

5

CONFIRMATION OF HYPOGONADOTROPIC HYPOGONADISM (HH) SUSPECTED AT PREPUBERTAL AGE. S. Gottlieb, G. Ropelato, C. Bergada. División de Endocrinología, CEDIE. Hospital de Niños Ricardo Gutiérrez. Buenos Aires, Argentina.

We have previously reported that prepubertal diagnosis of HH could be assumed on the basis of micropenis and cryptorchidism, olfactory disturbances, low LH response to GnRH infusion and subnormal clinical and histological response to prolonged treatment with hCG.

In order to confirm the diagnosis of HH at pubertal age, 12 patients with suspicious prepubertal diagnosis of HH were studied, due to the clinical appearance, hCG test; Testosterone (T: ng/dl) basal:  $31.9 \pm 25.9$ , T post hCG:  $111 \pm 97.8$  and with GnRH infusion ( $0.83 \mu\text{g}/\text{min}$ ): LH (IU/L) basal:  $2.8 \pm 1.9$ , LH Max:  $7.5 \pm 3.9$ ; FSH (IU/L) basal:  $2.1 \pm 1.9$ , FSH Max:  $5.1 \pm 2.8$ .

In all patients the clinical diagnosis of HH was confirmed at the last control carried out at the age of  $17.17 \pm 2.18$  years. Their height was  $170.6 \pm 5.62$  cm, testicular volume  $2.11 \pm 0.93$  ml and anosmia was detected in 6 out of 12. All of them required therapy with exogenous testosterone.

These results demonstrate the utility of hormonal tests for the prepubertal diagnosis of HH in boys with micropenis and cryptorchidism.

8

LONG-ACTING GnRH ANALOG (GnRHa) IN THE DIFFERENTIAL DIAGNOSIS OF MALE SEXUAL PRECOCITY. CC. Albano; C. Latronico; S. Domenice; IJP. Arnhold; W. Bloise; BB. Mendonca. Unidade de Gonadas e Intersexo, Disciplina de Endocrinologia, HC-FMUSP, Sao Paulo, Brasil.

GnRHa are potent inhibitors of LH and FSH release used in treatment of true precocious puberty (TPP). In 8 boys (ages 1y5m - 8y11m) with sexual precocity and advanced bone age we compared the pattern of gonadotropin response to the acute GnRH test ( $100 \mu\text{g}$ , iv) and the testosterone levels 30 days after administration of GnRHa (D-Trp6-GnRH 3 mg im or Goserelin 3.6mg sc). LH and FSH were measured by RIA or IFMA, and testosterone by RIA.

CASE	CA (Y)	LH U/L		FSH U/L		TESTOSTERONE (ng/dl) 30 days		DIAGNOSIS
		B	P	B	P	B	P	
1	1.41	6	36	3	7	213	13	TTP.Org
2	1.58	4*	26*	3*	4*	600	23	TTP.Org
3	8.91	6	46	7	15	378	22	TTP.Org
4	8.83	4	35	8	11	110	<10	TTP.Org
5	9.5	<0.6*	<0.6*	<1*	<1*	630	1165	Pseudo pp
6	7.41	4	4	<2	<2	118	69	Pseudo pp
7	5.58	8	8	4	4	164	235	Pseudo pp
8	2.83	<0.6*	<0.6*	<1*	<1*	392	282	Pseudo pp

All patients with TPP, but none with pseudo precocious puberty, had a pubertal LH rise on the acute GnRH test and prepubertal testosterone levels 30 days after GnRHa. However, one patient with a Leydig cell tumor had a partial decrease in testosterone levels. We conclude that prepubertal testosterone levels 30 days after administration of GnRHa is useful to confirm the diagnosis of TPP.

6

SERUM FSH AND LH AGE PROFILES IN NORMAL CHILDREN OF BOTH SEXES DURING PREPUBERTY AND IN EARLY PUBERTY. S. Chain, E. Chaler, A. Belgorosky, MA. Rivarola. Serv. Endocrin., Hosp. Garrahan, Bs. As., Argentina.

