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Revisión

Glycemic index role on visceral obesity, subclinical inflammation and associated chronic diseases

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Abstract

Background: It is believed that the glycemic index (GI) may be used as a strategy to prevent and control non-communicable diseases (NCD). Obesity is a multifactorial condition, a risk factor for development of other NCDs. Among the different types, abdominal obesity is highlighted, which is essential for the diagnosis of metabolic syndrome, and it is related to insulin resistance, dyslipidemia, hypertension and changes in levels of inflammatory markers. Such indicators are closely related to the development of Type 2 Diabetes and cardiovascular disease.

Objectives: Discuss the role of GI as a strategy for the prevention and/or treatment of visceral obesity, subclinical inflammation and chronic diseases.

Results and discussion: The intake of low GI diets is associated with glycemic decreases, and lower and more consistent postprandial insulin release, avoiding the occurrence of hypoglycemia. Moreover, consumption of a low GI diet has been indicated as beneficial for reducing body weight, total body fat and visceral fat, levels of pro-inflammatory markers and the occurrence of dyslipidemia and hypertension. The intake of low GI foods should be encouraged in order to prevent and control non-communicable diseases.

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Key words: Glycemic index. Obesity. Insulin resistance. Inflammation. Cardiovascular diseases.

Resumen

Introducción: Se cree que es posible emplear el índice glucémico (IG) como estrategia para prevenir y controlar enfermedades no-comunicables (ENC). La obesidad es un estado multifactorial, un factor de riesgo para el desarrollo de otras ENC. Entre las distintas manifestaciones de la obesidad, destaca la obesidad abdominal, que es fundamental para el diagnóstico del síndrome metabólico y está relacionada con resistencia a la insulina, dislipidemia, hipertensión y cambios en los niveles de marcadores inflamatorios. Estos indicadores están estrechamente relacionados con el desarrollo de diabetes de tipo 2, así como de enfermedad cardiovascular.

Objetivos: Debatar el papel del IG como estrategia para la prevención y/o tratamiento de obesidad visceral, inflamación subclínica y enfermedades crónicas.

Resultados y debate: La ingesta de dietas con bajo IG está asociada a incrementos glucémicos, así como una insulina postprandial más baja y más consistente, evitando la aparición de hipoglucemia. Además, el consumo de una dieta de bajo IG ha sido identificado como beneficioso para la reducción del peso corporal, la grasa corporal total y la grasa visceral, los niveles de marcadores pro-inflamatorios y la aparición de dislipidemia e hipertensión. Se debería fomentar la ingesta de alimentos con bajo IG para prevenir y controlar enfermedades no-comunicables.

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Abbreviations

BMI: Body mass index.
CD40L: Membrane glycoproteins expressed on the surface of T cells.
NCD: Non-communicable diseases.
FUNGENUT Study: Functional Genomics and Nutrition Study.
GI: Glycemic index.
GL: Glycemic load.
GPx: Glutathione peroxidase.
HDL: High density lipoprotein cholesterol.
ICAM-1: Intercellular adhesion molecule-1.
IL: Interleukin.
LDL: Low density lipoprotein cholesterol.
MCP-1: monocyte chemotactic protein-1.
NADPH: Nicotinamide adeninedinucleotide phosphate.
ON: Nitric oxide.
PAI-1: Plasminogen activator inhibitor-1.
CRP: C-reactive protein.
MRP: Myeloid related protein.
US-CRP: Ultra-sensitive C-reactive protein.
TNF α: Tumor necrosis factor.
VCAM-1: Vascular cell adhesion molecule-1.

Introduction

Obesity is currently considered a global epidemic and results from changes in living standards and the environment in which humans live, leading to a gradual genotypic and phenotypic adaptation. The number of overweight adults worldwide has surpassed 1.4 billion people, where 35% were considered overweight and 11% obese in 2008. Reduced physical activity, the socioeconomic environment and consumption of energy-dense and palatable foods are probably the greatest contributors for establishment of this pattern.7

Many non-communicable diseases (NCD), the main causes of morbidity and mortality, have obesity as the common risk factor. NCDs related to obesity include ischemic heart disease, diabetes, stroke, cancer and hypertension.4

The consumption of hypolipidic diets has been widely used as a strategy for prevention and control of obesity.3 However, reduced fat intake is usually accompanied by increased consumption of foods with a high glycemic index (GI).4 It is believed that, in relation to the low GI, consumption of foods with high GI favors the occurrence of hyperglycemia and hyperinsulinemia, as well as hypoglycemia, which increases the feeling of hunger, thus hindering the successful treatment of obesity.7

On the other hand, consumption of a low GI diet has been associated with lower levels of pro-inflammatory markers such as plasminogen activator inhibitor-1 (PAI-1), C-reactive protein (CRP) and tumor necrosis factor α (TNF-α), as well as improved levels of serum total cholesterol and the LDL fraction.8 Several studies have also presented the role of GI in adiposity, and thus in the occurrence of various diseases.11-13

Despite the numerous scientific reports on the potential preventive and therapeutic effect of low GI diets for obesity control, no consensus has been reached on this subject. Accordingly, the objective of this review study was to critically investigate the role of GI as a strategy for prevention and/or treatment of visceral obesity, subclinical inflammation and chronic illnesses.

