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Glycemic index, glycemic load, wellness and beauty: the state of the art

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Abstract The glycemic index (GI) is a ranking system for carbohydrates' effect on blood glucose levels. It compares available carbohydrates gram for gram in individual foods, providing a numerical, evidence-based index of postprandial glycemia. The glycemic load (GL) is a ranking system for carbohydrate content in food portions based on their GI and the portion size. These two markers increasingly are being used to prevent typical diseases of the Western world, including type 2 diabetes mellitus, cardiovascular disease, obesity, metabolic syndrome, and acne. Data on the efficacy of GI and GL in the treatment of Western population diseases are discussed and critically evaluated, with a particular focus on acne and other skin disorders.

Definition of glycemic index and glycemic load

In the past, carbohydrates were classified as simple or complex based on the number of monosaccharide present in the molecule. Carbohydrates composed of one or two sugars (like fructose, glucose, or sucrose) were labeled simple, while starchy foods were labeled complex. Advice to eat less simple and more complex carbohydrates was based on the assumption that consuming starchy foods would lead to smaller increases in blood glucose.[1] This assumption turned out to be too simplistic, because the blood glucose response to "complex" carbohydrates has been found to vary considerably. A more accurate indicator of the glycemia response to dietary carbohydrates is the glycemic index (GI).

The GI is a ranking system for carbohydrates, effect on blood glucose levels. It compares available carbohydrates gram for gram in individual foods, providing a numerical, evidence-based index of postprandial glycemia. The concept was proposed by Jenkins and colleagues in 1981.[2]

Carbohydrates that break down rapidly during digestion and are absorbed rapidly have the highest glycemic indices, while those that break down slowly, releasing glucose gradually into the blood stream, have a low glycemic index. A lower glycemic response often is thought to equate to a lower insulin demand, better long-term blood glucose control, and a reduction in blood lipids. But in fact, some foods having a low glycemic index or very little carbohydrate content cause a high insulin response or raise blood lipids; thus the insulin index also may be useful, because it provides a direct measure of the insulin response to a food.

The glycemic load (GL) is a ranking system for carbohydrate content in food portions based on their GI and the portion size. The usefulness of GL is based on the idea that a high GI food consumed in small quantities would have the same effect on blood sugar as larger quantities of a low GI food.

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Measurement of the glycemic index and glycemic load of food

To determine the glycemic index of a food, volunteers are typically given a test food, on different days, that provides 50 grams of carbohydrate and a control food (white bread or pure glucose) that provides the same amount of carbohydrate. The area under the two hours blood response curve (AUC) of the test food is divided by the AUC of the standard (either glucose or white bread, are giving two different definitions) and multiplied by 100.[3]

Glycemic load for a single serving of a food can be calculated as the quantity (in grams) of its carbohydrate content, multiplied by its GI, and divided by 100.[1]

The more recent and reliable data on glycemic index and glycemic load are reported by Foster et al.[4]

Glycemic index and glycemic load in disease prevention

Type 2 diabetes mellitus

After a high GL meal, blood glucose levels rise more rapidly, and insulin demand is greater than after a low GL meal. High blood glucose levels and excessive insulin secretion may contribute to the loss of the insulin-secreting function of the pancreatic beta-cells. High dietary GLs have been associated with an increased risk of developing type 2 diabetes mellitus in several large prospective studies.[5-7] The foods that most consistently were associated with increased risk of type 2 diabetes mellitus were potatoes (cooked or fried), white rice, white bread, and carbonated beverages.

