

RESEARCH ARTICLE

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Evaluation of frequency of erythropoietin use among end stage renal disease patients in Quetta, Pakistan

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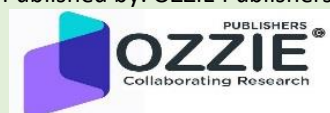
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Abstract

Objective: While treating anaemia in end stage renal disease (ESRD) patients, recombinant human erythropoietin (Epo) is the therapy of choice. However, it is rarely used in developing countries because of the financial constraints to the healthcare as well as the patient. Keeping the point of view in mind, the objective of this research was to identify the use of Epo, its frequency, and dosage in the patients of ESRD receiving continuous haemodialysis in Quetta city, Pakistan. **Methods:** This was a retrospective, single centered study. The selected population was subject with ESRD and on dialysis with prolonged anaemia. All recipients of dialysis in the past one year were targeted for the study. Data of the patients regarding anaemia and the use of erythropoietin was collected through a data collection sheet. Evaluation of the bio-chemical parameters of ESRD patients on haemodialysis was also be taken into consideration. Demographics of the selected patients were recorded carefully for the evaluation and analysis. SPSS 20.0 was used for data analysis and based on the objectives; both descriptive and inferential statistics were used for data elaboration. **Results:** A total of 97 ESRD patients that fulfilled the inclusion criteria were enrolled. Out of the 97, (52.6%) had age of more than 47 years and the cohort was dominated by males (63, 64.9%). Seventy two patients were on Epo use with majority on dose of 10000 IU with once a week frequency. The Man Whitney U test was used to compare erythropoietin use / non use and biochemical parameters. Haemoglobin percentage was significantly associated with erythropoietin use ($p < 0.05$). The mean rank interpretation revealed erythropoietin users significantly associated with improved haemoglobin percentage. The Kruskal Wallis test was used to compare erythropoietin usage frequency and biochemical parameters. Haemoglobin percentage was again significantly associated with erythropoietin use frequency. The Bonferroni correction revealed erythropoietin frequency of twice a week was significantly associated with improved haemoglobin percentage. **Conclusion:** Although the use of Epo among ESRD was reasonable, few patients were not prescribed Epo for anaemia associated with ESRD. We do understand that availability and affordability can be a major reason here; policy makers should make sure about the use of Epo because of its evidence-based advantages over other procedures.

Keywords: Frequency, erythropoietin, end stage renal disease, Quetta

INTRODUCTION

Anaemia is one of an important complications of End Stage Renal Disease (ESRD).^[1] The condition is coupled with deprived survival in persons who have complex and continual kidney ailments. Such patients are therefore recommended to undergo continuation of dialysis procedures.^[1] In terms of treatment rationality, the foremost intention of the dialysis procedure targets to increase patients' continued survival, decreasing the morbidity rates and humanizing the overall Quality of Life (QOL).^[2] Nevertheless, this does not happen in real time practice as regardless of technological improvements of pharmaceutical care, high rates of mortality and morbidity and poor QOL of dialysis patients is reported in literature.^[3] Quality of Life in ESRD patients is recovered at higher haematocrit levels.^[4] Within this context, severe anaemia is a major confine to psychoanalysis in patients with ESRD.^[1] Preceding approximation of storage iron in patients with dialysis linked anaemia reported that that unprocessed

haemodialysis patients experience total iron insufficiency of roughly 1 mg per day during dialyzer and blood loss.^[5] In line to what is reported in literature, the identified pathogenetic factor causing anaemia in ESRD population is the reduced production of erythropoietin in the diseased kidneys.^[6, 7]

While treating ESRD and anaemia as an associated disorder, recombinant human erythropoietin (Epo) is the therapy of choice for the last ten years.^[8-10] Conversely, previous to the accessibility of epoetin, the stronghold of anaemia treatment in ESRD was blood transfusions.^[11, 12] Erythropoietin is advanced when compared with blood transfusions as it has fewer undesirable reactions. Furthermore, epoetin is the reason of fabrication and discharge of young blood cells via bone marrow into systemic circulation.^[13, 14] The Health-Related Quality of Life (HRQoL) also exhibits the usefulness of epoetin remedy when managed as a usual clinical

procedure.^[15] When related to ESRD, the K/DOQI guiding principles advocate that the haemoglobin levels should stay at 11 - 12 g/dL.^[16] Therefore, patients treated with oral iron therapy demonstrate affirmative iron balance hence confirming that bowel iron assimilation is not disturbed in ESRD patients undergoing dialysis.^[16] The valuable outcome of stabilizing the haematocrit levels in ESRD is positively linked to advancement observed in both cognitive and corporeal functions and an improved QOL.^[2] Therefore based on the recommendations of the guidelines, it is hypothesized that a good level of haematocrit balance maintains the quality of life among dialysis patients.

