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SUBCUTANEOUS CONTINUOUS ADMINISTRATION OF RECOMBINANT HUMAN LUTEINIZING AND FOLLICLE-STIMULATING HORMONES IS AN EFFECTIVE TREATMENT FOR MICROPENIS DURING MINI-PUBERTY

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Background

- Early postnatal administration of recombinant gonadotropins has been shown to achieve elevated levels of gonadotropins, comparable to those of infants during mini-puberty.
- The stimulation of Leydig and Sertoli cells increases penile length and testicular volume respectively.
- We report the first evidence that this treatment can be effective in partial androgen insensitivity syndrome (PAIS).

Objectives

To evaluate the benefits of continuous subcutaneous infusion of recombinant human gonadotropins (CSCI-HGon) on penile length and hormonal response, in a group of infants with micropenis.

Subjects and Methods

- Prospective study of 6 male patients with micropenis due to isolated CHH (n=4), panhypopituitarism (n=1) and PAIS (n=1) diagnosed during 2011-2012 at Necker University Hospital.
- Continuous subcutaneous infusion of recombinant human gonadotropins (CSCI-HGon) via a pump:
  rLH (Luveris®, Merck Serono) and rFSH (Gonal-F®, Merck Serono).
  Initial infusion rate was 75 IU/24h for both rLH and rFSH and was modified according to hormonal and clinical response.
- Evaluation at baseline, during (monthly) and at the end of the treatment of:
  Clinical: stretched penile length (SPL), testicular position and volume
  Hormonal: testosterone, LH, FSH, AMH and inhibin B
  Radiological parameters: testicular position and size

Results

Patient with PAIS

PAIS was diagnosed during prenatal period (micropenis, hypospadias) and confirmed at birth. A missense mutation in exon 3 of AR was identified (c.1786G>A).
Treatment started at 45 days of life.
High rLH administration (225 IU/24h) increased SPL from 13 to 38 mm, at age of 6 months *(Figure 1).*

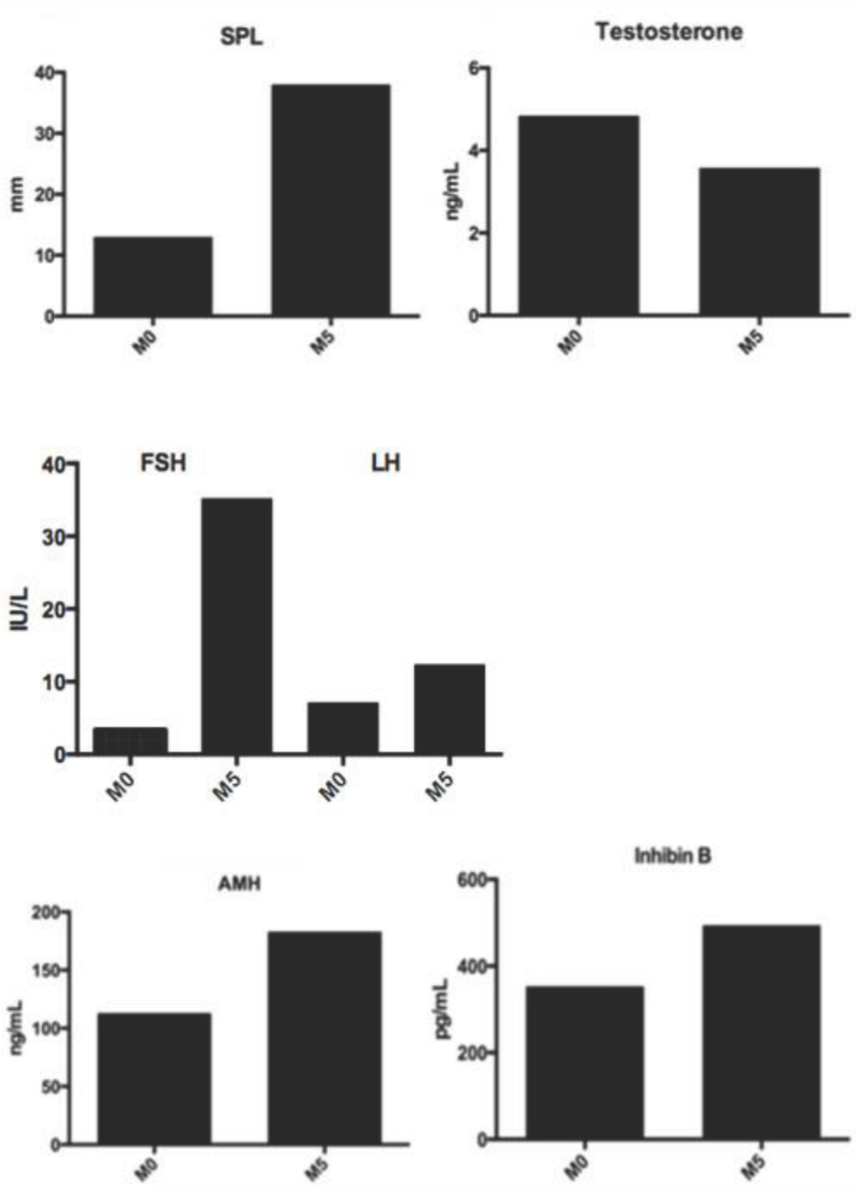

Figure 1: Infant with PAIS, changes in SPL and hormone levels from baseline (M0) to the end of treatment (M5) with continuous rLH and rFSH

Patients with CHH

Mean age at treatment initiation was 4.2±0.9 months and mean duration 4.2±1.2 months. CSCI-HGon increased significantly LH and testosterone, and therefore SPL in 5 patients with CHH.
FSH and Sertoli cell markers (AMH, inhibin B) also responded to treatment *(Table 1).*
No adverse effects were observed during treatment.

	Baseline	End of treatment	*P* value
LH (IU/L)	0.4±0.2	5.4±2.7	0.01
FSH (IU/L)	1.2±1.7	23.1±13.3	0.02
Testosterone (ng/mL)	undetectable	3.5±4.06	NA
AMH (ng/mL)	49.6±30.6	142±76.5	0.03
Inhibin B (pg/mL)	94.8±74.9	469.4±282.5	0.04
Stretched penile length (mm)	13.8±4.5	42.6±5	<0.0001
Right testis size (mm)	11.8±3.6	17.6±7.1	0.2
Left testis size (mm)	11.8±4.1	16.1±3	0.1

Table 1: Hormonal and clinical effects of CSCI-HGon in the 5 patients with CHH

Conclusions

- Our results corroborate previous evidence about beneficial effects of early CSCI-HGon for micropenis in infants with CHH.
- This is the first report regarding its efficacy in PAIS, depending on the genetic anomaly of androgen receptor.
- Whether the benefits extend to the puberty and improve reproductive function and fertility in adulthood needs to be evaluated.

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