Adherence to Growth Hormone Treatment: Impact of Height, Age, and Puberty

J Rothermel¹, J Scheitel², N Nazari³, B-P. Hauffa⁴, T Reinehr⁵

¹Department of Pediatric Endocrinology, Diabetes and Nutrition Medicine, Venlocher Hospital for Children and Adolescents Datteln, University of Witten/Herdecke, Datteln, Germany; ²GSK Gesellschaft für Therapieforschung mbH Munich, Germany; ³Merck Serono, Germany; ⁴Department of Pediatric Endocrinology and Diabetology, University Children’s Hospital, University Duisburg-Essen, Germany

Introduction

- Maintaining adherence to growth hormone treatment is difficult, because the burden of daily drug administration is often more apparent than the long-term benefits of therapy.
- Studies about treatment adherence (TA) to recombinant human growth hormone are rare and the results are controversial.
- The aim of our study was to identify factors that influence TA.

Methods

- The easygo® device was developed for the administration of rhGH; it automatically records the date, injected dose (mg) and injection status.
- All patients treated with easygo® in the Observational Study Saison—online study (an online prospective, multicentre, open-label, non-interventional study) with treatment data over at least 6 months and age, height and pubertal stage data available were included in our study.
- We analysed TA in 6-month periods. TA was evaluated using cut-offs (good adherence: <1 missed dose/week; medium adherence: 1–3 missed doses/week; poor adherence: >3 missed doses/week). The characteristics of the children are shown in Table 1.

Table 1. Characteristics of the 168 children treated with rhGH in this study

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td></td>
</tr>
<tr>
<td>Growth hormone deficiency: n=119</td>
<td></td>
</tr>
<tr>
<td>6-month observation periods: 462</td>
<td></td>
</tr>
<tr>
<td>6-months observation periods: 44</td>
<td></td>
</tr>
<tr>
<td>Chronic renal insufficiency: n=3</td>
<td></td>
</tr>
<tr>
<td>6-month observation periods: 14</td>
<td></td>
</tr>
<tr>
<td>SGA: n=34</td>
<td></td>
</tr>
<tr>
<td>6-month observation periods: 21</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>11.6 [IQR 9.9 – 13.9]</td>
</tr>
<tr>
<td>Gender</td>
<td>61.9% male</td>
</tr>
<tr>
<td>Pubertal Stage</td>
<td>67.1% prepubertal</td>
</tr>
<tr>
<td>Height – SDS</td>
<td>−2.0 [IQR −2.5 – 1.2]</td>
</tr>
<tr>
<td>Delta height-SDS between actual height-SDS and height-SDS at onset of treatment</td>
<td>0.4 [IQR 0.0 – 1.1]</td>
</tr>
<tr>
<td>Treatment duration (years)</td>
<td>0.9 [IQR 0.3 – 3.0]</td>
</tr>
</tbody>
</table>

Results

- 168 children treated with rhGH (71% growth hormone deficiency, 7% Turner-Syndrome, 24% chronic renal insufficiency, 20% small-for-gestational age) were included (641 6-month observation periods).
- TA did not differ significantly between treatment indications (p=0.713) or gender (p=0.167).
- Younger age, prepubertal stage, and lower height-SDS were associated with better TA, while better treatment success and longer treatment duration were related to lower TA (Table 2, Figures 1, 2).

Table 2. Influence factors on treatment adherence

<table>
<thead>
<tr>
<th></th>
<th>Good adherence</th>
<th>Medium adherence</th>
<th>Poor adherence</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of 6-month observation periods</td>
<td>373 (58.2%)</td>
<td>135 (21.1%)</td>
<td>133 (20.7%)</td>
<td>&lt;0.001²,³</td>
</tr>
<tr>
<td>Age (years)</td>
<td>11.6 ±3.2</td>
<td>13.4 ±3.1</td>
<td>12.0 ±3.1</td>
<td>&lt;0.001²,³</td>
</tr>
<tr>
<td>Height – SDS</td>
<td>−1.9 ±1.1</td>
<td>−1.7 ±1.2</td>
<td>−1.3 ±1.3</td>
<td>&lt;0.001²,³,0.038⁴,0.017⁴</td>
</tr>
<tr>
<td>Prepubertal</td>
<td>57.3%</td>
<td>32.2%</td>
<td>48.7%</td>
<td>&lt;0.001²,³,0.012⁴</td>
</tr>
<tr>
<td>Treatment success (actual height-SDS – height-SDS at onset of treatment with easygo®)</td>
<td>+0.8 (IQR 0.2–1.4)</td>
<td>+0.7 (IQR 0.2–1.3)</td>
<td>+1.0 (IQR 0.5–1.5)</td>
<td>0.004²,0.002⁴,0.005⁴</td>
</tr>
<tr>
<td>Treatment duration on easygo® (years)</td>
<td>1.8 (IQR 0.6–3.6)</td>
<td>3.0 (IQR 1.5–4.5)</td>
<td>2.5 (IQR 1.6–3.6)</td>
<td>&lt;0.001²,³</td>
</tr>
</tbody>
</table>

Conclusions

- Good TA was only achieved in approximately half of all 6-month observation periods in children treated with rhGH.
- Prevention and treatment efforts should, therefore, be undertaken to improve TA in GH-treated children.
- Pubertal stage and longer treatment duration seem to be a risk factor for low TA.
- The indication for rhGH treatment and gender were not associated with TA.

Acknowledgments

The trial was sponsored by Merck Serono GmbH®. Germany. The authors would like to thank the patients and their families, investigators, co-investigators and the study teams at each of the participating centres and at Merck Serono GmbH®, Germany. The authors would like to thank the Principal Investigator PD Dr Klaus Hartmann, Frankfurt/Main.

Disclosures

J Rothermel: support for congress participation
K Scheitel: is a current employee of GSK Gesellschaft für Therapieforschung mbH Munich, Germany which received consultancy fees for performing the study.
N Nazari: is a current employee of Merck Serono GmbH®
B-P. Hauffa, T Reinehr: have received consultancy fees from Merck Serono GmbH and are members of advisory boards and the AKES group, which is financially supported by Merck Serono GmbH®.

* An affiliate of Merck KGaA, Darmstadt, Germany