High-Fiber Cereal Reduces Postprandial Insulin Responses in Hyperinsulinemic but not Normoinsulinemic Subjects

Thomas M.S. Wolever, DM, PhD1,2
Janice E. Campbell, MSC1
Daniela Geleva, PhD3
G. Harvey Anderson, PhD1

OBJECTIVE — The objective of this study was to compare the plasma glucose and insulin responses elicited by two ready-to-eat breakfast cereals (one being high and the other being low in cereal fiber) and to see if the differences in response depended on subjects’ fasting plasma insulin.

RESEARCH DESIGN AND METHODS — Nondiabetic men (n = 77) were studied on two occasions after 10- to 14-h overnight fasts. They consumed 25 g of available carbohydrate from high- or low-fiber breakfast cereals in random order with blood taken at intervals for 2 h. Data from the 42 men with high fasting plasma insulin (FPI) on screening (>40 pmol/l) were compared with those from the 35 men with normal FPI (≤40 pmol/l).

RESULTS — Hyperinsulinemic men had significantly higher waist circumference and BMI, lower HDL cholesterol, and a trend toward higher triglycerides than control subjects. All 77 subjects, the incremental area under the glucose response curve (AUC) after high-fiber cereal was 11.8 ± 5.5% (P = 0.036) less than after low-fiber cereal with the reductions being equivalent in the hyperinsulinemic (12.6 ± 8.3%) and control (10.9 ± 9.1%) groups. However, insulin peak rise was reduced by the high-fiber cereal only in hyperinsulinemic men (351 ± 29 vs. 485 ± 55 pmol/l) but not in control subjects (211 ± 20 vs. 220 ± 20 pmol/l, cereal × group interaction P = 0.044). Insulin AUC after the high-fiber cereal, expressed as a percentage of that after low-fiber cereal, was negatively related to FPI (P = 0.009) but not to age, BMI, or waist circumference.

CONCLUSIONS — The high-fiber cereal reduced glucose responses to the same extent in normal and hyperinsulinemic men, but reduced insulin responses only in hyperinsulinemic subjects.

Diabetes Care 27:1281–1285, 2004

Insulin resistance, a decrease in the response of target tissues to insulin, is an important public health issue because it is associated with impaired glucose tolerance (IGT), obesity, hypertension, and cardiovascular disease (1). In individuals with normal blood glucose, insulin resistance is usually associated with a compensatory increase in plasma insulin (2). High plasma insulin may, at least in part, be responsible for the deleterious effects associated with insulin resistance; there is evidence that hyperinsulinemia exacerbates insulin resistance (3) and may increase cardiovascular risk through a variety of mechanisms (4). Thus, it is generally considered that dietary treatments that reduce postprandial plasma insulin are beneficial in the management of insulin resistance (5,6).

Postprandial plasma insulin can be reduced either by reducing carbohydrate intake (7) or by reducing the rate of carbohydrate absorption with α-glucosidase inhibitors (8) or low-glycemic index carbohydrate foods (9). Postprandial glucose and insulin responses have been measured for many hundreds of foods, but usually this has been done either in normal subjects or those with diabetes (10). It is not known if these results can be applied to nondiabetic subjects with insulin resistance. In preliminary studies (unpublished data), we showed that a ready-to-eat breakfast cereal rich in cereal fiber elicited a modestly lower acute glycemic response than a portion of low-fiber cereal containing an equal amount of available carbohydrate. The purpose of this study, therefore, was to determine the effect of the high-fiber cereal on plasma glucose and insulin responses and to see if the effect on glucose and insulin responses was the same in insulin-sensitive and insulin-resistant subjects.

RESEARCH DESIGN AND METHODS — Recruited by a newspaper advertisement from the general population of Toronto, healthy men aged 18–75 years; with BMI 18.5–34 kg/m², with fasting serum triglycerides <10.0 mmol/l; without diabetes (fasting glucose <7.0 mmol/l); who were not taking diuretics, β-blockers, or weight reducing agents; without evidence of gastrointestinal disorders, impaired liver (serum aspartate transaminase >2 times upper limit of normal) or renal (serum creatinine >1.5 mg/dl) disorders.