Cardiovascular disease

Impaired glucose tolerance and insulin resistance are known risk factors for cardiovascular disease. In addition to increased blood glucose and insulin concentrations, high dietary GLs are associated with increased serum triglyceride concentrations and decreased high-density lipoprotein cholesterol concentrations, both of which are cardiovascular disease risk factors.[8,9] High dietary GLs also have been associated with increased serum levels of C-reactive protein, a marker of systemic inflammation that is also a sensitive predictor of cardiovascular disease risk.[10]

In the Nurses' Health Study, women with the highest dietary glycemic loads had a risk of developing coronary heart disease over the next 10 years, which was almost twice as high as those with the lowest dietary GLs.[11] The relationship between dietary GL and coronary heart disease risk was more pronounced in overweight women, suggesting that people who are insulin resistant may be most susceptible to the adverse cardiovascular effects of high dietary GLs.[1]

Obesity

In the first 2 hours after a meal, blood glucose and insulin levels rise higher after a high GL meal than they do after a low GL meal containing equal calories. Due to the excess insulin secretion, blood GLs rise over the next few hours after a high GL meal than they do after a low GL meal. This may explain why 15 out of 16 published studies found that the consumption of low GI foods delayed the return of hunger, with subsequent decrease of food intake and increase of satiety, when compared to high GI foods.[12] The results of several small short-term trials (1-4 months) suggest that low GL diets result in significantly more weight or fat loss than high GL diets.[13-15] Although long-term randomized controlled trials of low-GL diets in the treatment of obesity are lacking, the results of short-term studies on appetite regulation and weight loss suggest that low GL diets may be useful in promoting long-term weight loss and decreasing the prevalence of obesity.

Metabolic syndrome

The constellation of dyslipidemia (hypertriglyceridemia and low levels of HDL—cholesterol), elevated blood pressure, impaired glucose tolerance, and central obesity is identified as the metabolic syndrome. In the very near future, metabolic syndrome will overtake cigarette smoking as the number one risk factor for heart disease among the United States population. Effective interventions include diet, exercise, and judicious use of pharmacologic agents to address specific risk factors. Weight loss significantly improves all aspects of the metabolic syndrome. Increasing physical activity and decreasing caloric intake by reducing portion sizes will improve metabolic syndrome abnormalities, even in the absence of weight loss. Specific dietary changes that are appropriate for addressing the different aspects of the syndrome include reducing saturated fat intake to lower insulin resistance, reducing sodium intake to lower blood pressure, and reducing high GI carbohydrate intake to lower triglyceride levels. A diet that includes more fruits, vegetables, whole grains, monounsaturated fats, fat fishes (and/or long chain polyunsaturated omega-3 fatty acids, long-chain polyunsaturated fatty acid omega-3), and low-fat dairy products will benefit most patients with the metabolic syndrome.[16]

Acne

Acne is a common and complex skin disease that affects individuals of all ages. In Western populations, acne is estimated to affect 79%–95% of the adolescent population, 40%–54% of individuals older than 25 years, and 12% of women and 3% of men of middle age.[17] In contrast, acne remains rare in non-Westernized societies, such as the Inuit,[18] Okinawan Islanders,[19] Ache hunter-gatherers, and

Kitavan Islanders.[17] Although familial and ethnic factors are implicated in acne prevalence, this observation is complicated by the finding that incidence rates of acne have increased with the adoption of Western lifestyles.[18] These observations suggest that lifestyle factors, including diet, may be involved in acne pathogenesis.

Although the pathogenesis of acne is not understood fully, recent epidemiological studies suggest that dietary factors, including the GL, my be involved.[20] Even if the relationship between GI, GL, and acne is controversial, a recent randomized controlled trial showed an improvement of acne, which is related to an enhancement of insulin sensitivity.[20,21]

The relationship of acne to foods certainly is not new. The United States textbooks of dermatology,[22-24] published in the early 1950s, contained information regarding specific foods to be avoided. The admonition to avoid chocolate, fats, sweets, and carbonated beverages commonly was given to patients as part of acne therapy. But all of this dietary advice was removed from more recent standard textbooks, and it has been many years since restriction of specific foods has been recommended in managing acne. It should be noted, however, that an article published in 2001[25] reported that many patients believed acne was influenced by diet.

