Serum α-klotho levels are not informative for the evaluation of GH secretion in short children.

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OBJECTIVES

α-klotho is a transmembrane protein which can be cleaved and act as a circulating hormone. Since low α-klotho levels were found in organic growth hormone deficiency (GHD) and high levels in acromegaly, an interaction between α-klotho, GH and linear growth has been suggested.

We investigated the role of α-klotho protein as a reliable marker of GH secretion in short children and the factors influencing its secretion. For this purpose, we used the pegvisomant-primed GH stimulation test, since pegvisomant acts as enhancer of GH secretion.

METHODS

We enrolled 20 Egyptian short children with reduced GH secretion (GH peak <10 ng/ml) after two pharmacological stimuli (clonidine and insulin tolerance test) and 20 subjects with normal GH secretion. Chronological age was 9.48±2.84 and 10.49±1.98 years, BMI -0.96±0.90 and -1.26±1.33 SDS and height -0.49±0.63 and -3.25±0.58 SDS in GHD and ISS, respectively. Then, pegvisomant was injected subcutaneously and after three days a GH stimulation test (insulin tolerance test) was performed. The baseline samples obtained before and after pegvisomant were used for measuring IGF-I and α-klotho. α-klotho levels were measured by a commercially available ELISA assay; IGF-I and GH levels were determined by a chemiluminescent assay which has no cross-reaction with pegvisomant.

FIG. 1

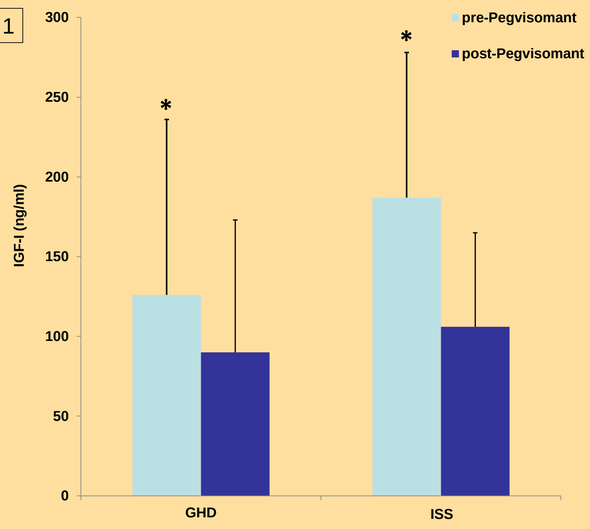


FIG. 2

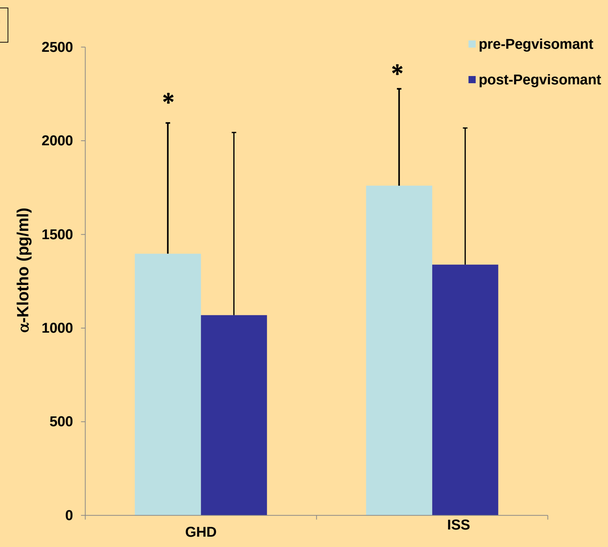
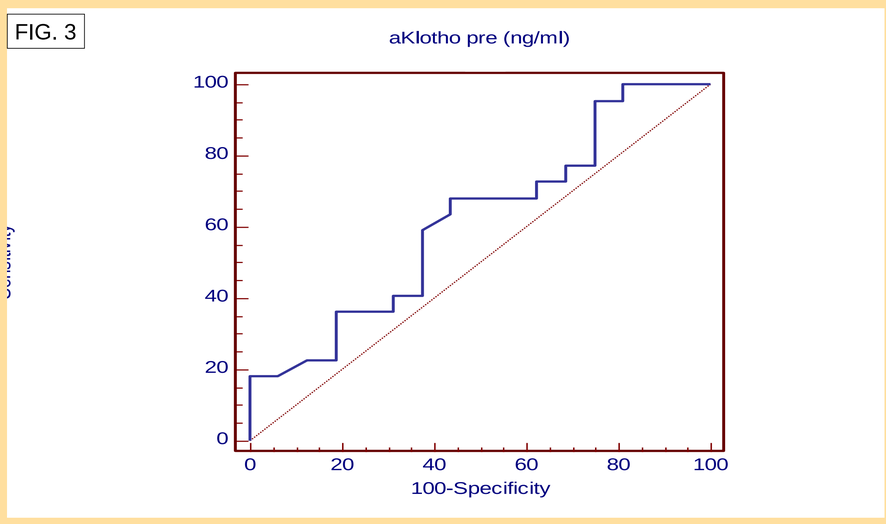


FIG. 3



RESULTS

IGF-I serum levels were lower in GHD compared to ISS (125±110 vs 188±91 ng/ml) (Fig. 1) although the difference was not statistically significant (p=0.059). Furthermore, α-klotho basal levels were not significantly different between GHD and ISS children (1397±697 vs 1760±975 pg/ml; p>0.1) (Fig. 2).After pegvisomant priming, a significant reduction of IGF-I was observed in the GHD group (90±83 ng/ml; p<0.002) as well as in the ISS group (107±59 ng/ml; p<0.001) (Fig. 1). The delta of IGF-I was greater in the ISS than in the GHD group (84.3±59.9 vs 35.7±41.8; p<0.03). α-klotho significantly decreased also both in the GHD group (1069±516 pg/ml; p<0.002) and in the ISS subjects (1339 ±728 pg/ml; p<0.001) (Fig. 2), but the delta of α-klotho (395±422 vs 570±331; p>0.1) and the post pegvisomant values were not different between the two groups.

Roc analysis could not identify a threshold to differentiate GHD from non-GHD children (Fig. 3).

α-klotho basal levels significantly correlated with IGF-I levels in GHD (before priming R=0.4173, p=0.05; after priming R=0.5604, p=0.0298) and ISS subjects (before priming R=0.7098, p=0.0002; after priming R=0.5428, p=0.009).

In the multiple regression analysis, basal IGF-I was the only factor influencing basal α-klotho (p=0.002).

CONCLUSIONS

In conclusion, IGF-I and the nutritional status have a role in the regulation of circulating α-klotho. Therefore, α-klotho is a good marker of the IGF-I status but not a reliable one for the evaluation of GH secretion in children.

References

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Growth

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