Shifting our concerns to conditions in a developing country like Pakistan, Pakistan is one of the largest and most populous countries of the South Asian region. Among multiple concerns, a great apprehension for the healthcare system today is the increased frequency of NCDs including chronic kidney disease or end-stage kidney disease thus resulting in an increase of haemodialysis recipients in recent years. In Pakistan, around 20 million people are suffering from kidney diseases and nearly 16,000 new cases of kidney failure are registered.^[17] Furthermore, 40-50 percent of the patients are not surgically fit for transplantation, while only 15 percent donate their kidneys to relatives.^[17] This ultimately results in the increased frequency of haemodialysis across the country as there is no other treatment option available for kidney patients in Pakistan. Even at the treatment level, compounds like erythropoietin are rarely used because of the financial constrains to the healthcare as well as the patient. Consequently, this imposes a huge financial, economical and societal burden on the deprived healthcare system as the conditions worsen and there is no choice of treatment available. Therefore, it is wise to initiate rational treatment in the initial stages so that the complications of ESRD can be minimized later. Keeping the point of view in mind, the objective of this research was to identify the use of Epo, its frequency, and dosage in the patients of ESRD receiving continuous haemodialysis in Quetta city, Pakistan. We also aimed that the results of the study will urge the physicians to start using erythropoietin early in the treatment plans so that the patients can get maximum benefits of the therapeutic plans.

METHODS

Study design and settings

This was a retrospective, single cantered study. The research was carried out at Baluchistan institute Of Nephrology and Urology Quetta (BINUQ). BINUQ was established in November 2006 for kidney related diseases. It is a well-equipped institute with all modern treatment facilities, providing care for patients in the field of urology and nephrology. A twelve bedded well equipped haemodialysis unit provides services in three shifts and an extension program of haemodialysis unit is almost near completion. This added program will enable the institute to become a 40 bedded haemodialysis unit to facilitate the increasing number of haemodialysis patients.

Study population, sampling and inclusion criteria

The selected population was subject with ESRD and on dialysis with prolonged anaemia. All recipients of dialysis in the past one year (2019) and attending the above mentioned healthcare facilities were targeted for the study. Patients having ESRD & congestive heart failure on dialysis, receiving

any surgical intervention or receiving renal transplant were excluded from the study.

Data collection and analysis

Data of the patients regarding anaemia and the use of erythropoietin was collected through a standardized data collection sheet. Evaluation of the biochemical parameters of ESRD patients on haemodialysis was also be taken into consideration. The use of erythropoietin and other hematinic ratios, frequency and dosage were recorded and analysed. Demographics of the selected patients were recorded carefully for the evaluation and analysis. SPSS 20.0 was used for data analysis and based on the objectives; both descriptive and inferential statistics were used for data elaboration.

Ethical approach

Ethical approval was taken from Faculty of Pharmacy & Health Sciences, University of Balochistan Quetta. Additionally, permission from the Executive Director of BINUQ was also taken before data collection.

RESULTS

Demographic characteristics of the study respondents

The demographic information of the study respondents is presented in Table 1. A total of 97 ESRD patients that fulfilled the inclusion criteria were enrolled. Out of the 97, (52.6%) had age of more than 47 years and the cohort was dominated by males (63, 64.9%). Seventy two patients were on EPo use with majority on dose of 10000 IU with once a week frequency.