The proximate etiology of acne vulgaris

Acne is thought to result from the interplay of three factors: 1) hyperkeratinization and obstruction of sebaceous follicles caused by abnormal desquamation of the follicular epithelium, 2) increases sebum production from androgen stimulation, and 3) colonization of the follicle by *Propionibacterium acnes,* which generates inflammation.[26,27] The ultimate mechanism responsible for factors one and two is not well understood.[27,28] It is likely that any environmental element underlying the development of acne must operate via modulation of the known proximate or ultimate (genetic) causes.

Diet, hyperinsulinemia, and acne

Although diet is considered infrequently as an etiologic agent in the development of acne,[29] it represents a well-recognized factor in acute[30] and chronic[31,32] hyperinsulinemia. Recent evidence has demonstrated that the hormonal cascade triggered by diet-induced hyperinsulinemia elicits an endocrine response that simultaneously promotes unregulated tissue growth and enhanced androgen synthesis. Hence, hyperinsulinemic diets may represent a previously unrecognized environmental factor in the development of acne.

Hyperinsulinemia and free IGF-1 and IGFBP-3

Chronic and acute hyperinsulinemia initiate a hormonal cascade that favors unregulated tissue growth by simultaneously elevating levels of free insulin-like growth factor 1 (IGF-1) and reducing levels of insulin-like growth factor binding protein 3 (IGFBP-3).[33-36] Because free IGF-1 is a potent mitogen for virtually all body tissues,[37] elevated concentrations of free IGF-1 have great potential for stimulating growth in all tissues, including the follicle.

Data shows that IGF-1 is required for keratinocyte proliferation in humans[38] and that in transgenic mice, overexpression of IGF-1 results in hyperkeratosis and epidermal hyperplasia, which supports the notion that insulin-triggered elevations in free IGF-1 levels may promote acne via hyperkeratinization.[39] Furthermore, women with postadolescent acne maintain elevated serum concentrations of IGF-1[40] and are mildly insulin resistant.[41]

The reductions in IGFBP-3 levels stimulated by elevated serum insulin[33,34] or by acute ingestion of high–glycemic load carbohydrates[42] also may contribute to unregulated cell proliferation in the follicle. In murine knockout cells lacking the IGF receptor, IGFBP-3 acts as a growth inhibitory factor.[43] Accordingly, IGFBP-3 inhibits growth by preventing IGF-1 from binding to its receptor. Hyperinsulinemia indirectly increases the number of epidermal growth factor receptors by elevating levels of plasma nonesterified fatty acids,[44] and it also induces production of transforming growth factor 1.[45] Increased concentrations of these cytokines depress localized keratinocyte synthesis of IGFBP-3, thereby increasing the availability of free IGF-1 to its keratinocyte receptors,[46] which promotes keratinocyte proliferation. Consequently, hyperkeratinization of sebaceous follicles may result synergistically from elevations in free IGF-1 levels and/or reductions in concentrations of IGFBP-3.

IGBF-3 and retinoid receptors

Insulin-mediated reductions in IGFBP-3 levels may promote unregulated follicular growth further by affecting the nuclear retinoid signaling pathway. Retinoids are natural and synthetic analogues of vitamin A that inhibit cell proliferation and promote apoptosis.[46] The body's natural retinoids (*trans* retinoic acid and 9-*cis*-retinoic acid) act by binding two families of nuclear receptors: retinoic acid receptors (RARs) and retinoid X receptors (RXRs). Retinoid receptors, in turn, activate gene transcription by binding as RAR-RXR heterodimers or RXR-RXR homodimers to retinoic acid response elements located in the promoter regions of target genes, whose function is to limit growth in many cell types.[47]

IGBF-3 is a ligand for the RXR nuclear receptor and enhances RXR-RXR homodimer–mediated signalling.[48] Studies in knockout rodents show that the *RXR* gene is required for actions of the two endogenous retinoic acid ligands (*trans* retinoic acid and 9-*cis*-retinoic acid),[49,50] and RXR agonists and IGFBP-3 are growth inhibitory in many cell lines.[51] Additionally, RXR is the major RXR receptor in skin.[52] Consequently, low plasma levels of IGFBP-3

induced by hyperinsulinemia may reduce the effectiveness of the body's natural retinoids to activate genes that normally would limit follicular cell proliferation.

