Area Under the Curve (AUC) of Growth Hormone, an additional tool in assessing stimulation test results

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Introduction:
Growth hormone (GH) deficiency is diagnosed through the combination of clinical observation and low GH upon stimulation, in two separate stimulation tests. Normal response is considered as a single rise of GH above the local cutoff point which is used, and differs between countries and range between 7-10 mcg/L. The aim of our study was to assess whether a calculation of area under the curve (AUC) of GH can be used as an additional tool in the diagnosis of GH deficiency, and to find the level of AUC which correlates best with a GH peak of 7.5, which is considered normal in our country.

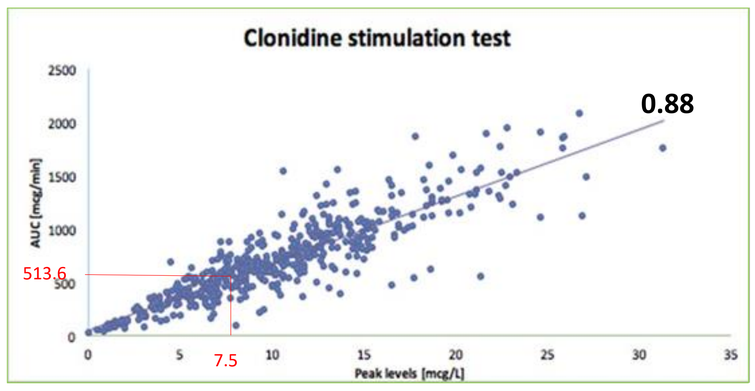
Methods:
Patients who underwent GH stimulation tests which were performed in our clinic during a 3 year period were analyzed and an AUC was calculated for each test.
Correlation between AUC and peak GH was calculated using pearson correlation coefficient, and using linear regression an AUC level was found which correlates with a peak GH of 7.5.
This level was used as an AUC cutoff for the diagnosis of GHD and false negative rates were calculated, using the traditional peak GH method compared to the AUC of GH during the test.

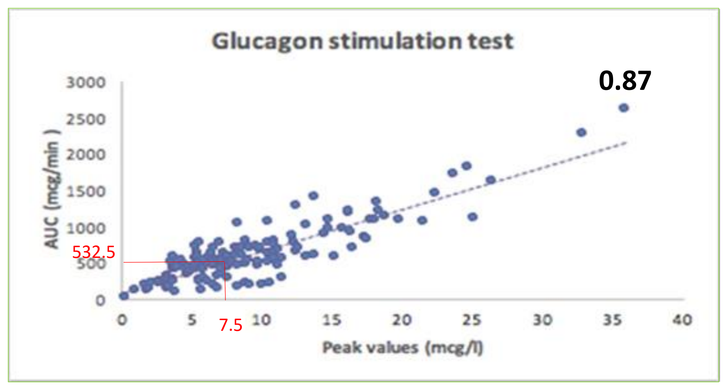
Results:
751 GH stimulation tests were performed. 527 clonidine, 150 glucagon, 74 arginine tests. A strong correlation was found between AUC and peak GH in all 3 tests (0.88, 0.87, 0.89 respectively). The AUC which correlated with a peak GH level of 7.5 in the 3 tests was 513.6, 532.5, and 398 mcg/L/min respectively.
Using these levels as cutoffs for the diagnosis of GHD we found false negative rates using the peak GH level as high as 10.9%, 23.8% and 23.5% in the above 3 tests respectively. False positive rates were 12.1%, 20%, 9.6% respectively. When limiting the analysis to a group with borderline peak GH of 7.5-10 mcg/L the false negative rates rose to 24%, 38%, 20% respectively.

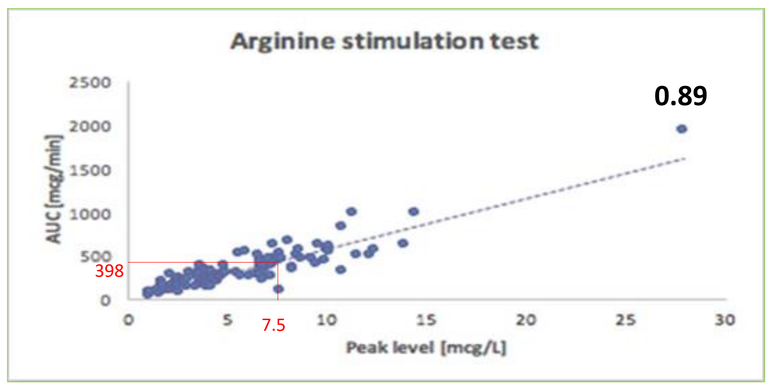
"Normal" Clonidine test result:
0' – 0.5
30' – 1.8
60' – 1.7
90' – 7.6
120' – 2.3

"Abnormal" Clonidine test result:
0' – 1
30' – 4.5
60' – 7.4
90' – 7.0
120' – 5.6

Patients and tests	
N (% males)	730 (61.2)
Mean Age	9.53y
Clonidine test (N)	527
Glucagon test (N)	150
Arginine test (N)	74







	GH level groups	x < 7.5	x > 7.5	7.5-10
Stimulation test	AUC cut off	False positive [%]	False negative [%]	False negative [%]
Clonidine	513.6	12.1	10.9	24
Glucagon	532.5	20.0	23.7	38.0
Arginine	398.0	9.6	23.5	20

Discussion:
The decision to treat children with daily injections of GH for many years is based on a single peak of GH during a supra physiologic test, which at times does not correlate with multiple other samples taken during that and a second test. Calculating an AUC could serve as an alternative or additional information in the diagnostic workup. When GH levels are borderline (7.5-10) higher rates of false negative tests are seen and AUC calculation may be of special benefit.