Table 1: Demographic characteristics of the study respondents

Characteristics	Frequency	Percentage
Age		
18-27	19	19.6
28-37	10	10.3
38-47	17	17.5
> 47	51	52.6
Gender		
Male	63	64.9
Female	34	35.1
Use of Erythropoietin		
Yes	72	74.2
No	25	25.8
Dose of Erythropoietin (IU)		
0	25	27.8
5000	4	2.1
10000	68	70.1
Frequency of Erythropoietin Use		
Once/Week	62	63.9
Twice/Week	12	8.2
None	25	27.8

Haemodialysis and blood transfusion related information of the study respondents

Out of the 97 patients, eighty six percent were on haemodialysis with a frequency of twice a week. Majority of the respondents were on arteriovenous access while 58 (59.8%) were on blood transfusion as shown in Table 2.

Table 2: Haemodialysis and blood transfusion related information of the study respondents

Characteristics	Frequency	Percentage
Frequency of Haemodialysis		
Once per week	11	11.3
Twice per week	84	86.6
Thrice per week	2	2.1
Duration of Haemodialysis		
1-12 months	64	65.9
1-3 years	8	8.2
> 3 years	25	25.7
Vascular Access		
Subclavian	9	9.3
Arteriovenous	88	90.7
Blood Transfusion		
Yes	58	59.8
No	39	40.2
Frequency of Blood Transfusion		
Once per week	11	18.9
Twice per week	23	39.6
Once in 2 Weeks	6	10.3
Once in 3 Weeks	6	10.3
Once in a month	12	20.6

Comorbid and bio-chemical information of the study respondents

Twenty (20.6%), 31 (32.0%) and 5 (5.2%), of the respondents were positive for Hepatitis-B, Hepatitis-C and HIV respectively. All patients were hypertensive while 77 (79.4%) had Type II diabetes mellitus. The mean values of biochemical parameters were assessed and are presented in Table 3.

Table 3: Comorbid and bio-chemical information of the study respondents

Disease related characteristics	Frequency	Percentage
HbsAg		
Positive	20	20.6
Negative	77	79.4
HCV		
Positive	31	32.0
Negative	66	68.0
HIV		
Positive	5	5.2
Negative	92	94.8
Diabetes		
Type II Diabetic	77	79.4
Type-I Diabetic	2	2.06
Non Diabetic	20	20.6
Hypertension		
Yes	97	100.00
Biochemical parameters		
	mean ± sd	
Haemoglobin %age (mg/dl)	9.05 ± 1.47	
Serum Urea (mg/dl)	70.61 ± 45.72	
Urea creatinine (mg/dl)	7.87 ± 2.55	
Serum Calcium (mg/dl)	7.68 ± 1.85	
Serum Sodium (mmol/l)	139.81 ± 15.34	
Serum Chloride (mmol/l)	116.16 ± 10.60	
Serum Potassium (mmol/l)	5.54 ± 0.91	

Fasting Blood Sugar (mg/dl)	147.01 ± 24.66
Systolic blood pressure (mm/Hg)	86.91 ± 16.63
Diastolic blood pressure (mm/Hg)	129.79 ± 47.41

Inter group comparison (erythropoietin use) and study parameters

The Man Whitney U test was used to compare erythropoietin use / non-use and biochemical parameters. Haemoglobin percentage was significantly associated with erythropoietin use. The mean rank interpretation revealed erythropoietin users significantly associated with improved haemoglobin percentage. No significant association was found among other study variables as shown in Table 4.

Table 4: Inter group comparison (erythropoietin use) and study parameters

Biochemical parameters	P-Value (compared with erythropoietin and non use)*
Systolic Blood Pressure	0.612
Diastolic Blood Pressure	0.707
Fasting Blood Sugar (mg/dl)	0.099
Serum Urea (mg/dl)	0.038
Blood Sugar (mg/)	0.626
Serum Calcium (mg/)	0.984
Serum Sodium (mmol/l)	0.533
Serum Chloride (mmol/l)	0.653
Serum Potassium (mmol/l)	0.423
Hb %age (mg/dl)	0.008

Inter group comparison (erythropoietin frequency) and study parameters

The Kruskal Wallis test was used to compare erythropoietin usage frequency and biochemical parameters. Haemoglobin percentage was again significantly associated with erythropoietin use frequency. The Bonferroni correction revealed erythropoietin frequency of twice a week was significantly associated with improved haemoglobin percentage. No significant association was found among other study variables as shown in Table 5.

