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Acarbose as an adjunct in the management of juvenile-onset diabetes

C.S. Bartsocas¹, C. Papachristou², I. Hillebrand³, and C.J. Papadatos¹
¹Second Department of Pediatrics, University of Athens at P. and A. Kyriakou Athens Children's Hospital; ²Bayer, Athens, Greece; and ³Bayer AG, Wuppertal, Federal Republic of Germany

Summary

Regulation of insulin-dependent diabetes with conventional methods of management presents several difficulties and problems. Hypoglycaemic attacks may occur as commonly as severe hyperglycaemic episodes. Therefore, an agent, which decreases the rate of carbohydrate absorption might help to diminish these problems. Acarbose was tested as such an agent on 8 insulin-dependent diabetic children, aged 7-15 years. They were studied for the effect and tolerance of acarbose. Follow-up was based on physical examination, daily urinary glucose determinations and various blood biochemical parameters (glucose, HbA₁c). The effect of the drug was studied on haematological parameters, liver and kidney function tests, serum proteins, Fe, Ca, Na, Mg, etc. No side-effects were reported and acarbose was well tolerated. In conclusion, acarbose should be considered a safe, useful adjunct in the management of juvenile diabetes, because of its effect on stabilizing blood glucose, therefore preventing severe postprandial hyperglycaemia or hypoglycaemic attacks.

Introduction

Regulation of insulin-dependent diabetes with conventional methods of management, i.e., 1 or 2 insulin injections daily, diet and exercise, presents several difficulties and problems particularly in children. Hypoglycaemic attacks may occur as common as severe hyperglycaemic episodes.

A new approach to the treatment of diabetes, obesity, hyperlipaemia, and other disorders due to an imbalance of carbohydrate metabolism may emerge from the therapeutic use of a novel α-glucosidase inhibitor, which has been found to limit intestinal carbohydrate digestion [1, 2]. Since there have
been several studies on adult insulin-dependent and non-insulin-dependent diabetics [3-14], and very few on the effects of the drug on juvenile diabetics [15], this investigation was carried out to determine the effect of acarbose on the daily balance, insulin requirements and possible side-effects in young diabetics.

Materials and methods

Acarbose was tested for its effect and tolerance on 9 insulin-dependent diabetics aged 7-15 years. All but one had diabetes for more than 2 years.

Throughout the 12-week study period dietary intake was regulated to provide a study amount of calories per day.

The research protocol was set so that following an initial clinical check-up, the patients received 3 or 4 placebo tablets daily (2 with breakfast and 1 or 2 with dinner) for 2 weeks. This was then followed with an 8-week period of acarbose administration in a 150- or 200-mg dose divided in 2 (breakfast and dinner). The study ended with another 2-week placebo period.

Haematological and biochemical parameters were investigated at the end of the first placebo period (at 2 weeks) and at the end of acarbose administration (at 10 weeks). These parameters included the following: determination of HbA1c (with the Helena Glycosylated (Fast Fraction) Hemoglobin Quick Column Method); 2-hour postprandial blood glucose and, glucose and protein quantities in 2, 12-hour urine specimens (8.00-20.00 and 20.00-8.00); complete blood count; total serum bilirubin, serum glutamic oxalacetic transaminase (SGOT); serum glutamic pyruvic transaminase (SGPT); alkaline phosphatase; creatinine; urea; uric acid; total protein; iron; calcium and sodium. Patients were asked to test and record their own glucosuria 3 times daily, throughout the placebo- and acarbose-administration periods. To check patient compliance, stool samples were sent once weekly for testing. Therefore, every individual studied acted as his own control. Patients were instructed to report any side-effects, illnesses, changes in insulin-dose requirements, or deviations from their diet.

Results and discussion

Three patients were withdrawn before completion of the study. Preliminary results showed that all patients tolerated the drug well, since no side-effects were reported. Five of the 6 patients who completed the trial reported a marked improvement of their status during acarbose therapy. They 'felt better' and did not present with headaches or any other symptoms related
to severe blood-sugar level deviations. There was an average weight gain of 2.64% (from 41.7 kg to 42.8 kg) during the study. It was remarkable, however, to note a significant reduction (55.6%) of urinary glucose excretion during the 20.00-8.00 period of the study (Table I).

