Role of glycemic index and glycemic load in the healthy state, in prediabetes, and in diabetes1–5

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ABSTRACT

The choice of carbohydrate-rich foods in the habitual diet should take into account not only their chemical composition but also their ability to influence postprandial glycemia (glycemic index). Fiber-rich foods generally have a low glycemic index (GI), although not all foods with a low GI necessarily have high fiber content. Several beneficial effects of low-GI, high-fiber diets have been shown, including lower postprandial glucose and insulin responses, an improved lipid profile, and, possibly, reduced insulin resistance. In nondiabetic persons, suggestive evidence is available from epidemiologic studies that a diet based on carbohydrate-rich foods with a low-GI, high-fiber content may protect against diabetes or cardiovascular disease. However, no intervention studies have so far evaluated the potential of low-GI, high-fiber diets to reduce the risk of diabetes, although in studies aimed at diabetes prevention by lifestyle modifications, an increase in fiber consumption was often part of the intervention. In relation to prevention of cardiovascular disease, intervention studies evaluating the effect of a low-GI diet on clinical events are not available; moreover, the results of the few available intervention studies evaluating the effects of GI on the cardiovascular disease risk factor profile are not always concordant. The best evidence of the clinical usefulness of GI is available in diabetic patients in whom low-GI foods have consistently shown beneficial effects on blood glucose control in both the short-term and the long-term. In these patients, low-GI foods are suitable as carbohydrate-rich choices, provided other attributes of the foods are appropriate. Am J Clin Nutr 2008;87(suppl):269S–74S.

KEY WORDS

Diabetes mellitus, cardiovascular disease, prevention, dietary fiber, glycemic index, dietary carbohydrates

POSSIBLE DRAWBACKS OF INCREASING THE AMOUNT OF FAT OR CARBOHYDRATE IN THE HABITUAL DIET

The so-called Mediterranean diet is a model of healthful eating habits for the prevention of coronary artery disease, which is the major cause of premature death and disability in industrialized countries (1, 2). Its main features are a moderate intake of total fat (predominantly monounsaturated fat while consumption of saturated fat and cholesterol-rich foods is low) and a high intake of starch (3). Although this type of diet has beneficial effects on lipid metabolism, its high carbohydrate content might hamper its potentially healthful effects in some population groups, in particular, in patients with diabetes or other conditions associated with insulin resistance (the metabolic syndrome) who are known to be particularly at risk of coronary artery disease (4–6). Dietary carbohydrate increases blood glucose concentrations, particularly in the postprandial period. Therefore, in diabetic patients, particularly those treated with insulin or who have more severe forms of type 2 diabetes, a carbohydrate-rich diet can have detrimental effects on glycemic control, which plays a major role in the development of coronary artery disease and other macrovascular and microvascular complications (7, 8). In parallel with the plasma glucose rise, plasma insulin and triacylglycerol concentrations also tend to increase with a high-carbohydrate diet, along with other cardiovascular disease risk factors (Figure 1) (9).

However, carbohydrate-rich foods represent a heterogeneous category and, therefore, may have a variable effect on energy and substrate metabolism in humans. In particular, it is known that not all carbohydrate-rich foods are equally hyperglycemic; differences in the postprandial blood glucose response to various carbohydrate-containing foods have been shown in both healthy subjects and diabetic patients, even when consumed in portion sizes containing identical amounts of carbohydrate (10–12).

METABOLIC HETEROGENEITY OF CARBOHYDRATE-RICH FOODS

Carbohydrates are traditionally classified as mono-, oligo-, and polysaccharides on the basis of their chemical structure. However, a classification based purely on their chemistry does not provide a true guide to their importance for health. More important seems a classification based on their ability to be digested and absorbed in the small intestine, thereby contributing directly or indirectly to the body carbohydrate pool (glycemic carbohydrates). In this classification, carbohydrates that are not digested and absorbed in the small intestine, namely dietary fiber, are kept separate from glycemic carbohydrates (13).

