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Review Article

Glycemic Control and Acne: A Review

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ABSTRACT

Acne as a chronic inflammation involves pilosebaceous unit and is associated with hyperkeratosis and sebaceous hypersecretion. A high glycemic index (GI) and glycemic load (GL) diet may stimulate acne proliferative pathways affecting biochemical factors in acne. Although GI and GL have a prominent role in acne pathophysiology, few literatures assessed this association. This review was undertaken to summarize the published data regarding the effect of low glycemic load diet on acne lesions. A literature search was conducted in PubMed, Science direct, Google scholar up to January 2019. GI and GL are implicated in acne pathogenesis due to diet-induced hyperinsulinemia, stimulating a rise in IGF-1 concentrations and androgen hormones and as a result, amplifying acne-promoting pathways.

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Introduction

Acne is still a common and complex skin disease manifested as a chronic inflammation of the pilosebaceous unit, leading to hyperkeratosis and sebaceous hypersecretion (1). The Global Burden of Disease Project estimates the prevalence of acne at 9.4%, ranked as the eighth most prevalent global disease (2). It is among the top three most prevalent skin diseases in the general population (3). Even acne is typically misconstrued as a aesthetic disease confined to adolescents, acne affects mostly all age groups and results in considerable psychological distress, physical morbidity, and social prejudice (4). Frequently, face is affected by acne, and it is difficult to hide the produced scars that can persist for years or for lifelong. Social isolation, depression, and suicidal ideation are frequent comorbidities observed in acne (5).

Various acne therapies exist, including oral, procedural and topical treatments. Although each of these remedies interfere different advantages for the management of acne, they may have unwanted side effects too including local irritations in topical treatments and systemic side effects such as liver function abnormalities and teratogenic ones (6). Moreover, treatment in acne is not cost-effective including the cost of brand-name too. Therefore, alternative prevention and treatment choices for patients with acne seem necessary (4). A high-GI diet is characterized by a relatively high intake of carbohydrate-containing foods that are rapidly digested and absorbed, rising the blood glucose and insulin levels. The GL takes the portion size of dietary carbohydrate into consideration and is a measure of quality and quantity of carbohydrate-containing foods (4, 7). GI and GL have important roles in acne pathogenesis and even they have a biologically plausible role in acne pathophysiology, few literature is available on the relationship.

Insulin Resistance and Prevalence of Acne

Insulin affects glucose uptake into the tissue, and its capability varies greatly among individuals. In insulin resistance, tissues have a decreased capability to respond insulin action. To overcome the resistance, more insulin is secreted from pancreas. So insulin-resistant persons show high plasma insulin levels (8). The role of insulin in development of acne is demonstrated by the high prevalence of acne in women with polycystic ovary syndrome (PCOS), a condition noted with insulin resistance, hyperinsulinemia, and hyperandogenism. Insulin resistance was found to be the underlying disturbance in PCOS, as it generally precedes and leads to the cluster of endocrine abnormalities that characterize PCOS (9).

Del Prete et al. studied on correlation between metabolic abnormalities and acne in a sample of male patients influenced by inflammatory acne resistant to common treatments (common topical antibacterials and retinoids, and oral retinoids and antibiotics after >1 year of therapy) and realized that these had an impaired metabolic profile and a declined insulin sensitivity (10). In fact, endocrine disorders with increased IGF-1 serum and insulin levels, like polycystic ovary syndrome, premature adrenarche, and acromegaly, are clinically associated with a high prevalence of acne (11).

The Mechanism of Insulin in Acne Pathogenesis

High insulin levels in fasting and/or postprandial conditions can exacerbate the acne. Postprandial insulin responses may have particular correlation with puberty and adolescence when whole-body insulin resistance naturally increases. Identically, compensatory hyperinsulinemia is associated with a decline in insulin-like growth factor binding protein-1 (IGFBP-1), corresponding to higher cellular concentrations of free insulin-like growth factor-1 (IGF-1) (12). Insulin affects hepatic secretion of IGF-1 (1). IR was also shown to increase the inflammatory responses within and near to the comedo (12). Insulin can influence the entire androgen axis; in the pituitary, where it plays a role as a gonadotrophin amplifier, the gonads where is stimulates androgen synthesis, the adrenal glands, where it stimulates production of androgenic precursors, and the liver, where it inhibits sex hormone binding globulin (SHBG) production and increase the free androgen index (FAI) (13).

