Circulating α-Klotho Levels Are Inversely Correlated to FGF23 in Tumor Induced Osteomalacia

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INTRODUCTION

- Tumour induced osteomalacia (TIO) is characterised by high circulating levels of fibroblast growth factor 23 (FGF23) due to ectopic secretion from typically small endocrine tumors.[1]
- An abundance of FGF23 drives the hypophosphatemia and low 1,25-dihydroxy vitamin D levels characteristic of this condition.[1]
- The single-pass trans-membrane protein α-Klotho is integral for FGF23-mediated receptor activation and its downstream effects.[2]
- The regulation of α-Klotho in the face of high circulating FGF23 is currently unknown.
- We investigated the relationship between circulating FGF23 and α-Klotho in patients with TIO.

METHODS

- We identified 15 consecutive plasma FGF23 requests in subjects with TIO for testing.
- FGF23 was measured using Immutopics C-term ELISA kit and soluble α-Klotho was measured using the IBL ELISA kit.
- Correlations between biochemical variables were examined using Pearson's product-moment correlation coefficient.
- Statistical significance of the correlation was tested using a two-tailed t test.

RESULTS

- The group consisted of 7 males and 8 females with an age of 53 ± 20 years (mean ± SD).
- Only one subject was not on treatment for TIO at the time of sampling.
- The average circulating levels of FGF23 and α-Klotho were 286 ± 244 RU/ml and 644 ± 309 pg/ml respectively.
- Although not significant, there was an inverse correlation between FGF23 and α-Klotho circulating levels, with a Pearson coefficient of – 0.28.

Age	Sex	Source / Other diagnoses	FGF23	α-Klotho
70	Male	Unknown, prostate cancer	102	486
29	Male	Unknown primary	105	834
65	Male	Unknown primary	134	807
85	Male	Unknown, prostate cancer	149	1350
50	Male	Unknown primary	158	384
53	Female	Unknown primary	170	339
53	Female	Unknown primary	173	474
10	Female	Neck haemangioma	444	845
22	Female	Unknown primary	217	474
67	Female	Unknown primary	221	1191
64	Female	Unknown primary	330	819
47	Female	Spindle cell lipoma	347	819
70	Male	Unknown primary	434	281
50	Female	Unknown primary	449	576
68	Male	Unknown primary	1104	357

Table1: Table showing age, gender, diagnosis and the levels of circulating FGF23 and α-Klotho in patients with TIO.

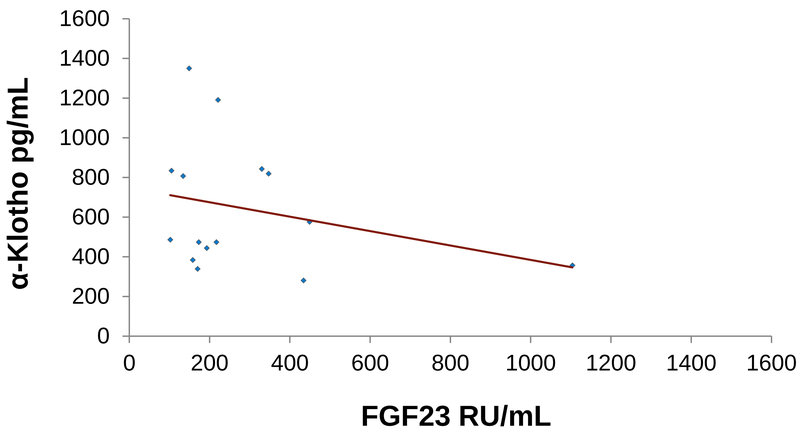

Figure 1: Graph showing the correlation between the levels of circulating FGF23 and α-Klotho in patients presenting tumor induced osteomalacia. There was no significant correlation between the two variables [r =-0.28; n =15, p =0.3].

DISCUSSION

- Given α-Klotho's role in mediating FGF23 signalling and that α-Klotho may be a phosphaturic factor in its own right,[3] its regulation in the face of high circulating FGF23 is of interest.
- The inverse correlation seen between FGF23 and α-Klotho may suggest that elevated levels of FGF23 in TIO down-regulate α-Klotho expression in the kidney and parathyroid glands leading to reduced circulating levels of α-Klotho.
- Such an adaptive mechanism would help partially reduce the renal phosphate wasting seen in TIO.
- A prospective larger scale study following FGF23 and α-Klotho levels over time in each patient is required to further evaluate this potentially key relationship in TIO.

CONCLUSION

- Circulating α-Klotho levels are inversely correlated to FGF23 in TIO.
- This may suggest there is a compensatory down-regulation of α-Klotho in TIO to limit the degree of phosphate wasting that is pathogenic of this condition.

REFERENCES

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