

Association between growth hormone peak at a stimulation test and pituitary morphological findings in children with growth hormone deficiency (GHD)

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BACKGROUND

According to the prevalence of growth hormone deficiency (GHD), it would be expected that 1 in 4000 patients (1), and the diagnosis includes clinical manifestations, laboratory tests and imaging (2). There are controversies about the validity of the growth hormone stimulation test, considering the fact that the tests are non-physiological, invasive, generating a dubious information about what happens on day-to-day of the child growth (3,4). A variety of stimulation tests are used in clinical practice, with different assays (5,8). The biochemical definition of GHD has generally been considered to be a peak stimulated GH concentration <10ng/ml. The aim of this study was to check if there is a statistically significant relation between GH peak in growth hormone stimulation test and pituitary morphological findings in children with GHD, assessing whether there is difference between GH peak in patients with and without pituitary morphological abnormalities.

METHOD

The study was conducted in the Pediatric Endocrinology Ambulatory at Regional University of Blumenau(Brazil). The tests were analyzed in 189 patients with GHD. It was analyzed the GH peak in growth hormone stimulation test with clonidine and hypoglycemia and correlate with the presence, or not, of pituitary morphological abnormalities (Magnetic Resonance Imaging and/or Computed Tomography). The laboratorial methods used to evaluate GH were IRMA, ICMA and IFMA. The variables analyzed were sex, H-SDS and chronological age in the diagnosis. This study was approved by the University ethics committee.

RESULTS

GH clonidine stimulation test was conducted in 139 patients, and GH insulin stimulation test in 9 patients. 37 patients that realized the test with clonidine had pituitary morphological abnormalities; 26 patients of them were males (70.3%). The peak of GH was higher after 60 minutes of clonidine stimulation test (83 patients) (mean 9.21 ng/ml). There wasn't a statistic difference between the peak of GH in patients with and without pituitary morphological changes, 8.52 ng/ml and 9.5 ng/ml, respectively(p=0,51). Comparing H-SDS and chronological age(CA) at diagnosis in patients with and without morphological pituitary abnormalities they showed no significant difference. (CA 10.09 with x 10.01without, p=0.89; H-SDS -2.04 with x -1.87 without, p=0.57).

Correlate between the GH peak in growth hormone stimulation test with clonidine at 60min(83 patients) according the presence, or not, of pituitary morphological abnormalities

	Patients with morphological pituitary abnormalities (n = 24)		Patients without morphological pituitary abnormalities (n = 59)		p(*)	p(**)
	Mean ± DP	Median ± DQ	Mean ± DP	Median ± DQ		
Growth hormone peak (clonidine 60min - ng/ml)	(8,52 ± 5,01)	(6,64 ± 2,4)	(9,5 ± 6,54)	(7,73 ± 3,5)	0,51269	0,65488

p value of the Student's t test (parametric test). p (**): p value Mann-Whitney test (nonparametric test).

DISCUSSION

Morphological pituitary abnormalities detecting in imaging are more common in patients with severe GHD (6). In this study there wasn't a statistic difference between the peak of GH in patients with and without pituitary morphological changes. There isn't a laboratory test with sufficient sensitivity and specificity to be the gold standard in the diagnosis of DHC (3). It should be considered that 10% to 35% of children without DHC may fail to get an adequate response during a GH stimulation test. And even when subjected to two distinct tests, 3% to 10% of normal children may fail to demonstrate a normal response in both tests (7). The determination of cutoff values in a pharmacological stimulation test to indicate where starts the deficiency can induce to a mistake (8). The analysis of the general context of children with short stature, growth data and clinical judgment remain the basis for the diagnosis of GHD to determine who is a candidate for treatment with GH (4).

CONCLUSION

There were more morphological pituitary abnormalities in males with GHD in this sample. There wasn't significant difference between GH peak stimulation test with clonidine in patients with and without morphological pituitary abnormalities. The presence of morphological pituitary abnormalities may indicate more severe deficiency, therefore it's necessary more discussions about the validity of the GH stimulation tests.

REFERENCES

1. Hoinoff C, Collet-Solberg PF. Crescimento Normal e Alterado. Tratado de pediatria: Sociedade Brasileira de Pediatria. São Paulo: Manole, 2010. p.768 – 779.
2. De Paula LP, Czepielewski MA. Avaliação dos Métodos Diagnósticos para Deficiência de GH (DGH) na Infância: IGFs, IGFbPs, Testes de Liberação, Ritmo de GH e Exames de Imagem. Arq Bras Endocrinol Metab. 2008; 52 (5):734-744.
3. Damiani D. Deficiência de hormônio de crescimento: até onde confiar em testes de estímulo?. Arq Bras Endocrinol Metab. 2005;49(4).
4. Takara Stanley MD. Diagnosis of Growth Hormone Deficiency in Childhood. Curr Opin Endocrinol Diabetes Obes. 2012;19(1): 47–52.
5. Smyczynska J, Stawerska R, Lewinski A, Hilczner M. Limited usefulness of the test of spontaneous growth hormone (GH) nocturnal secretion as a screening procedure in children with short stature. Ann Agric Environ Med. 2014;21(4):893-7.
6. Maghnie M, Ambrosini L, Di Iorgi N, Napoli F. Hypothalamic-Pituitary MRI Imaging: Normal And Abnormal Features In GH Deficiency. Department of Pediatrics, IRCCS Giannina Gaslini, University of Genova, Italy. <https://www.eurospe.org/clinical/CPC%20Docs/Hypothalamic-Pituitary%20MRI%20Imaging%20Normal%20And%20Abnormal%20Features%20In%20GH%20Deficiency.pdf>.
7. Sociedade Brasileira de Pediatria e Sociedade Brasileira de Endocrinologia e Metabologia. Projeto Diretrizes Associação Médica Brasileira e Conselho Federal de Medicina. Baixa Estatura por Deficiência do Hormônio de Crescimento: Diagnóstico. 31 de agosto de 2004.
8. Seick D, Boguszewski MCS. Testes de secreção de hormônio de crescimento e suas implicações no tratamento da baixa estatura. Arq Bras Endocrinol Metab. 2003; 47(4).