia of Chronic Kidney Disease (CKD) Stage IV and V

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ABSTRACT

Objective: To compare efficacy of Roxadustat with Erythropoietin in anemia of chronic kidney disease stage four and five patients.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Department of Nephrology, KRL Hospital Islamabad from 10 November 2025 to 10 May 2026.

Methods: Total 150 patients were included and divided into two groups, Roxadustat group n=75 and Erythropoietin group n=75. Patients aged 18–70 years with anemia of chronic kidney disease stage four and five were selected. Patients were followed for 12 weeks and haemoglobin levels were measured at 4, 6 and 12 weeks. Requirement of blood transfusion was also recorded. Independent sample t-test was applied for comparison of mean haemoglobin, while chi-square and fisher exact test were used for categorical variables.

Results: Mean age was 53.60 ± 12.05 years in Roxadustat group and 50.55 ± 11.41 years in erythropoietin group. Males were 48 (64.0%) and 43 (57.3%) respectively. At baseline haemoglobin was comparable (8.67 ± 0.77 vs 8.44 ± 0.82 g/dL, p=0.077). At 4, 6 and 12 weeks haemoglobin was significantly higher in Roxadustat group (9.41 ± 0.79 vs 9.05 ± 0.83, p=0.008; 10.02 ± 0.90 vs 9.57 ± 0.92, p=0.003; 11.06 ± 0.74 vs 10.37 ± 0.83, p<0.001). Blood transfusion was less in Roxadustat group at 4 weeks 7 (9.3%) vs 24 (32.0%), and at 6 weeks 3 (4.0%) vs 19 (25.3%) (p<0.001).

Conclusion: Roxadustat showed better haemoglobin improvement and less transfusion need as compared to erythropoietin in these patients.

Key Words: Anaemia, Chronic kidney disease, Erythropoietin, Haemoglobin, Roxadustat

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INTRODUCTION

Anaemia caused by CKD is a common and important medical condition, especially among patients with more severe forms of kidney disease where there is significantly impaired renal function.[1] This medical problem arises due to decreased production of erythropoietin by the kidneys, which is essential for erythropoiesis occurring in the bone marrow.[2] Additional causes of this form of anaemia may involve iron deficiency, inflammation, shortened red blood cell survival time, and bleeding during dialysis treatment.[3] In clinical practice, affected individuals usually suffer from fatigue, exhaustion, shortness of breath, and reduced quality of life. In addition, anaemia caused by CKD not only represents a symptom but is also associated with a higher risk of developing heart diseases and dying from them.[4] The severity of anaemia increases with declining glomerular filtration rate and affects patients with Stage IV and V CKD the most.

Roxadustat is a new oral pharmacologic drug that works through the stabilization of HIF, which further helps to increase the natural production of erythropoietin and iron metabolism.[5] It acts as a physiological stimulator of erythropoiesis along with a reduction in hepcidin, thus making iron available.[6] Clinical trials have shown that Roxadustat significantly increases the concentration of hemoglobin in patients suffering from CKD who require and do not require dialysis.[7] Administration of Roxadustat via the oral route represents a benefit because of its convenience, but there are issues with regard to its safety.

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The use of exogenous erythropoietin along with its derivatives has been used conventionally to manage anemia associated with CKD.[8] Exogenous erythropoietin promotes production of red blood cells in the bone marrow, and their administration can be performed either by the intravenous route or subcutaneously.[9] It is effective in managing anemia by correcting iron deficiency and reducing the need for transfusion of blood, but for an ideal result, there should be enough iron present.[10]

The prevalence of anaemia in patients with chronic kidney disease is on the rise, leading to low quality of life and increased susceptibility to adverse events. While erythropoietin is widely employed, the disadvantages of being expensive, requiring injection, and inconsistent treatment response make it necessary to consider more favourable options. Roxadustat is one of the newer agents that can be administered orally; nonetheless, there is a dearth of local studies regarding the drug's effectiveness compared to erythropoietin. Therefore, the purpose of this research is to evaluate the effectiveness of Roxadustat against erythropoietin in patients with stages IV and V CKD.

METHODS

A randomized controlled trial was carried out in the Department of Nephrology, KRL Hospital Islamabad, over a period from 10th November 2025 to 10th May 2026. Ethical approval had been taken from the institutional Ethical Review Board before start of study. The total sample size was 150, which had been calculated by WHO sample size software using 5% level of significance and 80% power, taking population mean values of 108±5.5 and 101±6. 75 patients were allocated in each group.

