



ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating 2017: 5.03
TPI 2017; 6(8): 325-327
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www.thepharmajournal.com
Received: 18-06-2017
Accepted: 20-07-2017

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A comparative study on the effectiveness of ferric citrate versus sevelamer plus iron supplement in patients with chronic kidney disease

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Abstract

Chronic Kidney Disease (CKD) includes the continuum of kidney dysfunction from mild kidney damage to kidney failure. Ferric citrate is an iron-containing phosphate binder which decreases serum phosphate, increases haemoglobin and replete iron stores in patients with CKD. Sevelamer is a phosphate binding drug used to treat hyperphosphatemia in patients with CKD.

Aim: To compare the effectiveness of ferric citrate versus sevelamer plus iron supplement in controlling hyperphosphatemia and iron deficiency anaemia in patients with chronic kidney disease.

Materials and Method: A prospective study was conducted in Department of Nephrology at Pushpagiri Medical College Hospital. About 50 patients was recruited according to the inclusion and exclusion criteria, where 25 receiving ferric citrate (210mg ferric iron equivalent to 1g ferric citrate, twice daily) and 25 receiving sevelamer (400mg, thrice daily) plus iron supplement in stage 5 CKD patients on dialysis. Informed consent of the patients was taken by explaining the whole procedure. Serum phosphorus and TIBC was in consideration. The residual blood sample was collected from the biochemistry lab and the parameters were measured using semi auto analyzer. Then the effectiveness of the two drugs in controlling hyperphosphatemia and iron deficiency were studied.

Result: Among the two drugs, ferric citrate had shown significant effect in reducing elevated phosphorus and TIBC level rather than sevelamer plus iron supplement.

Keywords: CKD, Hyperphosphatemia, Iron deficiency anemia, Ferric citrate, Sevelamer.

1. Introduction

Chronic kidney disease (CKD), also called chronic kidney failure. This term includes the continuum of kidney dysfunction from mild kidney damage to kidney failure, and it also includes the term, End-Stage Renal Disease (ESRD)^[1]. The symptoms of worsening kidney function are not specific, and might include feeling generally unwell and experiencing a reduced appetite. Some of the common complications of CKD include anaemia, heart disease, high potassium, bone disease and high phosphorus^[2]. Hyperphosphatemia in CKD patients is a potentially life altering condition that can lead to cardiovascular calcification, metabolic bone disease (renal osteodystrophy) and the development of secondary hyperparathyroidism (SHPT). It is also associated with increased prevalence of cardiovascular disease and mortality rates. There are three main strategies for correcting hyperphosphatemia are diet (restricting dietary phosphate intake), enhancing elimination (removing phosphate with adequate dialysis), minimizing phosphate absorption (reducing intestinal absorption using phosphate binders)^[3]. Iron deficiency anaemia develops when body stores of iron drop too low to support normal red blood cell (RBC) production. Anaemia tends to worsen as CKD progresses. Most people, who have total loss of kidney function, or kidney failure, have anaemia. A person has kidney failure that needs a kidney transplant or dialysis in order to live. Two forms of dialysis include hemodialysis and peritoneal dialysis. Hemodialysis uses a machine to circulate a person's blood through a filter outside the body. Peritoneal dialysis uses the lining of abdomen to filter blood inside the body^[4]. Ferric citrate is an iron-containing phosphate binder that has been shown to effectively decrease serum phosphate, increase hemoglobin and replete iron stores in patients with chronic kidney disease. Ferric citrate binds dietary phosphate in the gastrointestinal tract, thereby decreasing absorption and lowering concentration of serum phosphorus^[5]. Sevelamer is an orally administered non-absorbed phosphate-binding anion exchange resin used in the treatment of hyperphosphatemia in chronic kidney disease (CKD).

When taken with meals, sevelamer binds to dietary phosphate and prevents its absorption [6]. Serum phosphorus is the amount of reabsorbed phosphorus is the main regulator of the serum phosphorus level in subjects with normal renal function, or moderately reduced glomerular filtration rate. In CKD the kidney fails to excrete the phosphorus and the result is a positive phosphorus balance [6]. Total iron binding capacity (TIBC) is a blood test that shows if there is too much or too little iron in the blood. Iron is carried in the blood attached to the protein transferrin. This test helps measure the ability of a protein called transferrin to carry iron in the blood. In iron deficiency anemia TIBC is increased [8].

