

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

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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 (IGF1) since this is the main growth factor dependent upon endogenous GH secretion.

The goal of this study was to evaluate the interpretation of these tests depending on the drug administered despite the legal and unique threshold of 20 mIU/l. Then we compared it to IGF-1 results obtained, according to the standard reference values given by the supplier according to age.

MATERIALS ET METHODS

Chemiluminescent assays of hGH were performed in our laboratory in 2007 using Beckman Coulter's DXI instrument and somatomedin C assays were conducted using the Immulite 2000 from DPC (Siemens). hGH assays were calibrated to the international standard IS 98/574, as recommended.

416 dynamic tests using 7 different pharmacological agents were analysed.

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.

● Response to dynamic tests

Response varies according to:

→ substance administered

Of the 430 dynamic tests and regardless of the product(s) used, only 50% showed a positive response, with a secretion peak above 20 mIU/l. This percentage varied according to the product used:

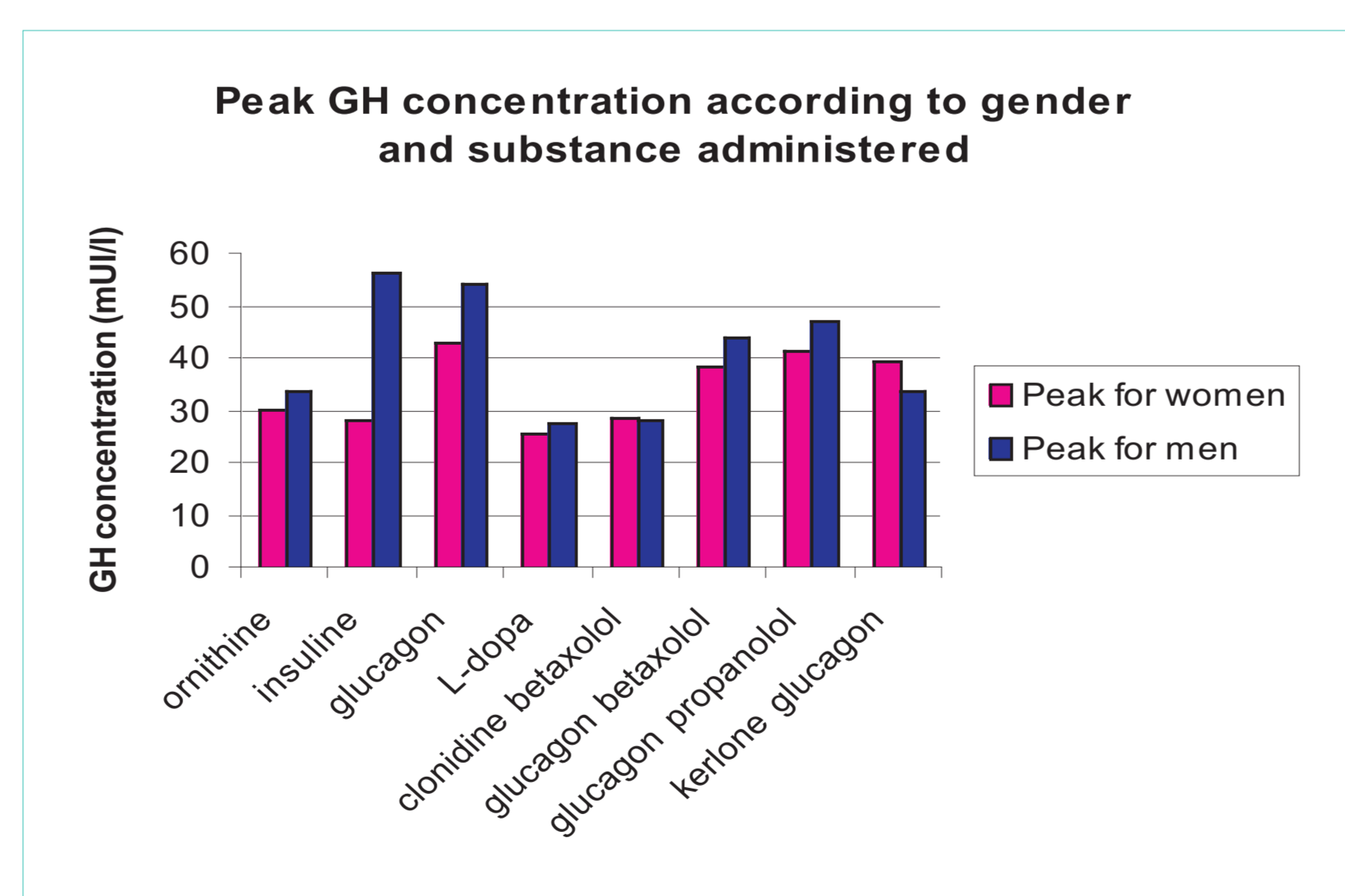
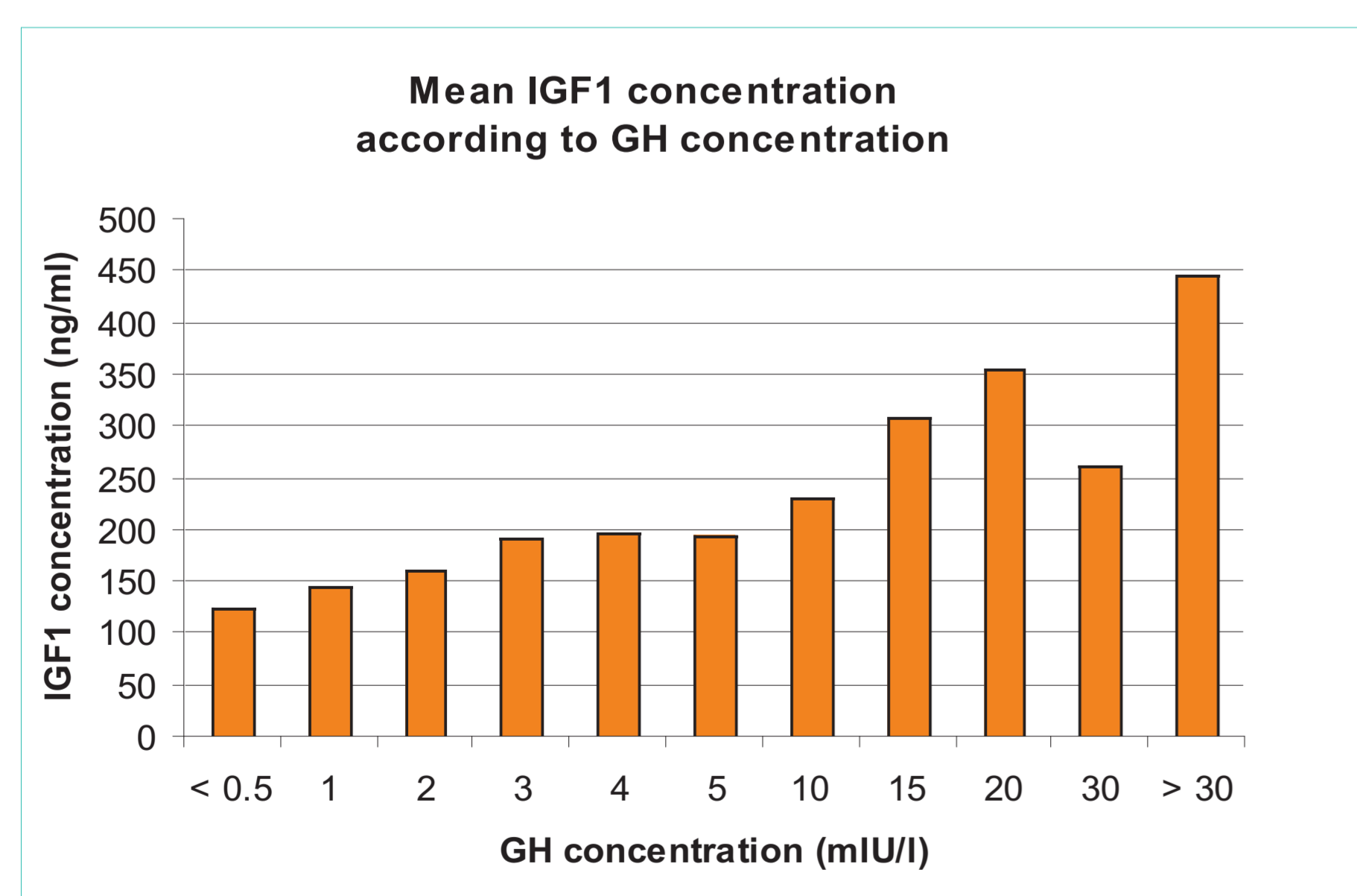
- ornithine (51.3%), insulin (22.8%), glucagon (42.8%), L-Dopa (50%)
- clonidine-betaxolol (28.6%), glucagon-betaxolol (64.8%), glucagon-propranolol (69%), kerlone-glucagon (65.5%)

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.



Substance administered	Peak GH concentration (mIU/l) by gender	
	women	men
ornithine	30.30	33.80
insulin	28.10	56.25
glucagon	43.30	54.50
L-dopa	25.80	27.90
clonidine-betaxolol	28.50	28.00
glucagon-betaxolol	38.70	44.19
glucagon-propranolol	41.40	47.11
kerlone-glucagon	39.70	33.70

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