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A study on utilisation pattern and treatment outcome of erythropoietin and iron sucrose in chronic renal failure patients undergoing hemodialysis

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ABSTRACT

Chronic renal failure (CRF) is a debilitating condition responsible for high morbidity and mortality and is a financial burden on government and society. The main purpose of the study is to evaluate the changes from baseline Hb and Hct level after erythropoietin therapy. And also the changes from baseline serum ferritin and transferrin saturation levels after iron sucrose therapy. For this a prospective observational study is carried out for 7 months between May 2006 to November 2006 including 55 patients in the renal unit at Kovai Medical Center and Hospital, a multi-speciality hospital in Coimbatore. Patients who were undergoing hemodialysis greater than 18 years of age during the study period and those patients who had a baseline Hb and Hct value of ≤ 10 g/dL and $\leq 30\%$ were enrolled in the study. Results showed that the prevalence of CRF was more in men when compared to women. The study conclusion is that the increase in Hb value is dependent on erythropoietin dose, higher the dose, higher in Hb value after 6 months of treatment. Thus erythropoietin is shown to be effective in treating anemia in patients with CRF, but it is associated with higher costs of therapy. Our results concluded that iron sucrose is safe and effective when given for the treatment of iron deficiency or for maintenance of iron stores.

Keywords: Chronic Renal Failure, Anemia, Renal Transplantation, Iron Sucrose therapy, Hemodialysis.

INTRODUCTION

Chronic renal failure is a major health issue in various parts of the world. The number of patients with end-stage renal disease (ESRD) is increasing in both developed and developing countries, greatly expanding the need for chronic dialysis and renal

transplantation. Although some dialysis patients live longer than 5-10 years and are able to work and contribute to the society in which they live, others are poorly and die within 2 to 3 years. Another issue surrounding ESRD is a rapidly aging dialysis population, in part related to the fact that the major proportion of new patients entering

dialysis programs comprises people with type 2 diabetes[1]. Because of the costs and the complexity of the treatment, very few patients are able to obtain adequate treatment, and CRF places a heavy financial burden on any society[2].

Another compounding issue of patients with ESRD is the aging population of chronic dialysis patients[1]. About 90 percent of patients undergoing of patients undergoing dialysis have anemia as a result of erythropoietin deficiency. The mean Hct of patients in the Medicare End Stage Renal Disease Program in 1995 was 31 percent. Consequently a number of strategies have been considered to improve the effectiveness of epoetin [3].

There is a evidence Hb concentration of less than 11g/dL is associated with an increased incidence of left ventricular hypertrophy, a known risk factor for death in patients with ESRD, there were insufficient data to support a recommendation to increase the Hct to the normal range [4]. Presumably then, some patients in the normal Hct group in whom the target Hct was not achieved must have died or had an acute myocardial infarction.

The objectives of the study include the evaluation of changes from baseline Hb and Hct level after erythropoietin therapy and also evaluating the changes from baseline serum ferritin and transferrin saturation levels after iron sucrose therapy, to analyse the cost and benefits for erythropoietin and iron, to describe the drug utilisation pattern in management of anemia in CRF patients and to review drug use and prescription pattern [5].

METHODOLOGY

A Prospective Observational Study was carried out is carried out for 7 months between May 2006 to November 2006 including 55 patients in the renal unit at Kovai Medical Center and Hospital, a multi-speciality hospital in Coimbatore. Patients who were undergoing hemodialysis greater than 18 years of age during the study period and those patients who had a baseline Hb and Hct value of ≤ 10 g/dL and $\leq 30\%$ were enrolled in the study. Patients who have undergoing blood transfusion and who have undergone kidney transplantation, who are resistant to erythropoietin therapy and who are allergic to parenteral iron therapy and also

patients with uncontrolled severe Hypertension are excluded from the study.