Inclusion criteria

Patients of either gender, aged 18–70 years and having anemia of CKD of stage 4 or 5 were included.

Exclusion criteria

Patients having NYHA Class III or IV congestive heart failure, CKD stage 1–3, history of myocardial infarction or acute coronary syndrome, hyperkalemia, pregnancy or lactation, history of stroke, epileptic disorder or any thromboembolic event within last 12 weeks, hypersensitivity to study drugs, or uncontrolled hypertension were excluded.

Anemia of CKD was taken as hemoglobin level less than 12 g/dL in females and less than 13 g/dL in males in presence of chronic kidney disease. Chronic kidney disease was graded on basis of eGFR as stage 1 (≥90), stage 2 (60–89), stage 3a (45–59), stage 3b (30–44), stage 4 (15–29), and stage 5 (<15). Written informed consent was taken from all patients before enrolment. Basic demographic details including age, gender, weight, baseline hemoglobin and eGFR were recorded at time of inclusion. All patients underwent detailed clinical assessment. Patients were then randomized into two groups by computer-generated random sequence. The Roxadustat treatment group was given a dosage of 70 mg thrice a week, whereas the erythropoietin treatment group (Epokine©) was given 100 U/kg thrice a week. Follow-up took place after 12 weeks, with evaluations taking place at four, six, and 12 weeks. Hemoglobin levels were determined during each evaluation, and the requirement for blood transfusions was assessed and documented. Non-completers were not included in the final analysis. Change in hemoglobin level was calculated by subtracting the baseline hemoglobin level from the hemoglobin level at four, six, and 12 weeks. The need for blood transfusions was determined by clinical indication in combination with a reduction in hemoglobin levels.

All collected data was entered and analyzed using SPSS version 26. Quantitative variables such as age, weight, eGFR and hemoglobin were presented as mean ± standard deviation. Qualitative variables including gender and CKD stage were expressed as frequency and percentage. Comparison of mean hemoglobin and its change between groups was done using independent sample t-test. Frequency of blood transfusion between groups was compared using chi-square test. A p-value ≤0.05 was taken as statistically significant.

RESULTS

A total of 150 patients were enrolled and divided equally into two groups, with 75 patients receiving Roxadustat and 75 receiving erythropoietin.

Table No.I: Patient Demographics in Both Groups n=150

Variables	Roxadustat n=75	Erythropoietin n=75
	Mean ± SD	Mean ± SD
Age (years)	53.60 ± 12.05	50.55 ± 11.41
Weight (kg)	69.04 ± 12.14	68.81 ± 12.31
eGFR	16.09 ± 7.91	14.80 ± 7.40
Gender	**n (%)**	**n (%)**
Male	48 (64.0%)	43 (57.3%)
Female	27 (36.0%)	32 (42.7%)
CKD Grade		
IV	35 (46.7%)	33 (44.0%)
V	40 (53.3%)	42 (56.0%)
Smoking		
Yes	18 (24.0%)	11 (14.7%)
No	57 (76.0%)	64 (85.3%)
Hypertension		
Yes	48 (64.0%)	51 (68.0%)
No	27 (36.0%)	24 (32.0%)
Diabetes Mellitus		
Yes	33 (44.0%)	38 (50.7%)
No	42 (56.0%)	37 (49.3%)

The mean age in the Roxadustat group were 53.60 ± 12.05 years as compared to 50.55 ± 11.41 years in the

erythropoietin group, whilst mean weight were recorded as 69.04 ± 12.14 kg and 68.81 ± 12.31 kg respectively. The mean eGFR were 16.09 ± 7.91 in the Roxadustat group and 14.80 ± 7.40 in the erythropoietin group. With regards to gender distribution, males were constituted 48 (64.0%) and 43 (57.3%) of the Roxadustat and erythropoietin groups respectively, whilst females were comprised 27 (36.0%) and 32 (42.7%). In terms of CKD grade, stage IV disease were present in 35 (46.7%) patients of Roxadustat group and 33 (44.0%) of erythropoietin group, whereas stage V were recorded in 40 (53.3%) and 42 (56.0%) patients respectively. Smoking history were reported in 18 (24.0%) of Roxadustat patients and 11 (14.7%) of erythropoietin patients. Hypertension were present in 48 (64.0%) and 51 (68.0%) patients, and diabetes mellitus were found in 33 (44.0%) and 38 (50.7%) patients across the two groups respectively (Table-I).

