



EFFECTIVENESS OF ERYTHROPOIETIN IN CORRECTING ANEMIA IN PATIENTS OF CHRONIC KIDNEY DISEASE.

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ABSTRACT... Objectives: The anemia of chronic kidney disease (CKD) is commonly normocytic and normochromic. The objective of current study was to see the effectiveness of erythropoietin in correcting anemia in children with CKD. **Study Design:** Descriptive case series. **Setting:** Department of Nephrology, at The Children's hospital and the institute of child health, Multan. **Period:** From March 2018 to September 2018. **Material & Methods:** A total of 79 children with CKD were enrolled in this study. A standard dose of erythropoietin 100 IU/kg was given s/c biweekly and after 4 weeks patients were assessed for improvement in Hemoglobin (Hb) level. Data were entered and analyzed using SPSS-18. **Results:** Of the 79 cases, 48 (60.8%) were boys and 31 (39.2 %) girls. Mean age amongst cases was 9.92 ± 2.60 years and mean weight 19.65 ± 4.71 Kilograms. Mean baseline hemoglobin level of our study cases was 7.88 ± 1.09 gm/dl. Mean hemoglobin level after 4 weeks of therapy with Erythropoietin was 9.22 ± 1.04 gm/dl. Majority of our study cases i.e. 56 (70.88 %) were having stage 1 and 2 of CKD. Correction of anemia (effectiveness) was seen in 72 (91.1%) of our study cases. **Conclusion:** Recombinant human erythropoietin aid major improvement / correction of anemia in children with CKD. This drug can be safely used in children with CKD disease without any side effects such as hypertension.

Key words: Anemia, Chronic Kidney Disease, Erythropoietin, Hemoglobin.

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INTRODUCTION

Chronic kidney disease (CKD) is defined as renal injury (proteinuria) and/or glomerular filtration rate when calculated less than $60 \text{ ml/min/1.73m}^2$ for more than 3 months.¹ In pediatric population, 11 to 12 / million cases for the stage 3 to 5 CKD are estimated in Europe whereas overall prevalence is reported as approximately 55 to 60 million cases.^{2,3}

Most common complication and well recognized cause of morbidity in CKD is anemia. Anemia is due to decrease production of erythropoietin from failing kidneys due to tissue damage and decrease oxygen delivery to renal tissues which develops easily during the course of illness and affects almost all patients who present with some degree of reduced renal function.^{4,5} Anemia in CKD is normochromic normocytic. Severity of anemia is associated with extent and duration of disease. Prevalence of anemia in CKD stage 1 is

31.2% and 93.3% in CKD stage 4 and 5.⁶⁻¹²

Erythropoietin is a hormone produced by per tubular capillaries of kidney that promotes red blood cells production (erythropoiesis) from bone marrow by increasing proliferation and maturation of erythroid progenitors.¹³ Use of exogenous erythropoietin in CKD improves hemoglobin level, reduces risk of cardiovascular disease, and improves patient wellbeing and exercise tolerance. Exogenous erythropoietin is started when hemoglobin level is below normal range of age and sex. It is given subcutaneously to maintain hemoglobin between 11-12 g/dl. According to National Institute of Health and Clinical Excellence (NICE) guidelines efficacy of erythropoietin in CKD is defined as rise of 1gm of Hb in 4 weeks.¹⁴ Regular use of erythropoietin improves anemia in these patients so reducing the transfusion demand in these patients.¹⁵ Data of erythropoietin response in pediatric patients

according to the different stages of CKD (stage 1-5) is not plentiful as compared to the adult patients and no study has shown the effectiveness of erythropoietin in all stages of CKD. Few studies here been done to check the response in pediatric patients. In a study conducted in the children's Hospital and the Institute of Child Health Lahore, 50 patients of pre-dialysis CKD were enrolled and given erythropoietin subcutaneously with 100 IU/kg/biweekly. Out of them 92% of patients improved. But this study did not include results of stage 5 CKD patients.⁸

The Children's hospital and the institute of child health Multan is a tertiary level pediatric care center catering services to the children of southern Punjab. The Nephrology department manages heavy burden of patients of CKD. The aim of my study was to evaluate effectiveness of erythropoietin in raising hemoglobin level in CKD patients coming to our nephrology department. If results show effectiveness then this will guide us in better management of anemia in CKD and improving the prognosis of our patients.

