EFFECT OF SUCROFERRIC OXYHYDROXIDE (PA21) ON
RENAL FUNCTION, MINERAL HOMEOSTASIS AND VASCULAR
CALCIFICATION IN A RAT MODEL WITH CHRONIC KIDNEY
DISEASE (CKD)

INTRODUCTION AND AIMS: PA21 (or sucroferric oxyhydroxide) is an iron-based phosphate binding agent and a promising alternative to existing compounds. Clinical trials have shown that PA21 is an efficacious and well-tolerated phosphate binder. We aimed to evaluate the effect of this iron-based phosphate binding agent on renal function, mineral homeostasis and vascular calcification in a rat model with adenine-induced CKD and vascular calcifications.

METHODS: To induce stable CKD, 64 male Wistar rats were administered a 0.25% adenine enriched diet with a low vitamin K content (0.25% adenine, 0.2 mg/kg Vitamin K, 1% Ca, 1% P, 1 IU/g vitamin D and 6% protein) during the entire study period of 8 weeks. CKD rats were randomly assigned to 4 treatment groups: (i) vehicle (n = 16), (ii) 2.5 g/kg/day PA21 (n = 16), (iii) 5.0 g/kg/day PA21 (n = 16) and (iv) 3.0 g/kg/day CaCO3 (n = 16). Evolution in renal function and mineral metabolism was followed at regular time points by measurement of serum creatinine, phosphorus and calcium. Ionized calcium, hematocrit, hemoglobin, pH and bicarbonate, were measured using an i-STAT 1 Point-of-Care analyzer immediately at the time of blood sampling. Calcification in the aorta, femoral and carotid artery was assessed by determining the calcium content via flame atomic absorption spectrometry.

RESULTS: Vehicle treated CKD rats developed severe renal impairment, with creatinine values around 3.5-4 mg/dL, and anemia as indicated by decreased serum hematocrit and hemoglobin levels. CKD went along with development of hyperphosphatemia and hypocalcemia. CKD rats treated with 2.5 or 5 g/kg PA21 resulted in significant lower serum creatinine and phosphorus levels and higher ionized calcium levels after 8 weeks of daily treatment as compared to vehicle treated CKD rats. The better preserved renal function with PA21 treatment was also reflected in parameters of anemia which showed significantly higher serum hematocrit and hemoglobin levels in CKD rats treated with this iron-based phosphate binder. In contrast, daily treatment of CKD rats with 3.0 g/kg CaCO3 did not modulate the development towards severe chronic kidney disease and concomitant anemia. PA21 treatment significantly reduced the calcium content in the aorta as well as the carotid and femoral arteries, whereas CaCO3 did not affect calcification in the arteries.

CONCLUSIONS: Treatment with the iron-based phosphate binder PA21 had, aside from its phosphate lowering capacity, a beneficial impact on the development towards severe CKD and anemia. Calcification in the aorta and peripheral arteries was significantly reduced by PA21 treatment.