Table No.2: Comparison of Mean Haemoglobin Levels in Both Groups n=150

Haemoglobin Levels	Roxadustat n=75	Erythropoietin n=75	t	P value*
	Mean ± SD	Mean ± SD		
Hb Baseline (g/dL)	8.67 ± 0.77	8.44 ± 0.82	1.78	0.077
Hb at 4 Weeks (g/dL)	9.41 ± 0.79	9.05 ± 0.83	2.701	0.008
Hb at 6 Weeks (g/dL)	10.02 ± 0.90	9.57 ± 0.92	2.989	0.003
Hb at 12 Weeks (g/dL)	11.06 ± 0.74	10.37 ± 0.83	5.43	<0.001

*Independent t test

Table No.3: Comparison of Blood Transfusion Requirement Between Both Groups n=150

Transfusion	Roxadustat n=75 n (%)	Erythropoietin n=75 n (%)	P value
At 4 Weeks			
Yes	7 (9.3%)	24 (32.0%)	<0.001**
No	68 (90.7%)	51 (68.0%)	
Total	75 (100%)	75 (100%)	
At 6 Weeks			
Yes	3 (4.0%)	19 (25.3%)	<0.001*
No	72 (96.0%)	56 (74.7%)	
Total	75 (100%)	75 (100%)	
At 12 Weeks			
Yes	3 (4.0%)	7 (9.3%)	0.327*
No	72 (96.0%)	68 (90.7%)	
Total	75 (100%)	75 (100%)	

*Fischer Exact Test **Chi-square test

At baseline, mean haemoglobin levels were appears comparable between the two groups, being 8.67 ± 0.77 g/dL in the Roxadustat group and 8.44 ± 0.82 g/dL in the erythropoietin group, and the difference were not statistically significant (p = 0.077). At 4 weeks, haemoglobin levels were risen to 9.41 ± 0.79 g/dL in the Roxadustat group as compared to 9.05 ± 0.83 g/dL in the erythropoietin group, with a statistically significant difference were observed (p = 0.008). At 6 weeks, the Roxadustat group were demonstrated a further rise to 10.02 ± 0.90 g/dL in comparison to 9.57 ± 0.92 g/dL in the erythropoietin group, and the difference were remained significant (p = 0.003). By 12 weeks, the mean haemoglobin in the Roxadustat group were reached 11.06 ± 0.74 g/dL versus 10.37 ± 0.83 g/dL in the erythropoietin group, and this difference were found to be highly significant (p <0.001) (Table-2).

With regards to blood transfusion requirement, at 4 weeks, significantly fewer patients in the Roxadustat group were required transfusion as compared to the erythropoietin group, being 7 (9.3%) versus 24 (32.0%) respectively, and the difference were statistically significant (p <0.001). At 6 weeks, transfusion requirement was also notably lower in the Roxadustat group, with only 3 (4.0%) patients were needed transfusion as compared to 19 (25.3%) in the erythropoietin group, and the difference were again found to be significant (p <0.001). At 12 weeks, transfusion was required in 3 (4.0%) patients of the Roxadustat group and 7 (9.3%) of the erythropoietin group, however this difference was not reached statistical significance (p = 0.327) (Table-3).

DISCUSSION

In present study, hemoglobin levels showed a significant rise in the Roxadustat group after 4 weeks

(9.41 ± 0.79 g/dL vs 9.05 ± 0.83 g/dL, p = 0.008), after 6 weeks (10.02 ± 0.90 g/dL vs 9.57 ± 0.92 g/dL, p = 0.003), and after 12 weeks (11.06 ± 0.74 g/dL vs 10.37 ± 0.83 g/dL, p < 0.001) when compared with those in the erythropoietin group. The reason for the improvement could be attributed to the mechanism of action of Roxadustat, which involves inhibiting the activity of hypoxia-inducible factor prolyl hydroxylase (HIF-PH) and consequently enhancing the stability of the HIF pathway to produce erythropoietin. As such, Roxadustat not only improves iron uptake but also increases erythropoietin production. Erythropoietin works through direct stimulation of erythropoiesis and does not address the deficiency of iron that occurs in CKD patients. In addition, the number of patients in the Roxadustat group who needed blood transfusion was significantly lower than those in the erythropoietin group after 4 weeks; 7 (9.3%) versus 24 (32.0%), respectively (p < 0.001), and also after 6 weeks; 3 (4.0%) versus 19 (25.3%), respectively (p < 0.001). In this regard, Roxadustat leads to sustained correction of anemia in CKD patients. Moreover, since CKD is characterized by chronic inflammation, it induces erythropoietin resistance by inhibiting its erythropoiesis effect. Roxadustat helps to overcome.

