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Comparing the effectiveness of Ferric Pyrophosphate and Ferrous Bis-glycinate in non-dialysis chronic kidney disease patients

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ABSTRACT

Introduction: Iron deficiency anaemia is common and consequential in nondialysis-dependent CKD (NDD-CKD), and are associated with higher risks of progressive loss of kidney function, cardiovascular events, and mortality. Aim: Comparing the effectiveness of Ferric pyrophosphate and Ferrous bis-glycinate in non-dialysis chronic kidney disease patientsandto observe the side effect profile of both the drugs. Methodology: A prospective study was conducted in the outpatient Dept. of Nephrology at Govt. Medical College, Kannur. The patients were grouped into two cohorts. Those patients prescribed with Ferric pyrophosphate (Ferisome) and Ferrous bis-glycinate (Bizfer XT) were included. Anemia profile Ferritin, % Transferrin saturation and serum creatinine were collected and documented and the patients were observed for adverse reactions during monthly outpatient visits. Result: A total of 67% patient completed the study . Both the drugs had shownclinical improvement in the anemia profile and haemoblobin level. By comparing, Ferrous bisglycinate shows better improvementthan Ferric pyrophosphate. ADRs were observed in patients on both the drugs. Conclusion:The study conclude that Ferrous bis-glycinate (Bizfer) is more effective than Ferric pyrophosphate (Ferisome) and is cost effective than latter.

INTRODUCTION

Chronic kidney failure is a syndrome characterized by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma eventually terminating in death when sufficient number have been damaged.(1) World Health Organization (WHO) defines Anaemia as a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet physiologic needs, which vary by age, sex, altitude, smoking, and pregnancy status.(2) Anemia is a common complication of chronic kidney disease and it is associated with increased cardiovascular morbidity and mortality and decreased quality of life.(3) The target Hb for maintenance in all CKD patients is 10-11.5 g/dL. Hb level of >11 g/dL should be aimed for all the CKD patients. (4)

According to the most recent definition in K/DOQI guidelines, anemia should be diagnosed at Hb concentration of 13.5 g/dL in adult male and 12 g/dL in adult female. (1) Frequency of testing for anemia: For CKD patients with anemia not being treated with an ESA, measure Hb concentration when clinically indicated: at least every 3 months in patients with CKD 35ND(5)

Anemia is twice as prevalent among patients with CKD compared with the general population (15.4% vs 7.6%), with the prevalence of anemia among patients with CKD rising from 8.4% in stage 1 to 53.4% in stage 5. Data from the KEEP study targeting a higher risk population, reports anemia to occur in 20% of the patient with stage 1 to 3 CKD , almost 65% of those with stage 4 CKD and in 75% of those with stage 5 CKD. A total of 22.8% of CKD patients with anemia reported being treated for anemia within 3 months14.6% of patients at CKD stages 12 and 26.4% of patients at stages 34.(6)

The progression of kidney damage is marked by the rise in two important chemical substances in the blood - creatinine and urea whose evaluation in serum helps to assess Glomerular Filtration Rate (GFR) followed by renal function. However, neither creatinine nor urea is directly toxic and they are only a measure of

kidney function.(7)

If treating anemia slows the progression of chronic kidney disease, the mechanism is still a matter of speculation. Some of the currently proposed mechanisms that the treatment may reduces oxidative stress, ameliorates the effects of hypoxia at the tubular level (thus protecting against nephron loss), lowers the accumulation of extracellular matrix, promotes angiogenesis, and prevents apoptosis.(8)

The objective of this study is to compare the effectiveness of Ferric pyrophosphate and Ferrous bis-glycinate in non-dialysis chronic kidney disease patients and to observe the side effect profile of Ferric pyrophosphate and Ferrous bis-glycinate.

METHODOLOGY

Theprospective study was conducted in the Outpatient Department of Nephrology at Govt. Medical College, Kannur, a tertiary care hospital of Kannur district from December 2018 to May 2019.The patients was selected based on the inclusion exclusion criteria. Inclusion: Patient above 18 years with estimated GFR < 60ml/mt based on EPI equation and who are willing to give the consent. Exclusion: Age< 18 years and CKD patients on dialysis.

