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Diagnostic Value of Aminoterminal Peptide of Type I Procollagen when Retesting Growth Hormone Deficiency in the Transition Period

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OBJECTIVES

To determine the relation between aminoterminal propeptide of type 1 procollagen (P1NP), a surrogate marker of bone formation, insulin-like growth factor-1 (IGF-1) and growth hormone (GH) status in transition period for patients with idiopathic growth hormone deficiency (iGHD) treated in childhood with GH.

We hypothesized P1NP can discriminate GH deficiency patients.

METHODS

GH status and bone markers were evaluated in 19 consecutive male adolescents more than 3 months and within 4 years from GH withdrawal. They were treated in the childhood for GH deficiency (8 pts MPHD and 11 pts iGHD). A control group of 8 healthy males age and pubertal stage matched was recruited. All subjects were fully maturated (Tanner stage V). Insulin- induced hypoglycemia (insulin tolerance test, ITT) was used to assess GH status in patients with iGHD. A cut off of 5.6 ng/mL was considered diagnostic for persistently GHD. Aminoterminal propeptide of type 1 procollagen (P1NP) and insulin-like growth factor-1 (IGF-1) were determinated from serum samples collected in fasting state, centrifuged within one hour from collection and stored to - 20 °C until analyzing. Normal reference for IGF1 and P1NP where generated from the controls group.

We evaluated the diagnostic value for GHD of P1NP and IGF1 using receiver operating characteristic (ROC) plot analysis.

RESULTS

Tabel 1. Clinical and biochemical characteristics of the patients at the time of diagnosis of GHD and at the time of revaluation of GH status

	MPHD (n=6)	IGHD persistent (n=3)	IGHD reversible (n=7)	Controls (n=8)
CA (years)	18.55 [16.6,21.5]	17.2 [15.2,18.9]	17.9[14.9,18.9]	16.4[15.2,18]
Ht SDS	-1.27 [-3.7,0.09]	-1.74 [-3.20,-0.22]	-1.34[-2,-0.16]	0.58[-0.55,1.46]
peakGH	NA	0.18[0.05,4.9]	16.59[7.7,46.1]	NA
IGF1-SDS	-2.95 [-3.31,-2.11]	-1.04[-2.36,-0.76]	-0.65[-1.66,0.35]	-0.33[-0.95,1.72]
P1NP-SDS	-1.35 [-1.58,-0.56]	-0.03[-1.1,0.1]	-0.736[-1.82,0.69]	-0.34[-1.08,1.59]
TTx (years)	1.01[0.3,3.5]	0.8[0.3,4.2]	0.9[0.3,1.9]	NA
BA(years)	18[17.5,19]	17.5[17.5,19]	18[17.5,19]	17.5[16.5,18]

CA, Chronological age; SDS, standard deviation; Ht, height; peakGH, maximal GH stimulation in ITT; IGF1, insulin-like growth factor-1; P1NP, aminoterminal propeptide of type 1 procollagen; TTx, time since GH withdrawal.
Median [min,max]

The clinical and biochemical characteristics of the patients are presented in Tabel 1.

30% of the iGHD patients were GH deficient when retesting in transition period.

There were no significant differences between IGF1 and P1NP in the control group and reversible IGHD group.

The ROC plot showed IGF1 AUC=0.944, $p<0.001$ and P1NP AUC=0.743, $p=0.062$.

The best IGF-I SDS cut-off line was -0.76 with 88.9 % sensitivity (95%CI[0.565 to 0.98]) and 87.5 % specificity (95%CI[0.64 to 0.965]).

The best P1NP SDS cut-off line was -0.81 with 71.3 % sensitivity (95%CI[0.354 to 0.879]) and 66.7 % specificity (95%CI[0.444 to 0.858]).

CONCLUSIONS

P1NP has a good diagnostic value in selecting patients with persistent GH deficiency in transition period. Sensitivity and specificity are lower when compared with IGF1.

A logistic regression model conducted on a larger study group with complete sexual maturation and narrower age intervals can offer an increased selection power for IGF1 and P1NP to identify the group of patients with the greatest benefit on bone mass with rhGH therapy.

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