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Efficacy of erythropoietin-stimulating medications in controlling anemia in CKD patients

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ABSTRACT

Iron deficiency, chronic inflammation, and decreased endogenous erythropoietin production are the main causes of anemia, a prevalent and crippling consequence of chronic kidney disease (CKD). To raise hemoglobin levels, lower the requirement for blood transfusions, and improve patient quality of life, erythropoietin-stimulating agents (ESAs) are now a mainstay in the treatment of CKD-associated anemia. This study evaluates the efficacy of erythropoietin-stimulating medications in treating anemia in patients with chronic kidney disease. Hemoglobin response, transfusion needs, and clinical improvement were examined as part of a thorough evaluation of CKD patients on ESA therapy. The results show that, when properly dosed and managed, ESA medication dramatically raises and keeps hemoglobin concentrations within therapeutic levels.

Keywords: Chronic kidney disease, Anemia, Erythropoietin-stimulating hemoglobin, Erythropoietin-stimulating agents, Chronic kidney disease, Renal anemia, ESA therapy.

INTRODUCTION

Chronic kidney disease (CKD) is a progressive and irreversible disorder characterized by a gradual decline in kidney function over time[1]. It is defined as abnormalities of kidney structure or function present for more than three months, including a reduction in glomerular filtration rate (GFR) below 60 mL/min/1.73 m² or markers of kidney damage such as albuminuria [1]. CKD has emerged as a major global public health concern because of its rising prevalence, high morbidity and mortality rates, and substantial economic burden on healthcare systems [2]. The disease affects millions worldwide and is strongly associated with aging, diabetes mellitus, hypertension, cardiovascular disease, and lifestyle-related risk factors.

The kidneys play a vital role in maintaining internal homeostasis by regulating fluid and electrolyte balance, removing metabolic waste products, maintaining acid–base equilibrium, controlling blood pressure through the renin–angiotensin–aldosterone system, and producing essential hormones such as erythropoietin and calcitriol. As kidney function progressively declines in CKD, these physiological processes deteriorate, leading to complications including fluid overload, electrolyte imbalance, metabolic acidosis, mineral and bone disorders, cardiovascular disease, and hematological abnormalities. Among these complications, anemia is one of the most common and clinically significant manifestations of CKD [3].

According to the World Health Organization (WHO), anemia is defined as haemoglobin levels below 13 g/dL in men and below 12 g/dL in women. Anemia in CKD develops early and worsens as kidney function declines. The primary cause is reduced production of erythropoietin, a glycoprotein hormone produced by peritubular fibroblast-like cells of the kidney that stimulates red blood cell production in the bone marrow. Progressive loss of

functional renal mass results in decreased erythropoietin synthesis, leading to diminished erythropoiesis and anemia [4].

In addition to erythropoietin deficiency, several other factors contribute to anemia in CKD. These include absolute and functional iron deficiency, chronic inflammation, reduced red blood cell lifespan due to uremic toxins, nutritional deficiencies such as vitamin B12 and folate deficiency, blood loss during dialysis, frequent phlebotomy, and the use of certain medications such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers [5]. Chronic inflammation increases hepcidin levels, which impairs intestinal iron absorption and iron mobilization from storage sites, thereby exacerbating anemia [6].

Anemia significantly reduces quality of life in patients with CKD, causing symptoms such as fatigue, weakness, pallor, dizziness, dyspnea, reduced exercise tolerance, and cognitive impairment. More importantly, anemia is strongly associated with increased cardiovascular morbidity and mortality. Chronic anemia contributes to left ventricular hypertrophy, heart failure, ischemic heart disease, arrhythmias, and increased cardiac output [7]. Studies have shown that anemic CKD patients experience higher hospitalisation rates, faster progression of renal disease, and increased mortality compared with non-anaemic patients [8].

Historically, blood transfusions were the primary treatment for severe anemia in CKD. However, repeated transfusions were associated with complications such as iron overload, transfusion reactions, infection transmission, and sensitisation to human leukocyte antigens, which could adversely affect future kidney transplantation outcomes [9]. The introduction of recombinant human erythropoietin revolutionised anaemia management in CKD. Epoetin alfa received approval from the United States Food and Drug Administration (FDA) in 1989 [10].

Erythropoiesis-stimulating agents (ESAs), synthetic derivatives of erythropoietin, stimulate erythroid progenitor cells in the bone marrow to increase red blood cell production. Available ESAs include epoetin alfa, epoetin beta, darbepoetin alfa, and continuous erythropoietin receptor activators, which differ in molecular structure, half-life, and dosing frequency but share the same mechanism of action [11].

ESA therapy has been shown to effectively increase haemoglobin levels, reduce the need for blood transfusions, improve anaemia-related symptoms, and enhance quality of life in CKD patients. However, targeting higher haemoglobin levels has been associated with adverse cardiovascular outcomes such as hypertension, stroke, myocardial infarction, and vascular access thrombosis [12]. Therefore, current clinical guidelines recommend individualised haemoglobin targets and cautious ESA dosing to balance benefits and risks.

Response to ESA therapy varies among patients. Factors such as iron status, inflammation, nutritional deficiencies, infection, dialysis adequacy, and medication adherence influence treatment effectiveness5. ESA hyporesponsiveness is associated with increased morbidity, mortality, and healthcare costs. Regular monitoring of haemoglobin levels and iron parameters is essential for optimal anemia management.

The burden of CKD and anemia is particularly high in developing countries such as India, where delayed diagnosis, limited healthcare access, and financial constraints contribute to advanced disease presentation. Effective multidisciplinary management is therefore essential. Clinical pharmacists play a crucial role in optimizing ESA therapy by ensuring appropriate dosing, monitoring therapeutic response, managing adverse effects, promoting iron supplementation, improving medication adherence, and providing patient counselling.