The study contains three stages, with the first patient visit in December 2018 (baseline), second visit in February 2019 (3rd month) and last visit in May 2019 (6th months). Initially the patient demographic details like age, sex, weight and the drug prescribed were collected and the patients were grouped into two cohorts, those prescribed with Ferric pyrophosphate (Ferisome) and Ferrous bis-glycinate (Bizfer XT). Laboratory investigations including Hemoglobin (Hb), Anemia profile Ferritin, % Transferrin saturation and serum creatinine were done on patient visits and the datas were recorded. They were subjected to follow up with laboratory investigations at baseline, 3rd month and 6th month of the study. The changes from baseline hemoglobin, ferritin and % transferrin saturation level were the most common efficiency outcome measure. The patients were also observed for adverse reactions during these period on patient visit and through telephones. The collected datas were entered into a spread sheet format using microsoft Office Excel. Data processing tabulation of descriptive statistics, calculation and graphical representation were done using statistical software SPSS (Statistical Package for the Social Sciences).

RESULTS

During the study period, a total of 60 patients were enrolled; of these, 44 patients completed the study. In the study 24 (55%) were male and 20 (45%) were female. Among 44 patients, 26(59%) patients were prescribed with ferrous bis-glycinate (Bizfer) and 18(41%) were prescribed with ferric pyrophosphate (Ferisome). Haemoglobin, Ferritin, TSAT & Serum Creatinine,e GFR level were estimated in the study patients at baseline, 3rd and 6th month of the study.