In the present study, mean haemoglobin were showed a progressive and statistically significant rise in the Roxadustat group at 4 weeks (9.41 ± 0.79 g/dL versus 9.05 ± 0.83 g/dL, p = 0.008), at 6 weeks (10.02 ± 0.90 g/dL versus 9.57 ± 0.92 g/dL, p = 0.003), and at 12 weeks (11.06 ± 0.74 g/dL versus 10.37 ± 0.83 g/dL, p <0.001). These results were in agreement with Li et al. [12] who were also reported superior haemoglobin outcomes with Roxadustat as compared to recombinant Erythropoietin in hemodialysis patients (p <0.05), and with Zhang et al. [13] who were observed significantly higher haemoglobin levels and better haemoglobin stability with Roxadustat as compared to Erythropoietin (p <0.001). Similarly, Zhang et al. [14] were reported a haemoglobin response rate of 78.7% with Roxadustat versus 54.1% with Erythropoietin in diabetic kidney disease patients, which were further supports the superior erythropoietic potential of Roxadustat. This superior haemoglobin response with Roxadustat were may be explained by its mechanism of action, whereby it was inhibits the hypoxia-inducible factor prolyl hydroxylase (HIF-PH) enzyme, thereby were stabilizing endogenous erythropoietin production and were improving iron absorption and utilization via the hepcidin suppression pathway, as were also highlighted by Lewandowski et al. [15] and Edwards et al. [16]

However, Jin et al. [11] in a large retrospective cohort of 790 CKD patients were reported no significant difference in haemoglobin correction between Roxadustat and Erythropoietin over 24 weeks after propensity matching, which were slightly differs from the present study findings. This difference was may be attributed to the retrospective design and heterogeneous patient population included in that study, as compared to the more controlled study design of the present study. Similarly, Uysal et al. [17] were reported haemoglobin improvement in only 68% of patients switched to Roxadustat from Erythropoietin, with 56% achieving target haemoglobin ≥11 g/dL, which were relatively lower than the haemoglobin levels were achieved in the present study. This were possibly because that study was included patients with pre-existing Erythropoietin hyporesponsive anaemia, who were likely to have more severe underlying inflammatory and iron-restricted states.

With regards to blood transfusion requirement, significantly fewer patients in the Roxadustat group were required transfusion at 4 weeks, 7 (9.3%) versus 24 (32.0%) (p <0.001), and at 6 weeks, 3 (4.0%) versus 19 (25.3%) (p <0.001), as compared to the Erythropoietin group. This finding was consistent with the observations of Barratt et al. [18] who were reported reduced intravenous iron requirements and improved iron utilization with Roxadustat in the DOLOMITES trial, which were indirectly reflects a more sustained correction of anaemia and reduced dependence on external iron and transfusion support. The lower transfusion requirement with Roxadustat were likely reflects its ability to were overcome the chronic inflammation-mediated Erythropoietin resistance that were commonly seen in CKD patients, as were also noted by Alanazi et al. [19] who were identified high ferritin, low transferrin saturation, and low albumin as key drivers of Erythropoietin hyperresponsiveness. Roxadustat, by were acting on the HIF pathway, were appears to were address these underlying factors more effectively, thereby were reducing the need for blood transfusion in this patient population.

There are several limitations associated with the current study that need to be considered. First, the current study was carried out at one research centre, thus reducing its validity for other populations. Second, only a 12-week follow-up was included in the current research, which can be regarded as too short for examining the efficacy and safety of Roxadustat in comparison with Erythropoietin. Moreover, the number of participants is rather low for certain types of analysis. Finally, the current study failed to control such variables as iron intake, use of concomitant medication, and residual renal function.

CONCLUSION

In the current study, it is established that Roxadustat offers greater efficacy than Erythropoietin in addressing anaemia in individuals suffering from chronic kidney disease stages IV and V. It is observed that there is a higher level of efficacy of haemoglobin in Roxadustat along with the lower incidence of blood transfusion during the entire duration of the medication.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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