From the 1Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; the 2Division of Endocrinology and Metabolism, St. Michael’s Hospital, Toronto, Ontario, Canada; and 3General Mills, Minneapolis, Minnesota.

Address correspondence and reprint requests to Thomas MS Wolever, DM, PhD, Department of Nutritional Sciences, 150 College St., Room 316, Toronto, Ontario, Canada M5S 3E2. E-mail: thomas.wolever@utoronto.ca.

Received for publication 5 December 2003 and accepted in revised form 20 February 2004.

T.M.S.W. is employed by Glycaemic Index Testing and has received grant support from General Mills. J.E.C. is employed by Glycaemic Index Testing. G.H.A. has received grant support from and is on an advisory committee for General Mills, Hesz, McDonalds, and the Canadian Sugar Institute.

Abbreviations: AUC, area under the curve; FPI, fasting plasma insulin; GIP, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide-1; IGT, impaired glucose tolerance; RGR, relative glucose response; RIR, relative insulin response.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

© 2004 by the American Diabetes Association.
Insulin response to high-fiber cereal

Table 1—Comparison of subjects with normal and high fasting plasma insulin (FPI) at screening

<table>
<thead>
<tr>
<th></th>
<th>Normal insulin (FPI &lt;41 pmol/l)</th>
<th>High insulin (FPI ≥41 pmol/l)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.4 ± 2.5</td>
<td>40.8 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>90.6 ± 2.5</td>
<td>101.5 ± 1.5</td>
<td>0.0003</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.51 ± 0.59</td>
<td>29.16 ± 0.52</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fasting insulin (pmol/l)</td>
<td>22.8 ± 1.5</td>
<td>62.7 ± 4.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>5.06 ± 0.10</td>
<td>4.93 ± 0.13</td>
<td>NS</td>
</tr>
<tr>
<td>Insulin resistance: HOMA†</td>
<td>0.72 ± 0.05</td>
<td>1.98 ± 0.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>β-Cell function: HOMA (%)</td>
<td>50.2 ± 6.3</td>
<td>166.0 ± 22.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.48 ± 0.17</td>
<td>1.91 ± 0.15</td>
<td>0.066</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>4.87 ± 0.18</td>
<td>5.33 ± 0.12</td>
<td>0.035</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.17 ± 0.18</td>
<td>0.94 ± 0.04</td>
<td>0.0004</td>
</tr>
<tr>
<td>Calculated LDL (mmol/l)</td>
<td>3.02 ± 0.16</td>
<td>3.53 ± 0.12</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Data are means ± SE unless otherwise indicated. *C, Caucasian; SA, South Asian; A, Asian; Af, African; H, Hispanic. †Relative insulin sensitivity and β-cell function calculated from fasting glucose and insulin using the homeostasis assessment model (HOMA) (30).

Results—We recruited 37 control and 42 hyperinsulinemic men. Because of missing data, the results for two control subjects were discarded, leaving a total of 77 subjects (35 control and 42 hyperinsulinemic subjects). Hyperinsulinemic subjects did not differ significantly from control subjects with respect to age or fasting glucose (Table 1). A higher percentage of control subjects compared with hyperinsulinemic subjects were Caucasian (80 vs. 74%), but this was not significant (P > 0.3). Hyperinsulinemic subjects exhibited features consistent with the insulin resistance syndrome, including higher waist circumference and higher BMI than control subjects. Although the difference in serum triglycerides was of borderline significance, hyperinsulinemic subjects had significantly lower HDL cholesterol and higher total and LDL cholesterol concentrations than control subjects.

