Long-term Effects of Water-soluble Corn Bran Hemicellulose on Glucose Tolerance in Obese and Non-obese Patients: Improved Insulin Sensitivity and Glucose Metabolism in Obese Subjects

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We examined the effect of soluble corn bran hemicellulose (CBH, 10 g/day) on glucose control and serum insulin in three groups: patients with impaired glucose tolerance (IGT) with (20 subjects) or without (8 subjects) obesity and with healthy non-obese controls (10 subjects). Long-term supplementation (6 months) with CBH decreased the post oGTT curve for patients with impaired mild Type II diabetes, but not that for the controls. Hemoglobin A1c decreased significantly during CBH supplementation in the obese patients, while the fasting glucose level decreased in all three groups, although not significantly. A decreased serum insulin response by oGTT was found in those patients with IGT.

The improved oGTT result was associated with improved insulin release and perhaps with peripheral insulin sensitivity. These findings suggest that CBH at a low dose might contribute to glycemic control and would play a useful role in treating Type II diabetes patients.

Key words: insulin resistance; obesity; dietary fiber

Obesity is a well-known risk factor for non-insulin-dependent (Type II) diabetes mellitus (NIDDM) patients. Many investigators have shown that tissue sensitivity to insulin declined by 30-40% when an individual became >35-40% above the ideal body weight.1,2) The sequence of events for obese diabetic individuals has been confirmed by a prospective follow-up of the same subjects who were subsequently restudied several years later.3) Normal-weight NIDDM individuals are also characterized by their insulin resistance.4) However, as opposed to obesity, where the defect in insulin action is acquired, the insulin resistance is genetically transmitted in patients with NIDDM.

The severity of the insulin resistance in NIDDM patients is of similar magnitude to that observed in non-diabetic obese subjects. From the standpoint of the insulin effect, it is difficult to distinguish between the non-diabetic obese individuals and patients of normal weight with NIDDM. What distinguishes the two groups is their plasma insulin concentration. In NIDDM patients of normal weight, the plasma insulin response, although higher compared with that in normal-weight control subjects, is significantly less compared with that in non-diabetic obese subjects.

High-fiber diets offer many health benefits for diabetic individuals. Jenkins has reported that incorporating such water-soluble fiber as guar or pectin into meal decreased the postprandial glycemic and serum insulin responses compared with those resulting from fiber-free meals.5) The aim of the present study is to investigate the long-term effects of water-soluble hemicellulose on glucose metabolism and insulin response in obese and non-obese patients with impaired glucose tolerance.

Subjects and Methods
In the present study, the usual diet for each group of patients with impaired glucose tolerance with (ten males and ten females) or without (four males and four females) obesity and for healthy volunteers (six males and four females) was supplemented with ten grams/day of CBH for 6 months (Table I). Obesity is defined here as patients whose BMI (body mass index) is higher than 26.4. None of the subjects was undergoing medical treatment, all worked full-time and none exercised regularly. Table I shows the clinical characteristics of the patients and control subjects. They were informed of the details of the aims, contents and methods of the study, and consented to participate in this study of their own free will.

Study Design
All subjects participated for one year, and the ingestion period was assigned for 6 months. CBH was given at a dose of five grams twice a day with meals. The control period (without CBH) was the 6-month period following ingestion. Body weight and height were measured and blood samples were collected on entry into the study and at 3, 6, and 12 months after the beginning of the study; 75-g oGTT was performed and the serum glucose level, insulin response, and HbA1c were examined at each time point. The subjects were asked not to alter their regular diet and physical activity habits at any time during the study period.

Nutrition Survey
Dietary contents were recorded on case cards immediately after each meal by the subjects (obese patients) themselves for three days before entry and after 3 months of CBH supplementation. Breakfast, lunch, and supper were separately recorded on the card, as well as snacks and beverages. The results of the nutrition survey were calculated by the NUT version 3.0 program (Human Science Laboratory).

