Secreted Klotho and FGF23 in chronic kidney disease Stage 1 to 5: a sequence suggested from a cross-sectional study

Pavik, Ivana; Jaeger, Philippe; Ebner, Lena; Wagner, Carsten A; Petzold, Katja; Spichtig, Daniela; Poster, Diane; Wüthrich, Rudolf P; Russmann, Stefan; Serra, Andreas L

Abstract: Background Klotho and fibroblast growth factor 23 (FGF23) are key regulators of mineral metabolism in renal insufficiency. FGF23 levels have been shown to increase early in chronic kidney disease (CKD); however, the corresponding soluble Klotho levels at the different CKD stages are not known.Methods Soluble Klotho, FGF23, parathyroid hormone (PTH), 1,25-dihydroxy vitamin D(3) (1,25D) and other parameters of mineral metabolism were measured in an observational cross-sectional study in 87 patients. Locally weighted scatter plot smoothing function of these parameters were plotted versus estimated glomerular filtration rate (eGFR) to illustrate the pattern of the relationship. Linear and non-linear regression analyses were performed to estimate changes in mineral metabolism parameters per 1mL/min/1.73 m(2) decline. Results In CKD 1-5, Klotho and 1,25D linearly decreased, whereas both FGF23 and PTH showed a baseline at early CKD stages and then a curvilinear increase. Crude mean Klotho level declined by 4.8 pg/mL (95% CI 3.5-6.2 pg/mL, P < 0.0001) and 1,25D levels by 0.30 ng/L (95% CI 0.18-0.41 ng/L, P < 0.0001) as GFR declined by 1 mL/min/1.73 m(2). After adjustment for age, gender, serum 25-hydroxyvitamin D levels and concomitant medications (calcium, supplemental vitamin D and calcitriol), we estimated that the mean Klotho change was 3.2 pg/mL (95% CI 1.2-5.2 pg/mL, P = 0.0019) for each 1 mL/min/1.73 m(2) GFR change. FGF23 departed from the baseline at an eGFR of 47 mL/min/1.73 m(2) (95% CI 39-56 mL/min/1.73 m(2)), whereas PTH departed at an eGFR of 34 mL/min/1.73 m(2) (95% CI 19-50 mL/min/1.73 m(2)). Conclusions Soluble Klotho and 1,25D levels decrease and FGF23 levels increase at early CKD stages, whereas PTH levels increase at more advanced CKD stages.

DOI: https://doi.org/10.1093/ndt/gfs460

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-69081

Originally published at:
Pavik, Ivana; Jaeger, Philippe; Ebner, Lena; Wagner, Carsten A; Petzold, Katja; Spichtig, Daniela; Poster, Diane; Wüthrich, Rudolf P; Russmann, Stefan; Serra, Andreas L (2013). Secreted Klotho and FGF23 in chronic kidney disease Stage 1 to 5: a sequence suggested from a cross-sectional study. Nephrology, Dialysis, Transplantation, 28(2):352-359. DOI: https://doi.org/10.1093/ndt/gfs460
Figure 1 Scatter plot graphs of with locally weighted scatter plot smoothing (LOWESS) lines of A) Klotho, B) 1,25-dihydroxy-vitamin D₃ (1,25D), C) carboxy-terminal fibroblast growth factor 23 (FGF23) and D) intact parathyroid hormone (PTH) versus estimated glomerular filtration rate (eGFR) in chronic kidney disease patients. Each symbol represents one patient.
Figure 2. Scatter plot graphs with locally weighted scatter plot smoothing (LOWESS) lines of A) serum phosphate, B) ionized calcium and C) 25-hydroxy-vitamin D (25D), versus estimated glomerular filtration rate (eGFR) in chronic kidney disease patients. Each symbol represents one patient.
Figure 3 Overlaid locally weighted scatter plot smoothing (LOWESS) lines for Klotho (pg/ml), 1,25-dihydroxy-vitamin D₃ (1,25D, ng/l x 10⁻³), carboxy-terminal fibroblast growth factor 23 (FGF23, RU/ml), intact parathyroid hormone (PTH, ng/ml) and serum phosphate (mol/l x 10⁻³) versus estimated glomerular filtration rate (eGFR, ml/min/1.73m²) in chronic kidney disease patients.