The Mechanism of Insulin-Like Growth Factor-1 in Acne Pathogenesis

Insulin-like growth factor-1 (IGF-1) is a pleiotropic growth factor affecting normal and pathological growth. It is part of the growth factor family structurally related to pro-insulin, enabling the growth factor to bind to insulin receptors. IGF-1 is produced by many tissues in response to stimulation by growth hormone (14). Although structurally and functionally identical to insulin, it has distinct metabolic effects based on the affinity to IGF-1 receptors, placed on the majority of cells. In skin, they are visible on sebocytes, epithelial cells, eccrine glands, follicular outer sheath cells, and matrix of hair cells (15).

IGF-1 is thought to regulate the proliferation of keratinocyte and production of sebum in physiological doses via activating P1-3 K and MAPK/ERK pathways and induces the SREBP-1 expression, leading to an increase in sebaceous lipogenesis (11, 14). A more recent hypothesis revealed that diet-induced hyperinsulinemia may improve acne at the cellular level by affecting IGF-1 levels and by activation of phosphoinositide-3-kinase/Atk pathway reducing the nuclear localization of the forkhead Fox-O1 transcription factor. Reduced forkhead Fox-O1 can increase the androgen receptor activity and decrease nutrient-sensitive kinase the activity of the mammalian target of rapamycin complex and sterol regulatory element-binding protein (4). IGF-1 influence on production of androgens by gonadal and adrenal glands and results in comedogenic effects for androgens, growth factors and corticosteroids (1). Indeed, the highest incidence of acne happens when IGF-1 concentrations reach the peak and patients with acne have high levels of IGF-1 (16, 17).

Androgens in Acne Pathogenesis

Androgen hormones have a great role in development of acne, stimulation of keratinocyte proliferation, production of sebum, and growth of sebaceous glands (18). Sebum production is regulated by androgens and has a prominent role in acne pathogenesis (19). The production of sebum begins during puberty in line with the peaking levels of insulin like growth factor (IGF)-1 and growth hormone that happens in midpuberty (20, 21).

Glycemic Index and Load

Glycemic index is the equation measure by a rise in postprandial glycemia over the baseline level during a 2-hour period after using a specified amount of carbohydrate (usually 100 g) in comparison to an equal amount of carbohydrate as a reference food (white bread or glucose). A low glycemic index is regarded to be less than 55, while an amount greater than 70 is regarded a high glycemic index. Many factors affect the glycemic responses to foods including the type of carbohydrate (e.g. glucose, sucrose, lactose, fructose, amylase, resistant starch), the cooking style (longer cooking periods results in more breakdown of the starch), the type of food processing, and other meal ingredients like proteins and fat. An additional reference guide is the glycemic load, denoting to the quantity and quality of the carbohydrate present in a meal and is measured by multiplying the glycemic index by the grams of carbohydrate in a food serving (22). The low glycemic load diet (LGLD) reveals mainly a modification in the type and amount of consumed carbohydrates (11). LGLD decreases fasting and postprandial insulinemia and IGF-1 levels, and is expected to decline the proliferation of keratinocytes and production of sebum (23).

Low Glycemic Load Diet and Insulin Sensitivity

It was shown that a high glycemic load diet can lead to significant hyperinsulinaemia, and result in a hormonal cascade causing androgen-induced keratinocyte growth and sebum production. While a low glycemic-load diet causes a promotion in insulin sensitivity (13), only in one randomized controlled trial Burris et al. reported that in spite of decrease in IGF-1 of LGL diet group compared to control group; there were no differences in glucose, insulin, or IGFBP-3 or insulin resistance changes between treatment groups (4).

