

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



Authors : E. RENARD, C. LEGAGNEUR, J. AUGER, B. LEBON LABICH, C. BAUMANN, B. LEHEUP
Endocrinology Unit, Children Hospital, University Hospital of Nancy, France



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 (Mairona *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 1 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

| | Mean | Median | Standard deviation |
|---------------------------|-------|--------|--------------------|
| Gestational Age | 37,8 | 39 | 3 |
| Length at birth SD | -3,1 | -2,8 | 1 |
| Midparental height | 162 | 162,5 | 11,9 |
| Midparental height SD | -0,9 | -0,9 | 0,9 |
| Age at start of treatment | 7,5 | 6,9 | 3,2 |
| Height SD | -3,3 | -3,2 | 0,7 |
| BMI | 15,02 | 14,9 | 1,9 |
| BMI SD | -0,8 | -0,9 | 1,4 |

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

Table 2 : rGH response after 1 year, 2 years and at the end of treatment

| | n | Mean | Median | Standard deviation |
|---|----|------|--------|--------------------|
| Height SD after 1 year of treatment | 87 | -2,6 | 2,6 | 0,8 |
| Height SD gain after 1 year of treatment | 90 | 0,8 | 0,7 | 0,7 |
| Height SD gain after 2 years of treatment | 80 | -2,2 | -2,1 | 0,8 |
| Height SD gain after 2 years of treatment | 80 | 1,1 | 0,6 | 1 |
| Height SD gain at the end of treatment | 42 | -2,1 | -2 | 0,8 |
| Height SD gain at the end of treatment | 42 | 1,2 | 1,2 | 1,2 |
| Adult final height SD | 16 | -2,7 | -2,8 | 1,3 |
| Height SD gain at adult final height | 16 | 0,4 | 0,3 | 1,4 |

- 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,...

BIBLIOGRAPHY :

Maiorana A, Cianfarani S. Impact of growth hormone therapy on adult height of children born small for gestational age. *Pediatrics*. 2009 Sep;124(3):e519-31.
Ranke MB, Lindberg A, Cowell CT, Wikland KA, Reiter EO, Wilton P, Price DA; KIGS International Board. Prediction of response to growth hormone treatment in short children born small for gestational age: analysis of data from KIGS (Pharmacia International Growth Database). *J Clin Endocrinol Metab*. 2003 Jan;88(1):125-31.
Ranke MB, Lindberg A. Predicting growth in response to growth hormone treatment. *Growth Horm IGF Res*. 2009 Feb;19(1):1-11.