Administration of acarbose had a remarkable effect on the 2-hour postprandial blood sugar level. A 22.5% decrease (from 293 to 227 mg/dl) was noted following the 8 weeks' acarbose administration. The pretreatment figure was quite high and was attributed to the small quantity of short-acting insulin which the patients injected in the mornings with the long-acting insulin in order to avoid hypoglycaemic episodes.

Mean HbA1c levels were 11.33% before treatment. This value decreased 9% to 10.3% following the 8 weeks' acarbose therapy. Liver function studies showed a 21.67% increase of SGOT mean levels (Table II), but this will have to be checked by further studies. No significant changes were observed in kidney function studies (Table III) and various serum minerals and electrolytes (Table IV).

The most important result was that 5 patients were able to decrease, by 11.26%, their daily insulin requirements (from 37 to 32.8 U), while on acarbose.

These preliminary studies confirm a beneficial effect of acarbose in the management of juvenile diabetes. This is obvious by the reduction of HbA1c, the urinary glucose excretion and the daily insulin requirements. Nonetheless,

Table I: Twelve-hour urinary glucose excretion.

<table>
<thead>
<tr>
<th>Time</th>
<th>Before acarbose</th>
<th>After acarbose</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.00-20.00</td>
<td>25.0</td>
<td>22.3</td>
<td>10.8</td>
</tr>
<tr>
<td>20.00-8.00</td>
<td>16.0</td>
<td>10.3</td>
<td>55.6</td>
</tr>
</tbody>
</table>

Table II: Liver function studies.

<table>
<thead>
<tr>
<th>Test</th>
<th>Before acarbose</th>
<th>After acarbose</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>0.97</td>
<td>0.68</td>
<td>30.0</td>
</tr>
<tr>
<td>SGOT (U)</td>
<td>30.0</td>
<td>36.5</td>
<td>21.67</td>
</tr>
<tr>
<td>SGPT (U)</td>
<td>23.0</td>
<td>23.17</td>
<td>NC</td>
</tr>
<tr>
<td>Alkaline phosphatase (U)</td>
<td>57.5</td>
<td>46.17</td>
<td>19.7</td>
</tr>
</tbody>
</table>

NC no change.
Table III: Kidney function studies.

<table>
<thead>
<tr>
<th></th>
<th>Before acarbose</th>
<th>After acarbose</th>
<th>Change (%)</th>
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</thead>
<tbody>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.88</td>
<td>0.92</td>
<td>4.54</td>
</tr>
<tr>
<td>Blood urea (mg/dl)</td>
<td>37.0</td>
<td>32.67</td>
<td>11.71</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>3.37</td>
<td>3.58</td>
<td>6.42</td>
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</table>

Table IV: Mineral and electrolyte studies.

<table>
<thead>
<tr>
<th></th>
<th>Before acarbose</th>
<th>After acarbose</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Fe (mg/dl)</td>
<td>98.0</td>
<td>91.83</td>
<td>6.29</td>
</tr>
<tr>
<td>Serum Ca (mg/dl)</td>
<td>9.47</td>
<td>9.2</td>
<td>2.85</td>
</tr>
<tr>
<td>Serum Na (mEq/l)</td>
<td>136.0</td>
<td>135.0</td>
<td>NC</td>
</tr>
<tr>
<td>Serum K (mEq/l)</td>
<td>3.75</td>
<td>4.32</td>
<td>5.11</td>
</tr>
</tbody>
</table>

NC = no change.

Further studies are required on more subjects, and for a longer period of time in order to confirm this beneficial effect. It is also important to assess the effect of acarbose on hormonal factors, before recommending this drug as a necessary adjunct in insulin-dependent-diabetes mellitus therapy in children.

References