Table 5: Inter group comparison (erythropoietin frequency) and study parameters

Biochemical parameters	P-Value (frequency of erythropoietin use)*
Systolic Blood Pressure	0.450
Diastolic Blood Pressure	0.231
Diabetes	0.955
Serum Urea (mg/dl)	0.550
Blood Sugar (mg/)	0.211
Serum Calcium (mg/)	0.099
Serum Sodium (mmol/l)	0.488
Serum Chloride (mmol/l)	0.560
Serum Potassium (mmol/l)	0.309
Hb %age (mg/dl)	< 0.001

DISCUSSION

Erythropoietin was introduced in clinical practice in late 1980's and since then it is considered as a standard of care for the treatment of anaemia in patients with chronic kidney disease.^[18] The extensive use of Epo and its analogues for the

purpose of anaemia correction has succeeded in improving functionality, cognitive performance and overall quality of life.^[18] However, the use of Epo from the developing countries like Pakistan is least reported. Therefore, the current study was aimed to evaluate the frequency of erythropoietin use among end stage renal disease patients in Quetta city, Pakistan.

Results of the current study reported that EPo was used among 72 (74.2%) of the patients while majority (70.1%) were administered with a dose of 10,000 IU. Although majority of the patients were administered EPo weekly, 12 (8.2%) of the patients were administered with EPo with a twice a week regimen. Within this context, even though the benefits of EPo administration in dialysis patients is well established, the best possible frequency schedule has not as yet been established. On the other hand, treatment with EPo is expensive and there is therefore a need for optimizing the effectiveness of its administration in patients with ESRD.^[19] Streja et al reported the relationship between the received dose of EPo and mortality in dialysis patients. The authors presented a positive dose-response relationship between weekly dose of EPo and the risk of death and higher dose of EPo was associated with increased mortality.^[20] Therefore, the scientific guidelines suggest modifying the partial haemoglobin levels in dialysis patients by EPo but it is not recommended obtaining the same haemoglobin level as the healthy people's standard levels in these patients.^[21] Connecting the observations with the current study results, the mean haemoglobin (Hb) percentage reported was 9.05 which is less than the normal ranges. Therefore, as per what is reported by Drüeke et al, practitioners at the hospital should reconsider the dose adjustment in patients with ESRD in the current cohort as higher doses are related to dose related complications.

Based on the literature review and as expected, the use and frequency of EPo use was significantly associated with Hg percentages. Our study findings are also evident from the literature as Panjeta and colleagues reported the same relationships between EPo use and Hb percentages.^[22] In line to what is reported earlier; the direct relationship was also reported in a study of the same nature.^[23] Therefore, the use of EPo as reported earlier is recommended in patients with ESRD. The only limitation with the use of EPo is the cost as EPo is relatively expensive and it is not always the treatment of choice for the developing healthcare systems. Furthermore, during the study it was also discussed that the availability of EPo in the said hospital is also an issue at certain periods of the year. Therefore, until or unless the EPo is available, it is used for patients with anaemia associated ESRD. Therefore, we do urge the practitioners in healthcare settings to focus on the use and regular availability of EPo at the healthcare centres as human EPo corrects anaemia and reduces the chances of blood transfusions.^[24]

Haemoglobin percentage was again significantly associated with erythropoietin use frequency. The Bonferroni correction revealed erythropoietin frequency of twice a week was significantly associated with improved haemoglobin percentage. It is obvious that the more EPo is administered the more are the chances of Hb increase.^[25] However, the presence of other predisposing factors, condition and stage of the kidney and other pathological conditions are not to be neglected. As mentioned earlier, the dosage of EPo should be thought of as there is no clinical evidence supporting higher doses of EPo

use in ESRD patients. Even though the percentage of twice a week administration is very few in our study cohort, twice administration of EPo should be avoided and other measures should be applied to increase Hb where feasible and are available.

CONCLUSION

Although the use of EPo among ESRD was fairly reasonable, few patients were not prescribed EPo for anaemia associated with ESRD. We do understand that availability and affordability can be a major reason here; policy makers should make sure about the use of EPo because of its evidence-based advantages over other procedures. Additionally, the dose of EPo and the rise in Hb should be monitored very carefully so that a change in dose can be recommended that can provide maximum therapeutic effect among patients with ESRD.

DISCLOSURE

The authors have no conflict of interest to disclose. No funding was received for the study.

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