Patient's demographics, history of disease, past medical history, social habits, ADR, treatment charts were documented. Baseline values of hematological parameters like Hb, Hct, Serum ferritin and transferrin saturation values were recorded and changes from the baseline value after the initiation of erythropoietin and iron sucrose therapy were noted every month. Monthly cost and consumption of erythropoietin and iron therapy as well as changes in the weight of patients from the baseline after hemodialysis were documented during the study period in a suitable developed data collection form. Protocol for anemia management in CRF was prepared.

The data was analysed using SPSS version 8. Percentage was used to analyse categorical data. The nature of the variable was studied with the help of descriptive measures mean and standard mean.

Correlation co-efficient was used to measure the degree of relationship between the etythropoitin dose and Hb response. The paired t test was used to test the significant differences between

- ❖ The baseline mean Hb and sixth month mean Hb.
- ❖ The baseline mean serum ferritin and sixth month mean ferritin.
- ❖ The baseline mean transferrin saturation and sixth month mean transferrin saturation.

RESULTS

A total of 55 patients were evaluated, in which 78% (n=43) were males and 22% (n=12) were females.

The most age group in this population was >60 years, which constituted 33% (n=18) of the patient population, followed by 24% (n=13) in the range of 51-60 years, 22% (n=12) in the range of 41-50 years, 16% (n=9) in the range of 31-40 years and 5% (n=3) in the range of 20-30 years. The mean age in the study population was 52.07 ± 12.09 years.

According to the marital status, 13% (n=7) were single and 87% (n=48) were married.

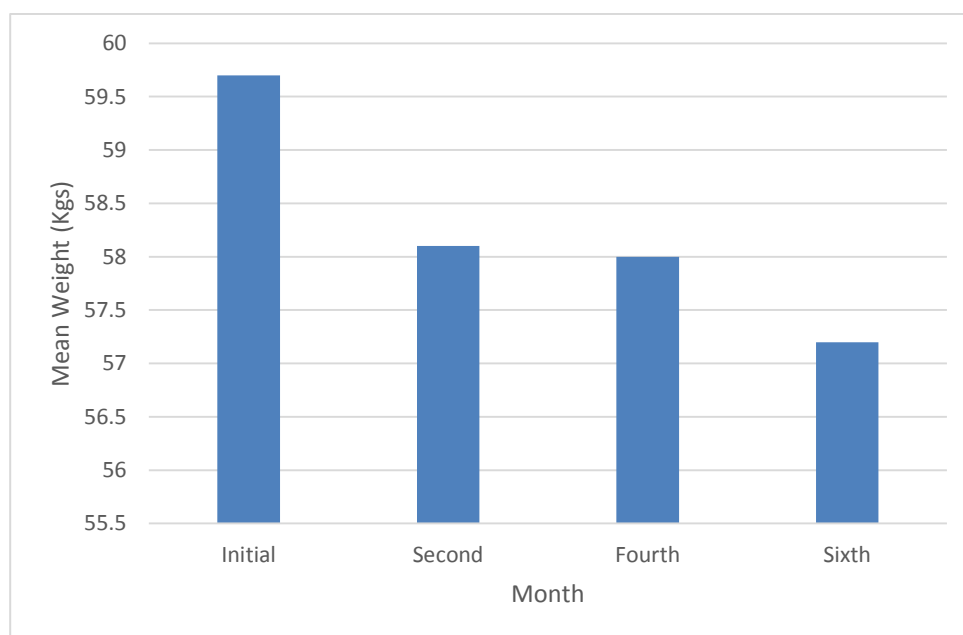
When the occupations were recorded, 31% (n=17) were in business, 24% (n=13) were agriculturists, 20% (n=11) were employees, 11% (n=6) were house wives, 14% (n=8) had no occupation.

The social habits of patients were recorded which showed that 25% (n=14) were in the habit of consuming alcohol, 18% (n=10) had the habit of smoking, 15% (n=8) had the habit of smoking and alcohol consumption and 42% (n=23) were not having the habit of either smoking or alcohol consumption.

