ACUTE EFFECT OF FERRIC CARBOXYMALTOSE ON OXIDATIVE STRESS IN NON-DIALYSIS CKD PATIENTS

AM Mehedinti[1,2], I Andreiana[1,2], G Mircescu[1,2], C Capusa[1,2]

[1] " Carol Davila " University of Medicine and Pharmacy, Bucharest, Romania

[2] "Dr. Carol Davila" Teaching Hospital of Nephrology, Bucharest, Romania

Background and aim

Ferric carboxymaltose (FCM), a nanomedicine with similar structure to serum ferritin, provides controlled delivery of iron into the reticuloendothelial system and, subsequently, onto the transport or deposit proteins. Therefore, its potential pro-oxidative effect by releasing "free" iron seems small, but has been incomplete investigated. The impact of FCM on oxidative stress is even less studied in patients with chronic kidney disease (CKD)[1]. Therefore, we assessed the effect of a single dose of 1000mg FCM on oxidative stress in non-dialysis CKD subjects with iron deficiency and anemia.

Subjects and Methods

Study design: unicenter, prospective, crossover.

Subjects: Forty-one stage G3-G5 non-dialysis CKD subjects [estimated GFR 24 (16-34) mL/min], median age 68 (58-70) years, 61% women, 90% with arterial hypertension and 41% diabetes mellitus. Anemia was only mild: hemoglobin (Hb) 10.6 (10-11) g/dL.

Inclusion criteria: age >18 years, eGFR <60mL/min, anemia (Hb <12g/dL in women and <13g/dL in men) and iron deficiency (serum ferritin <100ng/mL and/or transferrin saturation <20%) .

Exclusion criteria: iron or erythropoiesis-stimulating agents therapy in the last 6 months, Hb <7g/dL, other known causes of anemia, active liver disease, infectious and autoimmune diseases, neoplasia, inflammation (C-reactive protein >5mg/L), brachial flow-mediated dilatiation <7%, pregnancy.

Main studied parameters:

- **Total antioxidant capacity of serum (TACS)**
- **Advanced oxidation protein producs (AOPP).**

Intervention: control-infusion (250ml 0.9% NaCl) and studied-infusion (1000mg FCM in 250ml 0.9% NaCl), were administrated at 24 hours interval, in this order, intravenously, during 30 minutes.

Blood samples were collected before (0 minutes) and after each infusion (at 30 minutes, 6 hours and 24 hours, respectively) (*Fig. 1*):

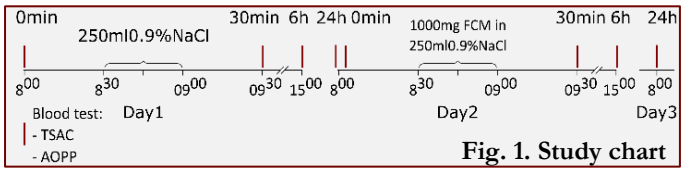

Fig. 1. Study chart

Statistical analysis: Kruskal-Wallis and Wilcoxon signed rank sum tests were used for the analysis.

Results

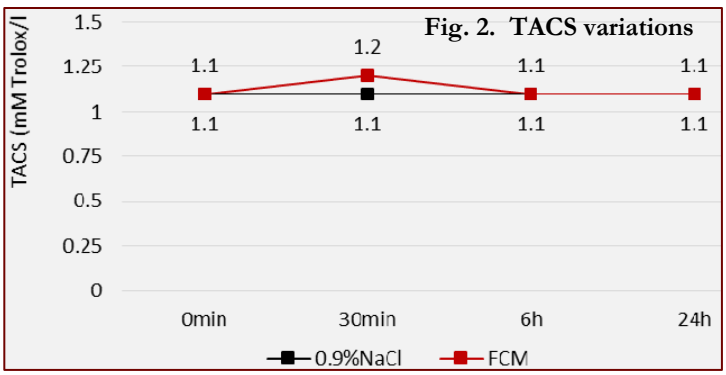

Fig. 2. TACS variations

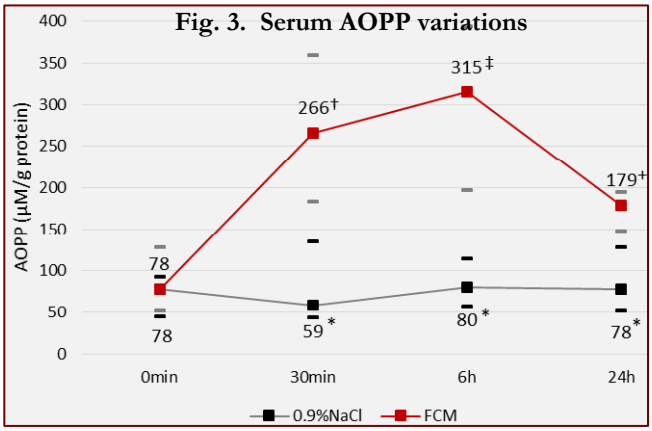

Fig. 3. Serum AOPP variations

FCM did not influence the total antioxidant capacity of serum at any study moment when compared with control-infusion (*Fig. 2*). Contrariwise, advanced oxidation protein products level increased only after FCM during the first 6 hours, with a decrease after 24 hours, but without returning to the baseline level (*Fig. 3*).

Conclusions

In non-dialysis CKD patients with mild anemia and iron deficiency, a single usual dose (1000mg) of ferric carboxymaltose seems to induce oxidative stress as suggested by the increase of protein oxidation biomarker, but does not influence the serum total antioxidant capacity.

References

1. Tovbin D, Mazor D, Vorobiov M, Chaimovitz C, Meyerstein N. Induction of protein oxidation by intravenous iron in hemodialysis patients: Role of inflammation. *AJKD* 40(5):1005-1012, 2002.

Further information
Cristina Capusa: ccalexandr@yahoo.com