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Carbohydrates that more strongly influence blood glucose concentrations and other metabolic parameters are those rapidly absorbed from the small intestine; conversely, dietary fiber reaches the colon undigested and there undergoes bacterial degradation. Dietary fiber, which is present in legumes, vegetables, and fruit, as well as in whole-meal cereals, acts on intermediate metabolism by slowing the absorption rate of glucose and fat from the small intestine (Figure 2); moreover, it ferments in the gut and produces short-chain fatty acids than can contribute to the modulation of glucose and lipid metabolism in the liver (14–20).

Carbohydrate-rich foods have also been classified on the basis of their effects on postprandial glycemia, as indicated by their glycemic index (GI). This is calculated by dividing the incremental blood glucose area measured after the ingestion of a portion of a test food containing 50 g carbohydrate by the incremental blood glucose area achieved with a portion of a reference food (glucose or white bread) containing the same amount (50 g) of carbohydrate and expressed as a percentage (21). Fiber-rich foods generally have a low GI, although not all foods with a low GI necessarily have a high fiber content (22–24). Because the postprandial blood glucose response is influenced not only by the GI of the food, but also by the amount of ingested carbohydrate, in epidemiologic studies, the concept of glycemic load (GL), the GI of a specific food multiplied by the amount of carbohydrate contained in an average portion of the food consumed) has been developed to better represent both the quantity and the quality of the carbohydrate consumed. Each unit of dietary GL represents the equivalent glycemic effect of 1 g carbohydrate from white bread, which is used as the reference food (25).

**THE POTENTIAL HEALTHFUL EFFECT OF SELECTING CARBOHYDRATE-RICH FOODS ON THE BASIS OF GI IN NONDIABETIC PERSONS**

Several beneficial effects of low-GI, high-fiber (LGI-HF) diets have been shown at the population level (Table 1). Epidemiologic studies have provided suggestive evidence that a diet in which carbohydrate-rich foods with high fiber and low GI are predominant may contribute to diabetes prevention. The Nurses’ Health Study, which includes 65,173 women followed for 6 y, reports an increased incidence of diabetes in those consuming a diet with a higher GI, especially if consumed in combination with a low intake of cereal fiber. In that study, the relative risk of developing type 2 diabetes was 2.50 (95% CI: 1.14, 5.51) for women with the combination of a high GI and low fiber intake compared with those consuming a diet with a low GI but rich in fiber (26). These results were confirmed in the Health Professionals’ Follow-Up Study (27), but not in the Iowa Women’s Health Study, which includes 35,988 older women who were followed for 6 y. In that study, glycemic load was not associated with the risk of diabetes, although the authors found an inverse relation between fiber intake and incidence of diabetes (28).

The association between low GI or GL and a reduced risk of type 2 diabetes might be mediated by an improvement in insulin resistance, because this condition is recognized as a metabolic derangement predisposing to diabetes in the large majority of individuals at risk. However, in relation to this variable, the available evidence on GI or GL fails to be convincing. The Insulin Resistance Atherosclerosis Study is the first study that tried to evaluate the effect of a higher versus a lower GI or GL diet on insulin sensitivity in a large epidemiologic setting; however, no relation between either GI or GL and insulin sensitivity was observed (29). A larger observational study in Denmark also failed to find any association between GI and insulin resistance as assessed by HOMA (a homeostasis model assessment of insulin resistance based on fasting glucose and insulin values);
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When GI was used instead of GI, however, the former was found to be inversely correlated with HOMA (30).

No intervention studies have so far evaluated the effect of fiber or GI on prevention of diabetes, although the most important intervention studies aiming at lifestyle modifications also included an increase in fiber consumption (most probably associated with a lower GI) in the intervention group (31, 32). Moreover, the evidence that consumption of low-GI foods reduces coronary artery disease and improves the coronary artery disease risk factor profile in the nondiabetic population is not overwhelming. In particular, many but not all epidemiologic studies have shown a direct linear relation between the GI or GL of the habitual diet and the incidence of cardiovascular events; however, so far, no intervention study has been undertaken to test this hypothesis (33–36). Also, in relation to the cardiovascular disease risk factor profile, observational studies show consistently that triacylglycerol concentrations tend to rise and HDL-cholesterol concentrations decline when the GI or GL of the habitual diet increases. Conversely, when these relations have been tested in intervention studies, the effect of the GI or GL on plasma lipid concentrations has been less consistent (36–39).

