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Full Length Research Paper

The new glucose revolution: Is the authoritative guide to the glycemic index the right dietary solution for lifelong health?

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The persistence of an epidemic of obesity, coronary heart disease and type 2 diabetes suggests that new nutritional strategies are needed if the epidemic is to be overcome. A promising nutritional approach suggested by this thematic review is carbohydrate restriction. Under conditions of carbohydrate restriction, fuel sources shift from glucose and fatty acids to fatty acids and ketones, and that *ad libitum*–fed carbohydrate-restricted diets lead to appetite reduction, weight loss, and improvement in surrogate markers of cardiovascular disease. Recent researches focus on the debate among professionals regarding the use of the glycemic index (GI) for meal planning. However, evidence from individual trials about benefits and risks of these diets to achieve weight loss and modify cardiovascular risk factors is preliminary. In epidemic studies, there is limited evidence that a low GI diet is beneficial for a reduced risk of developing diabetes or prevalence of insulin resistance, weight loss or satiety, and other cancers. The GI can be used as an adjunct for the fine tuning of postprandial blood glucose responses, particularly in diabetic patients. Other food/meal-planning interventions have been shown to be more effective than the use of the GI.

Key words: Glycemic index, Glycemic load, macronutrients metabolism, obesity, diabete, coronary heart disease.

INTRODUCTION

Our body is adapted to the diet that our ancestors followed for hundreds of thousands of years, but cannot properly handle "industrial foods", such as refined flour. These mechanically-processed foods flood the blood stream with glucose and provoke an outpouring of insulin. The excess insulin compels the body to burn carbohydrate (CHO), leaving the fat to accumulate in our bodies. The deranged insulin levels can also lead to diabetes and heart disease.

By choosing CHO with more care, we can restrain these outbursts of insulin and encourage the body to burn more fat. Glycemic index (GI) is thus, indeed a revolution to the human diet. The GI describes the ability of specific carbohydrate-rich foods to increase the concentration of glucose in the blood. It is calculated as the incremental area under the blood glucose response curve for the food relative to the incremental area under the blood glucose response curve for a reference food, which is set to be 100. Anything with a GI value of 70 or more is a High-GI food; Moderate-GI foods range from 56 - 69, and Low-GI foods have scores from 0 to 55. Table 1 lists samples of low, moderate, and high GI foods (Murakami et al., 2006; Foster-Powell et al., 2002). Choosing low-GI foods guarantees that we are eating with a low energy density and a high capacity to satisfy our appetites. Watch for it on food labels as the public catches on to the value of this information.

It has been proposed that eating high-GI carbohydrates is associated with increased risk of cardiovascular

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Table 1. Samples of glycemic index (GI) food classification.

High GI (> 70)	Moderate GI (56 - 69)	Low GI (< 55)
White bread	Brown rice	Barley
High sugar cereal	Banana, grapes	Milk, yogurt
Bagel	Ice cream	Beans, chickpeas
Pretzels	Corn tortilla	Tree fruit
Hard candy	Spaghetti	Tomato
Russet potatoes	Corn, peas	Apple
Carrots	Whole wheat bread	Chocolate
Pancakes/waffles	Red potatoes	Peanuts
Glucose, sucrose	Lactose	Orange
Sports drink	Soups	Fructose
Rice	Pizza	Non-starchy vegetable

disease (CVD), type 2 diabetes, and obesity because of postprandial hyperglycemia and hyperinsulinemia related to eating high-GI carbohydrates. Recently the experimental and clinical use of low GI foods has been enthusiastically used for diet counseling of diabetic or hyperlipidemic patients and even normal subjects at risk of CVD. A large number of studies have demonstrated the efficiency of diet counseling as regards the use of low GI foods in these patients (Slama et al., 2006). More striking effects were noted in the improvement of postprandial blood glucose excursions and, consequently, in glycated hemoglobin, in fasting plasma lipids, particularly triglyceride levels and, marginally, total and low density- lipoprotein (LDL) cholesterol

The aim of the present review is to establish whether there is sufficient evidence to support a general recommendation for lowering dietary GI and/or GL at this point in time and to evaluate the long-term effects of GI and GL on the development of lifestyle disease.