Hyperinsulinemia, IGF-1, androgenesis, and sebum production

Sebum production, which is essential to the development of acne,[27] is stimulated by androgens.[26,27] Consequently, hyperinsulinemia may promote acne by its well-established androgenic effect. Insulin and IGF-1 stimulate the synthesis of androgens in ovarian[53,54] and testicular[55,56] tissues. Furthermore, insulin and IGF-1 inhibit the hepatic synthesis of sex hormone binding globulin[57,58] thereby increasing the bioavailability of circulating androgens to tissues. Cross-sectional studies demonstrate inverse relationships between serum sex hormone binding globulin and insulin[59] and IGF-1.[60-62] Additionally, sebum production is stimulated not only by androgens,[26,27] but also by insulin[63] and IGF-1.[64] Direct injections of recombinant IGF-1 in humans elicit androgenesis and acne.[65] Higher serum androgen,[66] insulin,[40] and IGF-1[41] concentrations are associated with the presence of acne in women. Taken together, data suggests that the endocrine cascade induced by hyperinsulinemia enhances sebum synthesis and the development of acne.

The role of insulin in acne development also is supported by the high prevalence of acne in women with polycystic ovary syndrome (PCOS), a condition associated with insulin resistance, hyperinsulinemia, and hyperandogenism.[67] Insulin resistance is believed to be the underlying disturbance in PCOS, because it generally precedes and gives rise to the cluster of endocrine abnormalities that characterize PCOS (elevated androgen and IGF-I concentrations and low sex hormone–binding globulin).[68] Treatments for PCOS now include oral hypoglycemic agents, which improve insulin sensitivity, restore fertility, and alleviate acne.[69]

Despite the above mentioned evidences, few well-controlled dietary studies have examined the effect of diet on acne. Fulton et al,[70] in a crossover single-blind study, found no effect of chocolate on acne when compared with a placebo bar. However, a later examination of the ingredients in the placebo bar indicated that the fatty acid composition and sugar contents were virtually identical to that found in the chocolate.[71] Anderson examined the effect of the daily consumption of chocolate, milk, or nuts and found no effect on acne.[72] On the other hand, this study has been criticized for its small sample size, short follow-up, and lack of control.[73] Chiu et al[74] showed, in university students, an association between worsening diet quality and exacerbation of acne during a preexamination period. Nevertheless, stress was found to be the main contributing factor, and diet was assessed by using a non-quantitative, self-assessed measure of food quality. Recently, a retrospective evaluation of dietary intake showed a positive association between milk intake and severe acne.[75] However, this association may have been affected by the imprecision inherent in the measurement of dietary intakes via dietary recall, according to the authors.

Cordain et al[17] postulated that high-glycemic-load diets may be a significant contributor to the high prevalence of acne seen in Western countries. The authors speculate that the frequent consumption of high-GI carbohydrates may repeatedly expose adolescents to acute hyperinsulinemia. Therefore, low GL dietary interventions may have a therapeutic effect on acne based on the beneficial endocrine effects of these diets. The hypothesis was based on the fact that high GL diets may influence one or more of the four underlying causes of acne mentioned previously.[42]

To our knowledge, the study of Smith et al[20] is the first study to show a therapeutic effect of dietary intervention on acne. After 12 weeks, the low GL diet was shown to significantly reduce acne lesion counts and improve insulin sensitivity when compared with a high GL diet. Although the authors could not isolate the effect of the low GL diet from that of weight loss, their findings are consistent with the earlier suggestions of the association between hyperinsulinemia and acne. However, these observations will need to be substantiated and the underlying mechanisms determined in larger-scale studies.

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