Use of Cosmofer in Routine Practice in the Hemodialysis Department in Saint Anna Hospital Sofia and Behavior in Case of Adverse Medication Effects Manifestation

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Abstract: *Background*: CosmoFer® solution for injection contains stable aqueous solution of iron(III)-hydroxide dextran complex, which is equivalent to the physiological ferritin.

CosmoFer® has been used in the Hemodialysis Department/HDD/ at the Sofia St. Anna Hospital since June 2012.

Objective: Topresent the use of the medication in the routine practice in the Department.

Materials and Methods: The use of the medication in the routine practice for a period of 1 year and 4 months in 63 chroniodialysis patients was presented. Clinical cases with manifestations of adverse effects were reported.

Results and conclusions: CosmoFer® showed very good effects when used once or twice per month of renal anemia and chronic kidney disease (CKD) patients.

- The clinical cases presented are indicative of patients with severe clinical status and polymorbid patients.
- Comfort and safe administration are achieved in slow intravenous infusion of CosmoFer®

dissolved in 100ml physiological solution.

Keywords: Anemia, chronic kidney disease, chronic hemodialysis treatment, hemoglobin level, serum iron.

INTRODUCTION

Iron deficiency anemia is the leading cause of anemia, affecting approximately 1.6 billion people worldwide [1]. Studies have shown that oral iron supplementation in patients with chronic kidney disease /CKD/, especially those on hemodialysis, is inferior to intravenous iron administration [2,3]. Several reports have suggested an increased risk of ADEs associated with the use of higher molecular weight iron dextran preparations [4,5]. Recent studies announce for good safety profile in treatment ofchronic kidney disease / CKD/ patients with low-molecular iron dextran - CosmoFer® [6].

CosmoFer® solution for injection contains stable aqueous solution of iron (III)-hydroxide dextran complex, which is equivalent to the physiological ferritin.

- pH of the solution is fixed approximately to 5.2 – 6.5 by means of sodium base and hydrochloric acid.
- The solution contains a strong colloidal complex of an iron core enveloped by strongly bonded dextran chains.
- Free of added preservatives

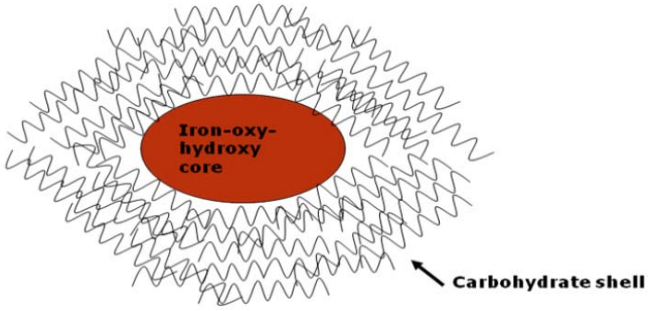

Figure 1: Schematic representation of the product built-up of an iron core and a carbohydrate shell of dextran chains.

OBJECTIVE

1. To follow up he Hemoglobin levels and serum iron levels in patients after 12 and 16 month treatment with CosmoFer®
2. To study the Advers Reaction incidenence and the tolerance of the patients to Cosmofer therapy.

CosmoFer® has been used in the Hemodialysis Department /HDD/ at the Sofia Saint Anna Hospital since June 2012. A so called test dose is used before the first administration, to exclude a patient's allergic reaction to the medication. 1 or 2 ampoules monthly

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were individually dosed depending on each patient's needs. The medication is administered through slow venous-drop infusion in 100 ml physiological solution.

The medication was given to 63 patients at an average age of 59.56 ± 1.9 years. The youngest patient (female patient) was 22, and the eldest patient (male patient) was 85. CosmoFer® was given to 24 female patients and 39 male patients in the Hemodialysis Department /HDD/.

RESULTS

The serum iron values (mmol/l) in patients in the beginning are presented on Diagram **1**.

