Effect of Sucroferric Oxyhydroxide (PA21) on renal function, mineral homeostasis and vascular calcification in a rat model with chronic kidney disease

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Background and Aim

Both in vivo and in vitro studies indicate that elevated phosphate levels contribute to the development of vascular calcifications which is recognized as an important risk factor for cardiovascular mortality in patients with chronic kidney disease (CKD).

PA21 (or sucroferric oxyhydroxide) is a novel iron-based phosphate binding agent and a promising alternative to existing compounds. Clinical trials have shown that PA21 is a well-tolerated phosphate binder and effective in lowering serum phosphorus in dialysis patients.

We aimed to compare the effect of this iron-based phosphate binding agent with a conventional calcium containing phosphate binding agent on renal function, mineral homeostasis and vascular calcification in a rat model with adenine-induced CKD and vascular calcifications.

Study design

- Male Wistar rats.
- Induction of CKD by administration of a 0.25% adenine enriched diet.
- Daily treatment with vehicle (1% carboxymethylcellulose), 2.5 or 5 g/kg PA21 or 3 g/kg CaCO3 from the start of CKD induction onward until the end of the study at week 8 by oral gavage.

Conclusions

- Both PA21 and CaCO3 treatment showed efficient phosphate binding capacity and prevented the pronounced increase in serum PTH.
- PA21 treatment partially protected renal function decline along with less severe anemia.
- Both PA21 doses prevented the dramatic increase in FGF-23, whereas CaCO3 did not affect the levels of this phosphaturic hormone.
- Daily treatment with PA21 did not increase circulating iron levels.
- The liver iron content was significantly increased in both PA21 treatment groups.
- In contrast to CaCO3, PA21 is able to significantly reduce CKD-related vascular calcification.

Results

1. Effect of PA21 on renal function and calcium/phosphorus metabolism

2. Effect of PA21 on hormones regulating mineral and bone metabolism

3. Effect of PA21 on iron metabolism

4. Effect of PA21 on hematocrit and hemoglobin levels

5. Effect of PA21 on vascular calcification

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