Long-term insulin sensitivity and beta-cell function in short children born SGA treated with GH and GnRHa: Results of a randomized, dose-response trial

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CONCLUSIONS

• Combined GH/GnRHa treatment has no long-term negative effects on insulin sensitivity and β-cell function in young adults compared to only GH
• Started in early puberty, a GH dose of 2mg/m²/day results in a similar insulin sensitivity and β-cell function at AH as GH 1mg/m²/day

Background
Children born SGA can benefit from combined treatment of GH and 2 years of GnRH analogue (GH/GnRHa). GnRHa treatment might have negative effects on insulin sensitivity. Long-term effects of combined GH/GnRHa treatment and GH-dose effects on insulin sensitivity and β-cell function at adult height (AH) are unknown.

Aims
I. To investigate insulin sensitivity and β-cell function during GH treatment, with or without 2 years of additional GnRHa.
II. To assess whether a higher GH dose results in a similar insulin sensitivity and β-cell function at AH.

Results
I. At AH, insulin sensitivity and β-cell function were similar between children treated with combined GH/GnRHa and those treated with GH only
II. A higher GH dose of 2mg/m²/day resulted in a similar insulin sensitivity and β-cell function as GH 1mg/m²/day

I. Insulin sensitivity and β-cell function at AH

<table>
<thead>
<tr>
<th></th>
<th>Total group</th>
<th>GH/GnRHa</th>
<th>GH</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>76</td>
<td>48</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>17.4 (1.2)</td>
<td>17.4 (1.1)</td>
<td>17.4 (1.3)</td>
<td>0.853</td>
</tr>
<tr>
<td>Si x 10⁻⁴/min (mU/l)</td>
<td>6.1 (5.2)</td>
<td>6.8 (5.8)</td>
<td>5.0 (3.9)</td>
<td>0.176</td>
</tr>
<tr>
<td>AIR (mU/l)</td>
<td>706.9 (564.4)</td>
<td>726.3 (516.7)</td>
<td>673.8 (470.2)</td>
<td>0.881</td>
</tr>
<tr>
<td>DI (Si x AIR)</td>
<td>2929.3 (1762.9)</td>
<td>3159.4 (1871.4)</td>
<td>2534.7 (1510.2)</td>
<td>0.066</td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>5.0 (0.5)</td>
<td>5.0 (0.5)</td>
<td>5.1 (0.6)</td>
<td>0.506</td>
</tr>
<tr>
<td>Fasting insulin (mU/l)</td>
<td>13.6 (6.6)</td>
<td>13.6 (7.3)</td>
<td>13.7 (5.2)</td>
<td>0.752</td>
</tr>
</tbody>
</table>

Methods
• 110 short SGA children, 11.4 years at start (59 girls)
• GH treatment until AH, mean follow-up 5.9 years
• At start of puberty
  Height < 140cm → additional GnRHa for 2 yrs
  GH/GnRHa-group: N=67 / GH-group: N=43
  Randomisation to GH 1mg/m²/day (~0.033mg/kg/d)
  or 2mg/m²/day (~0.067mg/kg/d)

II. GH-dose effect on insulin sensitivity and β-cell function in children with GH/GnRHa

FSIGT
Frequently Sampled Intravenous Glucose Tolerance (FSIGT) test to measure insulin sensitivity (SI), acute insulin response (AIR) and β-cell function (disposition index, DI)