In all 77 subjects, mean plasma glucose after the high-fiber cereal was significantly lower than after low fiber at 15, 30, 45 (P < 0.01 for all), and 60 min (P = 0.026) and significantly greater than after low fiber at 90 (P = 0.047) and 120 min (P < 0.001) (Fig. 1). Glucose peak rise and AUC after high-fiber cereal were significantly lower than after low fiber (Table 2). The high-fiber cereal elicited an 11.8% lower glucose AUC than the low-fiber ce-
real (relative response 88.2 ± 5.6%; P = 0.036).

Plasma glucose was significantly greater in hyperinsulinemic than control men at fasting and at 60, 90, and 120 min (Fig. 1). Peak rise and AUC tended to be lower in hyperinsulinemic men, although the differences were not significant (Table 2). There was no significant cereal × group interaction for glucose concentrations, peak rise, or AUC, indicating that the differences in glucose response between the high- and low-fiber cereals were the same in hyperinsulinemic as in control subjects. The glycemic response elicited by the high-fiber cereal relative to the low-fiber cereal in hyperinsulinemic men (87.4 ± 8.3%) was not significantly different from that in control subjects (89.1 ± 7.2%). The relative glycemic response of the high-fiber cereal in individual subjects was not related to fasting insulin at screening (Fig. 2).

In all 77 men, plasma insulin was significantly less after the high-fiber cereal at 15 and 30 min (P < 0.01) (Fig. 1). In addition, insulin peak rise and AUC were significantly lower after the high-fiber than the low-fiber cereal (Table 2). Hyperinsulinemic subjects had significantly higher plasma insulin than control subjects at every point in time (Fig. 1) along with significantly higher peak rise and AUC (Table 2). There was a significant cereal × group interaction for plasma insulin at 30 min (P = 0.011) and

![Figure 1](https://example.com/figure1.png)

**Figure 1**—Plasma glucose and insulin responses elicited by the low-fiber (●) or high-fiber (○) test meals in all subjects (left), subjects with normal fasting insulin (middle), or high fasting insulin (right). Data are means ± SE. *Significant main effect of cereal (P < 0.05). **Significant main effect of group (normal versus high insulin; P < 0.05). ***Significant cereal × group interaction (P < 0.05).

![Figure 2](https://example.com/figure2.png)

**Figure 2**—Glucose (top) and insulin (bottom) response AUCs after the high-fiber cereal expressed as a percentage of those after the low-fiber cereal in each subject plotted against FPI at screening. Regression lines are plotted. ○ an outlying value (3.4 × SD from the mean). RGR versus fasting insulin: r = 0.056 (NS). RIR versus fasting insulin: excluding outlier, r = 0.297 (P = 0.009); including outlier, r = 0.240 (P = 0.036).

### Table 2 —Peak rise and incremental area under the curve (AUC) of plasma glucose and insulin after the high- and low-fiber treatments

<table>
<thead>
<tr>
<th></th>
<th>All subjects</th>
<th>High-insulin subjects</th>
<th>Normal-insulin subjects</th>
<th>ANOVA*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low fiber</td>
<td>High fiber</td>
<td>Low fiber</td>
<td>High fiber</td>
</tr>
<tr>
<td>Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak rise (mmol/L)</td>
<td>2.73 ± 0.12</td>
<td>2.06 ± 0.10</td>
<td>2.64 ± 0.15</td>
<td>1.97 ± 0.14</td>
</tr>
<tr>
<td>AUC (mmol×min/l)</td>
<td>130 ± 8</td>
<td>107 ± 7</td>
<td>130 ± 11</td>
<td>102 ± 10</td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak rise (pmol/L)</td>
<td>365 ± 35</td>
<td>287 ± 20</td>
<td>483 ± 55</td>
<td>351 ± 29</td>
</tr>
<tr>
<td>AUC (nmol×min/l)</td>
<td>18.7 ± 1.5</td>
<td>16.6 ± 1.3</td>
<td>24.2 ± 2.2</td>
<td>20.8 ± 2.0</td>
</tr>
</tbody>
</table>

