Serum soluble alpha-klotho concentrations are not dependent on vitamin D status in maintenance dialysis patients

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Introduction

The long extracellular chain of the single-pass transmembrane protein klotho may be released into the blood (soluble klotho). Circulating blood levels of alpha-klotho in haemodialysis (HD) patients are low. Clinical significance of circulating klotho is extensively studied. Vitamin D may increase the klotho gene expression. However, the relation between serum vitamin D concentrations and serum soluble klotho is not known (references 1-6).

Objective

To determine serum values of novel markers of bone mineral metabolism, including soluble alpha-klotho, before and after correction of vitamin D deficit in maintenance HD patients. Especially, we focused on the relation between soluble klotho and serum vitamin D metabolites (25D and 1,25D).

Patients and methods

- N = 80 clinically stable maintenance HD patients (50 M; mean age 66 years)
- low vitamin D status at baseline (serum 25D below 50 nmol/l)
- supervised administration of cholecalciferol (5000 IU once weekly)
- laboratory parameters assessed at baseline and after 15 weeks
- clinical follow-up continued for 36 months (outcome)

Fig. 1: Soluble alpha-klotho (pg/ml; ELISA; IBL, Germany)

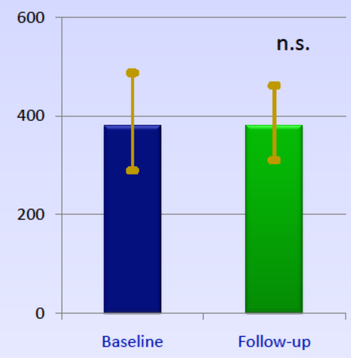


Fig. 2: 25D (nmol/l; CLIA; DiaSorin, USA)

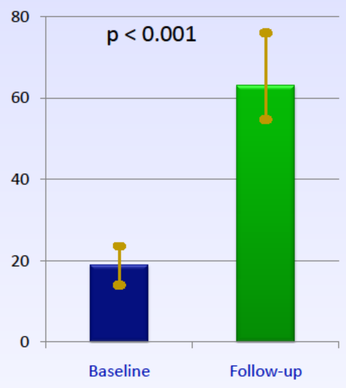
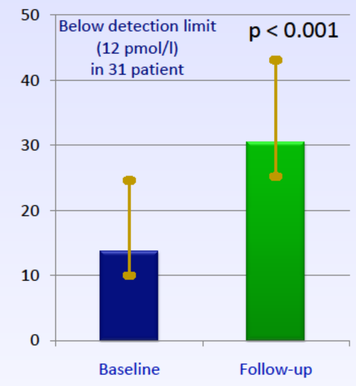


Fig. 3: 1,25D (pmol/l; CLIA; DiaSorin, USA)



Results

Data are given as median (interquartile range) and are presented in figures.

Fig. 4: Vitamin D binding protein (ug/ml; ELISA; RD System, USA)

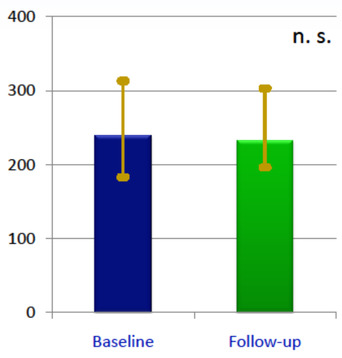


Fig. 5: Sclerostin (pmol/l; ELISA; Biomedica, Austria)

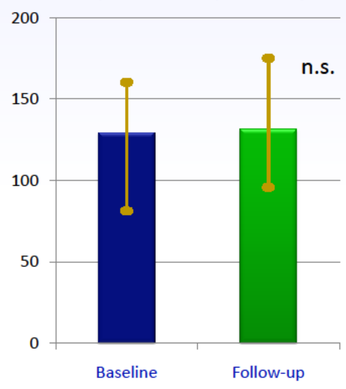


Fig. 6: Fetuin A (ug/ml; ELISA; BIoVendor, CZ)

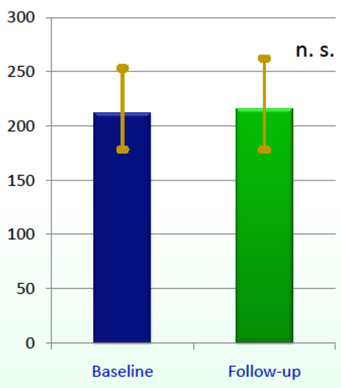


Fig. 7: Intact FGF-23 (pg/ml; ELISA; Immunotopics, USA)

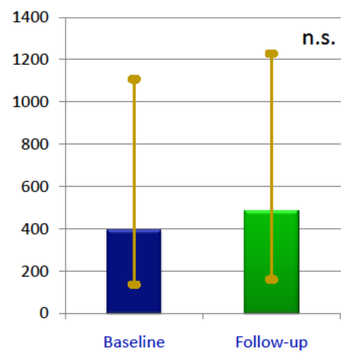


Fig. 8: iPTH (pmol/l; Immulite; Siemens, USA)

