Endocrine and metabolic parameters before onset of rGH treatment: potential predictive factors of rGH response in children born SGA?

Results from cohort of Nancy, France

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 CONTEXT:  
- Children born Small For Gestational Age (SGA) without catch up at 4 years can benefit of rGH treatment to improve adult final height  
- Great variability of response is observed: 15% of unsatisfactory response (Mairaona et al., 2009)  
- Predictive factors described in literature: age at start of treatment, midparental height, rGH dose, bone age retardation, IGF1 levels ... (Ranke et al., 2003; Ranke et al., 2009)

→ We analyze the effects of pretherapeutic data such as weight evolution during first years of life, before onset of treatment, on rGH response in children born SGA.

MATERIAL AND METHOD:  
- Retrospective and monocentric study in Nancy, France  
- Children born SGA, treated by rGH since at least one year in endocrinology unit of University Hospital of Nancy are included  
- Amplitude of rGH response is defined as variation of height (DS) at 1 year, 2 years of treatment, at the end of treatment, and at adult final height  
- Regression analysis, bivariate and multivariate, were performed to calculate regression coefficient (r) for each variable studied

RESULTS:

91 children were included.

Table 1: Clinical cohort description at start of rGH treatment

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Age</td>
<td>37,8</td>
<td>39</td>
<td>3</td>
</tr>
<tr>
<td>Lenght at birth SD</td>
<td>-3,1</td>
<td>-2,8</td>
<td>1</td>
</tr>
<tr>
<td>Midparental height SD</td>
<td>162</td>
<td>162,5</td>
<td>11,9</td>
</tr>
<tr>
<td>Midparental height SD</td>
<td>-0,9</td>
<td>-0,9</td>
<td>0,9</td>
</tr>
<tr>
<td>Age at start of treatment</td>
<td>7,5</td>
<td>6,9</td>
<td>3,2</td>
</tr>
<tr>
<td>Height SD</td>
<td>-3,3</td>
<td>-3,2</td>
<td>0,7</td>
</tr>
<tr>
<td>BMI</td>
<td>15,02</td>
<td>14,9</td>
<td>1,9</td>
</tr>
<tr>
<td>BMI SD</td>
<td>-0,8</td>
<td>-0,9</td>
<td>1,4</td>
</tr>
</tbody>
</table>

Pretherapeutic factors associated with amplitude of rGH response (bivariate analysis):

- At 1 year of treatment (n=91):
  - Paternal height: \( r = 0,03, p = 0,0003 \)
  - Height (DS):  
    - At 9 months: \( r = -0,09; p = 0,01 \)
    - Between 2 and 3 years: \( r = -0,1; p = 0,035 \)
    - Between 3 and 4 years: \( r = -0,12; p = 0,032 \)
  - Age at onset of rGH: \( r = -0,003; p = 0,0103 \)
  - IGF-1 level before rGH: \( r = -0,001, p = 0,0199 \)
  - Bone age at onset of rGH: \( r = -0,08, p = 0,0009 \)

- At 2 years of treatment (n=82):
  - Paternal height: \( r = 0,02, p = 0,0386 \)
  - Pretherapeutic TSH: \( r = 0,09, p = 0,0449 \)
  - Height (DS):  
    - At 9 months: \( r = -0,14; p = 0,028 \)
    - Between 2 and 3 years: \( r = -0,15; p = 0,019 \)
    - Between 3 and 4 years: \( r = -0,25; p = 0,019 \)
  - IGF-1 level before rGH: \( r = -0,004; p = 0,002 \)
  - Age at onset of rGH: \( r = -0,01; p = 0,0033 \)
  - Bone age at onset of rGH: \( r = -0,12; p = 0,0005 \)
  - Height at onset of rGH: \( r = -0,31; p = 0,0035 \)

- At the end of treatment (n=42):  
  - Bone age retardation: \( r = 0,04; p = 0,0046 \)
  - Bone age at onset of rGH: \( r = -0,14; p = 0,034 \)
  - Height (SD) between 2 and 3 years: \( r = -0,42; p = 0,004 \)
  - Height (SD) at onset of rGH: \( r = -0,57; p = 0,0012 \)

- At adult final height (n=16):  
  - Pretherapeutic total cholesterol: \( r = 1,64; p = 0,0341 \)
  - Pretherapeutic cortisol: \( r = 0,02; p = 0,0217 \)
  - T4 at onset of rGH: \( r = -0,31; p = 0,0417 \)

Pretherapeutic factors associated with amplitude of rGH response (multivariate analysis):

- At 2 years of treatment: TSH before onset of rGH: \( r = 1,1; p = 0,0204 \)

CONCLUSION:

- Weight evolution before onset of rGH is not associated with rGH response in our study.
- This study highlights potential role of thyroid hormone in rGH response in children born SGA: SGA phenotype and rGH response may be linked to a global hormonal resistance.
- Others results are consistent with literature such as age at start of treatment, IGF-1 level, bone age,...