CRITERIA FOR FIRST-YEAR GROWTH RESPONSE TO GROWTH HORMONE TREATMENT IN PREPUBERTAL CHILDREN WITH GROWTH HORMONE DEFICIENCY: DO THEY PREDICT POOR ADULT HEIGHT OUTCOME?

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1. Background / Aim

Several criteria for first-year growth response (FYGR) to growth hormone (GH) treatment have been proposed. We explored which FYGR criteria predicted best a poor final height outcome after GH treatment in prepubertal children with GH deficiency (GHD).

2. Subjects and methods

Height data of 129 (non acquired) GHD children (83 boys) who attained adult height and had been treated with GH for at least 4 consecutive years with at least 1 year before pubertal onset, were retrieved from the Belgian GH Registry.

First-year growth response (FYGR) parameters were: (1) increase in height (∆Ht) SDS, (2) height velocity (HV) SDS, (3) ∆HV (cm/year), (4) index of responsiveness (IoR) in KIGS prediction models1, (5) first-year HV SDS based on the KIGS expected HV curve (HV KIGS SDS), (6) near final adult height (nFAH) prediction after first-year GH treatment.

Poor final height outcome (PFHO) criteria were: (1) total ∆Ht SDS < 1.0, (2) nFAH SDS < -2.0, (3) nFAH minus midparental height (MPH) SDS < -1.3.

ROC curve analyses were performed to define the optimal cut-off for FYGR parameters to detect PFHO. Only ROC curves with an area under the curve (AUC) of more than 70% were further analyzed.

3. Results

• Characteristics (mean): age at start 6.8 years, height SDS at start -3.31, duration of GH treatment 9.7 years, total ∆Ht SDS 2.23, nFAH SDS -1.17, nFAH minus MPH SDS -0.16

• PFHO: total ∆Ht SDS < 1: 12%, nFAH SDS < -2: 22%, nFAH minus MPH SDS < -1.3: 10%

• The currently used FYGR criteria (in bold tables) had low specificities and sensitivities to detect PFHO (table 1 + 2) (no results presented for nFAH minus MPH SDS < -1.3 as all AUC’s were <70%).

• To obtain a 95% specificity, the cut-off value (and sensitivity) of FYGR parameters were:

- ∆Ht SDS < 0.35 (40%), HV SDS < -0.85 (43%), ∆HV < 1.3 cm/year (36%), IoR < -1.57 (17%), HV KIGS SDS < -0.83 (40%) to predict total ∆Ht SDS < 1
- predicted nFAH SDS (with GH peak) < -1.94 (25%), predicted nFAH SDS (without GH peak) < -2.02 (25%) to predict nFAH SDS < -2

• At these cut-offs, the amount of correctly diagnosed poor final responders equals the amount of false positives.

Table 1. ROC curve analysis: cut-off values for first-year response and responsiveness parameters, with their sensitivity and specificity to predict total ∆Ht SDS < 1 (%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cut-off value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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</thead>
<tbody>
<tr>
<td>∆Ht SDS</td>
<td>0.35 (40%)</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>HV SDS</td>
<td>-0.85 (43%)</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>∆HV</td>
<td>1.3 (36%)</td>
<td>57</td>
<td>100</td>
</tr>
<tr>
<td>IoR</td>
<td>-1.57 (17%)</td>
<td>57</td>
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</table>

Example: first-year ∆Ht SDS < 0.5 has a sensitivity of 60% and a specificity of 86% to predict total ∆Ht SDS < 1.

Sens 60% = 60% of poor final responders (FR) has a poor first-year response (FYR), 40% of poor FR has a good FYR. Spec 86% = 86% of good FR has a good FYR, 14% of good FR has a poor FYR.

4. Conclusion

First-year growth response criteria perform poorly as predictors of poor final height outcome after long-term GH treatment in prepubertal GHD children.


Acknowledgements: The authors express their thanks to all patients, parents and to all BESPEED members who provided data.

The 58th Annual ESPE Meeting, 19-21 September 2019, Vienna, Austria