RESEARCH METHODOLOGY

Observational, interventional and experimental studies were identified through a literature search in PubMed. The search terms glycemic index or glycemic load and epidemiolog were combined with heart disease, coronary heart disease (CHD), diabetes, insulin, HbA1c, blood lipid, high-density-lipoprotein (HDL), LDL, triacylglycerol (TAG), cholesterol, obesity, respectively. Studies on humans published in English before 2010 were considered. Reference lists in identified papers were cross-checked manually to ensure that all relevant papers were identified. Only studies using a measure of the habitual dietary GI or GL were included.

RESULTS

Metabolic theory

CHO can be classified based on their chemical structure and/or based on their physiological effects. Based on chemical structure, the major dietary CHO groups are: Sugars, starch, and fiber. Defining CHO by chemical structure, however, does not take into account their physiologically differing responses, such as differences in satiety value, gastric emptying times, and effects on glucose and insulin levels. To better define physiological responses, the concept of GI was developed by David Jenkins and colleagues (Jenkins et al., 1981) in 1980 – 1981 at the University of Toronto in their research to find out which foods were best for people with diabetes. The GI is a measure of the effects of CHO on blood glucose levels. CHO that break down rapidly during digestion releasing glucose rapidly into the bloodstream have a high GI; CHO that break down slowly, releasing glucose gradually into the bloodstream, have a low GI. For most people, foods with a low GI have significant health benefits (Jenkins et al., 1981).

The mechanism based on the GI effects on the diabetes milieu is: Increasing postprandial plasma glucose and insulin excursions are assumed to increase the severity of diabetes and to be independent predictors of the risk of atherosclerotic diseases and adiposity. Many possible connections have been found between postprandial events and the development of diabetes complications (Ceriello, 2003). Lowering postprandial plasma glucose and insulin responses are relevant in preventing and managing diabetes mellitus. Therefore, interventions to reduce postprandial plasma glucose and insulin spikes are one of the essential goals in the therapeutic strategy in diabetic patients and could reduce the risk of developing cardiovascular complications (Slama et al., 2006).

It has been hypothesized that the metabolic effect of low-GI foods relates to the rate at which CHO are absorbed from the gut (Wong and Jenkins, 2007). Low-GI foods are characterized by the slower rate of CHO absorption resulting in a lower rise in blood glucose levels. When a glucose solution was sipped at an even rate over 180 min compared with the same amount of glucose taken as a bolus at zero time (Jenkins et al., 1990), a marked economy in insulin secretion and lower serum

free fatty acid (FFA) levels were observed with sipping. A similar improvement is also observed with low-GI meals, where a slower rate of glucose absorption reduces the postprandial rise in gut hormones (e.g., incretins) and the demand for insulin. Furthermore, the prolonged absorption of CHO over time will suppress FFA synthesis (Jenkins et al., 1990; Wolever et al., 1988) and counter-regulatory responses (Jenkins et al., 1990; Ludwig et al., 1999). Over time, with lower FFA concentrations and sustained tissue insulinization, glucose is withdrawn from the circulation at a faster rate. As a result, blood glucose concentrations return toward baseline despite continous glucose absorption from gut. Therefore, a reduction in the rise in peak postprandial and incremental area under the curve for blood glucose is observed. Furthermore, there is a "second meal" effect such that an intravenous glucose tolerance test shows more rapid uptake of glucose after sipping than after the bolus drink (Jenkins et al., 1990).