MATERIAL & METHODS

This descriptive case series was done at The Department of Nephrology, at The Children's hospital and the institute of child health, Multan, from March 2018 to September 2018.

A total of 79 cases during the study period, having CKD (either GFR less than 60 ml/min/1.73m² or evidence of kidney injury i.e. proteinuria > 30mg/dl, scarring on ultrasound, with or without decrease in GFR),¹ aged > 1 year and < 15 year, Hb < 10 gm/dl and medically stable, were enrolled. Patient with iron deficiency anemia with serum ferritin < 7 ng/ml, previous history of adverse reaction to erythropoietin, already taking erythropoietin or having blood transfusion in last 4 weeks, were excluded.

Before starting study, permission was taken from institutional ethical review committee. Informed consent was taken from parents/guardians after discussing all details, benefits and risks of the study. Blood sample for hemoglobin (Hb), peripheral film and serum ferritin level were sent

to our hospital's laboratory. Variables recorded for each case included name, age, gender, height, weight, surface area. Basic investigations including complete blood count, renal parameters, urinalysis, ultrasound kidney, ureter, bladder (KUB) and glomerular filtration rate were calculated by schawrtz formula and patients were categorized according to GFR (eGFR). All the patients were stabilized to minimum Hb level of 6 gm/dl. A standard dose of erythropoietin 100 IU/kg was given s/c biweekly and after 4 weeks patients were assessed for improvement of Hb level. All data was entered in a pre-designed proforma. Outcome variable in term of improvement of Hb > 1 gm/dl in 4 weeks was taken as effectiveness.¹⁴

Data was analyzed using SPSS version 18.0. Frequency and percentage were calculated for gender, stages of CKD, and effectiveness of erythropoietin. Stratification was done with respect to age, gender, base line Hb, and stages of CKD. Post stratification chi square test has been applied. P value less than or equal to 0.05 have been taken as significant.

RESULTS

Of the 79 cases, 48 (60.8%) were boys and 31 (39.2 %) were girls. Mean age of our study cases was 9.92 ± 2.60 years (ranging 5 to 14 years). Study results have also indicated that majority of our cases i.e. 59 (74.7 %) were in the range of age groups 9 to 15 years. Mean weight of our study cases was 19.65 ± 4.71 Kilograms (minimum weight was 12 Kg while maximum weight was 30 Kg). Majority i.e. 52 (65.8%) of our study cases had weight in the range of 10-20 Kg. Mean height of the study cases was 116.95 ± 18.14 cm (minimum height was 96 cm while maximum height was 149 cm). Majority of our study cases i.e. 53 (67.1%) had height in the range of 95 - 125 cm. Mean baseline hemoglobin level of our study cases was 7.88 ± 1.09 gm/dl (with minimum Hb level was 6.1 gm/dl while maximum Hb level was 9.9 gm/dl). Mean hemoglobin level after 4 weeks of therapy with Erythropoietin was 9.22 ± 1.04 gm/dl (with minimum Hb level was 7.4 gm/dl while maximum Hb level was 11.2 gm/dl).

Majority of our study cases i.e. 56 (70.88 %) were

having stage 1 and 2 of CKD, 16 (20.3%) were in stage 3 of CKD, 5 (6.3%) with stage 4 and only 2 (2.5%) presented with stage 5 of CKD.

Correction of anemia (effectiveness) was seen in 72 (91.1%) of our study cases. This effectiveness was stratified with regards to the gender (p = 0.068), age of patients (p = 0.836), weight (p = 0.743), height (p = 0.798), baseline Hb levels (p = 0.430) and stages of CKD (p = 0.001).

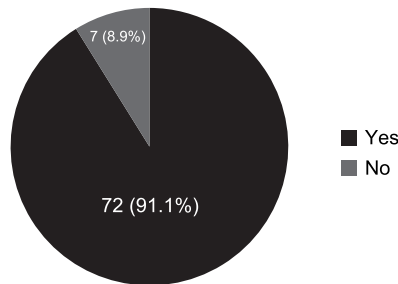


Figure-1. Effectiveness of erythropoietin (n=79).

DISCUSSION

Renal anemia is a well-recognized complication of CKD with erythropoietin deficiency being the primary cause. Lower levels of glomerular filtration rate (GFR) are associated with lower levels of hemoglobin, and in adults the latter is most pronounced when the GFR falls below 60 mL/min per 1.73 m.¹ This condition is associated with multiple adverse clinical consequences and its management is a core component of nephrology care. Increased morbidity and mortality, increased risk of cardiovascular disease and decreased quality of life have been associated with anemia of CKD in children. Our study included 79 children with CKD, 48 (60.8%) were male and 31 (39.2 %) were female. Our study findings are similar to that of Akhtar N et al⁵ who have also reported that anemia being more prevalent in male patients rather than female patients (62 % male versus 38% females) in their study.