Methodology

The study was conducted using online databases (Web of Science, Science Direct, Pubmed and Scopus) with the following keywords: “glycemic index”, “glycemic load” and/or “obesity”, “visceral obesity”, “central obesity”, “body fat”, “body fat distribution” and “inflammation”. Papers were selected which related to population studies and clinical trials with humans or animals, published from 2003 to 2013, as well as other relevant studies published prior to these dates.

Carbohydrates, fibers and glycemic index

The GI was proposed by Jenkins et al.4 for classification of carbohydrates with regards to their physiological effects. This index is an indicator of the ability of the carbohydrate food source to increase postprandial glycemia. The GI is determined from the area below the glycemic response curve after consumption of a portion of the test food, containing 50 g or 25 g of available carbohydrates, expressed as a percentage of the same type of response obtained from the consumer for a standard food (normally glucose or white bread) by the same individual.10

In addition to the GI, the glycemic load (GL) is another parameter that has been used in studies to evaluate the impact of foods and meals on glycemia. The GL is obtained by multiplying the GI of the test food or meal, considering glucose as the standard food, with its available carbohydrate content.11 The result of this product should thus be divided by 100.12

The quantity and quality of carbohydrates may have an effect on cardiovascular risk factors. During the grain refinement process, there occurs the removal of original fibers, making these high GI foods. Intake of these foods results in rapid increase of glycemia and insulinemia, which may decrease satiety and increase the level of circulating free fatty acids.7 Acute hyperglycemia, along with other consequences, reduces the availability of nitric oxide and worsens endothelial vasodilation, with consequent increase in blood pressure, a precursor to cardiovascular diseases.17

The intake of dietary fiber may play a protective role against disorders associated with inflammation in obesity.15,16 However, the mechanisms involved in this process are not yet clear. In a study performed with adolescents, it was observed that dietary fiber intake was
associated with lower visceral adiposity and improved inflammatory profile (CRP, leptin, fibrinogen and adiponectin). The deposit of fat in the visceral region is closely related to subclinical inflammation. This type of low-grade inflammation plays a central role in the mechanisms that link obesity to cardiometabolic risk factors, and consequently, non-communicable diseases. It is interesting that the researchers evaluated the relationship between the fiber content consumed and GI of the tested meals, as well as insulinaemia of the participating individuals, since it is suggested that the increased fiber intake has positive effects on insulin sensitivity.

Abdominal obesity, inflammation, endothelial dysfunction and atherosclerosis: general considerations

Central obesity, characterized by fat accumulation in the central region of the body, is a public health problem. The incidence of this type of obesity is higher than being overweight as diagnosed by the body mass index. Central obesity is more strongly associated with metabolic changes that result from the deposition of fat in other regions. Excess abdominal fat has recently been considered a sine qua non for diagnosis of metabolic syndrome, which is associated with increased risk for cardiovascular disease. Accumulation of abdominal fat results in excessive liberation of fatty acids from the visceral adipose tissue, favoring the occurrence of hyperinsulinemia and insulin resistance, which are associated with an inflammatory and thrombogenic profile.

In this sense, obesity is considered a chronic systemic inflammatory disease, characterized by increased levels of pro-inflammatory markers, such as adhesion molecules, including vascular adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1); cytokines such as tumor necrosis factor α (TNF-α) and interleukin 1, 6 and 18 (IL-1, IL-6 and IL-18); proteases such as matrix metalloproteinase-9 (MMP-9); platelet products such as CD40L and myeloid related proteins (MRP); acute phase proteins such as ultra-sensitive C-reactive protein (US-CRP), PAI-1; serum amyloid A and fibrinogen, and anti-inflammatory adipokines, such as adiponectin. Moreover, other clinical markers of inflammation have been reported, such as oxidized LDL and homocysteine.

Atherosclerosis results from chronic inflammation in response to interactions between plasma lipoproteins, cellular components including monocytes/macrophages, T lymphocytes, endothelial cells, smooth muscle cells and the extracellular matrix of arteries. Atherosclerotic lesions are considered inflammation producers, while high levels of CRP can induce atherosclerosis. Moreover, the release of inflammatory markers from visceral adipose tissue damages the vascular endothelium. The CRP appears to induce endothelial dysfunction, reduced nitric oxide production, hypertension and cardiovascular diseases (fig. 1).