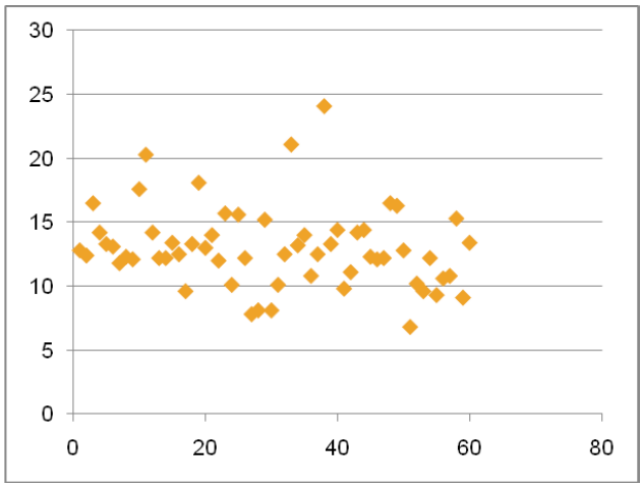

Diagram 1: Serum iron values (mmol/l) in patients in the beginning of the trial monitoring.

The serum iron values (mmol/l) in patients in following one-year-therapy with CosmoFer® are presented on Diagram **2**.

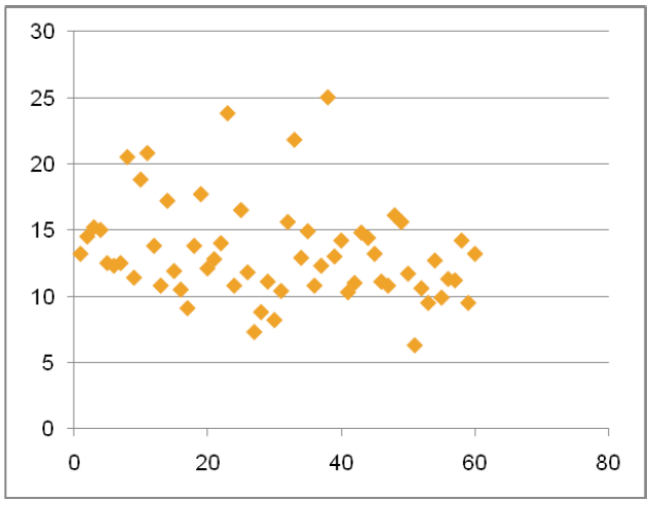

Diagram 2: Serum iron values (mmol/l) in patients following one-year-therapy with CosmoFer®.

The serum iron values (mmol/l) in patients in following sixteenth-month-therapy with CosmoFer®, i.e. in the end of the trial are presented on Diagram **3**.

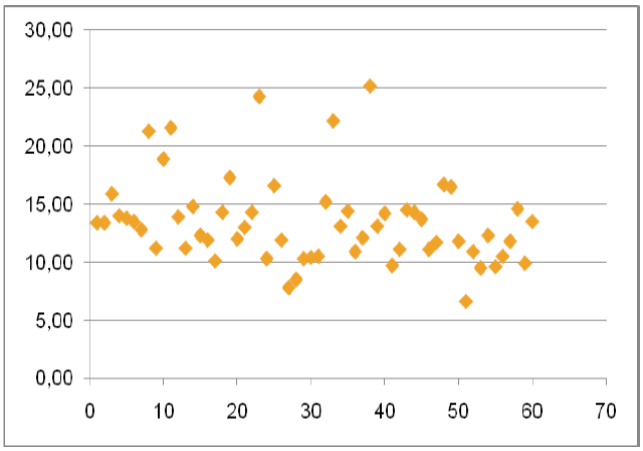

Diagram 3: Serum iron values (mmol/l) in patients following sixteenth-month-therapy with CosmoFer®, i.e.in the end of the trial.

The average level of the serum iron in patients in the beginning of the trial was 12.9 mmol/l ± 0.4. Minimum value 6.8 mmol/l, maximum value 24.1 mmol/l.

One year following CosmoFer® administration the average level of the serum iron was 13.28 mmol/l ± 0.48. Minimum value 6.3 mmol/l, maximum value 25 mmol/l.

In the end of the period the average level of the serum iron was 13.43 mmol/l ± 0.48. Minimum value 6.6 mmol/l, maximum value 25.2 mmol/l (Diagram **4**).