The initial mean weight was 59.69 ± 9.08 Kg. During the second and fourth month the mean weight was reduced to 58.1 Kg and was slightly decreased to 57.18 ± 9.23 Kg at the sixth month after hemodialysis (**Table-1**).

Table 1: Changes in mean weight from the baseline after hemodialysis

MONTH	Mean Weight
Initial	59.7
Second	58.1
Fourth	58
Sixth	57.2



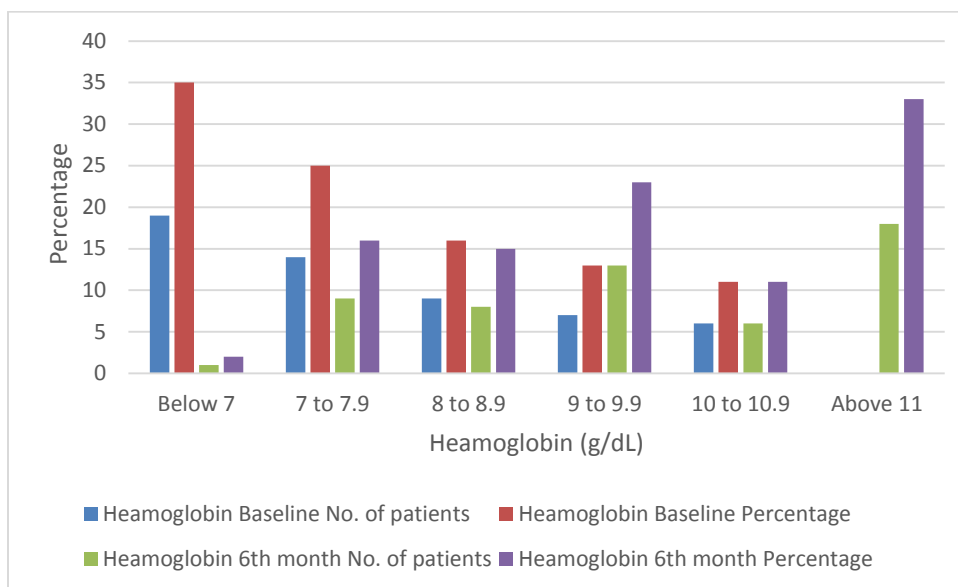
According to the patients report, the percentage of patients with a baseline Hb value less than 7g/dL was 35% (n=19) of the patient population, between 7 to 7.9g/dL was 25% (n=14), 8 to 8.9g/dL was 16% (n=9), 9 to 9.9g/dL was 13% (n=7), 10 to 10.9g/dL was 11% (n=6) and none of the patients have baseline Hb value greater than 11g/dL. While considering the sixth month Hb concentrations, only 2% (n=1) of the study population had Hb

value below 7g/dL, 16% (n=9) had the Hb value of 9 to 9.9, 11% (n=6) had the Hb value of 10 to 10.9g/dL and 33% (n=18) had reached the Hb value above 11g/dL, the target range recommended by dialysis outcome quality initiative guidelines (**Table-2**). The average (\pm SD) baseline Hb concentrations was 7.8 ± 1.4 g/dL and increased to 9.6 ± 1.6 g/dL at sixth month.

Table 2: Baseline and 6th month Haemoglobin concentration among the study group.

Heamoglobin Values (g/dL)	Heamoglobin Baseline		Heamoglobin 6th month	
	No. of patients	Percentage	No. of patients	Percentage
Below 7	19	35	1	2
7 to 7.9	14	25	9	16
8 to 8.9	9	16	8	15

9 to 9.9	7	13	13	23
10 to 10.9	6	11	6	11
Above 11	0	0	18	33



The results showed that the average monthly consumption of erythropoietin by patient who attained Hb concentrations of 10g/dL or above. The average monthly dose was 39625 IU, 37708 IU, 40458 IU, 34583 IU and 325421 IU during the first, second, third, fourth and fifth months.