In practice, the actual CHO load from a normal portion varies considerably. It is well known now that both type and amount of CHO influence the glycemic response (Wolever and Mehling, 2003; Barclay et al., 2005). In order to address this problem, the concept of glycemic load (GL) was introduced. GL calculated as the amount of CHO in one serving multiplied by the GI of the food, allows comparisons of the likely glycemic effects of realistic portions of different foods (Schulz et al., 2004).

Supporting/refuting research

It is likely that most people already eat a moderate GI diet. In the Nurses Health Study, the lowest quintile of GI for women was 64 and in the highest quintile 77, a difference of only 13 units (Salmeron et al., 1997b). In the Health Professional Study, GI was 65 in the lowest quintile for men and 79 in the highest, again a difference of only 14 units (Salmeron et al., 1997a). In the Insulin Resistance and Atherosclerosis Study, the average caloric intake was reported to be 1,987 kcal/day with 220 g/day of digestible carbohydrate, 19 g/day of fiber, and an average GI of 58 and an average GL of 128 (Leise et al., 2005). It is unknown if further lowering of the GI can be achieved in a long-term. Such small differences suggest that it may be both impractical and unreasonable to drive the GI down in the general population. In the only 1-year study published thus far, one group of individuals attempted to follow a low GI diet while the other group ate their usual foods (Gilbertson et al., 2001). At the end of the year there was no significant difference in the GI between groups.

The major problem is the reproducibility and variability of the glucose response. Reproducibility of the glucose response in the same subject has not been adequately studied, and the individual blood glucose response to any food or meal is highly variable, both within and between individuals – ranging from 23 to 54% (Pi-Sunyer, 2002; Wolever et al., 1998). Another major problem is that the GI is not the best indicator of healthy food choices. Although many healthy foods have a low GI (whole grains, fruits, vegetables, legumes, dairy products), there are also foods of questionable value with low or moderate GI values. For example, soft drinks, candies, sugars, and high fat foods fall into this questionable category. The GI of foods can be lowered by adding or substituting sugars, especially fructose, sugar alcohols, or fat.

In addition, the insulin response to a given food is not linear and is not consistently related to either the carbohydrate content or glycemic effect of food (Holt et al., 1997). Postprandial insulin responses to isocaloric amounts of food are not closely related to either the carbohydrate content or the glycemic effects of food; the glycemic response accounts for only 23% of the variability in insulin (Holt et al., 1997). Thus, GI may not be a good marker to predict insulin response.

GI/GL and obesity controversy

Although Brand-Miller et al. (2006) in their popular diet book promotes the use of low GI foods in their diets, there is minimal evidence to suggest that a low GI diet contributes to weight loss. The diet book claims that high GI foods are digested rapidly causing blood glucose to surge, and an over secretion of insulin, both contributing to insulin resistance, increased appetite, overeating, and weight gain. However, Table 2 showed that the contributions of low GI to weight loss were really minor. Although subjects may report feeling more satisfied after consuming different meals, this does not always translate into eating fewer calories. For example, Stubbs et al. (1996) in a 1-day study reported that although subjective hunger was less after a high protein breakfast compared to a high fat or high carbohydrate breakfast, lunch time intake 5 h later and energy intake for the rest of the day were similar after all three breakfasts. Currently the majority of research on satiety is very short-term and the effect of satiety on future calorie intake is rarely studied.

GI/GL and diabetes

Early epidemiological studies suggest that a low GI/GL diet may play a role in the prevention of diabetes (Salmeron et al., 1997a, b). Although different CHO do produce differing glycemic responses, to be of benefit clinically, this benefit should translate into long term improvements in glycemia or lipids. Table 3 summarizes the outcomes from later studies and from different countries other than the United States. There are controversial evidences that people with diabetes can in

Table 2. Recent research articles on the GI and weight loss.

