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COMPARISON OF ROXADUSTAT VS ERYTHROPOIETIN FOR THE TREATMENT OF ANEMIA IN PATIENTS WITH CHRONIC KIDNEY DISEASE AT BAHRIA INTERNATIONAL HOSPITAL RAWALPINDI

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Abstract

Background:
Anemia is a common complication of chronic kidney disease (CKD), traditionally treated with erythropoietin. However, limitations such as adverse events and injection requirements have prompted exploration of alternatives like roxadustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor.

Objective:
This study compared the efficacy and safety of roxadustat versus erythropoietin for treating anemia in CKD patients.

Methods:
A prospective, observational study was conducted with 187 CKD patients (stages 3–5) randomized to roxadustat (oral, n=94) or erythropoietin (injectable, n=93). Hemoglobin levels, iron parameters (ferritin, TSAT), blood pressure, and adverse events were monitored over 12 weeks.

Results:
Roxadustat showed superior hemoglobin improvement (11.1 ± 1.1 g/dL vs. 10.2 ± 1.0 g/dL, p=0.001) and better iron utilization (ferritin +10 ± 15 ng/mL vs. -5 ± 12 ng/mL, p=0.01; TSAT +4.2 ± 3.0% vs. +1.8 ± 2.6%, p=0.03). Adverse events were significantly lower with roxadustat (23.4% vs. 39.8%, p=0.01), including fewer cases of hypertension (10.6% vs. 23.6%) and no injection site reactions (0% vs. 16.1%).

Conclusion:
Roxadustat demonstrated greater efficacy in correcting anemia and improved safety profile compared to erythropoietin, with the added advantage of oral administration. These findings support its use as a first-line therapy for CKD-related anemia, though longer-term studies are needed.

INTRODUCTION

In China, there are an estimated 120 million people with chronic kidney disease (CKD) [1], of which 2% will likely progress to end-stage renal disease (ESRD). Anemia is a common complication of CKD caused by impaired oxygen sensing during renal failure. It decreases erythropoiesis, influences the survival of red blood cells, induces inflammation, and blocks metabolism. More than 90% of dialysis patients have been reported to suffer from renal anemia [2].

Conventionally, recombinant human erythropoietin (rhEPO) is used to treat anemia in patients with CKD. It not only improves hemoglobin (Hb) levels but also delays the progression of CKD, reduces hospitalization and all-cause mortality, and improves the quality of life of patients with CKD [3]. However, the increase in adverse events associated with disease progression is disturbing. Owing to the frequent incidence of treatment-related adverse events, such as tumors, endocrine system dysfunction, and cardiovascular events, rhEPO doses are often reduced [4]. In addition, erythropoietin resistance can occur in some patients, resulting in treatment failure, the risk of needle-stick injury for nurses, and the inconvenience of frequent subcutaneous injections [5]. As a hypoxia-inducible factor prolyl hydroxylase inhibitor, the novel agent roxadustat may increase endogenous erythropoietin concentrations by mediating the hypoxia-inducible factor, which is regulated via the inhibition of certain activated domains, such as pan-prolyl hydroxylase [6]. Subsequently, it has been incorporated into the therapeutic regimen for anemia in CKD [7].The incidence of renal anemia is significantly higher in DKD patients (68.0% in DKD versus 56.6% in hypertensive nephropathy, and 46.1% in chronic glomerulonephritis) as reported in a muti-center cross-sectional study [8]. A nested case-control study also demonstrated a high incidence rate of anemia in DKD patients [9]. DKD patients usually develop more severe anemia than patients with non-DKD. Study enrolled 106 DKD and 100 non-DKD participants showed that in stage 3 and 4 CKD, Hb levels were lower in DKD [10].

Methodology

This study was designed as a prospective, comparative, observational study to assess the efficacy and safety of Roxadustat compared to Erythropoietin in treating anemia among patients with chronic kidney disease (CKD). The study focused on patients diagnosed with CKD stages 3–5 who exhibited anemia.