Scarce information is available on serum FSH and LH levels, determined by highly sensitive assays. We evaluate gonadotropin age profiles in children of both sexes using an enzyme immunoassay, in presence of two monoclonal antibodies (MEIA). 124 females (F) were studied: 55 prepubertal (Group G1) with a chronological age (CA) of  $13.47 \pm 0.03$  months, 51 prepubertal (G2), CA  $4.66 \pm 1.93$  years, and 18 pubertal F, 8 of them in breast stage 2 (G3), CA  $10.3 \pm 0.69$  y and 10 in breast stage 3 (G4), CA  $12.3 \pm 1.71$  y; 185 males (M) were studied: 81 prepubertal (G1), CA  $12.1 \pm 6.68$  m, 75 prepubertal (G2), CA  $4.81 \pm 2.07$  y, and 29 pubertal M (G3) genital stage 2 CA  $10.8 \pm 1.76$  y. In both F and M, G1 was subdivided in 3 subG according to age: 0-3 m, 4-12 m and 12-24m. In F, serum FSH in G1 was higher than in G2 or G3 ( $5.12 \pm 2.63$ ,  $2.76 \pm 1.9$  and  $2.89 \pm 2.0$  U/L respectively,  $p < 0.05$  by ANOVA) and similar to G4 ( $5.88 \pm 2.91$ ). Serum LH similar in G1, G2 and G3 but higher in G4 ( $0.19 \pm 0.23$ ,  $0.23 \pm 0.88$ ,  $0.71 \pm 1.87$  and  $4.04 \pm 3.19$  U/L,  $p < 0.05$ ). In M, serum FSH was similar in G1 and G2, but higher in G3 ( $1.15 \pm 0.78$ ,  $1.10 \pm 0.82$  and  $2.26 \pm 0.96$  U/L,  $p < 0.05$ ) while serum LH in G1 was higher than in G2 but similar to G3 ( $0.78 \pm 1.33$ ,  $0.13 \pm 0.32$  and  $0.72 \pm 0.99$  U/L,  $p < 0.05$ ). However, in the different M sub G1 LH was high between 0-3m and 4-12m ( $2.39 \pm 1.35$  and  $1.25 \pm 1.65$ ) but similar to G2 between 13-24m ( $0.154 \pm 0.17$ ). In F, serum FSH was higher than in M in G1 and G2 and serum LH was lower in G1. It is concluded that serum FSH in the first 2 years of life in F and in the first one in M are similar to pubertal values. Sex differences can be due to different sensitivity of the gonadostat to the inhibitory effects of gonadal steroids and peptides or to differential secretion of the hormones.

9

PROGRESSIVE DECREASE OF SERUM FREE IGF-I IN NORMAL CHILDREN DURING THE FIRST SEVEN YEARS OF LIFE. A. Belgorosky; MA. Rivarola. Laboratorio de Investigación, Hospital de Pediatría Garrahan, Buenos Aires, Argentina.

Most of serum IGF-I circulates as a complex bound to a specific binding protein (BP 3) and to an acid-labile subunit. It has been described that in adults 5% of total serum IGF-I can circulate as a free (F) fraction and it has been proposed that the free fraction would be a better marker of biological actions than the bound fraction. The aim of the present work was to evaluate serum F IGF-I by absorbing the F fraction with a cartridge of octadecyl silyl silica (SEP-PAK C18) and eluting it with 75% ethanol acid  $0.01$  M HCl, following the technique of Hizuka et al. Twenty one normal children (chronological age 0.32-7 years) and 5 normal adults were studied. A significant decrease of serum F IGF-I ( $y = 7.26 \text{ ng/ml} - 0.48 x$ ,  $r = -0.445$ ,  $p < 0.043$ ) and of % F IGF-I ( $r = -0.55$ ,  $p < 0.01$ ) as a function of age was observed in children, to reach adult values ( $X \pm DS$  F IGF-I:  $5.04 \pm 1.97 \text{ ng/ml}$ , percentage of total  $4.15 \pm 1.7$ ) by the age of 7 years. It is concluded that, different to serum total IGF-I, serum F IGF-I shows parallelism with growth velocity during the first years of life.

7

SHORT TERM TREATMENT WITH TWO DIFFERENT aLH-RH IN CENTRAL PRECOCIOUS PUBERTY (CPP). E. Boulgourdjian; G. Ropelato; M. Gryngraten; A. Martínez; ME. Escobar; C. Bergada. División de Endocrinología, CEDIE, Htal. de Niños R. Gutiérrez, Bs. As. Argentina.