Role of the glycemic index on prevention and control of chronic diseases associated with obesity

Studies involving human subjects

Postprandial hyperglycemia is more strongly associated with increased release of free radicals and pro-inflammatory cytokines than fasting hyperglycemia.
The increased release of these factors is responsible for the deleterious effect of hyperglycemia on the vasculature. A cross analysis of the intake data from 780 diabetic men participating in the Health Professionals’ Follow-Up Study indicated that consumption of low GL diets, independent of fiber content, may increase the serum concentrations of adiponectin, independent of the dose; this is an anti-inflammatory adipokine that, among other important effects on the metabolism, contributes to increased sensitivity to insulin. In another study involving 511 elderly, higher levels of TNF-α and IL-6 were observed in the in the upper quartile of GI compared to the lower quartile in the baseline. After one year of monitoring, there was a decrease in levels of adiponectin and leptin in those who consumed diets with higher contents of GI and GL. Leptin is a hormone produced by the adipose tissue, which controls food intake. Thus, results of the study performed by Bulló et al. suggested that consumption of diets rich in GI and GL favor the occurrence of obesity and diabetes mellitus type 2.

In this context, in a study conducted among women with type 2 diabetes, it was found that consumption of whole grains and low GI reduced systemic inflammation. Thus, scientific evidence suggests that different carbohydrate types can modulate circulating levels of pro- and anti-inflammatory cytokines.

The typical western diet, rich in GI carbohydrates, including potatoes, bread and refined grains is rapidly digested and absorbed, resulting in increased insulin secretion. Therefore, consumption of high GI foods by insulin-resistant individuals intensifies the increase in postprandial glycemia and insulinemia, contributing to depletion of beta cells and development of type 2 diabetes (fig. 2).

On the other hand, consumption of a low GI diet may maintain and/or improve insulin sensitivity, and also assist in weight loss. Conversely, consumption of a low GI diet may help control obesity by promoting greater satiety and increased fat oxidation, resulting in reduction of total body fat and abdominal body fat, which is known to participate in development of chronic diseases. These effects are summed with slower digestion and absorption with consequent effects on the reduction of postprandial glycemia and insulinemia.

In a study involving the participation of 933 Korean individuals, it was found that women who consumed a diet rich in GI and GL were more likely to be obese. On the other hand, a negative association was confirmed between the prevalence of obesity in men and consumption of the GI-rich diet. These results suggest that the mechanisms which contribute to prevalence of obesity may differ among genders. Similarly, in another study involving Korean adults, it was reported that intake of diets rich in GI and GL increased the risk of women presenting hypertriglyceridemia and HDL-cholesterol lower than ideal. The risk of developing metabolic syndrome was increased among overweight women who consumed larger quantities of carbohydrates and diets rich in GI and GL. However, this increased risk was not observed among eutrophic women. The results of this latest study suggest that body weight can modulate the effect of carbohydrate quantity and quality consumed on the manifestation of metabolic syndrome.
In a crossover study, overweight volunteers randomly participated in two stages (high GI or low GI), each lasting thirty consecutive days. During the study, volunteers ate two meals daily in the laboratory and an isocaloric portion of fruit outside the laboratory, with GI in accordance with the stage in which they participated. A significant reduction in measures of waist circumference and waist-hip ratio were observed after the low GI stage. However, no differences were observed in the BMI and total body fat. These results reinforce that the consumption of low-GI diets may play an important role in reducing abdominal obesity and consequently chronic diseases, such as diabetes and cardiovascular diseases.

Similarly, in a prospective study with 48,631 men and women from five European countries, the influence of dietary factors on changes in abdominal adiposity was evaluated for an average period of 5.5 years. A significant increase in waist circumference was observed in both genders for a given BMI in those consuming the GI-rich diet with higher energy density. Among women, low fiber intake, increased GL and higher alcohol consumption were also predictors of increased abdominal adiposity. Thus, the results suggest that consumption of the low-GI diet associated with low caloric intake may prevent visceral adiposity.

Similar results were observed in a 12 week study, in which women (BMI 25-45 kg/m²) who consumed a Mediterranean diet showed reductions in body weight, systolic blood pressure, triglyceride levels, total cholesterol and LDL-cholesterol. It should be noted, however, that study participants differed with regards to their level of adiposity, since participants included those considered overweight as well as morbidly obese. Thus, the variation in adiposity presented by study participants may have differently influenced the glycemic response and consequently the levels of the biochemical parameters evaluated.

Participants from Christchurch, New Zealand, were involved in dietary intervention programs via the internet, targeting the consumption of low GL diets. After 6 months, significant losses were observed regarding average weight (3.5 kg), along with reductions in BMI (1.2 kg/m²) and waist circumference (4.8 cm). However, intake of a low GI diet for 18 months did not affect body weight of eutrophic Brazilian women between 25-45 years old.