Reference	Duration	Diets	Weight loss difference
Jenkins et al., 1985	4 weeks	L-GI vs. L-Fat	L-GI > H-GI
Jenkins and Jenkins, 1987	2 weeks	L-GI vs. H-GI	NS
Jenkins and Jenkins, 1987	4 weeks	L-GI vs. H-GI	L-GI > H-GI
Santacroce et al. ,1987	2 weeks	L-GI vs. H-GI	H-GI > L-GI
Frotvielle et al., 1992	5 weeks	L-GI vs. H-GI	NS
Wolever et al., 1992	6 weeks	L-GI vs. H-GI	NS
Frost et al., 1994	12 weeks	L-GI vs. H-GI	L-GI > H-GI
Slabber et al., 1994	12 weeks	L-GI vs. H-GI	L-GI > H-GI
Raben et al., 1997	2 weeks	L-GI vs. H-GI	H-GI > L-GI
Frost et al., 1998	3 weeks	L-GI vs. H-GI	NS
Luscombe et al., 1999	4 weeks	L-GI vs. H-GI	NS
Jarvi et al., 1999	24 weeks	L-GI vs. H-GI	NS
Agus et al., 2000	6 days	L-GI vs. H-GI	NS
Giacco et al., 2000	24 weeks	L-GI vs. H-GI	NS
Spieth et al., 2000	4 months	L-GI vs. L-Fat	L-GI > L-Fat
Ebbing et al., 2003	6 months	L-GI vs. H-GI	NS
Frost et al., 2004	12 weeks	L-GI vs. L-Fat	NS
Sloth et al., 2004	10 weeks	L-GI vs. H-GI	NS
Alfenas and Mattes 2005	8 days	L-GI vs. H-GI	NS
Raatz et al., 2005	12 weeks	L-GI vs. H-GI vs. H-Fat	NS
Pittas et al., 2006	24 weeks	L-GI vs. H-GI	L-GI > H-GI
Das et al., 2007	1 year	L-GL vs. H-GL	NS
Sichieri et al., 2007	10 months	L-GI vs. H-GI	NS
Aston et al., 2008	12 weeks	L-GI vs. H-GI	NS
Epidemiology studies	Sample	**Diets**	**Weight/BMI difference**
Jacos et al., 1998	34,492F	L-GI vs. H-GI	L-GI < H-GI
Liu et al., 2000	75, 512F	L-GI vs. H-GI	NS
Van Dam et al., 2000	646M	L-GI vs. H-GI	H-GI < L-GI
Ma et al., 2005	572 M and F	L-GI vs. H-GI	L-GI < H-GI
Sahyoun et al., 2005	2248 M and F	L-GI vs. H-GI	NS
Liese et al., 2006	979 M and F	L-GI vs. H-GI	NS
Hare-Brunn et al., 2006	376 M and F	L-GI vs. H-GI	L-GI < H-GI (Men)

Note: NS- Non significantly different.

the long-term change the GI of their usual diet. In a 1-year study, children in the low GI group did have significantly better HbA1c levels than the group using a CHO exchange diet (Gilbertson et al., 2001). However, the study reported no differences in mean GI between the 2 groups at study end and even the authors stated it was difficult to attribute the difference in HbA1c to diet when there was no apparent difference in the mean GI. The majority of studies comparing low and high GI diets have been short-term. Furthermore, it is likely that most people already eat a moderate GI diet and it is not known if it is necessary changed long-term to a low GI diet.

GI/GL and CHD

Epidemiological studies have suggested that low-GI diets may play a role in reducing the risk of CHD (Dickinson and Brand-Miller, 2005). Low-GI diets have been observed to be negatively associated with high density lipoprotein cholesterol (HDL-C), suggesting that low-GI diets may preserve HDL-C (Ford and Liu, 2001; Frost et al., 1999). In the Women's Health Study, GI was positively associated with C-reactive protein (Liu et al., 2002), a marker for systemic inflammation that is associated with an increase in cardiovasular disease (CVD)

Table 3. Recent research articles on the association between GI and diabetes.

