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Safety and Efficacy of Erythropoietin in CKD Patients

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Abstract: ***Background: Chronic Kidney Disease is a permanent loss of kidney function. Erythropoietin is a hormone produced by kidney which play an important role in the production of RBC, that carry oxygen from the rest of the body. Lack of oxygen activates EPO production as erythropoietin is sensitive to oxygen levels in the blood that passes through the kidney. EPO production is less in CKD patients and it leads to anaemia. Man- made version of human erythropoietin is epoetin injection. It is used to treat severe anaemia in CKD patients. Objectives: The main objective of the study was to assess the safety and efficacy of erythropoietin in CKD patients. Materials and Methods: Study was carried out at Department of Nephrology, Mysore Medical College & Research Institute and K R Hospital, Mysore, India, from March 2020 to May 2020. A total of 40 patients were enrolled in the study as per inclusion and exclusion criteria. Patient's demographic data were collected by using patient data collection form and severity of the ADR was assessed by Hartwigs Severity Assessment Scale. Result: Among to patients 23 were female and 17 patients were male. In this study most patients were at age group 45-54years.About 65% (n=26)of the population was on dialysis. Only 4 patients had experienced ADR and the ADR was mild. Average increase in the Hb level in the study population was 3.78gm/dl. Conclusion: The study was conducted to ensure the safety and efficacy of erythropoietin used by CKD patients. The drug show mild adverse drug reactions and the level haemoglobin raised in patients and improve overall health related quality of life.***

Keywords: Chronic Kidney Disease, Erythropoietin, Adverse Drug Reaction, Anaemia

1. Introduction

Chronic Kidney Disease (CKD) or Chronic Renal Failure is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for life. In India, there is a rising incidence and prevalence of CKD.[1]

Anaemia is a common complication of chronic kidney disease resulting from insufficient release of the hormone erythropoietin by the damaged kidney leading to a decreased red cell production by the bone marrow. [2][3]

Erythropoietin (EPO) is a sialoglycoprotein hormone (MW34000) produced by peritubular cells of the kidney that is essential for normal erythropoiesis. Kidney cells senses anaemia and hypoxia and induce rapid secretion of EPO which acts on erythroid marrow. It stimulates proliferation of colony forming cells of the erythroid series there by inducing hemoglobin formation and erythroblast maturation. Proliferation of the cells release recticulates in the circulation. EPO binds to specific receptors on the surface of its target cells. The EPO receptors on the surface is a JAK-STAT-binding receptor that alters phosphorylation of intracellular proteins and activates transcription factors to regulate gene expression. It induces erythropoiesis in a dose dependent manner, but has no effect on RBC lifespan. The recombinant human erythropoietin (Epoetin α, β) is administered by i. v or s.c injection and has plasma t- ½ life of 6-10hour, but action lasts several days .The primary indication for epoetin is anaemia of chronic renal failure which is due to low level of EPO. Only symptomatic patients with hemoglobin less than 8g/dl should be considered for EPO therapy[4][5]

In CKD, anaemia can develop at early stages (stages 2 and3, of the KDOQI guidelines). As estimated glomerular filteration rate is around 70 ml/min/1.7m^2(men) and 50ml/min/1.73m^2 (women), Hb level decreases. [6]

Establishment of EPO in clinical practice, more than two decades ago, altered completely the management of patient with chronic kidney disease (CKD). The successful management of anemia of CKD has resulted in reduction of associated morbidity and improvement of functionality, exercise tolerance ,cognitive function and overall quality of life.