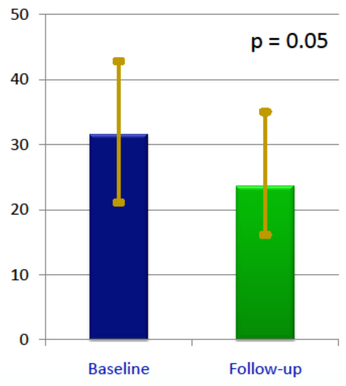


Fig. 9: Ca (mmol/l; routine analysis; COBAS 8000, Roche, Switzerland)

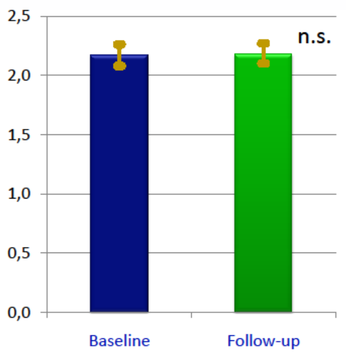


Fig. 10: P (mmol/l; routine analysis; COBAS 8000, Roche, Switzerland)

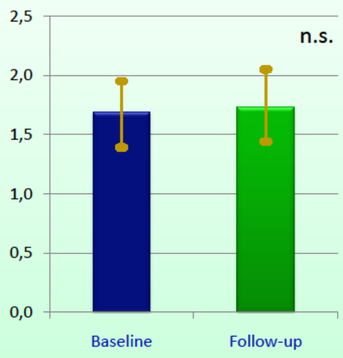


Fig. 11: Beta-cross-laps (ug/l, routine analysis; COBAS 8000, Roche, Switzerland)

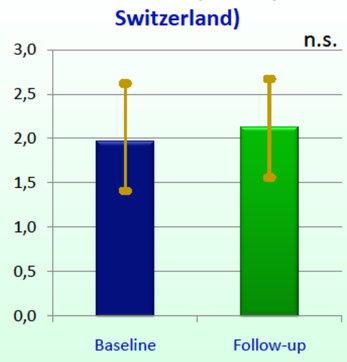
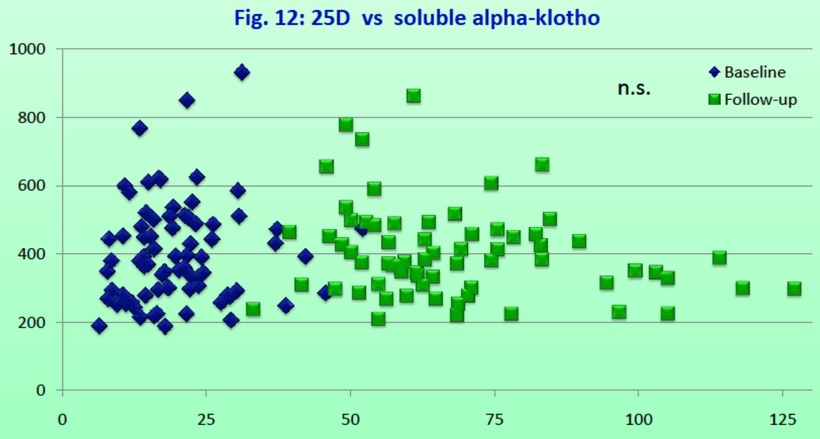


Fig. 12: 25D vs soluble alpha-klotho



Comments

- Serum 25D increased markedly after vitamin D supplementation. However, also serum 1,25D increased after correction of low vitamin D status.
- No associations between serum soluble alpha-klotho and baseline vitamin D metabolites were observed.
- Similarly, after vitamin D supplementation, no associations between serum soluble alpha-klotho and vitamin D metabolites were observed.
- No correlations between serum soluble alpha-klotho concentrations and any other bone metabolism parameters were found.
- Vitamin D supplementation (5000 IU weekly for 15 weeks) did not increase intact FGF-23.
- Twenty three patients died during 36 months of follow-up. Their baseline serum alpha-klotho concentration did not differ from those who survived on dialysis or were transplanted.

Conclusion

Soluble alpha-klotho serum concentrations are independent on vitamin D status in HD patients, both before and after vitamin D supplementation.

References

1. Haussler MR et al: 1,25-Dihydroxyvitamin D and Klotho: A tale of two renal hormones coming of age. Vitam Horm 2016;100:165
2. Hu MC et al: Klotho deficiency causes vascular calcification in chronic kidney disease. J Am Soc Nephrol 2011;22:124
3. Hu MC et al: Renal and extrarenal actions of klotho. Semin Nephrol 2013;33:118
4. Kim HR et al: Circulating alpha-klotho levels in CKD and relationship to progression. Am J Kidney Dis 2013;61:899
5. Lau WL et al: Vitamin D receptor agonists increase klotho and osteopontin while decreasing aortic calcification in mice with chronic kidney disease fed a high phosphate diet. Kidney Int 2012;82:1261
6. Yokoyama K et al: Serum soluble alpha-klotho in hemodialysis patients. Clin Nephrol 2012;77:347

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