Reference	Sample	Outcomes: Association
Feskens et al., 1994	Zutphen elderly study	GI (Ø)
Salmeron et al., 1997	84,360 F	GI and GL (+)
Salmeron et al., 1997	42, 759 M	GI (+); GL (Ø)
Stevens et al., 2002	Atherosclerosis risk in communities study	GI and GL (Ø)
McKeown et al., 2004	Framingham Offspring Cohort	GI and GL (+)
Schulze et al., 2004	91, 249 F	GI (+); GL (Ø)
Lau et al., 2005	Inter99 Study	GI and GL (Ø)
Sahyoun et al., 2005	2248 M and F	GI (+)in men ; GL (Ø) GI and GL (Ø) in women
Liese et al., 2006	979 M and F	GI and GL (Ø)
Sahyoun et al., 2008	3,075M&F	GI and GL (Ø)
Hardy et al., 2010	13,051F&M	GI and GL (Ø)

Note: (+)- positive association; (Ø)- no association.

Table 4. Recent research articles on the association between GI and heart disease.

Reference	Sample	Outcomes: association
Frost et al., 1999	2,200	GI(+) w/. HDL-C
Liu et al., 2000	75, 512F	GI&GL (+) in women
Van Dam et al., 2000	646M	GI (Ø) in men
Ford and Liu, 2001	13,907MandF	GI&GL (+) w/. HDL-C
Tavani et al., 2003	881	GI&GL (Ø)
Holton et al., 2006	82,802F	GL (+) in women
Beulens et al., 2007	15,714F	GI&dGL (+) in women
Levitan et al., 2007	36, 246M	GI&GL(Ø) in men
Levitan et al., 2009	4, 617M	GI&GL(Ø) in men
Hardy et al., 2010	13,051F&M	GI and GL (+)

Note: (+) - positive association; (Ø) - no association.

risk. Many studies have explored the effect of low-GI diets on coronary heart disease risk factors while some remain conservatives (Table 4) (Hare-Bruun et al., 2008). In one study, plasminogen activator inhibitor-1 (PAI-1) levels, a marker of impaired fibrinolysis, was reduced (Jarvi et al., 1999), and in another concerning hyperlipidemia, 1 month on a low-GI diet reduced LDL-C and triglycerides (TG) in those with higher TG levels, despite no significant difference in body weight (Jenkins and Jenkins, 1987). A low-GL diet has been compared with a low-fat diet during weight loss, where a low-GI diet showed marked improvements in heart disease risk factors such as insulin resistance, TG, C-reactive protein, and blood pressure while subjects consumed the low-GL diet (Pereira et al., 2004). In studies that have assessed its effect on the development of CVD directly, low-GI diets appear to have a protective role. The Nurses' Health Study demonstrated a direct relation between fatal and nonfatal myocardial infarction and GI as well as GL (Liu et al., 2000). On the other hand, no significant association of GI or GL and CHD was seen in the Zutphen study of older men (van Dam et al., 2000).

GI/GL and cancer

Direct associations between GI and colorectal and breast cancer have been observed in epidemiological studies (Table 5) (Salttery et al., 1997; Fransceschi et al., 2001; Augustin et al., 2001). McKeown-Eyssen (1994) and Giovannucci (1995) were among the first to hypothesize a link between hyperinsulinemia and the development of colorectal cancer and possibly other types of cancer such as breast and prostate (Boyd, 2003). This is possibly related to increased insulin-like growth factors in conjunction with a sedentary lifestyle including higher intake of energy and refined carbohydrates and lower intake of fruits and vegetables; however, human data are

Table 5. Recent research articles on the association between GI and cancers.