EPO and its receptors are regarded as essential modulators of the physiologic response to hypoxia and EPO administration decreases acute ischemic injury in a variety of tissues. Epo receptors are present in vascular and other sites of the adult kidney, mainly in tubular. Epo act as a renoprotective during acute kidney injury. Particularly, Epo administration activates protective intracellular pathways that results in increased expression of antiapoptotic protein expression and reduce caspase activity, that leads to reduction in apoptotic cell death and increased proliferation of tubular endothelial cells. Betterment in anemia and symptoms such as headache, dizziness were decreased and blood pressure modestly raised. There is no deviation in serum protein, lipid, electrolytes and liver enzymes. The result indicate treatment is effective.[7]. There can be rise in hematocrit, increase in blood pressure in four patients and

majority had an increase serum creatinine and potassium levels. Not even reported any organ dysfunction and other toxic effects.[8]

2. Materials and Methodology

This is a hospital based prospective observational study, it was conducted at Mysore medical college and research institute and associated hospitals, (K R hospital); Mysuru. The study was carried out at Department of Nephrology .The study duration was the period of 3 months from March 2020 to May 2020. During the study period we attended 40 patients who are above for above 18 years Patient prescribed with erythropoietin injection. Female patients with pregnancy and lactation, incomplete information, alcoholic patients with comorbidities of physical are excluded from the study. The patients who satisfy the inclusion criteria will be enrolled in to the study after obtaining their consent. The pharmacist activities like participating in ward round, patient counseling, medication review (medication chart and relevant documents), providing the drug information, monitoring and documenting of ADR will be done.

A suitably designed data collection form will be used to record all the necessary data (patient demographic details, patient medication history, and reason for admission, any allergic reaction, medication details and lab investigations). The patient will be followed from the date of admission to date of discharge. The drug use pattern will be assessed using various resources. If any ADRs identified, ADRs will be documented in ADR reporting form. The obtained data will be subjected for suitable study. Ethical approval was obtained from the institutional ethical committee of Mysore Medical College and Research Institute, KR Hospital; Mysuru.

