

The Diagnosis of Growth Hormone Deficiency in Obese Children and Adolescents

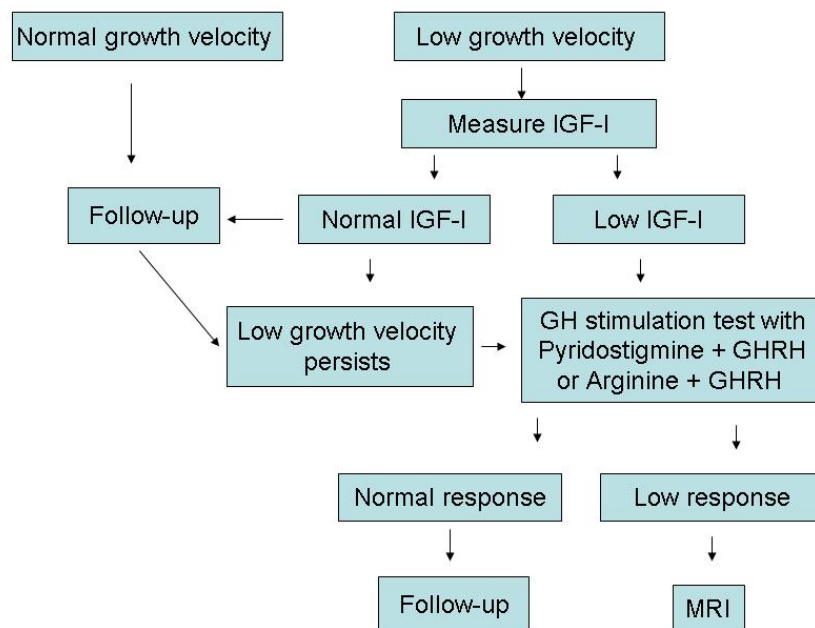
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In children with short stature the diagnosis of growth hormone deficiency (GHD) is classically established when GH concentrations do not reach an arbitrary cut-off value (usually between 7-10 $\mu\text{g/L}$) after two pharmacological stimuli (1, 2). In addition, subnormal serum levels of insulin-like growth factor I (IGF-I) strongly support a diagnosis of GHD (high specificity), although normal IGF-I concentrations do not exclude a diagnosis of GHD in about 30% of cases (1-3).

Truncal obesity is one of the clinical features of severe growth hormone deficiency (1). On the other hand, reduced GH secretion is a consistent finding in obese children, a phenomenon caused by increased body weight since it is partially or totally reversible with weight loss (4). Spontaneous GH secretion in obese children and adolescents increases also after a short-term hypocaloric diet. In adult obese subjects, a dual defect in GH secretion and clearance has been proposed as the underlying cause. Although the exact neuroendocrine mechanism of the reduced GH concentrations in obesity is not known, the finding of decreased spontaneous GH secretion suggests decreased release/action of hypothalamic GH-releasing hormone and/or increased somatostatin tone. Pharmacologic manipulation with a number of agents partially restores the GH response to exogenous GH-releasing hormone in obese children (5). A chronic somatotrope inhibition by an excessive release of endogenous somatostatin would explain why, although normalized, the GH response to GH-releasing hormone after pharmacologic manipulation still remains lower than that observed in normal weight children given the same treatment. Nonetheless, combined administration of GHRH with arginine, piridostigmine or GH-secretagogue analogues, elicits marked GH responses in obese subjects and are to be preferred to the classical GH stimulation tests which, in this case, yield a great number of false positive results.

Obese children usually have normal stature or are even taller than their peers. Furthermore, obese children usually have normal or elevated IGF-I concentrations (4), while IGF-I is reduced in most GHD patients (1, 2). Although truncal obesity may be present in children with short stature and severe unequivocal GHD, there still may be an occasional short obese child who requires investigation for GHD. Before undergoing endocrine investigation, however, other causes of short stature associated with obesity such as Prader-Willi syndrome or pseudohypoparathyroidism type Ia must be excluded (1, 2). Chronic renal and bowel diseases also have to be ruled out. A short child, either obese or not, needs a careful evaluation of growth velocity as the first step. Afterwards a meaningful diagnostic algorithm could be proposed as follows:



REFERENCES

1. Cappa M, Loche S Evaluation of growth disorders in the paediatric clinic. *Journal of Endocrinological Investigation* 2003; 26 (suppl to n. 7):54-58
2. GH Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. *J Clin Endocrinol Metab* 2000; 85:3990-3993
3. Badaru A, Wilson DM. Alternatives to growth hormone stimulation testing in children. *Trends Endocrinol Metab* 2004; 15:252-258
4. Loche S, Cappa M, Borrelli P et al. Reduced growth hormone response to growth hormone-releasing hormone in children with simple obesity: evidence for somatomedin C mediated inhibition. *Clin Endocrinol (Oxf)* 1987; 27:145-53
5. Loche S, Pintor C, Cappa M et al. Pyridostigmine counteracts the blunted growth hormone response to growth hormone releasing hormone of obese children. *Acta Endocrinol (Copenh)* 1989; 120:624-628