ESPN research grant 2018 final report

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Impact of active vitamin D on left ventricular hypertrophy and FGF23/klotho system in renal failure

We are pleased to announce that our study on the impact of active vitamin D on left ventricular hypertrophy (LVH) and FGF23/klotho system in renal failure is finished. We investigated the cardiac phenotype and activation of the intra-cardiac renin-angiotensin system (RAS) in 5/6 nephrectomized (5/6Nx) rats that were treated with and without calcitriol. Additionally, we performed a nested case-control study within the Cardiovascular Comorbidity in Children with CKD (4C) study including children with CKD stages 3-5 treated with and without active vitamin D and echocardiograms, plasma FGF23 and soluble klotho were assessed at baseline and after nine months.

In rats with 5/6Nx, LVH, LV fibrosis and upregulated intra-cardiac RAS were dose-dependently attenuated by calcitriol. Calcitriol further stimulated FGF23 synthesis in bone but not in the heart, and normalized suppressed renal Klotho expression. In the 4C study cohort, treatment with active vitamin D was associated with increased FGF23 and phosphate, and decreased soluble klotho and eGFR compared to controls, whereas LV mass index did not differ between groups. We conclude that active vitamin D ameliorates cardiac remodeling and normalizes renal Klotho expression in 5/6Nx rats, but does not improve the cardiac phenotype in children with CKD stages 3-5. This discrepancy may be due to further enhancement of circulating FGF23 and faster progression of CKD associated with reduced soluble klotho and higher serum phosphate in vitamin D-treated patients.

We are happy that the manuscript of our study with the title "Active vitamin D is cardioprotective in experimental uremia but not in children with CKD stages 3-5" was recently accepted by NDT. Of course, the ESPN grant was acknowledged. We thank the ESPN once again for supporting our study.

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