The study population included adults aged 18 years or older, diagnosed with CKD (stage 3–5), either on dialysis or pre-dialysis, and with hemoglobin (Hb) levels below 11 g/dL. Participants were required to provide informed consent. Exclusion criteria comprised active malignancy, uncontrolled hypertension, recent blood transfusions within the past four weeks, a history of hypersensitivity to the study drugs, and pregnant or lactating women.

A total of 187 patients were enrolled and evenly divided into two groups: Group A (Roxadustat group) received oral Roxadustat, while Group B (Erythropoietin group) received subcutaneous or intravenous Erythropoietin. The treatment protocol involved administering Roxadustat orally at a specified dose three times weekly, and Erythropoietin was given according to standard clinical guidelines. Doses were adjusted based on hemoglobin response and clinical judgment.

Data collection occurred at baseline and monthly intervals over three months. Key parameters measured included hemoglobin levels, serum ferritin, transferrin saturation (TSAT), blood pressure, and any adverse drug reactions. The primary outcome was the change in hemoglobin levels from baseline to 12 weeks. Secondary outcomes included changes in ferritin and TSAT, the incidence of adverse events, and blood pressure fluctuations.

For statistical analysis, the study utilized SPSS software (version specified). Quantitative variables, such as hemoglobin levels, were presented as mean ± standard deviation and analyzed using paired and unpaired t-tests. Categorical variables were compared using the Chi-square test, with a p-value of less than 0.05 considered statistically significant.

Results

A total of 187 patients with CKD-related anemia were enrolled and evenly distributed into two groups: Group A received Roxadustat and Group B received Erythropoietin. Baseline characteristics were comparable between groups. Over the 12-week study period, patients in the Roxadustat group showed a significantly greater increase in hemoglobin levels compared to the Erythropoietin group (mean Hb at week 12: 11.1 ± 1.1 g/dL vs. 10.2 ± 1.0 g/dL, p = 0.001). Improvements in iron indices were also more

pronounced in the Roxadustat group, with significant increases in ferritin and TSAT (p = 0.01 and p = 0.03, respectively). Moreover, Roxadustat was associated with fewer blood pressure elevations and a lower incidence of adverse events such as hypertension and injection site reactions (overall adverse events: 23.4% vs. 39.8%, p = 0.01). These findings suggest that Roxadustat may offer a more effective and better-tolerated alternative to Erythropoietin in managing anemia in CKD patients.

Table 1: Baseline Characteristics of Patients

Characteristic	Group A (Roxadustat)	Group B (Erythropoietin)	p-value
Number of patients	94	93	-
Age (years)	57.4 ± 10.2	56.9 ± 9.8	0.68
Male/Female	50/44	48/45	0.81
CKD Stage 3/4/5	20/35/39	22/33/38	0.91
Baseline Hb (g/dL)	8.6 ± 1.0	8.7 ± 1.1	0.74
Ferritin (ng/mL)	180 ± 60	175 ± 55	0.56
TSAT (%)	22.3 ± 6.4	21.8 ± 6.1	0.59
Systolic BP (mmHg)	138 ± 15	140 ± 16	0.48
Diastolic BP (mmHg)	84 ± 10	85 ± 9	0.52

Table 2: Hemoglobin Changes Over 12 Weeks

Time Point	Group A (Roxadustat)	Group B (Erythropoietin)	p-value
Baseline	8.6 ± 1.0	8.7 ± 1.1	0.74
Week 4	9.7 ± 1.1	9.3 ± 1.0	0.04*
Week 8	10.5 ± 1.2	9.9 ± 1.1	0.01*
Week 12	11.1 ± 1.1	10.2 ± 1.0	0.001*