3. Results

Demographics

Table 1: Gender Distribution of the study population

Gender	No of patients	Percentage
Female	23	57.5%
Male	17	42.5%
Total	40	100%

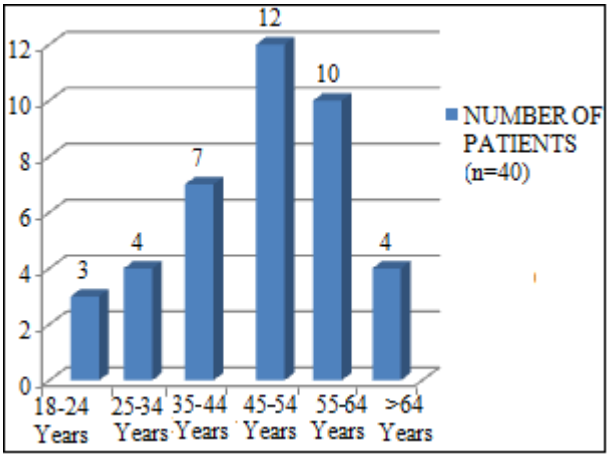

Figure 1: Age Distribution in the study population

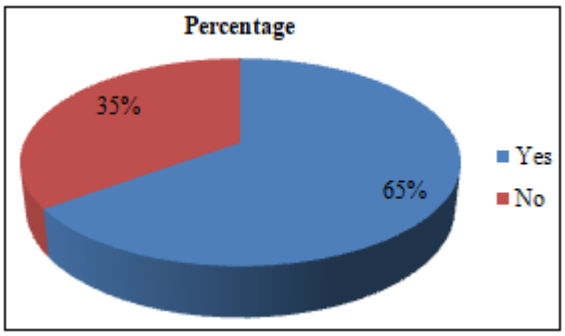

Figure 2: Study Population according to Dialysis

Adverse Drug Reaction

Table 2: Adverse Drug Reaction in the study population

ADR	Number of patients	Percentage
Yes	4	10%
No	36	90%
Total	40	100%

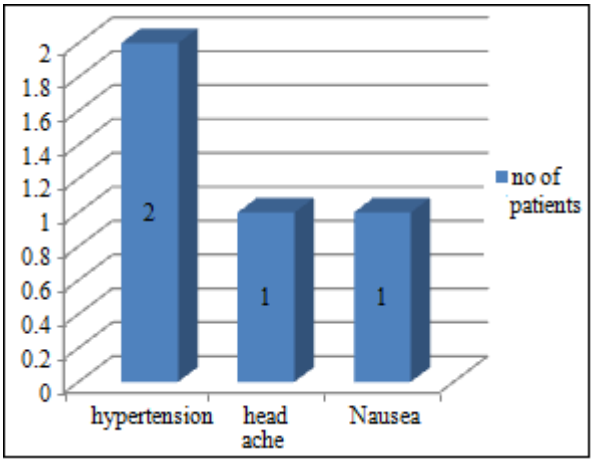

Figure 3: Suspected Adverse drug reactions

Table 4: Severity of the ADR

Severity	No of patients
Mild	4
Moderate	0
Severe	0

Table 5: Average increase in the Heamoglobin level

Patients on dialysis	3.6gm/dl
Patients not on dialysis	3.9gm/dl

Table 6: Average Hb level before and after administration of eythropoetin in the study population

Before Administration	After Administration
5.47	9.23

Table 1 shows that, out of 40 patients , 57.5% where males (n=23) and 42.5% were females (n=17). Figure 1 shows that out of 40 patients, majority of the people belong to the age group of 45-54 years followed by the age groups 55-64 years and 35-44 years. By analysing these results, it is understood that CKD patients taking erythropoietin showed a maximum among patients of age group 45-54 years. Figure 2 explains out of 40 patients, according to dialysis 65% are on dialysis and 35%not on dialysis.

Table 2 shows adverse drug reaction in the study population, out of 40 (n=4) reports ADR that is 10% and (n=36) that is 90% not report ADRs. Figure 3shows suspected ADRs while taking erythropoietin drug. ADRs (n=2) were seen as hypertension followed by nausea (n=1), and headache (n=1). Table5 out of 40 patients, shows average increase in haemoglobin level in which patient on dialysis 3.6gm/dl (n=26) and patients not on dialysis 3.9gm/dl (n=14). Table 6 shows that average haemoglobin level before administration was 5.47 and after administration it was increased to 9.23 therefore average increase in the Hb level in the study population was 3.78gm/dl.

4. Discussion

Demographic

The study was carried out in the nephrology of Mysore Medical college and research institute (KR hospital) over a period of 3 month from March 2020 to May 2020. This is a prospective study on safety and efficacy of erythropoietin in patients with CKD. In this study of 40 patients about 17 patients (45.5%)were male and 25(57.5%) patients were female. Most of the patients were between the age of 45-54yeas. This can be supported by a study conducted by Vareesangthip K et.al [9]. in his study about 64.10% of the CKD patients were female. About 65% (n=26) of the study population were on dialysis and rest without dialysis.

Safety

In the study population only 4 patients experienced ADR .this can be supported by the study conducted by JW Eschbach et.al on correction of the anaemia[10] .According to the study recombinant human erythropoietin ineffective except for slight increase in the BP, serum creatinine , and potassium levels.

Efficacy

In the study population, average Hb level before and after administration of eythropoetin 5.47 and 9.23 respectively. This study can be supported by Angelo karaboyas et.al.[11]in which about 53% of study population increased haemoglobin level upto 10g/dl 3 months later after administration of erythropoietin .

5. Conclusion

Eythropoietin has proved to be effective to treat anaemia of end stage of renal disease (ESRD). The aim of this study was to assess the efficacy and safety of EPO .EPO is effective to treat anaemia in patients on maintenance hemodialysis with an acceptable safety profile. There was no difference in response observed neither between men and women nor between patients with different levels of chronicity of ESRD. In the study population there was an average increase in the hb level in ckd patients with anemia. The ADR observed while using erythropoietin was mild and safe to use.

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