206

INFLUENCE OF BODY MASS INDEX (BMI) ON GROWTH HORMONE (GH) STIMULATION TESTS IN SHORT PREPUBERTAL CHILDREN.

L PATEL, PE CLAYTON, DA PRICE.
Dept of Child Health, University of Manchester, UK.

Simple obesity reduces peak GH concentrations during stimulation tests in children and adults. It is not known how factors such as sex, pubertal status, stature and distribution of body fat may influence this relationship. We therefore retrospectively analysed the effect of percent ideal BMI (%BMI) on peak GH concentration after arginine infusion (0.5g/kg) in 117 short prepubertal children without GH deficiency (SN) and 42 prepubertal girls with Turner syndrome (TS), who had received no hormonal therapy. Physical characteristics [Mean (SD)] and regression analysis of %BMI versus log peak GH concentration are shown:

	n	Ht SDS	%BMI	GH(mU/l)	r	r^2%
SN Boys	65	-2.8(0.9)	95(11)*	23(15)	-0.05	0
SN Girls	52	-2.7(1.2)	99(21)	26(15)	-0.49#	24
TS	42	-2.7(0.8)	107(18)	22(25)	-0.19	4

# $p<0.01$; * $p<0.01$ compared to TS, No difference between SN Girls and TS.

In these prepubertal children, only SN girls show an inverse relationship between %BMI and peak GH concentration. There is therefore a dichotomy not only between girls and boys but also between SN girls and those with TS. We hypothesise that oestrogenic effects on body composition may be critical to the relationship between fat and GH secretion.

207

THE INSULIN-LIKE GROWTH FACTOR-I (IGF-I) GENE IS EXPRESSED IN SKIN FIBROBLASTS FROM CHILDREN WITH LARON GROWTH HORMONE (GH) INSENSITIVITY.

PE CLAYTON, DA PRICE.
Dept of Child Health, University of Manchester, UK.

The IGF-1 gene contains 6 exons, distributed over 90kB of genome. A complex array of mRNA species can be transcribed, which vary in 5' (leader) and 3' (terminal) exon usage, and polyadenylation site. Four IGF-I mRNA transcripts encode putative preprohormones: IGF-IA (exons 1,3,4,6), the dominant species expressed in liver, IGF-IB (exons 1,3,4,5), IGF-IA' (exons 2,3,4,6) and IGF-IB' (exons 2,3,4,5). Interest has focused on the differential expression of these mRNAs, their relevance to IGF-1 action and hormonal mechanisms, which may induce their expression. The Laron syndrome is characterised by insensitivity to the actions of GH. Hence the IGF-I gene will be expressed independent of GH control. We have therefore examined the expression of the IGF-I gene in total RNA extracted from confluent skin fibroblast cultures, taken from 3 children with Laron syndrome and 1 normal child. This was achieved by reverse transcription of mRNA followed by PCR amplification of the 4 transcripts with oligonucleotide primers specific to 5' (exons 1 or 2) or 3' (exons 5 or 6) IGF-I sequences. IGF-IA and IB mRNA were expressed in 2 of the 3 Larons and the normal child, and IGF-IB mRNA only in the oldest of the Laron children. Transcripts containing the alternative leader exon 2 were not identified. Fibroblasts from those with Laron syndrome may form an important tissue in which to study IGF-I gene expression independent of GH action.

208

VARIABILITY IN THE URINARY EXCRETION OF GROWTH HORMONE (GH) AND CREATININE IN CHILDHOOD.

AM SKINNER, PE CLAYTON, DA PRICE, GM ADDISON, CYW MUI.
Royal Manchester Children's Hospital, Manchester, UK.

As a basis for assessment of the clinical validity of urinary GH measurements in children, the variability in renal handling of GH was compared to that of creatinine in 93 healthy children (aged 4-16 years), 20 of normal stature and 73 with growth disorders. 10 were classified as GH deficient (GHD), 48 as short normal (SN) and 15 had Turner syndrome (TS). 5 overnight urine samples were collected over 2 weeks, and the variability of excretion expressed as a coefficient of variation (CV) of the total overnight amount of GH or creatinine. There was considerable night to night variability in the excretion of both substances:

MEAN CV (%)	Normal	SN	GHD	TS
GH	37	35	52'	46
Creatinine	22	29	30	36'

* $p<0.05$ compared to Normal + SN, # $p<0.05$ compared to Normal.