Study Variables	Effectiveness		P-Value
	Yes (n=72)	No (n=07)	
Gender			
Male	46 (63.9%)	02 (28.6%)	0.068
Female	26 (36.1%)	05 (71.4%)	
Age Group (years)			
1-8	18 (25.0%)	2 (28.6%)	0.836
9-15	54 (75.0%)	5 (71.4%)	
Weight (kg)			
10-20	47 (65.3%)	5 (71.4%)	0.743
21-30	25 (34.7%)	2 (28.6%)	
Height (cm)			
95-125	48 (66.7%)	5 (71.4%)	0.798
126-150	24 (33.3%)	2 (28.6%)	
Stages of CKD			
Stage 1	23 (31.9%)	00	0.001
Stage 2	33 (45.8%)	00	
Stage 3	16 (22.2%)	00	
Stage 4	00	05 (71.4%)	
Stage 5	00	02 (28.6%)	
Baseline Hemoglobin (gm/dl)			
6-8	42 (58.3%)	3 (42.9%)	0.430
8.1-10	30 (41.7%)	4 (57.1%)	

Table-I. Stratification of Effectiveness with regards to Study Variables (n= 79).

However our findings are different from that of Jungers et al¹⁶ who reported significantly more prevalent anemia in female patients than male patients. Another trial reported 65% male patients with anemia, these findings are in consistence with our findings.¹⁷

Mean age of our study cases was 9.92 ± 2.60 years (ranging 5 to 14 years). Study results have also indicated that majority of our cases i.e. 59 (74.7%) were in the range of age groups 9 to 15 years. Akhtar N et al⁸ reported 7.68 years mean age which is a bit low than ours.

Mean weight of our study cases was 19.65 ± 4.71 Kilograms (minimum weight was 12 Kg while maximum weight was 30 Kg). Majority i.e. 52 (65.8%) of our study cases had weight in the range of 10-20 Kg. Akhtar N et al⁸ reported 21.65 Kg mean weight of their study participants, similar to our study.

Mean baseline hemoglobin level of our study cases was 7.88 ± 1.09 gm/dl (with minimum Hb level was 6.1 gm/dl while maximum Hb level was 9.9 gm/dl). Akhtar N et al⁸ reported 8.20 ± 1.28 gm/dl, which is close to our findings. Jungers et al reported 8.8 ± 0.7 g/dl baseline Hb levels. While mean Hb level was 9.5 ± 0.6 gm/dl in another trial.¹⁷

Mean hemoglobin level after 4 weeks of therapy with Erythropoietin was 9.22 ± 1.04 gm/dl, with minimum Hb level was 7.4 gm/dl while maximum Hb level was 11.2 gm/dl. Akhtar N et al reported 10.94 ± 1.04 , which is close to our study findings. Jungers P et al¹⁶ reported a bit higher mean levels for of Hb i.e. 11.3 ± 0.9 gm/dl. Mean Hb levels were 10.8 ± 1 gm/dl in a large population trial of 403 patients.¹⁷

Majority of our study cases i.e. 56 (70.88%) were having stage 1 and 2 of CKD, 16 (20.3%) were in stage 3 of CKD, 5 (6.3%) with stage 4 and only 2 (2.5%) presented with stage 5 of CKD. Our findings are in contrast to that of Akhtar et al⁵ while are in compliance with that Jungers P et al.¹⁶ Correction of anemia (effectiveness) was seen in 72 (91.1%) of our study cases. Akhtar et

al⁸ reported 92% correction of anemia in such cases. In our findings, erythropoietin was found to be safe in children with CKD without any side effects such as hypertension.

CONCLUSION

Recombinant human erythropoietin has significant impact on the improvement/ correction of anemia in children with CKD. This drug has potential to improve the quality of life of these patients and lower the burden on health authorities in terms of hospital stays and delayed start of dialysis.



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2	Asim Khurshid	Ideae, Methodology, Literature Review, Data analysis, Proof reading.	
3	Muhammad Abu Talib	Data collection, Methodology, Literature Review, Discussion.	