Material
The water-soluble hemicellulose used in this study was extracted from corn bran (Nihon Shokuhin Kako Co., Tokyo, Japan) by the method of Ayano et al. with a slight modification.6) This soluble CBH consisted mainly of 1-arabinono-o-xylan, and its molecular weight was estimated to be about 10^3 by the gel-filtration method. Mean values and SEs were

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Abbreviations: CBH, corn bran hemicellulose; IGT, impaired glucose tolerance; oGTT, oral glucose tolerance test; NIDDM, non-insulin-dependent diabetes mellitus.
Table I. Anthropometric Data for Each Group

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<tr>
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<th>IGT (-)</th>
<th>IGT (+)</th>
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<tr>
<td></td>
<td>Control (non-obese)</td>
<td>Non-obese</td>
</tr>
<tr>
<td></td>
<td>20 ≤ BMI &lt; 24</td>
<td>20 ≤ BMI &lt; 24</td>
</tr>
<tr>
<td>N (M/F)</td>
<td>10 (6/4)</td>
<td>8 (4/4)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>Before CBH intake</td>
<td>Before CBH intake</td>
</tr>
<tr>
<td></td>
<td>58.1 ± 4.6</td>
<td>56.1 ± 5.3</td>
</tr>
<tr>
<td></td>
<td>6 months after</td>
<td>6 months after</td>
</tr>
<tr>
<td></td>
<td>57.2 ± 3.8</td>
<td>54.8 ± 4.9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.7 ± 5.8</td>
<td>158.8 ± 5.2</td>
</tr>
<tr>
<td>(35–68 y)</td>
<td>48.7 ± 5.9</td>
<td>57.5 ± 8.1</td>
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N.S.

Table II. Mean Daily Intake of Nutrients

<table>
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<tr>
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<th>Non-obese (N=8)</th>
<th>Obese (N=10)</th>
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<tr>
<td></td>
<td>Before</td>
<td>Fiber diet</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>1620 ± 265</td>
<td>1586 ± 248</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>62.4 ± 6.8</td>
<td>58.9 ± 7.4</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>37.7 ± 5.2</td>
<td>34.3 ± 7.1</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>243 ± 26</td>
<td>254 ± 36</td>
</tr>
<tr>
<td>Dietary fiber (g)</td>
<td>16.8 ± 1.9</td>
<td>25.9 ± 2.6</td>
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calculated by conventional methods, and Friedman’s two-way analysis of variance and a paired t-test were used for statistical analyses.

Results

Nutritional survey

Table II shows the mean values for each nutritional component taken by patients with IGT before and 3 months after the start of supplementation with CBH (Table II). Throughout the test period, the intake of energy, protein, fat and carbohydrate exhibited no significant differences compared with the corresponding values before CBH ingestion. The values for dietary fiber, however, differed significantly (p < 0.01) from those before fiber supplementation in both groups. Consistent with this, the body weight remained constant throughout the 6 months of the study.

Glucose response to oral glucose tolerance testing

The serum glucose response by the subjects of each group to a 75-g oral glucose loading are presented in Fig. 1 (Fig. I). The glucose response curves before supplementation with CBH in those subjects with impaired glucose tolerance revealed an abnormal glucose tolerance: their mean (± SE) serum glucose concentrations at 120 min after ingesting 75 g of glucose were 186 ± 27 (obese subjects) and 172 ± 31 (non-obese subjects). After 6 months on the usual diet supplemented with CBH, the glucose intolerance in the obese subjects had improved, with mean glucose concentrations at 60, 90, and 120 min after ingesting 75 g of glucose of 190 ± 34, 168 ± 31, and 131 ± 22 mg/dl, respectively (open circles). In the non-obese patients (N = 8), the glucose response curves had also improved significantly from 225 ± 28 mg/dl to 176 ± 25 mg/dl at 90 min after ingesting 75 g of glucose. However, there was no difference in the glucose response curves between the periods with and without fiber supplementation in the control subjects without impaired glucose tolerance (n = 8). Six months after discontinuing the CBH ingestion, the improvement in glucose tolerance had been lost (data not shown).

Effect of the fiber diet on HbA1c

The changes in HbA1c were similar to those exhibited by the glucose tolerance curves (Fig. 2). Although HbA1c did not change significantly when the non-obese group and control group ingested CBH, HbA1c in the obese group fell significantly (p < 0.05) to 6.3 ± 0.2% 6 months after entry from 6.8 ± 0.2% before entry. An increase in HbA1c was recognized at 6 months after ceasing the fiber treatment in all groups; moreover, HbA1c in the obese subjects did not differ significantly from that before entry.