The present study aims to evaluate the effectiveness of erythropoiesis-stimulating agents in managing anemia among patients with chronic kidney disease in a tertiary care hospital setting. By assessing changes in haemoglobin levels before and after ESA therapy and analyzing associated clinical parameters, this study seeks to support rational ESA use and improve quality of life in CKD patients [13].

MATERIALS AND METHODS

Study Site: GSL General Hospital and Medical College, Rajahmundry

Study Duration: The study will be conducted for a period of 6 months from October 2024 to March 2025.

Study Design: Prospective observational study

Sample Size: 70 patients

Study Criteria: Inpatients and outpatients of the nephrology department are included in the study.

Inclusion criteria

All the inpatients and outpatients of chronic kidney disease at any stage (preferably Stages 3-5, including those on dialysis, are included in the study.

Both males and females who are above 30 years are included in the study.

Male & female Patients with social habits like active smoking & alcohol intake are included in the study.

Patients with comorbidities like hypertension, diabetes, and CAD are included in the study.

Patients were either currently on ESA therapy or initiating ESA therapy during the study period.

Exclusion criteria

Patients who are not diagnosed with chronic kidney disease will be excluded.

Patients with anemia primarily due to causes other than CKD (blood loss, bone marrow disorders).

Patients with known hypersensitivity to erythropoietin-stimulating agents or severe ADR.

Patients who are dropping without treatment are excluded from the study.

Sources of data collection

Case sheets of patients admitted to the Nephrology department.

Interview of the patient and their representatives and research articles.

Patient admission record.

Laboratory test record.

Materials and methods used for data collection

Data will be collected directly from the case sheet of individual patients from the hospital on a specially designed data collection form.

Data will be collected after filling the informed consent forms from each patient.

Data will be qualitatively analyzed using Microsoft Excel 2007.

Descriptive data was presented as mean, standard deviation, and percentage.

Data was tabulated and graphically represented.

A two tailed t-test was used to assess statistical significance between variables.

RESULT

Table 1: Baseline demographic and clinical characteristics (N=70)

PARAMETER	VALUES
Age (years) means+ SD	52.3 ±11.4
Gender (Male/Female) n%	42(60%)/ 28(40%)
CKD with Hypertension	55(79%)
CKD with Diabetes mellitus	48(69%)
On Dialysis	20(29%)
Presence of Edema	45(64%)
ESA' s used	61(87%)

Table 4: Comparison of haemoglobin levels before and after ESA therapy

PARAMETER	MEAN±SD
Haemoglobin before treatment	7.86±1.79
Haemoglobin after treatment	9.26±1.72
Mean difference	1.40
t- value	10.86
p-value	<0.001*

DISCUSSION

This is a prospective observational study (cohort study) involved 70 patients, male patients were found to more susceptible to Anemia in CKD than female mostly in the age group 46-65(45%) adults, (15%) in age group (65-85), whereas (9%) of patients in the age group (36-45) and (1%) of patients in age group (25-35). Almost all the Patients had a history of deficiency of Erythropoietin, which is a leading cause of anemia in CKD. Along with the decreased level of haemoglobin, which is also the second leading cause of Anemia in CKD.

Therefore, treatment of anemia becomes crucial in the study, and it has been found that almost all the patients, nearly 67(87%), were prescribed injection erythropoietin for intensive increase in Hb levels, has been given in I.V form until the Hb levels reached the desired level.

This study suggests that Erythropoietin Stimulating Agents will be more effective in increasing Hb levels to increase Hb level at desired level and reducing the risk of anaemia. Erythropoietin was given in I.V form until the Hb levels reached normal, and continuous monitoring is required.

Almost all the male patients had a history of smoking and alcohol consumption. Nearly 22 patients were found to be alcoholics, and 23 patients were found to be smokers.

Along with anemia patients had co-morbidities like hypertension in (55) patients, Diabetes (48) and CAD (7). Therefore, treatment for hypertension is crucial, and it has been found that almost all the patients were prescribed Telmisartan, followed by Amlodipine and Metoprolol for a significant decrease in blood pressure.

For Diabetes mellitus, most of the patients were prescribed Metformin, followed by Insulin and Glimipride for a significant decrease in blood glucose levels.

Comparing Hb levels before and after treatment shows a significant raise in the levels of Hb. After treatment with the ESAs, there is a decrease in anemia and improvement was observed and concluded that this therapy plays a significant role to treat anemia in CKD.

For hypothetical test, In our study there are more than 70 samples for analysis, Z-test is required with the level of significance 0.05 and found that the result value was very less than level of significance and conclude that acceptance of alternative hypothesis, mean result was highly significance between haemoglobin before – haemoglobin after medication along with this also performed the correlation test between this parameter and found to be positive value, concluded that the high positive value indicates the high Correlation.

CONCLUSION

Chronic kidney disease is a fatal nephrological emergency condition that requires prompt recognition of clinical signs and symptoms, early diagnosis and early medical management of decreased haemoglobin levels. In this study, we conclude that the use of ESA's in treating anemia in CKD patients. The average Hb levels before administration were 7.85g/dl, and after administration, the average levels increased to 9.26g/dl. The present study concludes based on the statistical evidence. The effect of Erythropoietin-

stimulating agents in treating anemia in CKD patients was significantly observed, and found that there was an intensive increase in Hb levels, which plays a crucial role in the improvement of the condition. Maintaining haemoglobin levels in anemic CKD patients is extremely beneficial for physical and mental health and overall well-being. Quality of life improves in patients when haemoglobin is actively increased above 11.5g/dl. Treatment of anemia with ESAs in patients with CKD is indicated to improve quality of life and decrease morbidity and mortality.

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