Effects of the α-Glucosidase Inhibitor 1 Desoxynojirimycin (BAY M 1099) on Postprandial Blood Glucose, Serum Insulin and C-Peptide Levels in Type II Diabetic Patients

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Summary. Bay m 1099 is a newly developed inhibitor of intestinal α-glucosidase. Its ability to lower postprandial plasma glucose, serum insulin and C-peptide levels in Type II diabetics has been investigated. Fifteen obese Type II diabetic patients with inadequate metabolic control during sulphonylurea treatment received a standardized diet and were treated either with Bay m 1099, b.d. (100 mg before breakfast and dinner) or placebo for 3 days, according to a double-blind cross-over design. The postprandial blood glucose level was significantly lower during Bay m 1099 treatment compared to placebo after breakfast and dinner (AUC after breakfast \( p < 0.001 \)). The reduced postprandial hyperglycaemia was associated with a decrease in meal stimulated serum insulin and C-peptide levels. Thus, Bay m 1099 may be a useful addition in the treatment of Type II diabetic patients.

Key words: diabetes mellitus, Bay m 1099; Type II diabetic patients, desoxynojirimycin, α-glucosidase inhibitor, metabolic effects

Modulation of absorption processes by specific enzyme inhibitors that retard the break-down of carbohydrates may represent a new approach to the treatment of diabetes mellitus [1]. The administration of acarbose, an α-glucosidase inhibitor, has been reported to lead to significantly improved metabolic control in Type I and Type II diabetic patients in short- and long-term studies [2].

A new α-glucosidase inhibitor, 1-desoxynojirimycin, Bay m 1099 has recently been developed, using culture liquid from various types of streptomyces and bacilli [3, 4]. Bay m 1099 reduces postprandial plasma glucose and serum insulin levels after carbohydrate ingestion in normal volunteers and it has been suggested that it might improve metabolic control in patients with diabetes mellitus [5].

The aim of the present study was to investigate whether the administration of Bay m 1099 was of benefit in the treatment of obese Type II diabetics. These patients are only poorly controlled on diet plus sulphonylurea treatment and they should not receive insulin.

Subjects and Methods

The study was performed in 15 obese Type II diabetic patients (13 female, 2 male) with inadequate metabolic control (mean HbA1c 9.2 ± 1.2%, SD) during sulphonylurea treatment. The mean age of the study population was 66.8 ± 7.5 years and their mean relative body weight was 120 ± 13%. The mean duration of diabetes was 10.4 ± 5.3 years. All patients were being treated with glibenclamide, mean daily dose 14.2 ± 1.8 mg and it was continued unchanged throughout the study period. All patients gave their informed consent to the study. They were hospitalized one week before the study for stabilization of metabolic control. According to a double blind cross-over design, patients were treated for 3 days either with Bay m 1099 or placebo tablets, with a 1-day washout between treatments.

Blood samples were taken one day before the study began (prevalue) and at the end of each treatment period, always at the same times of day, starting at 8.00 a.m., immediately before breakfast and continuing postprandially for up to 3 hours. The patients had three meals at fixed times, at 8.00 and 12.00 a.m., and 6.00 p.m. The diet consisted of three mixed meals per day, containing 35.52 and 34 g carbohy-
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**Table 1.** Increments above baseline for 3 h of blood glucose after breakfast expressed by the area under curve (AUC) and the 1 h postprandial increase of blood glucose after breakfast, lunch and dinner in 15 obese Type-II diabetics, Bay m 1099 compared to placebo

<table>
<thead>
<tr>
<th></th>
<th>Bay m 1099</th>
<th>Placebo</th>
<th>Bay m 1099 versus placebo: p &lt; 0.001</th>
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<tr>
<td><strong>AUC breakfast</strong></td>
<td></td>
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<tr>
<td>(mean ± SD)</td>
<td>35966 ± 14919 (min × mg/dl)</td>
<td>45857 ± 14175 (min × mg/dl)</td>
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<tr>
<td><strong>One hour p.p. increase (means ± SD, mg/dl)</strong></td>
<td></td>
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<tr>
<td>breakfast</td>
<td>23 ± 21</td>
<td>92 ± 34</td>
<td></td>
</tr>
<tr>
<td>lunch</td>
<td>24 ± 29</td>
<td>16 ± 21</td>
<td></td>
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<tr>
<td>dinner</td>
<td>-69 ± 40</td>
<td>2.5 ± 51</td>
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</tbody>
</table>

Fig. 1. Effects of Bay m 1099 (100-0-100 mg) on fasting and postprandial blood glucose levels in 15 obese Type-II diabetics (mean values ±SEM represented by vertical bars)

Fig. 2. Effects of Bay m 1099 (100-0-100 mg) on fasting and postprandial C-peptide levels in 15 obese Type-II diabetics (means ± SEM represented by vertical bars)

Fig. 3. Effects of Bay m 1099 (100-0-100 mg) on fasting and postprandial serum insulin concentrations in 15 obese Type II diabetics (means ± SEM represented by vertical bars)

**Results**

**Blood Glucose**

As shown in Fig. 1, diurnal profiles of blood glucose were markedly smoothed during Bay m 1099 treatment compared to placebo, although the fasting blood glucose levels remained unchanged. AUC after breakfast (Table 1) was significantly reduced by Bay m 1099 medication compared to placebo.

drates (1200 kcal, 40% carbohydrates, 40% fat, 20% protein). It was identical on all days when blood samples were taken. Bay m 1099 100 mg (2 tablets of 50 mg) was administered twice daily, together with breakfast and dinner.

Routine clinical and laboratory examinations were performed before and after the study in all patients: Full blood count, blood urea nitrogen, creatinine, uric acid, bilirubin, alkaline phosphatase, glutamic oxalacetic transaminase, glutamic pyruvic transaminase, glutamyl transpeptidase, lactate dehydrogenase, cholesterol, triglycerides, serum electrolytes and electrocardiogram.

Blood glucose was measured by a SMAC (American Monitor Parallel Analyser). Serum insulin and C-peptide levels were determined by standardized radio-immunoassays. HbA1c values were tested by microcolumn chromatography, using an aldimine eliminator.

The 1 h postprandial increases in blood glucose, serum insulin and C-peptide were determined after each meal. The area under the curve (AUC) was calculated for the postprandial rises in blood glucose, serum insulin and C-peptide after breakfast. The data were analysed by analysis of covariance using program BMD P2 V of the University of California, L.A.