Effect of the fiber diet on the serum insulin response

The fasting level of serum insulin in the non-obese and control groups was decreased by CBH supplementation, but not to a significant extent. However, 7 of 20 obese patients were hyperinsulinemic (15 μU/ml >) (Fig. 3). The value for them of 18.8 ± 2.8 μU/ml fell significantly (p < 0.05) to 11.9 ± 3.8 μU/ml after 6 months of supplementation with CBH. The change in mean insulin response to oGTT before fiber supplementation (solid circles) followed a pattern similar to those of glucose, and serum insulin in the fasting obese patients (13.1 ± 3.8 μU/ml) was higher than that in the fasting non-obese (8.9 ± 2.8 μU/ml) and control subjects (8.1 ± 2.3 μU/ml). In the obese patients, supplementation with 10 g of CBH to the usual diet for 6 months resulted in serum insulin levels at 60 min (from 63.7 ± 8 μU/ml to 48 ± 7 μU/ml, p < 0.05) and at 90 min (from 65.8 ± 8 μU/ml to 43 ± 5 μU/ml, p < 0.01) significantly lower than those.
Numerous studies have shown that the plasma glucose and insulin responses to an oral carbohydrate load can be modified by the addition of dietary fiber.\textsuperscript{5,8,9} Furthermore, a number of studies have shown a decreased insulin concentration during guar treatment, both in the fasting and postprandial states, in insulin-resistant patients.\textsuperscript{10-13} It has been pointed out that findings obtained by using the euglycemic clamp technique appear to reflect tissue sensitivity to insulin.\textsuperscript{14} In the present study, supplementation with 10 g of CBH significantly reduced the mean serum glucose and the insulin requirements of those patients with impaired glucose tolerance, especially those who were also obese. Unfortunately, we did not determine the insulin sensitivity by the clamp technique. Since no weight changes were found during the study, the reduced insulin concentration cannot be attributed to weight loss. Therefore, our findings are compatible with the view that the observed reduction in insulin resistance might be related to an enhanced sensitivity to insulin in peripheral tissues. Improvement to the glycosylated hemoglobin concentration (HbA\textsubscript{1c}) occurred despite a simultaneous decrease in the insulin requirements of obese patients being treated with CBH. This finding also indicates improved peripheral insulin sensitivity.

The effects of dietary fiber on carbohydrate metabolism might be related to its composition rather than to the amount consumed.\textsuperscript{15} The type of CBH used in the present study was water-soluble and viscous. The physiological effects of insoluble dietary fiber differ from those of water-soluble dietary fiber.\textsuperscript{16} The viscosity of the fiber, which increases the gastric emptying time and prolongs the intestinal absorption phase of carbohydrates without inducing malabsorption, could be the reason for its efficacy.

Our study was undertaken for a relatively long term (6 months), and the long-term effects of CBH may differ from its short-term effects. It might be supposed that flattening before supplementation. Although the differences did not reach the 5% significance level, the serum insulin levels at 60 min and 90 min in the non-obese group were also below the level before CBH supplementation. In the control subjects, the serum insulin level did not differ before and after treatment with CBH.

Discussion
When a non-diabetic individual consumes excessive calories and gains weight, the body becomes markedly resistant to the effect of insulin. If insulin resistance with compensatory hyperinsulinemia plays a role in the development of NIDDM, atherosclerosis, hypertension, and an abnormal serum lipid profile, the development of anti-diabetic drugs whose primary mechanism of action is to improve the body's sensitivity to insulin would seem to be reasonable.\textsuperscript{7}
of the post-oGTT blood glucose level induced by acute fiber supplementation would be accompanied by less stimulation of islet cells and a compliant reduction of the serum insulin response. If prolonged, this could result in a depression of the basal plasma insulin level, even if not to a significant extent, and improved peripheral sensitivity due to down-regulation.\(^\text{17}\) At 6 months after ceasing the CBH supplementation, however, fasting blood glucose, the post-oGTT glucose curve, fasting serum insulin, the post-oGTT insulin response, and the HbA\(_1c\), glycosylated hemoglobin concentration had all unfortunately returned to their respective levels present before the fiber treatment. Nevertheless, this is the first report concerning the efficacy of long-term supplementation for a new product, water-soluble hemicelulose isolated from corn bran, on impaired glucose tolerance, particularly for patients with mild Type II diabetes.

Takent together, the findings reported here suggest that the CBH could be used in the chronic management of Type II diabetes. A key feature in the present study is the low dose of CBH employed (10 g/day), which was unaccompanied by any of the gastro-enteric side effects that were noted when 15–30 g/day of dietary fiber has been used.\(^\text{18–20}\) This low-dose, long-term administration of CBH to patients with Type II diabetes, particularly those who are obese, resulted in a high degree of compliance and could provide a means for improving blood glucose control and perhaps peripheral insulin sensitivity.

References