The Haemoglobin level of the patient on ferrous bis-glycinate

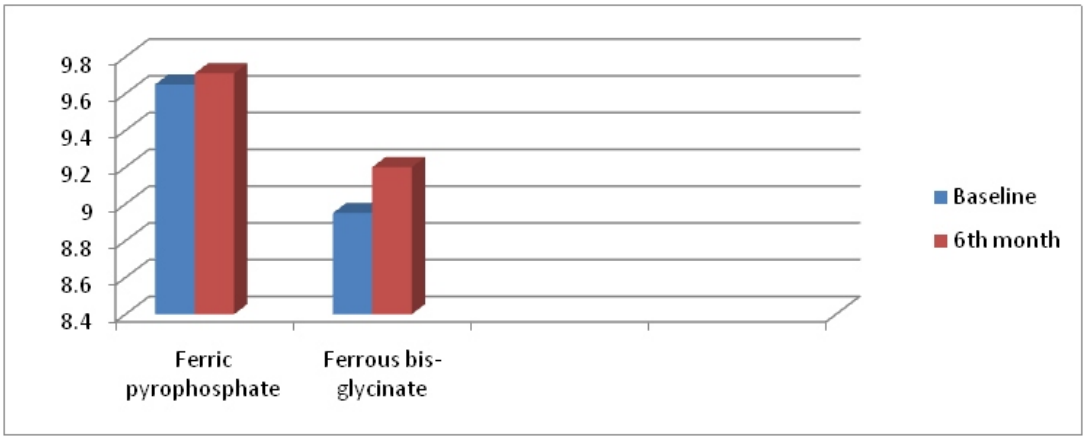

Fig. 1 : Mean haemoglobin level

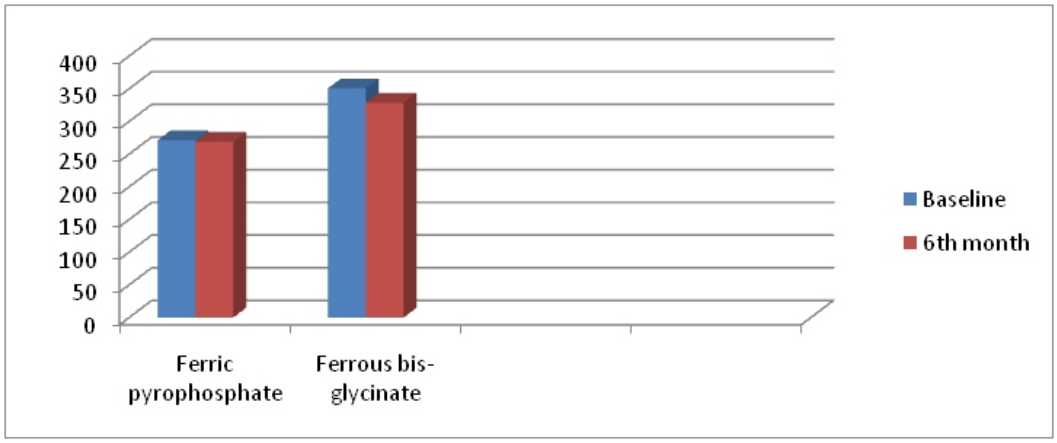

Fig. 2 : Mean ferritin level

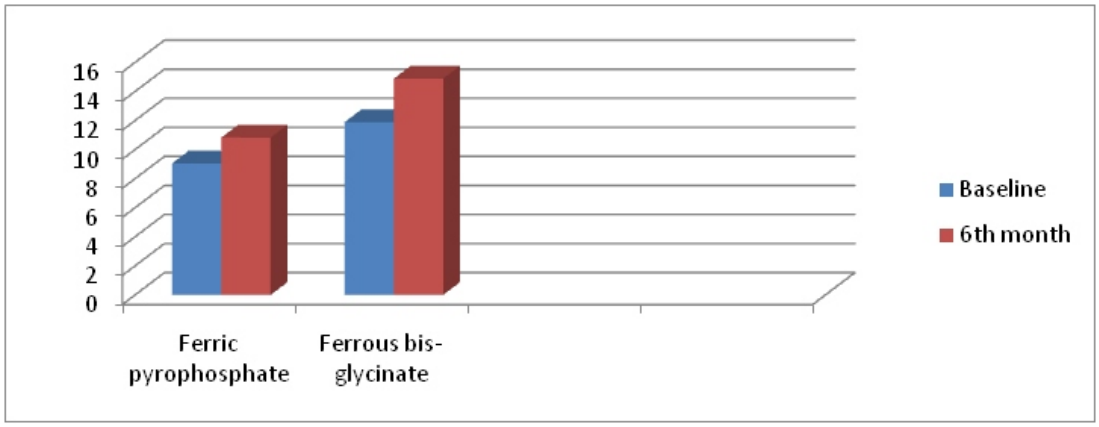

Fig. 3 : Mean TSAT level

shows 0.25 units improvement from baseline to 6th month and the patient on ferric pyrophosphate shows 0.06 units improvement from the baseline to 6th month. (Fig no:1)

The ferritin level of the patient on ferrous bis-glycinate shows 21.85 units decrease from baseline to 6th month and the patient on ferric pyrophosphate shows 2.38units decrease from the baseline to 6th month. (Fig no:2)

The TSAT level of the patient on ferrous bis-glycinate shows 3 units increase from baseline to 6th month and the patient on ferric pyrophosphate shows 1.78 increase from the baseline to 6th month. (Fig no:3)

Serum creatinine, the most frequently measured biomarker of GFR is found to be stable or slight decrement during the study duration. The creatinine level of both the study patients shows improvement on follow up. The eGFR level also shows improvement on follow up.

OBSERVED ADVERSE DRUG REACTION

Safety monitoring of the study drugs was carried out with the help of recording adverse drug reaction in all the clinical visit. The ADR profile of patients received ferrous bis-glycinate and ferric pyrophosphate was represented graphically. (Fig no:4)

The observed ADRs of both the drugs were not seriously effecting the quality of life. From the collected data, ADR was shown to be more in patients on ferrous bis-glycinate than ferric pyrophosphate.

DISCUSSION

According to several studies of oral iron v/s intravenous iron therapy, intravenous iron was found to be more effective. Ferric pyrophosphate is as effective as intravenous iron in chronic kidney disease patients. Here we compared the efficacy of Ferric pyrophosphate with a new oral formulation Ferric bis-glycinate. So it is important to determine the best efficacious oral iron therapy in non-dialysis chronic kidney disease patients.