2. Materials and Method

A prospective study was conducted in Department of Nephrology at Pushpagiri Medical College Hospital after getting approval from Institutional Ethics Committee. All patients were given a brief introduction regarding the study and confidentiality of data. A written consent form was obtained from the patient or care giver. Patients diagnosed with stage 5 CKD identified and their hospital record in the department was studied. After obtaining their hospital number, name and other demographic details, from the Biochemistry lab residual blood was obtained. Residual blood was the blood remaining after the blood routine analysis in the lab. Blood was not withdrawn directly from the patient and any financial burden was not imposed on the patient. The collected residual blood from the lab was analyzed for serum phosphorus and Total Iron Binding Capacity (TIBC) using semi auto analyzer in the Pushpagiri College of Pharmacy.

2.1 Measurement of serum phosphorus.

Standard: 20 µL standard solution and 1000 µL reagent were pipetted out into a micropipette.

Mixed well and incubated at 37°C for 5 minute. Then absorbance was measured at 340 nm and corresponding concentration was read.

Test: 20 µL of sample solution and 1000 µL were pipetted out into a micropipette. Mixed well and incubated at 37 °C for 5 minute. Then absorbance was measured at 340 nm and

corresponding concentration were read.

Reference range: 2.5 – 4.5 mg/dL

2.2 Measurement of TIBC

Procedure for determination of iron: 200 µL patient’s sample, 1000 µL of reagent 1 and 1 tsp reagent 2 was pipetted out and mixed well and kept for 30 minutes then centrifuged the same at 4000 rpm for 10 minute. [Reagent1: Iron Buffer reagent, Reagent2: ascorbic acid]

Procedure for determination of TIBC: 200 µL of the above supernatant solution was pipetted out then added 1000 µL of reagent 1 and kept it for 5 minute. Then added reagent 2 and again wait for 5 minute. The corresponding concentration was read. [Reagent 1:FeCl₃, Reagent 2: colouring agent]

Reference range: 54-73µmol/L in men, 45-63µmol/L in women.

3. Results and discussion

Patients receiving ferric citrate: Serum phosphorus of the 100% patients was initially above the normal range. After one month 32% of the patients had the normal range of serum phosphorus. The normal TIBC value was initially 6.0% and after one month the percentage become 37.0% in male patients. The normal TIBC value was initially 0% and after one month the percentage become 44% in female responders.

Patients receiving sevelamer plus iron supplement: Serum phosphorus of the 4% patients was initially above the normal range. After one month 16.0% of the patients had the normal range of serum phosphorus. The normal TIBC value was initially 6% and after one month the percentage become 22% in male patients. The normal TIBC value was initially 24% and after one month there is no relevant variation in female patients.

Ferric citrate was 16% more effective in controlling hyperphosphatemia than sevelamer plus iron supplement. Ferric citrate was 15% more effective in improving iron levels than sevelamer plus iron supplement in male respondents. Ferric citrate was 20% more effective in improving iron levels than sevelamer plus iron supplement in female respondents.

