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).

Subjects and Methods

- Prospective study of 6 male patients with micro penis 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

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 micro penis.

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).

Results

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.

Conclusions

- Our results corroborate previous evidence about beneficial effects of early CSCI-HGon for micro penis 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.

<table>
<thead>
<tr>
<th>Baseline</th>
<th>End of treatment</th>
<th>P value</th>
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<tbody>
<tr>
<td>LH (IU/L)</td>
<td>0.4±0.2</td>
<td>5.4±2.7</td>
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<tr>
<td>FSH (IU/L)</td>
<td>1.2±1.7</td>
<td>2.3±13.3</td>
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<tr>
<td>Testosterone (nm/L)</td>
<td>undetectable</td>
<td>3.5±4.06</td>
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<tr>
<td>AMH (nm/mL)</td>
<td>49.6±30.6</td>
<td>142±76.5</td>
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<tr>
<td>Inhibin B (pg/mL)</td>
<td>94.8±74.9</td>
<td>469±282.5</td>
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Table 1: Hormonal and clinical effects of CSCI-HGon in the 5 patients with CHH

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