In relation to body weight regulation, the evidence for a possible role of GI is far from conclusive. As a matter of fact, most short-term, small-scale studies in humans that evaluated the role of GI on body weight control showed a reduction in subsequent hunger or increased satiety after consumption of low-GI compared with high-GI foods; however, it is still controversial whether these short-term changes in satiety persist in the long term and induce or facilitate changes in energy intake that will eventually be translated into weight loss (39, 40). So far, no long-term clinical trials have examined the effects of dietary GI on body weight regulation. Moreover, at the epidemiologic level, a relation between dietary GI and body weight has not been shown consistently (30, 35, 41).

THE EFFECT OF LOW-GI, HIGH-FIBER FOODS IN DIABETIC PATIENTS

The beneficial effects of low-GI foods are more pronounced in diabetic patients than in nondiabetic persons, because the regulation of glucose metabolism is impaired in the former, particularly in the postprandial period, which makes these patients more susceptible to the influence of diet on plasma glucose (Figure 3; 8, 36, 42). However, both supporters and detractors of GI claim that long-term studies are needed to clarify whether it has any relevant effect on the metabolism of diabetic patients; in this respect, particularly important is the evaluation of natural foods with a low GI that also have a high fiber content, because the association between a low dietary GI and the improved health outcomes observed in epidemiologic studies is largely mediated by fiber-rich foods.

To clarify this issue, we undertook a study in a group of unselected patients with type 1 diabetes to evaluate 1) the feasibility in the long-term (6 mo) of a LGI-HF diet composed exclusively of natural foodstuffs that are easily available in ordinary supermarkets and 2) the efficacy of such a diet in relation to blood glucose control and rate of hypoglycemic events (43). The study was based on a randomized, parallel group design. A total of 63 patients with type 1 diabetes were randomly assigned to either the LGI-HF (n = 32) or the high-GI, low-fiber (HGI-LF) diet (n = 31) for 24 wk. The 2 diets, which were composed exclusively of natural foodstuffs, were weight-maintaining and, aside from their GI and fiber content, were similar for all nutrients. Of the 63 study subjects, 29 in the LGI-HF group (91%) and 25 in the HGI-LF group (81%) completed the study. Compared with the HGI-LF diet, after 24 wk, the LGI-HF diet decreased both mean daily blood glucose concentrations (P < 0.05) and the number of hypoglycemic events (P < 0.01) (Figure 4 and Table 2). When compliance with the diet was taken into account, 83% of the subjects consuming the LGI-HF diet and 88% consuming the HGI-LF diet were compliant until completion of the study. In this subgroup, compared with the HGI-LF diet, the LGI-HF diet induced even more clinically relevant effects in relation to mean daily blood glucose concentrations (P < 0.001), glycated hemoglobin (P < 0.05), and number of hypoglycemic events (P < 0.01) (43).

This study shows that in patients with type 1 diabetes, an increased consumption of natural foods with a low GI and rich in dietary fiber is both feasible and effective for blood glucose control in the long term. The diet prescribed was based exclusively on natural foodstuffs (the consumption of any food artificially enriched with fiber was not allowed); in particular, in the experimental diet, an increased consumption of fruit, legumes, and vegetables was encouraged. Along with olive oil, these foods represent the cornerstones of the traditional Mediterranean diet (3, 4).

FIGURE 3. Working hypothesis on the potential mechanisms linking a high glycemic load with the development of type 2 diabetes.