Table 3: Changes in Iron Indices and Blood Pressure

Parameter	Group A (Roxadustat)	Group B (Erythropoietin)	p-value
Ferritin Change (ng/mL)	+10 ± 15	-5 ± 12	0.01*
TSAT Change (%)	+4.2 ± 3.0	+1.8 ± 2.6	0.03*
Systolic BP Change	+2 ± 5	+7 ± 6	0.04*
Diastolic BP Change	+1 ± 4	+5 ± 5	0.02*

Table 4: Adverse Events

Adverse Event	Group A (n = 94)	Group B (n = 93)	p-value
Hypertension	10 (10.6%)	22 (23.6%)	0.02*
Headache	12 (12.8%)	9 (9.7%)	0.48
Nausea	7 (7.4%)	11 (11.8%)	0.29
Injection site reaction	0 (0%)	15 (16.1%)	<0.001*
Overall adverse events	22 (23.4%)	37 (39.8%)	0.01*

Discussion:

Roxadustat has shown superior efficacy over erythropoietin in enhancing hemoglobin levels and improving iron parameters, while also exhibiting a better safety profile with fewer adverse events. Its oral formulation offers a

significant advantage by improving patient compliance and eliminating complications associated with injections. These findings position Roxadustat as a viable alternative for chronic kidney disease (CKD) patients, particularly those who do not respond well to or experience intolerance with erythropoietin therapy.

The results of this study align closely with prior research. For instance, similar to referenced studies, our data revealed no significant differences in baseline characteristics between treatment groups. Notably, Roxadustat was associated with a reduced incidence of hypertension and fewer adverse events compared to erythropoietin, further supporting its favorable safety profile [11].

Consistent with comparative studies, Roxadustat demonstrated a significantly greater increase in hemoglobin levels than erythropoietin at comparable time points. In our study, the Roxadustat group achieved a 2.5 g/dL rise in hemoglobin at 12 weeks, compared to 1.5 g/dL in the erythropoietin group (*p* = 0.001), mirroring results from external research [12].

These findings are also corroborated by Jin et al. (2022), who reported that Roxadustat led to more pronounced improvements in hemoglobin levels and iron parameters in CKD patients with anemia, alongside a lower incidence of adverse events such as hypertension and injection site reactions [13].

While our study highlights Roxadustat's superiority in hemoglobin elevation (mean increase of 2.5 g/dL vs. 1.5 g/dL for erythropoietin, *p* = 0.001), other trials have observed smaller yet still significant differences (e.g., 0.77 g/dL vs. 0.68 g/dL). This reinforces the conclusion that Roxadustat is at least non-inferior—and often superior—to erythropoietin in managing anemia [14].

Further supporting these observations, both our study and referenced literature found that Roxadustat significantly elevated hemoglobin levels over a 12-week period. For example, our results showed a week-12 hemoglobin level of 11.1 g/dL for Roxadustat versus 10.2 g/dL for erythropoietin (*p* = 0.001), consistent with the referenced study's findings of greater ΔHb and ΔHct in the Roxadustat group [15].

However, some studies suggest that Roxadustat's initial hemoglobin advantage may diminish over extended periods. While our data demonstrated significant improvements at 12 weeks, referenced trials reported no notable difference in hemoglobin levels after 24 months [16].

Conclusion:

The study demonstrates that Roxadustat is a highly effective and safer alternative to Erythropoietin for treating anemia in patients with chronic kidney disease (CKD). Over the 12-week period, Roxadustat showed superior efficacy in increasing hemoglobin levels and improving iron parameters compared to Erythropoietin, with a mean hemoglobin rise of 2.5 g/dL versus 1.5 g/dL (*p* = 0.001). Additionally, Roxadustat was associated with fewer adverse events, particularly hypertension and injection site reactions, and exhibited better tolerability. Its oral administration also offers practical advantages, enhancing patient compliance and eliminating the risks associated with injections. These findings support Roxadustat as a promising first-line treatment for CKD-related anemia, especially for patients who are intolerant or resistant to Erythropoietin therapy. Further long-term studies are recommended to confirm these benefits over extended periods.

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