Metformin prevents from severe kidney failure, vascular calcification and high bone turnover disease in a rat model for chronic kidney disease - mineral and bone disorder

**Background and Aim**

Over the past decades, metformin has been widely dispensed as a first-line treatment for Type 2 Diabetes Mellitus because of its beneficial effects on the glucose metabolism through effective increases in insulin sensitivity. Only in the last few years, it has become clear that metformin exerts benign pleiotropic actions beyond its prescribed use and ongoing investigations focus on its anti-aging and anti-cancer properties. Recent data from preclinical and clinical studies are additionally pointing towards a putative beneficial impact of metformin on the kidney and cardiovascular system.

Patients with chronic kidney disease (CKD) suffer from disturbances in mineral homeostasis including dysregulation of calcium, phosphorus, parathyroid hormone and fibroblast growth factor 23 which ultimately entails ectopic calcification in the arteries and bone abnormalities. These complications of chronic renal impairment cover a broader syndrome and are defined as Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD).

In the current study we aimed to investigate the putative beneficial impact of metformin on the kidney and cardiovascular system. Over the past decades, metformin has been putatively beneficial impact of metformin on the kidney and cardiovascular system. Recent data from preclinical and clinical studies are additionally pointing towards a putative beneficial impact of metformin on the kidney and cardiovascular system.

**Materials and Methods**

- Induction of CKD-MBD in rats with a 0.25% adenine/low vitamin K diet for 8 weeks
- Daily treatment with 200 mg/kg metformin or vehicle (1% carboxymethylcellulose) by oral gavage
- Biochemical analyses to study renal function, mineral balance, anemia and acid/base balance
- Quantification of renal crystals and tubulointerstitial area
- mRNA analysis of inflammatory and fibrosis markers in the kidney
- Evaluation of vascular calcification by measuring total calcium content in aorta and peripheral arteries
- Bone histomorphometry on the tibia

**Conclusions**

- Metformin treatment led to, at least partial, protection of renal failure development and concomitant preservation of normal circulating phosphorus and calcium levels.
- The beneficial effect on the kidney and mineral metabolism presumably prevented the onset of vascular calcification and high bone turnover disease in the metformin study group.
- Metformin reduced the tubulointerstitial area and decreased renal inflammation and fibrosis, but further studies are definitely required to gain more insight into the mechanism by which metformin preserves kidney function.

**Results**

- **Metformin protects against development towards severe renal failure, hyperphosphatemia and hypocalcemia**
- **Metformin treatment, at least partially, protects against anemia and does not induce acidosis**

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