FIGURE 4. Postprandial blood glucose concentrations in patients with type 1 diabetes treated with a low–glycemic index (GI), high-fiber diet or with a high-GI, low-fiber diet (a long-term, 24-wk, randomized controlled study; n = 63 patients) (39).
In the group treated with the LGI-HF diet, the improvement in blood glucose control was paralleled by a sharp reduction in the rate of hypoglycemic events; this result is particularly remarkable and deserves to be underlined (43). As a matter of fact, in patients with type 1 diabetes, any attempt to intensify the hypoglycemic treatment to improve blood glucose control would result almost inevitably in an increased risk of hypoglycemia. By contrast, by increasing the consumption of low-GI and fiber-rich foods, it is possible to improve blood glucose control and at the same time reduce the incidence of hypoglycemic events. Similar results have been obtained with LGI-HF diets in patients with type 2 diabetes, in whom the beneficial effects of this type of diet were also observed in relation to lipid metabolism and insulin sensitivity (44).

**GLUCOSE RESPONSES OF LOW-GI STARCHY FOODS THAT ARE NOT RICH IN FIBER**

Scanty information is available on the metabolic effects of low-GI, carbohydrate-rich foods with low fiber content, because not many foods have these features (45). Indeed, it may be appropriate to screen large numbers of low-fiber starch-rich foods (particularly cereal products) in diabetic patients to enlarge the number of foods with a low GI that can be used in the diabetic diet and to assess the importance of food characteristics able to reduce the effect of food carbohydrates on postprandial blood glucose concentrations.

With this aim, postprandial plasma glucose concentrations were evaluated in a group of patients with type 2 diabetes in response to isoglycemic portions (50 g available carbohydrate) of 3 starch-rich foods: 65 g spaghetti, 90 g white bread, or 285 g potatoes; each was consumed on different days, in random order, as part of a standard meal (46). This study showed that when spaghetti was replaced by a portion of bread containing the same amount of available carbohydrate, the glycemic response (evaluated for 5 h after the meal) increased by as much as 68%. When spaghetti was replaced by potatoes, the glycemic response was 48% higher. These differences cannot be accounted for by variations in any of the food constituents known to influence blood glucose metabolism, because the amount of simple and complex carbohydrate as well as the amount of dietary fiber were similar in the 3 test meals. The results of this study are particularly relevant because, unlike most other studies on this subject, the evaluation of the glycemic response of the different foods was performed within a composite meal. This guarantees that the results are applicable to everyday life.

We have also tried to increase our knowledge of the postprandial responses to other starchy foods typical of the Mediterranean diet and to elucidate the importance of different food characteristics able to influence the GI. To this aim, we have evaluated, in type 2 diabetic patients, plasma glucose responses to 50 g available carbohydrate provided by 90 g white bread and to an equivalent amount of carbohydrate provided by 3 other different starchy foods frequently consumed in Italy: pizza, 85 g; potato dumplings (gnocchi), 165 g; and bread crisps, 60 g. These foods were similar for their nutrient composition but were prepared with different technological processes. The GI of the test foods with use of the white bread (100) scale was 114% for pizza and 104% for bread crisps. In contrast, potato dumplings, a typical potato-wheat food that is often used as a substitute for pasta, were able to reduce glycemia during the whole postprandial period (glycemic index = 74% on the bread scale or 52% on the glucose scale) (47).

Pizza and bread crisps, which are prepared with leavened white wheat flour, elicited a blood glucose response similar to that of white bread, despite the fact that their cooking procedures are very different. Conversely, a significantly lower plasma glucose response was observed after potato dumplings. The GI of the potato dumplings (74%) was lower than that previously reported for freshly boiled potatoes of the same cultivar; this suggests that the low rate of carbohydrate digestion observed for this food is due to the particular way it is prepared, ie, mixing potato and wheat starch. To explain the different effects of the test foods on postprandial glucose metabolism, food characteristics able to reduce α-amylase accessibility and therefore to influence blood glucose response—ie, viscosity, resistant starch and fiber content, physical structure of food—were evaluated. In our study, neither viscosity nor variations in resistant starch, sugars, or dietary fiber justified the reduced influence of potato dumplings on postprandial glycemia. However, scanning electron microscopy showed for this food a compact structure similar to that observed in other low-GI starchy foods. This is consistent with a reduction in the rate of starch accessibility, predominantly as a result of to its compact form. In contrast, for leavened foods, the high porosity caused by the entrapment of gas bubbles that expand during cooking greatly increases the surface exposed to enzyme activity (47).