Assay variation rather than a change in renal protein handling accounted for the large variation in low uGH concentrations, thus contributing to the high uGH CV of the GHD group. Increasing the number of samples collected (upto 5) decreased the expected sample variation (error) for uGH but not significantly in all groups, and reduced the convenience and practicality of the test. These results indicate that variation in GH and creatinine excretion is considerable in both normal children and those with growth disorders. The use of multiple samples (upto 5) does not significantly reduce the variability inherent in uGH measurement.

209

U-hGH ASSAY IN LARON DWARFISM

I LORDEREAU-RICHARD ,P GEORGES ,JL CHAUSSAIN :
Department of Pediatric Endocrinology
Hospital Saint Vincent de Paul, PARIS, FRANCE.

U-hGH was measured before and during IGF 1 therapy in 4 prepubertal children with LARON dwarfism, 2 boys and 2 girls, aged 4 to 14 years, severely growth retardated (- 4,5 SD to -5,5 SD).
Urine specimen were collected for 3 consecutive nights using plastic container after addition of BSA solution (30 % w/v) and u-hGH was measured using EIA commercial kit (NorditestR).
Results (mean of 3 u-hGH measurements) in ng/mmol of creatinine were:

Patients	without treatment	With IGF1 (Month 9 (240 µg / kg / day)
A	5,1	3,2
B	6,4	6,6
C	10,3	3,9
D	5,4	ND

Mean u-hGH (U) in untreated Laron dwarfism (U=6,8) was as expected strongly higher than in normal prepubertal children (U=1,63 ±0,14 SD) and in other severe (<-3SD) growth retardations (U=2,24 ± 0,32 SD).
IGF 1 did not significantly decreased u-hGH excretion (U=6,8 to 4,6) nor plasma basal hGH secretion (mean 19,9 mUI/l to 20, 9 mUI/l) .
We concluded that u-hGH is of good predictive value for the diagnosis of LARON dwarfism but is not affected by IGF 1 therapy, despite growth acceleration. The role of IGF1 in the feed back regulation of GH secretion in Laron dwarfism remains questionnable.

210

ACTUAL VERSUS PREDICTED FINAL HEIGHT IN PATIENTS WITH INTRA-UTERINE GROWTH RETARDATION (IUGR).

J.L. Chaussain, J.F. Ducret, J.C. Job,
Pediatric Endocrinology, St Vincent de Paul, Paris, FR.

The methods used by pediatricians to predict final height in children with IUGR have not been validated. We were able to compare actual vs predicted adult height in 44 patients (21M/23F) born at term (39±1.8wks) with height 43.6±2.8 cm and weight 2200±500 g. Their fathers'height averaged 170±6 cm and mothers'height 157±5 cm. All children were evaluated for short stature between 4 and 12 yrs of age: all had normal GH values, skeletal X-rays, and caryotype.

Final height was calculated using Bailey-Pinneau prediction abaques: 170±4 cm in boys and 157.5±3.5 cm in girls. These values were higher than the actual heights of these adult individuals: 162±8 cm in boys ($p<0.001$) and 147.6±7 cm in girls ($p<0.001$). Adult height correlated with height at birth ($r=0.45$, $p<0.02$) and at 2 yrs of age ($r=0.56$, $p<0.01$), but not with parental height.

Our conclusion is that the height prognosis based on available prediction techniques is too optimistic by a mean of 8-10 cm, an important indication if GH therapy is contemplated in children with IUGR.

211

LONG TERM CONTROL OF GROWTH RATE AND BONE MATURATION BY LH RH AGONIST IN GIRLS WITH TRUE PRECOCIOUS PUBERTY (TPP).

J. Zeller, PF Bougnères, JL Chaussain. Pediatric Endocrinology, St Vincent de Paul, Paris, France.

TPP reduces adult height. During its first year of administration, the LH RH agonist D-Trp6 (Decapeptyl®) decreased growth velocity and bone maturation, but its long term effects have not been analyzed. Fourteen girls had onset of idiopathic TPP at 6.3±1.2 yrs: their growth rate was 9.7±3.5 cm/yr and bone age 8.9±1.9 yr. The girls received 1 injection/mo of a depot preparation of the agonist during 4.8±1.2 yrs. Growth rate stabilized at 4±1.2 cm per yr ($p<0.005$ vs pretreatment) and bone age increased by only 0.85±0.15 yr/yr. At the end of treatment, height was 151.5±6.2 cm and bone age 12.3±0.6 yrs. Growth rate remained at 4.4±2 cm/yr during the following 6-34 months. Therefore, 7±1.3 yrs after the onset of treatment with the LH-RH agonist, height was 157±8 cm and bone age 13.2±1.1 yrs, producing a final height prognosis of 162±5 cm. We conclude that treatment of true precocious puberty with D-Trp6-LH-RH increases final height prognosis.