DIFFERENT TOXICITY ON RENAL TISSUE BETWEEN NEW AND OLD ORIGINAL INTRAVENOUS IRON PREPARATIONS IN NORMAL RATS.

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At present, different IV iron compounds are commonly used in patients with CKD. Though useful, IV iron may cause a different degree of oxidative stress and tissue inflammation depending on the nature of each iron complex. In this study, we evaluated possible differences on hemodynamic, oxidative stress and inflammatory response between classic and new currently available original IV iron compounds in normal rats. Six groups of Sprague Dawley rats: G1 (Ferric Carboxymaltose); G2 (HMW Iron-Dextran); G3 (LMW Iron-Dextran); G4 (Ferric-Gluconate); G5 (Iron Sucrose Complex); G6 (Control). G1,G2,G3,G4 and G5 with a single equivalent IV dose of the corresponding iron compound, and G6 normal saline solution at 1,7,14, 21 and 28 days. Animals were killed 24hr after the last IV dose (day 29). In kidneys, TBARS, GSH/GSSH, CuZnSOD, Catalase and GPx were evaluated. LM and Immunohistochemistry (IHC) techniques using antibodies against Ferritin, IL6 and TNF-alpha, were also performed. At 4weeks: 1)SBP(mmHg) G1 123±2.4, G2 117±3, G3 114±2.5*, G4 118±2.6; G5 122.2±2.6, G6 124±2.4; 2)Proteinuria (mg/day) G1 5.1±2.6, G2 7.9±3.9, G3 6.9±4, G4 22.3±5*; G5 4.7±3, G6 2.1±3; 3)Cr.Clearance (ml/min) G1 2.8±0.1, G 2.9± 0.2, G3 2.6±0.1, G4 2.4±0.1*; G5 2.8±0.2, G6 2.9±0.1; Serum Iron (μg/dl) G1 409±17, G2 415±19, G3 423±23, G4 540±19*; G5 396±27, G6 299±15*; TSAT(%) G1 75±6, G2 72±6, G3 75.5±5.5, G4 83.2±6*; G5 73±4, G6 44±3*. Oxidative stress in kidney homogenates: TBARS (nmol MDA/mg prot) G1 67.9±8.9, G2 64,9±10, G3 70±10, G4 87.5±7*; G5 72±10, G6 68±8; GSH/GSSG ratio G1 7.2±0.7, G2 4.9±0.7**, G3 5.1±0.8**, G4 4.1±0.6*; G5 7.1±0.4, G6 7.8±0.5; CuZn SOD (U/mg prot) G1 6.4±1, G2 7.2±1.2**, G3 7.8±1.4**, G4 9.3±1.7*; G5 6.7±1.3, G6 6.1±1.2; Catalase (U/mg prot) G1 156±12, G2 158±10, G3 166±7, G4 200±21*, G5 167±15, G6 160±21; GPx (U/mg prot) G1 118±16, G2 198±22**, G3 208±18**, G4 295±34*; G5 121±12, G6 103±15. IHC at day 29: 1-Ferritin (%/area): G1 8.8±0.7, G2 6.1±0.6**, G3 5.9±0.7**, G4 4.1±0.6*; G5 7.9±0.5, G6 0.3±0.2*; 2-IL6 (%/area): G1 1.1±0.3, G2 2.6±0.6**, G3 2.9±0.5**, G4 6.1±0.5*; G5 1.2±0.4, G6 0.1±0.3*; 3-TNFalpha (%/area): G1 1.4±0.3, G2 3.6±0.4**, G3 3.9±0.3**, G4 4.8±0.6*; G5 1.5±0.2, G6 0.3±0.3*. *p<0.01 versus all groups **p<0.01 versus G1, G5 and G6. These findings suggest that after a four-week therapy, Both Ferric Carboxymaltose and Iron Sucrose Complex present a more favorable safety profile concerning hemodynamic and inflammatory tissue response compared with the other IV iron compounds in normal rats.