To analyze the effect of two aLH-RH, Triptorelin (T) dose  $\times 100 \mu\text{g}/\text{Kg}$  and Leuprolide (L) dose  $200-300 \mu\text{g}/\text{Kg}$  administered every 28 days, 25 girls with CPP treated for 0.5-2 years, were studied. Three groups were analyzed: A (n=7) treatment with medroxyprogesterone (MPA) and then T; B (n=11) only T; C (n=7) only L. Secondary sexual development was arrested or decreased in all cases. Urocytogram (mauration index score) decreased in all cases. As there were not significant differences in the baseline levels of LH, FSH and E, A and B were analyzed together.

W/T	1st month		6th month		12th month			
	A+B	C	A+B	C	A+B	C		
LH	$4.0 \pm 4.7$	$2.5 \pm 1.7$	$5.7 \pm 4.1$	$6.0 \pm 4.2$	$3.0 \pm 2.8$	$3.7 \pm 2.5$	$3.8 \pm 3.3$	$8.4 \pm 5$
FSH	$4.4 \pm 2.6$	$2.8 \pm 1.6$	$1.3 \pm 0.8$	$< 1^*$	$1.1 \pm 0.2$	$< 1^*$	$1.2 \pm 4.0$	$< 1^*$
E	$47 \pm 31$	$28 \pm 10$	$13 \pm 4.2$	$9.3 \pm 2.4$	$12 \pm 4.8$	$11 \pm 3.31$	$3 \pm 6.9$	$11 \pm 5^*$

\*  $p < 0.01$  vs W/T LH and FSH (UI/L) E2 (pg/ml)  
Height velocity decreased in both groups (A and B) after 6 months of therapy (A) and 12 months (B); in the C group the decrease was not significant. The ABA/ACA was  $1.2$ ,  $1.02$  and  $1.06$  after one year treatment in A, B and C group respectively and decreased to  $0.72$  and  $0.71$  at two years of treatment in A and B respectively. The high levels of immunological LH during treatment could be due to the presence of alpha subunit chains not inhibited by the analogue. No differences were found in the effectiveness between the two compared analogues.

10

HEIGHT AND BONE AGE RECOVERY IN ACQUIRED HYPOTHYROID CHILDREN. A. Chiesa, PL. Gruffeiro, A. Keselman, J. Heinrich, C. Bergada. División de Endocrino. Hospital de Niños R. Gutiérrez. B. A., Argentina.

We studied retrospectively 24 acquired hypothyroid children. All of them were prepubertal, well treated, and followed from starting of hormone replacement to final height. They were divided in 2 groups according to the age it starting treatment: Group 1:  $3.09 \pm 0.83$  years (n: 17 15 girls, 2 boys) Group 2:  $9.2 \pm 1.4$  years. (n: 7 6 girls, 1 boy). Bone ages (B.A.) were evaluated with Greulich and Pyle (G) and TWIRUS. In 10 children of groups 1 and 6 of groups 2 final height was compared with target height.

	GROUP 1		n	GROUP 2		n
	Mean	SD		Mean	SD	
Initial Height (H)	$-3.74 \pm 1.2$		17	$-4.10 \pm 1.4$		7
H. onset puberty	$-1.06 \pm 1.1$		17	$-2.80 \pm 1.4$		7
H. menarcho G5	$-0.63 \pm 1.09$		17	$-1.80 \pm 1.2$		7
Final Height	$-0.85 \pm 0.91$		17	$-1.86 \pm 1.2$		7
Target Height	$-1.22 \pm 0.78$		10	$-1.10 \pm 0.95$		6
Initial B.A. (G)	$-4.90 \pm 0.85$		7	$-7.40 \pm 2.9$		6
B.A. onset puberty	$-0.26 \pm 1.74$		7	$-1.65 \pm 1.6$		6
B.A. menarcho (G)	$0$		7	$0$		3
Age onset puberty	$10.3 \pm 1.1$		years 15	$10.6 \pm 0.91$		6
Age menarcho	$13.28 \pm 1.2$		years 15	$13.5 \pm 1.04$		6
B.A. menarcho (TW)	$13.4 \pm 0.3$		years 10	$13.9 \pm 0.25$		3
Onset-menarcho G5	$2.85 \pm 1.2$		years 17	$2.78 \pm 0.16$		7

Target height correlated with final height significantly in Groups 1  $p < 0.02$  and in G2  $p < 0.01$ . (Spearman). We conclude that height recovers and reaches target height in both groups. Puberty developed normally in all patients.