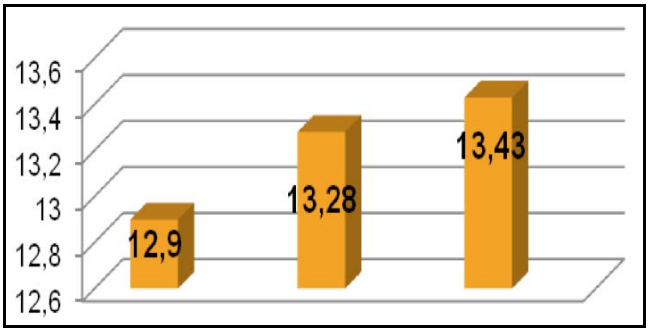

Diagram 4: Trial monitoring and comparison of the average values of the serum iron (mmol/l) in the beginning of the trial, one year later and in the end of the trial monitoring of the CosmoFer® therapy.

- 12.69% patients /8 patients out of 63/ in the end of the period were with serum iron values below the reference range /reference range 10 – 28 mmol/l/ only. This may be explained with the fact that by these dates part of the patients

experienced active infections and were on an antibiotic therapy. After completing the antibiotic course those patients were given iron intravenously. In the beginning of the period this percent amounted to 15.83 Diagram **5**.

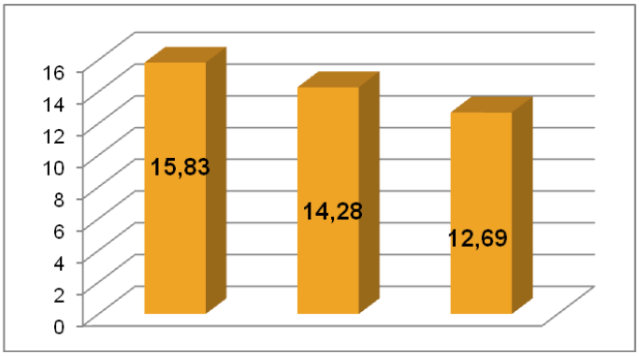

Diagram 5: Percentage of patients with serum iron values (mmol/l) below the reference ranges in the beginning, in the end of the trial, and one year following the CosmoFer® therapy.

The results of the hemoglobin level (g/l) in patients in the beginning of the trial are presented on Diagram **6**.

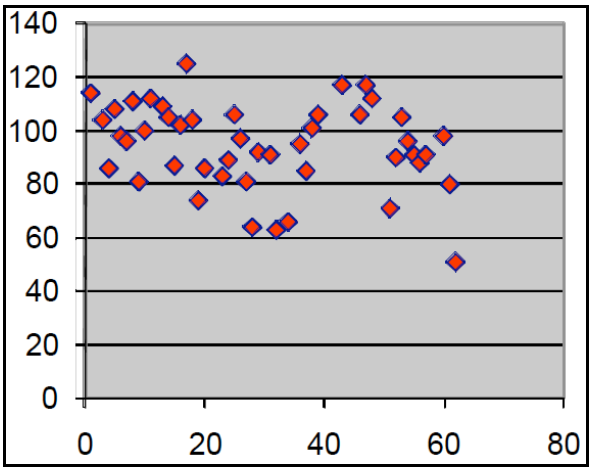

Diagram 6: Trial monitoring of the hemoglobin level (g/l) in patients in the beginning of the trial.

The results of the hemoglobin level (g/l) in patients 1 year following CosmoFer® administration are presented on Diagram **7**.

The results of the hemoglobin level (g/l) in patients in the end of the trial are presented on Diagram **8**.

The average hemoglobin level in patients in the beginning of the trial was 94.21 g/l.

One year following CosmoFer® administration the average hemoglobin level in patients was 98.65 g/l.