The report showed that the average monthly consumption of iron sucrose was 1029.1 mg during the first month, 229.1 mg in the second month, 210.9mg in the third month, 216.4mg in the fourth month, 209.1mg in the fifth month and 205.5mg during the sixth month. For maintaining the adequate iron stores, the average monthly consumption of iron was high during the first month.

The results showed that the changes in average monthly Hb level were 8.16g/dL during the first month, 8.53g/dL in the second month, 8.82 g/dL in the third month, 9.19 g/dL in the fourth month, 9.48 g/dL in the fifth month and 9.65g/dL in the sixth month. Thus, the results showed that average monthly Hb kept steadily increasing.

The results showed that the average monthly cost of erythropoietin for a patient who reached the Hb level of 10g/dL or above was Rs.15750.83 in the first month, Rs.14989.00 in the second month, Rs.16082.17 in the third month, Rs.13747.00 in the fourth month, Rs.12935.67 in the fifth month and

Rs.9225.17 in the sixth month. The cost was high during the initial stage and decreased gradually.

The report showed that the average monthly cost of Iron sucrose for patients who attained the adequate iron sucrose stores was Rs.4048 in the first month, Rs.917 in the second month, Rs.800 in the third and fourth, Rs.819 in the fifth month and Rs.810 in the sixth month.

The baseline mean Hb was 7.8164g/dL and the sixth month mean Hb was 9.650g/dL. The difference of mean was tested by using paired t test. Since the observed t value was 6.905 (t0), which is greater than the critical value 2.326 (t0.01) at 1% level for 54 degrees of freedom. So the difference is significant (p < 0.01).

The baseline mean serum ferritin was 168.25ng/mL and the sixth month mean serum ferritin was 212.9582ng/mL. The difference of mean was tested by using paired t test. Since the observed t value was 3.509 (t0), which is greater than the critical value 2.326 (t0.01) at 1% level for 34 degrees of freedom. So, the difference is significant (p < 0.01).

The baseline mean transferrin saturation was 17.1455% and the sixth month mean transferrin saturation was 21.6727%. The difference of mean was tested by using paired t test. Since the observed t value was 4.5272 (t0), which is greater

than the critical value 2.326 (t0.01) at 1% level for 54 degrees of freedom. So the difference is significant ($p < 0.01$).

The results showed that the correlation coefficient (r) between erythropoietin dose and Hb concentrations is positive. From second month onwards the correlation kept increasing, ($r=0.084$) in the second month, ($r=0.0413$) in the third month, ($r=0.0497$) in the fourth month, by the fifth month, the correlation was high ($r=0.558$) and in the sixth month, the correlation ($r=0.471$) was again decreased.

DISCUSSION

Severe anemia is a major impediment to the rehabilitation of patients with End Stage Renal Disease. The major contributor to anemia is the deficiency of erythropoietin produced by the diseased kidneys [6].

Since the introduction of erythropoietin, many studies have confirmed the value of treating anemia in patients with kidney disease. Reduced dependence on transfusions has diminished transfusion-related complications, such as iron overload, blood borne infections, and the development of cytotoxic antibodies. The treatment of anemia in patients with End Stage Renal Disease has led to a reduction in left ventricular hypertrophy, an enhanced quality of life, a greater for work and exercise and enhanced immune function [7].

Because of the cost and complexity of its treatment, very few patients are able to obtain adequate treatment, and chronic renal failures places a very heavy financial burden on the Government and society. At this period of time, when the prevention of chronic renal failure (CRF) is becoming an important for planning the care of patients afflicted by it [2].

It is hoped that surveys such as Pre Dialysis Anemia Survey Management (PRESAM) and Early Renal Insufficiency Referral Survey (ERIPS) will draw attention to the risks of late treatment of anemia and help to improve anemia management during the initial stage of chronic kidney disease [8].

In our study many patients have extremely advanced renal insufficiency at referral. Nearly 89% had a Hb value $<10\text{g/dL}$ at the time of

referral. From this it reveals that many patients are late referrals for an adequate treatment of anemia.

