A STUDY OF IGF-1 SERUM CONCENTRATIONS AND KINETICS OF GROWTH HORMONE ASSAYS IN STIMULATION TESTS USED FOR DIAGNOSING INSUFFICIENT SOMATOTROPE SECRETION

Monge M.
Laboratoire Pasteur Cerba - Cergy-Pontoise - FRANCE

INTRODUCTION

The diagnosis of insufficient somatotrope secretion (growth hormone deficiency or GHD) is important in children.

This diagnosis was based on interruption of the growth curve and/or height below 2 SD. Treatment with GH was long-term (until the end of growth), intensive (generally, one SC injection per day) and costly (on average, 10 to 12 thousand euros per year).

Because of the extremely short half-life of GH as well as its irregular pulsatile secretion, assays performed on limited samples yield little useful information. Investigation for hormone deficit was therefore performed using dynamic tests. A number of different pharmacological agents stimulate GH secretion, either by inhibiting the hypothalamus from producing somatostatin or by directly stimulating production of GRF. GH levels are determined at various intervals after administration of the substance according to clearly defined test protocols.

In France, a child is considered to have a deficit if no serum GH concentrations greater than 20 mIU/l are recorded in 2 different stimulation tests. One of the tests must be “coupled”, i.e. combining 2 pharmacological agents.

However, this 20 mIU/l threshold does not take account of the type of test and large response variances that can be reported, depending on the drug used. Nor does it factor in the patient’s weight, age and pubertal development.

Diagnosis may be assisted by determining concentrations of insulin-like growth factor (IGF) since this is the main growth factor dependent upon endogenous GH secretion.

Response to dynamic tests
 Response varies according to:
- substance administered
  Of the 430 dynamic tests and regardless of the product(s) used, only 55% showed a positive response, with a secretion peak above 20 mIU/l. This percentage varied according to the product used:
  - ornithine (51.5%), insulin (22.8%), glucagon (42.8%), L-Dopa (50%)
  - clonidine-betaxolol (28.6%), glucagon-betaxolol (64.8%), glucagon-propanolol (69%), kerlone-glucagon (65.5%)
  In light of these results and because the highest GH concentrations are observed at very different times from one patient to the next, it is important to comply with the different protocol times to avoid overlooking an unrecorded peak.
- gender
  GH concentrations obtained by stimulation vary according to the substance injected and also according to gender for certain substances.

Despite the relationship between GH and IGF-1, the percentage of low IGF-1 concentrations in patients with a positive response to dynamic tests (15% of the 73 tests with ornithine) does not differ considerably from that observed in those presenting a response less than 20 mIU/l (19.7% of the 66 tests with ornithine). Therefore IGF-1 assays cannot be used as a substitute for dynamic tests in diagnosing a GHD.

RESULTS

GH/IGF1 correlation
In healthy adults, GH levels may fluctuate throughout the day between largely undetectable concentrations and peaks of up to 30 μg/l (90 mIU/l).

Since IGF1 is the main effector of growth hormone in target tissues and GH is the primary agent responsible for regulating IGF1 secretion, there is normally a correlation between GH and IGF1, as described earlier.

BIBLIOGRAPHY

Suberbielle X.
A propos de l’exploration fonctionnelle de l’axe somatotrope.

Lahbhi N, Roger M.
Hormone somatotrope.

Rochciclen P, Enjoujane C, Taibier M, Pierkonwski C.
Statistical study of 5473 results of nine pharmacological stimulation tests : a proposed weighting index.