The beneficial effects of consuming low GI/GL diets on obesity control have been reported by several authors. In one of these studies, the authors concluded that the low GI diet, offered for 5 weeks to overweight individuals, promoted greater weight loss than the high GI diet. Similarly, consumption of a low GI diet by overweight or obese young adult women promoted greater weight and body fat losses when compared to the high GI diet. In obese adolescents, it was found that consumption of lower GL diets resulted in a greater reduction of BMI and body fat mass when compared to those consuming high GL diets.

Regarding the lipid, glycemic and insulinemic profiles and inflammatory markers, results of the studies also show positive effects of the low-GI diet on total cholesterol and LDL cholesterol in humans. Furthermore, reductions in the LDL/HDL-cholesterol and total cholesterol/HDL-cholesterol ratios were reported, with no effect on insulin sensitivity in adult men and women.

However, in a cross-sectional population study with 668 non-diabetic subjects between 18 and 75 years old, no association was found between GI and insulin resistance. Nevertheless, a positive effect was observed in an intervention study with obese children and adolescents, 7-13 years old, who consumed a low GI diet for 6 months. It is believed that the beneficial effects of consuming the low GI diet were found only in the intervention study due to greater control of the nutritional composition of the diet consumed during the study.

Regarding the levels of inflammatory markers, the results of the studies are also conflicting. Consumption of the low GI diet by overweight women during 10 weeks reduced levels of the PAI-1 inhibitor, which participates in the regulation of angiogenesis and apoptosis. In a study with type 2 diabetics, consumption of two meals daily with high GI for 30 days resulted in higher levels of TNF-α when compared to the low GI diet. From the results of another study involving adult men and women with BMI of 27.4 ± 5.4 kg/m² and age of 48 ± 12 the existence of an inverse association was reported between GI and US-CRP levels among obese individuals. Therefore, the results of recent studies suggest that consumption of high GI diets favor the installation of a profile of inflammatory markers capable of mediating installation of subclinical inflammation, which can promote the expression of NCD.

**Studies involving animals**

In relation to human studies, those involving laboratory animals have the advantage of providing information on the mechanisms and effects resulting from chronic consumption of low or high GI diets, as well as greater control over possible interfering factors.

In one of these crossover studies, the effect of ingesting diets with differing GI was assessed in adult rats for 32 weeks. Consumption of the GI-rich diet resulted in two times greater visceral fat, even after adjustment for total body fat. Contrarily, the subcutaneous adipose tissue did not differ between groups after adjustment for total fat. Lower levels of fat oxidation were observed in the high-GI group.

Furthermore, in C5BL/6 mice the effect of high or low GI diets was evaluated for 16 weeks, presenting high or low fat content. It was found that the postprandial glycemic response was greater in the high GI diet, independent of fat content. Although body weight did not differ between groups, mice fed a hypolipidic diet with high GI showed much higher adiposity than those fed a low-fat diet with low GI.
Glycemic index applicability

Insulin is a hormone involved in energy metabolism. Some of its various roles comprise enhancing glucose uptake and its utilization in the muscle and liver, increasing the hepatic conversion of glucose into glycogen, and inhibiting hormone-sensitive lipase leading to reduced release of fatty acids from adipose tissue, and thus presenting an anabolic function. The increase in serum insulin levels hinders weight loss and is a predictor of the development of type 2 diabetes. Therefore, it is considered that the GI be used in nutritional interventions aimed at reducing body weight and improving the cardiometabolic profile.

The GI of specific foods can be obtained using international tables and websites (www.glycemicindex.com), which were created in order to avoid unnecessary repetition of tests for its determination. However, use of these values in research has its limitations, since many times these values may not accurately reflect the value displayed by a given type of food grown in different countries. The GI for a given food may vary in function of the preparation method of a food or meal, even if it presents the same nutrient composition.

However, estimated values of the GI obtained from the previously mentioned table and website can be used to estimate the GI, important tools for use in nutrition education. The consumption of low GI foods has been recommended, especially among those who are already overweight and/or present glucose metabolism disorders.

In countries like Australia, various commercialized foods present seals that facilitate the identification and preferential selection of low GI foods by the population (www.glycemicindex.com). The GI concept has been widely disseminated and used by the Australian population. This is a result of the efforts of researchers for practical application and for returning the results obtained in the laboratory to the population. Considering the expected overall increase in diabetes from 366 million in 2011 to 552 million in 2030, the use of GI as a tool for nutrition education may be useful in weight control, cardiovascular risk and glycemic control.

Final considerations

The results of several studies suggest that the use of low GI foods favors the reduction of body weight, total and visceral adiposity, levels of pro-inflammatory markers, dyslipidemia and blood pressure. Thus, the GI should be considered an additional tool to be used for the selection of carbohydrate food sources, which should be included in a nutritionally balanced diet, able to promote and/or maintain proper health.

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