Our study results showed that the iron parameters initial average ($\pm\text{SD}$) serum ferritin of $168.25\text{ ng/mL} \pm 124.81$ with transferrin saturation of $17.15\% \pm 4.40$. These parameters improved ferritin of $212.96\text{ ng/mL} \pm 102.27$ and transferrin saturation $21.67\% \pm 3.56$ at sixth month after intravenous iron supplementation. Out of 55 patients, 75% of patients achieved adequate iron stores, the DOQI recommended target with serum ferritin of greater than or equal to 100 ng/mL and transferrin saturation of greater than or equal to 20%. Out of 55 patients, 7% showed a ferritin less than 100 ng/mL , indicating absolute iron deficiency and remaining 18% showed functional iron deficiency in sixth month. This results can be compared and correlated with the results of other studies [9].

Our study report showed that for maintaining the Hb greater than or equal to 10g/dL , the average monthly cost of erythropoietin was high during the first month and decreased gradually after reaching the Hb greater than 10g/dL . These results confirmed that erythropoietin therapy have pharmacoeconomic beneficial effects. A the study conducted by Takeshi Kimura et.al., revealed that pharmacist's activities had not only therapeutic but also pharmacoeconomically beneficial [10].

The target Hb of 11 to 12 g/dL was reached by 84.6% of patients. The difference between the baseline and treatment Hb was statistically significant ($p < 0.01$). Our study results reveal that the difference between the baseline and 6 month Hb, serum ferritin, and transferrin saturation were statistically significant (i.e., calculated 't' value is greater than table value of 2.326). So our study confirms that there is difference between baseline and 6 months after therapy is statistically significant ($p < 0.01$). This result showed similarity with the other studies [9].

While comparing the correlation between erythropoietin dose and Hb concentration, our results showed a statistically significant, but weak correlation. These results are supported by a study conducted by Christopher Burton et.al.

Anemia management is recognized as an extremely important factor in improving the outcomes of hemodialysis patients. Because anemia management is largely a medication related activity, pharmacists are in a position to make

valuable contributions to this aspect of patient care. Pharmacists may be able to optimize drug utilization and manage drug costs for hemodialysis facilities. The use of effective anemia management protocols can help hemodialysis facilities improve patient outcomes, lower erythropoietin doses, and promote the use of iron supplementation. Pharmacist can contribute to a multidisciplinary team approach to the management of anemia in this vulnerable population by monitoring Hb status, transferrin saturation levels, and serum ferritin concentrations and managing erythropoietin dose and iron administration [11].

CONCLUSION

We can conclude that the increase in Hb value dependent on erythropoietin dose, higher the dose, higher the Hb value after 6 months of treatment. Thus erythropoietin is shown to be effective in treating anemia in patients with Chronic Renal Failure, but it is associated with higher costs of therapy.

Iron supplementation is required to avoid functional or absolute iron deficiency in anemic patients undergoing hemodialysis and our results concluded that iron sucrose is safe and effective

when given for the treatment of iron deficiency or for maintenance of iron stores.

The Pharmacist has a unique opportunity to assist in ensuring optimal management of anemia in the hospitalized population as well. By being aware of the signs and symptoms of anemia, the pharmacist can identify the patients at risk and advise them on proper medical care. Pharmacists should be involved in the appropriate initiation, titration and discontinuation of erythropoietin agents to ensure that economic and clinical outcomes are maximized. A Pharmacist can ensure appropriate use of iron replacement to optimize erythropoietic therapy and prevent or treat iron deficiency through monitoring serum ferritin, transferrin saturation and Hb values. The Pharmacist is the ideal profession to counsel patients regarding treatment and potential adverse effects and to address patients questions and concerns. Pharmacists should be the primary members of health care teams developing anemia management guidelines for their institutions. Follow-up on adherence to guidelines can be accomplished by a pharmacist can participate in formulary decisions and balance economic and outcomes data to optimize patient care.

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