Data are means ± SE. *F and P values for main effects of cereal (low vs. high fiber), group (high vs. normal insulin), and cereal × group interaction by ANOVA.
for insulin peak rise ($P = 0.044$) with the interaction for insulin AUC just missing significance ($P = 0.061$) (Table 2). This indicates that the difference in insulin response between high- and low-fiber cereals differed in hyperinsulinemic and control subjects. In hyperinsulinemic subjects, plasma insulin 30 min after the high-fiber cereal was significantly less than after low fiber ($293 \pm 30$ vs. $486 \pm 58$ pmol/l); however, in control subjects, the respective values were virtually identical ($210 \pm 22$ vs. $211 \pm 21$ pmol/l) (Fig. 1). Similarly, in hyperinsulinemic subjects, insulin peak rise was significantly lower after the high-fiber cereal, but in control subjects, the values were virtually identical (Table 2).

Insulin AUC after the high-fiber cereal was $102 \pm 5.6\%$ that of low-fiber cereal in all 77 subjects ($98.6 \pm 4.4\%$ after excluding a value $5.4 \pm 5.4$ from the mean, which was considered to be an outlier) (Fig. 2). However, the relative response in hyperinsulinemic subjects ($89.9 \pm 5.5\%$) was significantly less than that in control subjects, $108.8 \pm 6.7\%$ (outlier excluded, $P = 0.026$). Also, the relative insulin response in individual subjects was negatively related to their fasting insulin at screening ($r = 0.297$, $P = 0.009$) (Fig. 2). If the outlying point was included in the analysis, the correlation remained significant ($r = 0.240$, $P = 0.036$). Relative insulin response was not related to age ($r = 0.139$, $P = 0.23$), BMI ($r = -0.169$, $P = 0.015$), or waist circumference ($r = -0.147$, $P = 0.021$).

**CONCLUSIONS** —This study shows that a ready-to-eat breakfast cereal rich in cereal fiber elicited lower plasma glucose responses than a low-fiber cereal in both normal and hyperinsulinemic men but reduced postprandial insulin responses only in the hyperinsulinemic subjects. This supports previous assertions that the relative glycemic effects of carbohydrate foods are the same in different subjects (12,13) but suggests that the relative insulinemic effects of foods are not.

Carbohydrates can elicit different glycemic responses because of the nature of the sugars absorbed (e.g., glucose versus fructose) or because of differences in the extent or rate of absorption from the small intestine (14). Differences in the nature of the sugars absorbed cannot explain our results. The low-fiber cereal contained only a small amount more sucrose than the high-fiber cereal (2.5 vs. 0.1 g), and this cannot explain its higher glycemic response. Paradoxically, sucrose-sweetened breakfast cereals elicit lower glycemic responses than unsweetened ones (15) because fructose has a lower glycemic index than glucose (10,16).

After the high-fiber cereal, plasma glucose was reduced at 30 min but increased at 120 min, which is a pattern that suggests delayed carbohydrate absorption. The high-fiber cereal contained corn and wheat fiber, of which $>95\%$ was insoluble fiber. Insoluble cereal fibers are generally considered to have little or no ability to delay glucose absorption (17). It is of interest that adding wheat bran to a 50-g oral glucose load significantly reduced plasma glucose at 30 min to a similar extent as shown here (18); however, bran had no effect on plasma glucose at 120 min. Recently, a high-fiber cereal was shown to reduce plasma glucose responses by increasing postprandial insulin (19). It was suggested this was due to the ~11-g higher protein content of the high-fiber control. However, the protein contents of the cereals we tested here did not differ.

It is possible that the high-fiber cereal contained more slowly digested starch than the low-fiber cereal. Unfortunately, we did not analyze the resistant starch content of the two cereals, although no resistant starch was added as an ingredient. Nevertheless, it seems unlikely that the high-fiber cereal contained significantly more undigested starch, because this would have resulted in a lower intake of available carbohydrate. Reducing available carbohydrate intake results in a more rapid return of postprandial glucose to baseline (16), whereas, here we observed the opposite effect after the high-fiber cereal.