Cancer type and author	Sample	GI/GL and cancer risk
Breast cancer		
Augustin et al., 2001	2,569 F	GI and GL (+)
Cho et al., 2003	90, 655 F	NA
Jonas et al., 2003	63,307 F	NA
Silvera et al., 2005	49, 613 F	NA
Giles et al., 2006	12, 273 (PM)	NA
Sieri et al., 2007	8,926 F	GI and GL (+)
Larsson et al., 2009	61,433 F	GI and GL (+)
Endometrial cancer		
Folsom et al., 2003	23, 335 F(PM)	NA
Silvera et al., 2005	49, 613 F	NA
Larsson et al., 2007	61, 226 F	GL (+)
Ovarian cancer		
Augustin et al., 2003	3, 442 F	GI and GL (+)
Silvera et al., 2007	49, 613 F	GL (+)
Prostate cancer		
Augustin et al., 2004	2, 556 M	GI and GL (+)
Colorectal cancer		
Higginbotham et al., 2003	39, 876 F	GL (+)
Oh et al., 2003	34, 428 F	NA
McCarl et al., 2006	35, 197	NA
Weijenberg et al., 2007	120, 852 M and F	NA
Strayer et al., 2007	45, 561 F	NA
Larsson et al., 2007	61, 433 M	NA
Gastric cancer		
Augustin et al., 2004	2, 850 M and F	GL (+)
Larsson et al., 2006	61, 433 F	NA
Pancreatic cancer		
Michaud et al., 2002	88, 802 F	NA
Johnson et al., 2005	41, 836 F (PM)	NA
Patel et al., 2007	124, 907 M	NA
Heinan et al., 2008	120, 852F&M	NA

are currently limited. Therefore, low-GI and -GL diets show promise for the prevention and treatment of chronic diseases.

Conclusion

Taken together, the associations between GI or GL and obesity, diabetes, heart disease, or cancers were mixed. The reasons for those inconsistent results are probably due to: (1) GI does not take into consideration other factors besides glycemic response, such as insulin response, which can be more appropriate in representing the effects from some food contents other than CHO; (2) a person's glycemic response varies (not the GI) depending on the kind of food, its ripeness, the length of time it was stored, how it was cooked, and its variety; (3) GI of a food varies from person to person and even in a single individual from day to day, depending on blood glucose levels, insulin resistance, and other factors; (4)

GI of a mixed meal is very difficult to predict. For example, fats and proteins can make a meal sit in the stomach longer, which reduces a food's GI; (5) problems with the GI – methodology and variability; the AUC of GI does not reflect the actual amount of CHO contributed by individual foods in the usual diet.

The evidence from this review is not strong enough to include GI in the dietary recommendation for healthy populations. The current low GI diet fad is phasing out and, therefore, food companies may be looking for a new marketing approach. With the current publicity regarding the GI in diet books and by many health providers, it would appear logical to think that knowing the GI of foods would be useful. The low fat diet approach stopped working when food companies flooded the market with low fat foods that were not necessarily lower in calories. The same can be said regarding the low GI approach. Instead of avoiding CHO foods which would lead to a reduction in calories the market became flooded with low CHO foods that also were not necessarily lower in calories (Franz, 2006). This can potentially happen to low GI foods as well.

The problem with the low GI approach will be similar to the problems that occurred with the development of low fat and low CHO foods. Food companies can develop low GI foods. This can be done by adding or substituting sugars, especially fructose, and fat to foods. However, this may change the 'healthy' image of low GI foods and turn off health providers and potentially the public to low GI foods.

Until research demonstrates long-term benefits for people with diabetes in the use of the GI, making food choices should be kept as easy and simple as possible. Understanding what foods are CHO, knowing portion sizes, and knowing how many servings to select for meals, and, if desired, for snacks, will benefit the majority of the people with diabetes and can increase variety and flexibility in food choices.

In summary, GI is not user friendly, the procedure of measurement is a complex physiological measure; and GI of a given food is readily altered by variety, origin, cooking and processing; GL has not been sufficient validated; GI or GL have been shown to be valid predictors of satiety or satiation, and insulin response; neither GI nor GL have been definitively shown to influence the risk of obesity, diabetes, CHD and cancer. Lowering the GL of the diet may be an effective adjunct treatment for diabetes.

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