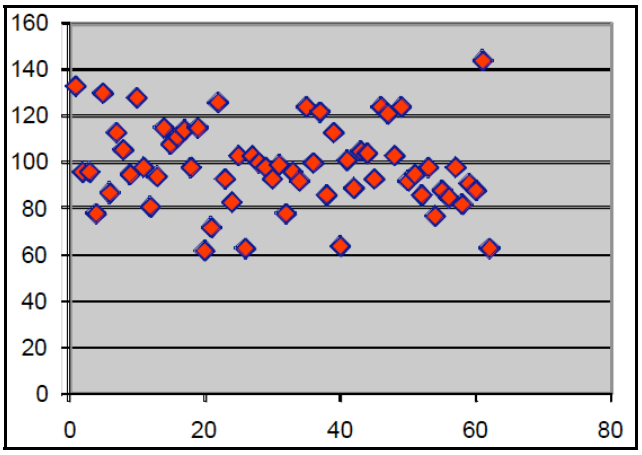

Diagram 7: Trial monitoring of the hemoglobin level (g/l) in patients 1 year following CosmoFer® administration.

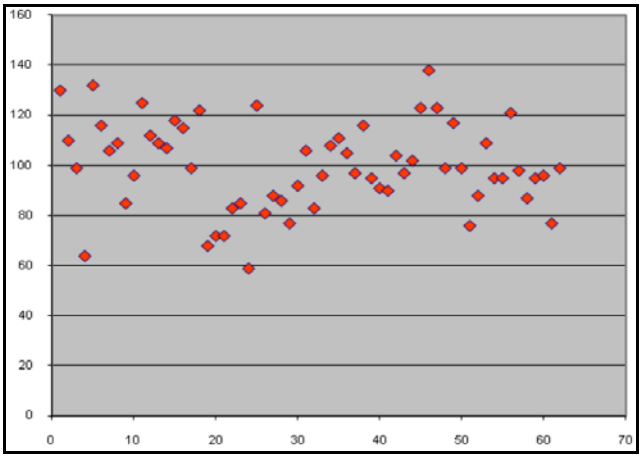

Diagram 8: Trial monitoring of the hemoglobin level (g/l) in patients in the end of the trial.

In the end of the period the average hemoglobin level in patients was 99.63 g/l (Diagram **9**).

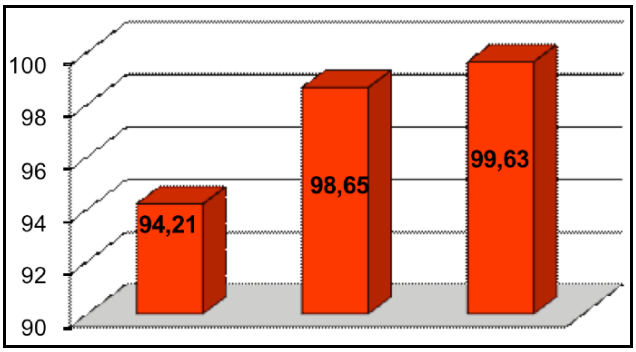

Diagram 9: Trial monitoring of the average hemoglobin level in patients in the beginning of the trial, in the end of the trial and one year following CosmoFer® administration.

CLINICAL CASE REVIEW

- Clinical case 1.A.D. aged 42
- Chronic calculous pyelonephritis since 1990.

- Chronic kidney disease */*CKD/ since 2003. Renal anemia.
- Hemodialysis therapy and arterial hypertension since January 2005.
- Poly allergy to medications, dust mites, household chemicals, and cosmetics.
- The first allergic reaction to medications was in 2008 and was to Ospexin– 2008, expressed in suffocation, face edema, skin rash.
- In 2010 manifestations of allergy to Heparin were reported (edemas on the extremities and the face - from then on low-molecular weight heparin – Clexane was given to the patient as an anticoagulant in hemodialysis. Before that she had experienced allergic reactions to various dialysis membranes. Since 2010 hemodialysis with polysulphonic membrane has been conducted.
- At that period, but in different months of 2010 the patient experienced allergy to Renagel and Mimpara – clinical manifestation consisting in suffocations, edemas, and skin rash. The clinical situation was controlled after the use of corticosteroids and anti-allergic agents, and such medications are no longer administered.
- The last allergic reaction to a medications was on October 1st, 2013, MIRCERA
- Many years ago tests and consultations with allergologists were carried out – proven allergy to dust mites, local anesthetics, cytoplast, cosmetics – shampoos, shower gels, sunscreen oils, hair colors, synthetic tissues.