The relative insulin response (RIR) of the high-fiber cereal differed in normal and hyperinsulinemic subjects in the face of virtually identical relative glucose responses (RGR) in the two groups of subjects. This is important because the lack of close correlation between postprandial glucose and insulin responses elicited by different foods is a criticism of the glycemic index and an argument for the need to develop an insulinemic index (20). However, if the RIR of foods varies in different groups of subjects, then insulinemic index values may not be as valid as glycemic index values. We know of only one other study directly comparing the RGR and RIR of carbohydrate test meals in different groups of subjects. The insulin response of a mixed test meal, relative to that of oral glucose, was found to be significantly greater in subjects with IGT than obese normal subjects and even greater in subjects with type 2 diabetes, despite the same RGR in all groups (13). Such differences may be due to defects of insulin secretion in subjects with IGT and type 2 diabetes (21). However, the hyperinsulinemic subjects in the present study had normal glucose tolerance, suggesting that their $\beta$-cells were able to compensate adequately for insulin resistance by secreting more insulin. Therefore, it seems unlikely that a defective $\beta$-cell response to glucose can explain the reduction in RIR we observed in high-insulin subjects.

The rise in plasma insulin after eating is determined partly by its rate of secretion into the bloodstream and partly by its rate of removal from the circulation, both of which may vary over a postprandial time course of several hours (22). Decreased hepatic insulin extraction may contribute to peripheral hyperinsulinemia in insulin-resistant subjects with abdominal obesity (23), such as the hyperinsulinemic men in this study. However, this also cannot explain the difference in RIR. In addition, there is evidence that dietary fat and protein may have abnormal effects on postprandial insulin responses in insulin-resistant subjects (24), but this cannot account for the difference in RIR between hyperinsulinemic and control subjects we observed because the high- and low-fiber test meals contained similar amounts of fat and protein.

Reducing the rate of glucose absorption is associated with a reduced insulin response (25), such as that seen in the hyperinsulinemic subjects after the high-compared with low-fiber cereal. In the control subjects, the early rise in plasma insulin (15 min) was reduced by high fiber; but from 30 to 60 min, mean plasma insulin after high fiber was identical to that after low fiber despite significantly reduced plasma glucose. This suggests that something was enhancing the ability of glucose to increase insulin secretion in control but not hyperinsulinemic subjects. Such a factor could be the hormones of the enteroinsulin axis. As much as 70% of the peripheral insulin response after glucose ingestion is due to the effect of gut hormones on insulin secretion (24). Reducing the rate of glucose absorption reduces postprandial responses of gastric
inhibitory polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) (25), and there is evidence that this occurs in both normal and diabetic individuals (26). However, high-fiber meals with no effect on glycemic response have been shown to increase postprandial GIP (27) and possibly cholecystokinin (28) responses, although the effects on GLP-1 are not known. If the effect of fiber on incretin secretion or the effect of incretins on insulin secretion was reduced in hyperinsulinemic subjects, this could explain why the high-fiber cereal reduced insulin responses in hyperinsulinemic subjects not control subjects. Although this hypothesis is purely speculative, there is some evidence that a high carbohydrate meal elicits lower GLP-1 responses in obese subjects than in age- and sex-matched control subjects (29).

In conclusion, a ready-to-eat breakfast cereal, rich in non viscous cereal fiber, reduced glucose responses to the same extent in normal and diabetic men but reduced insulin responses specifically and solely in the hyperinsulinemic men. Longer-term studies are required before conclusions can be drawn as to whether a high-fiber breakfast cereal has any long-term benefits for the management of insulin resistance or obesity.

Acknowledgments—This study was supported by General Mills (Minneapolis, MN) and the Canadian Institutes of Health Research Grant U/O/P-51599.

References


5. Reaven GM: Do high carbohydrate diets prevent the development or attenuate the manifestations (or both) of syndrome X: a viewpoint strongly against. Curr Opin Lipidol 8:23–27, 1997