The cause of iron deficiency anemia in NDD-CKD is usually a combination of relative erythropoietin deficiency and iron deficiency. Whereas aneamic patients receiving dialysis usually require ESAs (and supplemental iron) due to the severity of

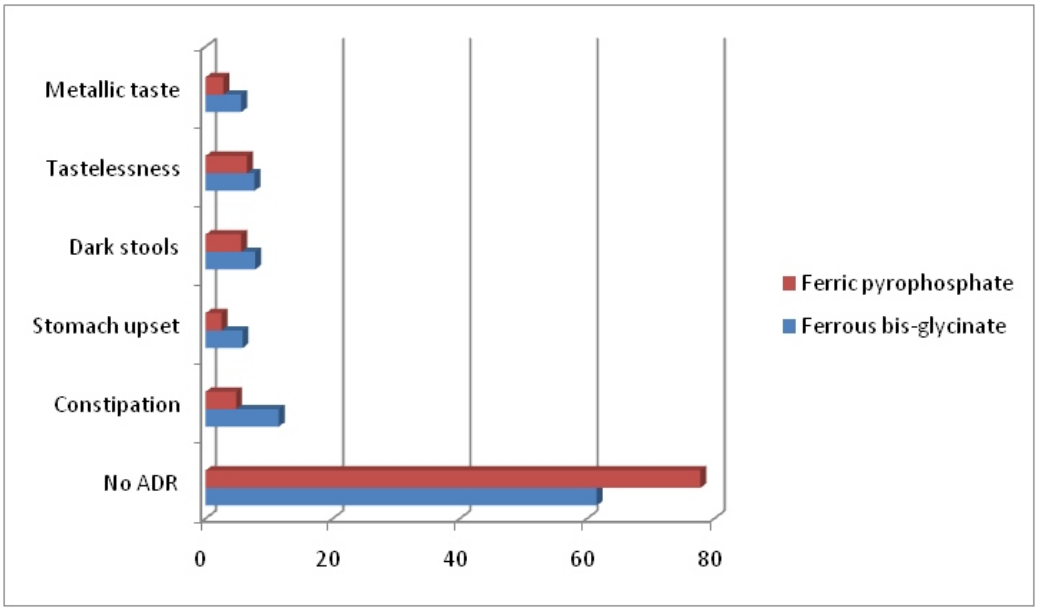

Fig. 4 : Observed ADR of both study drugs

erythropoietin deficiency, patients with NDD-CKD differ in that they have greater relative erythropoietin production. The relative preservation of erythropoietin production at earlier stages of CKD suggests that anemia may be treated in this population by effectively correcting iron deficiency as an initial step. Indeed, clinical practice guidelines suggest a trial of iron supplementation for adult patients with CKD (including ESRD) and anemia not on iron or ESA therapy.

The present study describes the outcomes of patients treated with ferrous bis-glycinate and ferric pyrophosphate for 6 months in a tertiary care hospital setting. At the end of 6 months of follow up, all patients showed a significant improvement in hematological parameters, showing the efficacy of both the drugs. The high patient compliance to this new oral iron therapy seems to be a key factor in the treatment success. A treatment effect was seen as early as 1month after start of treatment. The response was durable and achieved without the use of ESAs.

In this study, both the drugs were seem to be well tolerated and no serious adverse reactions were reported. Adverse effects were generally modest. Gastrointestinal effects were most common, as expected, with nominally higher rates of stomach upset and constipation in both the study group. Dark stools and metallic taste were also observed in few patients.

The average cost incurred to the patient treated with ferric pyrophosphate was highest compared to ferrous bis-glycinate. The cost of therapy per patient for 1 month with ferric pyrophosphate was Rs.492 and ferrous bis-glycinate was Rs.330. Ferrous bi-glycinate was best cost effective drug when compared to ferric pyrophosphate.

CONCLUSION

In conclusion it was observed that, Ferrous bis-glycinate (Bizfer) was more effective than Ferric pyrophosphate (Ferisome). The ADRs observed with both the drugs were not seriously effecting the quality of life of the patient. Ferrous bis-glycinate is cost effective than the latter. Beneficial effects on the treatment of iron deficiency anemia in non-dialysis Chronic kidney disease patients were observed. Anemia profile and haemoglobin shows clinical improvement in patients on both the study drugs.

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