Impaired adrenal function in pediatric patients with Diabetes Mellitus type 1 evaluated with low-dose Synacthen test

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Background

- Primary adrenocortical insufficiency (Addison’s disease) is reported to be five more times frequent in adult patients with type 1 diabetes mellitus (T1DM) than in the general population with a multifactorial aetiology involving autoimmune, inflammatory and metabolic mediators.
- Recent data indicate that more than half of children with T1DM show subnormal cortisol response.

Objective

To evaluate adrenal function in pediatric patients with T1DM and correlate these results with demographic and anthropometric data as well as data from metabolic control, presence of severe or recurrent hypoglycemia, other autoimmune diseases and the presence of autoantibodies against adrenal cells.

Methods

Patients with T1DM, aged > 6 years, with no history of corticosteroids or immunosuppressive drugs were assessed with a low-dose Synacthen test.

Results

Thirty-five patients (19 boys and 16 girls) with T1DM and a mean age of 13.26 ± 4.10 years (range: 6-19 years) were finally analyzed. In 30 of them a history of recurrent hypoglycemia was recorded. Mean glycosylated hemoglobin (HbA1c) was 7.60 ± 1.19 and duration of diabetes was 5.46 ± 3.58 years, widely ranging from 1 to 15 years.

In 10 patients (28.57%) a subnormal cortisol response was recorded with predominance in male patients (9 out of 10, p=0.01). No statistical significant difference was observed between patients with normal and sub-normal cortisol response regarding HbA1c levels, age, z-scores of anthropometric parameters (weight, height, BMI), or the presence of other autoimmune diseases. Years since diagnosis were lower in patients with normal compared to those with subnormal response to Synacthen test with a difference that was approaching significance (4.76 ± 3.31 versus 7.20 ± 3.82, p=0.07).

No patient in our study showed positivity to adrenal autoantibodies.

Conclusion

Approximately one-third (1/3) of pediatric patients with T1DM in our study showed subnormal response in low-dose Synacthen test despite the absence of autoantibodies against adrenals and this should be taken into consideration especially when evaluating T1DM patients with recurrent hypoglycemia.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Normal cortisol response</th>
<th>Subnormal cortisol response</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>25 (71.43)</td>
<td>10 (28.57)</td>
<td></td>
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<tr>
<td>Male</td>
<td>10/25 (40%)</td>
<td>9/10 (90%)</td>
<td>0.010</td>
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<tr>
<td>Age (years)</td>
<td>12.80 ± 4.40</td>
<td>14.40 ± 3.17</td>
<td>0.304</td>
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<tr>
<td>Disease duration (years)</td>
<td>4.76 ± 3.31</td>
<td>7.20 ± 3.82</td>
<td>0.075</td>
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<tr>
<td>HbA1c (%)</td>
<td>7.50 ± 1.03</td>
<td>7.85 ± 1.54</td>
<td>0.784</td>
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<tr>
<td>Height Z-score</td>
<td>0.14 ± 0.72</td>
<td>0.27 ± 0.90</td>
<td>0.342</td>
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<tr>
<td>BMI Z-score</td>
<td>0.03 ± 1.10</td>
<td>0.24 ± 0.63</td>
<td>0.674</td>
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</table>

References

4. Cortisol hyporesponsiveness to the low dose ACTH test is a frequent finding in a pediatric population with type 1 diabetes mellitus. Garza X et al, Pediatric Diabetes 2013; 14, 429-434
5. Newly diagnosed T1 diabetes presenting with hypoglycaemia due to simultaneous coexistence of Addison disease: Case report. Glynn et al, Pediatric Diabetes 2014; 15, 464-467
7. Additional autoimmune disease found in 33% of patients at type 1 diabetes onset. Triko et al, Diabetes Care 2011; 34: 1211–1213