The evidence that a low-GI diet can improve long-term blood glucose control in diabetic patients, independently of its fiber content, is scanty. The difficulty in performing intervention studies on this subject arises from the limited availability of starchy foods with a low fiber content that have a low GI. This scarcity does not allow sufficient diversification of food choices to be included in the intervention diet and makes compliance difficult. So far, only one study evaluated the effect on glycemic control in
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TABLE 3
Recommendations on glycemic index (GI) by the Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD)

<table>
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<th>Recommendation</th>
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<tr>
<td>● Carbohydrate-rich, low-GI foods are suitable as carbohydrate-rich choices provided other attributes of the foods are appropriate.</td>
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<tr>
<td>● The GI concept should in principle be used to classify carbohydrate-rich foods and is only meaningful when comparing foods within a comparable food group, eg, breads, fruit, and different types of pasta or rice.</td>
</tr>
<tr>
<td>● GI values should not be used in isolation but should be interpreted in relation to other relevant food characteristics, eg, energy, content of other macronutrients, available carbohydrates, and dietary fiber.</td>
</tr>
<tr>
<td>● Despite this qualified support for the use of the GI concept as it relates to natural foods, it should be noted that most studies showing beneficial effects have been relatively short term.</td>
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1 From reference 45.

patients with type 2 diabetes of 2 diets differing solely in their GI and containing the same amounts of nutrients and dietary fiber. Changes in GI were achieved by appropriate food technology, without modifying the chemical composition of the foods. The study showed that after 24 d on the low-GI diet, not only was blood glucose control better but insulin sensitivity, LDL cholesterol, and plasminogen activator inhibitor-1 activity were also improved in comparison with a diet of similar composition but with a high GI, thus suggesting a therapeutic potential of this type of diet in diabetes (48). Other possibilities of reducing GI rely on the addition of fat (which delays gastric emptying) (49) or fructose (which has a very low GI) (50); however, neither of these approaches is advisable because of their obvious potential untoward effects on body weight, insulin sensitivity, and lipid metabolism.

CONCLUSIONS

The GI concept should in principle be used to classify carbohydrate-rich foods and is only meaningful when comparing foods within a comparable food group, ie, breads, fruit, and different types of cereal foods. GI values should not be used in isolation but should be interpreted in relation to other relevant food characteristics, ie, energy content, amount of other macronutrients, available carbohydrates, and dietary fiber. Provided all qualities of the food are taken into account, the available evidence supports the use of GI as a helpful additional marker of which carbohydrate-containing foods to include preferentially in the diet. This is particularly relevant for diabetic patients in whom postprandial glucose regulation is impaired (Table 3) (51).

It is important to note that the window of glycemic index variability in a free-living population is quite narrow and depends on the paucity of low-GI foods so far available. If food technologies will contribute to increasing the availability of low-GI foods, it will probably be easier to implement a low-GI diet at the population level (45). If this were the case, it could be hypothesized, on the basis of the evidence from epidemiologic end mechanistic studies, that the low-GI diet would have a beneficial impact on diabetes and cardiovascular disease prevention (Table 1). However, future research should aim not only at characterizing food technologies apt to produce a larger number of low-GI foods but also at identifying more appropriate markers to assess their functional role in humans. In this respect, it is important to take into account pathophysiologic processes linked, but not confined, to blood glucose regulation (52–54).

For the time being, however, GI and GL are to be considered among the parameters to be used for selecting appropriate foods for the diet of people with diabetes or impaired glucose regulation (Table 3); at the general population level they may be potentially useful for the food choices of people with insulin resistance/metabolic syndrome in whom the impact of dietary carbohydrate on intermediate metabolism is more pronounced (51).

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