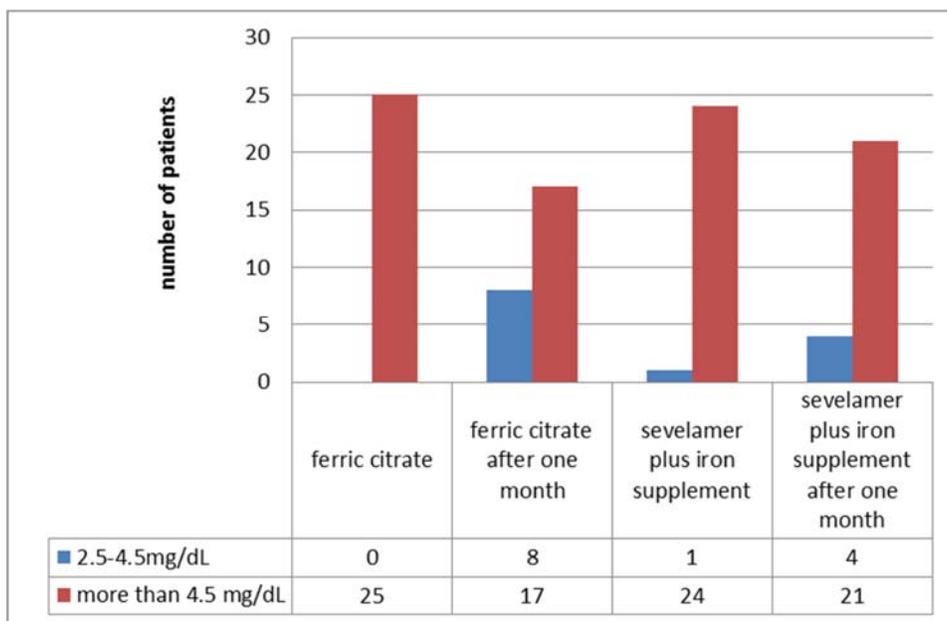


Fig 1: Comparison of serum phosphorus (ferric citrate versus sevelamer plus iron supplement)

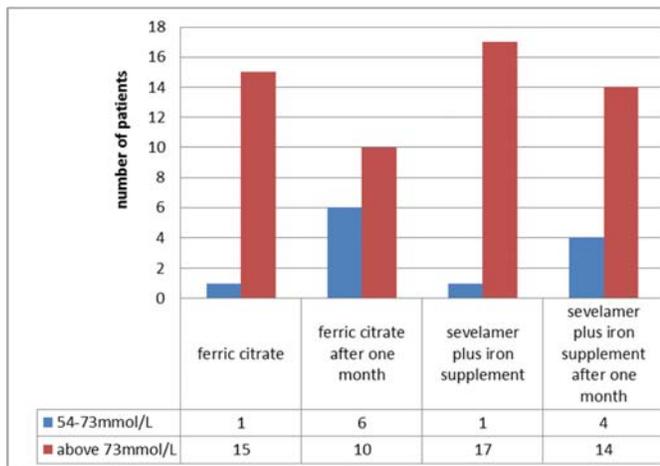


Fig 2: Comparison of TIBC value in men (ferric citrate versus sevelamer plus iron supplement)

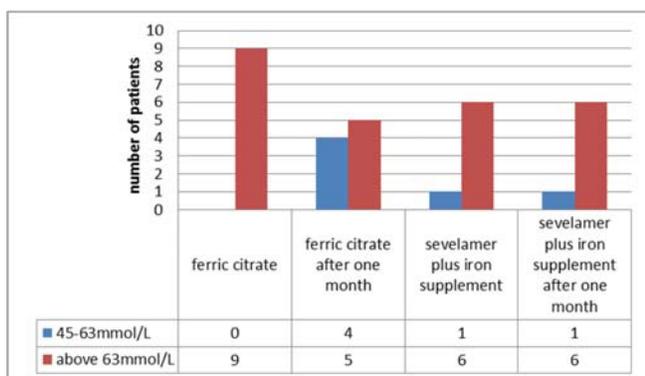


Fig 3: Comparison of TIBC value in female (ferric citrate versus sevelamer plus iron supplement)

4. Conclusion

A prospective study was conducted to compare the effectiveness of ferric citrate versus sevelamer plus iron supplement in controlling hyperphosphatemia and iron deficiency anaemia in patients with chronic kidney disease. The total sample size was 50 patients 25 receiving ferric citrate (210 mg ferric iron equivalent to 1 gram ferric citrate, twice daily) and 25 receiving sevelamer (400 mg, thrice daily) plus iron supplement. Patient’s demographic details were collected, residual blood sample were analysed for finding serum phosphorus and TIBC to compare the effectiveness of ferric citrate versus sevelamer plus iron supplement in controlling hyperphosphatemia and iron deficiency anemia. Patient counselling was provided to the patients and no adverse reactions were found associated with the use of ferric citrate and sevelamer in the study population during the study period.

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