Clinical case 2.T. A. aged 79

- Diabetes mellitus type 2. Psoriatic arthritis.
- Parkinson's disease – for 12 years
- Arterial hypertension for 30 years
- Chronic kidney disease */*CKD/ since 2006. Hemodialysis treatment since June 28th, 2012.
- Renal anemia.
- The patient is allergic to Venofer and Cosmofer – with the occurrence of suffocation, which faded away after the use of venous methylprednisolone. Currently the patient administers iron-containing medication per orally and during the last study her serum iron was reported to be 11.2 mmol/l.

Clinical case 3.S. M. Aged 41

- Interstitial nephritis since 1988
- Chronic kidney disease */*CKD/ since 2003.
- Hemodialysis treatment since October 16th, 2006. Renal osteodystrophy
- Arterial hypertension. Renal anemia
- Drug allergy to Eprex in 2004.
- No complaints were reported when a test dose of CosmoFer® was administered. There were no problems in the administration of the first dose. When the second ampoule /15 days later/ oppression in the chest, suffocation, and tachycardia were detected which faded away after the administration of venous methylprednisolone. Further, as home therapy, antihistamine agents were administered per orally.

Clinical case 4.I. P. aged 59

- Diabetes mellitus type 2.
- Arterial hypertension. Status post cerebral insult.
- Status post fracture of the right thigh joint.
- Hemodialysis therapy since November 17th, 2011. Renal anemia.
- No complaints were reported when a test dose of CosmoFer® was administered. When the dose was administered oppression in the chest and suffocation occurred which faded away after the administration of venous methylprednisolone.

Clinical case 5.I. K. aged 83.

- Status post rectum carcinoma surgery in 2009.
- Four-time implementation of TUR because of a urinary bladder tumor.
- Status post cerebral insult.

- Status post fracture of the right thigh – pertrochanteric fracture.
- Hemodialysis therapy since May 30th, 2013. Renal anemia.
- No complaints were reported when a test dose of CosmoFer® was administered. When the dose was administered oppression in the chest and suffocation occurred which faded away after the administration of venous methylprednisolone. Further, as home therapy, antihistamine agents were administered per orally.

Clinical case 6.G.D.T. aged 58

- Diabetes mellitus type 2.
- Arterial hypertension. Ischemic heart disease/ IHD/. Triple vessel disease. Status post stent placement.
- Chronic arterial insufficiency of the extremities, grade 4. Thrombosis of the right superficial femoral artery.
- Cirrhosis. Ascites.
- Ulcer of the duodenum. Erosive gastritis.
- Hemodialysis therapy since November 10th, 2011. Renal anemia.
- No complaints were reported when a test dose of CosmoFer® was administered. No complaints were reported when the dose was administered. Maculopapular itching rash occurred on the following day.

Clinical case 7.B. D. age 60

- Chronic pyelonephritis. Renal anemia.
- Lower paraplegia following fracture at C7 and Th12
- Hemodialysis therapy since July 8th, 2011.
- Tremor occurred four hours after the administration of the test dose and the first CosmoFer® dose. The tremor was regarded as an onset of an infection and an antibiotic therapy was started.

DISCUSSION SAFETY SUMMARY

- Total number of reactions 8 out of 63 observed patients:
- *8 Adverse effect – 12.7%* /in the first year of administration of a particular medication the number of the reported side effects is always higher/.
- Some of the patients /3 patients/ experienced psychological effect consisting in moderately manifested tachycardia and general weakness, which disappeared without any therapy when administration was suspended.
- Generally, the observed reactions were reported in patients predisposed to allergic reactions, who in most of the cases experience allergic responses to other medications as well.
- Another part of the patients experienced the Fishbane reaction: myalgia, pains behind the chest bone, which faded away spontaneously.
- Cosmofer increased the Hemoglobin and serum iron levels and reduced the anemia- related symptoms..
- The incidence of advers drug reactions is equal to that of other iron products[6].

CONCLUSIONS

- The CosmoFer® showed very good effects when used once or twice per month on renal anemia and chronic kidney disease (CKD) patients. The clinical cases presented are indicative of patients with severe clinical status and polymorbid patients
- Comfort and safe administration are achieved in slow intravenous infusion of CosmoFer® dissolved in 100ml physiological solution.

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