Low Glycemic Load Diet and IGF-1

IGF-1 levels significantly decreased among subjects randomized to a low GI and GL diet between pre- and postintervention time points (4). Also, LGL diets were demonstrated to affect IGF-I activity by alterations in IGF-binding proteins levels (IGFBPs). The LGL diet increased concentrations of IGFBP-1 by 28% and IGFBP-3 by 27%, when compared to the pretreatment values. These modifications may be described by alterations in the metabolic milieu happened with the consumption of an LGL diet (13).

Low Glycemic Load Diet and Androgens

HGL diet increased androgen bioavailability by 19% and decreased SHBG levels by 9%, when compared to pretreatment values (13). The effect of dietary treatment on FAI (free androgen index) was marginally significant (24). LGL diets were shown to decrease the androgen bioavailability and rise the SHBG levels (13).

Low Glycemic Load Diet and Lipid Profile

Fabbrocini et al. reported that metformin together with a hypocaloric low glycemic load diet resulted in a decline in total cholesterol of the LGL diet group (1). Smith et al. found that a 7-day LGLD could decline the triglycerides, while the HGL group declined HDL and both groups exhibited significant decreases from baseline in LDL and total cholesterol (13). Based on Smith et al.'s study, no influence was noted for dietary intervention on sebum output or the composition of individual fatty acids, and they realized opposing trends in the SFAs/MUFAs ratio of skin surface triglycerides. Subjects on the LGL diet showed a rise in the SFAs/MUFAs ratio when compared to a decline observed in the control group. The LGL group also revealed an increase in the 16:0/16:1D6+D9 ratio, thereby indicating to a decrease in the enzymatic desaturation of 16:0 with a LGL diet (25).

Low Glycemic Load Diet and Immunohistochemical Findings

Mean scores for H&E staining displayed reductions after dietary intervention. However, there was no significant modification in mean intensity of TGF-β1 (11). IL-8 immunostaining of acne lesions illustrated a declined inflammation in the LGLD group. Increased IL-8 expression in skin has been indicated to be significantly associated with follicular hyperkeratosis, and acne inflammation (26).

Low Glycemic Load Diet and Body Composition

In primary researches such as Smith et al.'s study, participants in the LGL group lost weight, therefore, they cannot preclude the change in BMI to the overall treatment effect (9). Accumulating documents point that LGL interventions may facilitate weight loss in overweight and obese adolescents, without the necessity for an imposed energy restriction (27, 28). The participants in the LGL group lost weight despite receiving dietary advice to keep their baseline energy intake due to the dual effect of added low-GI foods and proteins, affecting the hunger and satiety. It was shown that low-GI foods increase the satiety, delay the hunger, and decrease food intake in comparison to the high-GI foods (9, 29). Similar effects on satiety have been reported for high-protein meals when compared with high-fat meals or isocaloric high-carbohydrate (30). So it was hypothesized that the context of weight maintenance, fiber intake and identical macronutrient are of great importance (12). The results pointed to no differences in body

Table 1: Selected studies analyzing glycemic control and acne

Author	Year	Location	Design	Duration of trial	Inclusion criteria	Type of intervention	Participants	Age (years)	Male %	Results
Burris J et al. (4)	2018	United States	Randomized controlled trial	2 weeks	(1) Between 18 and 40 years old; (2) had a BMI >18.5 or <30.0; (3) had moderate or severe facial acne as determined by a dermatologist; (4) had self-reported moderate or severe acne for at least 6 months prior to study enrollment; (5) were able to read and speak the English language.	Participants randomized to the intervention diet received nutrition education on a low GI and GL diet from a registered dietitian nutritionist	Case: n=34 Control: n=32	22±4	18	Decrease in IGF-1 in LGLD group compared to control group and no differences in changes in glucose, insulin, or IGFBP-3 or insulin resistance and body composition (BMI,waist circumference, waist-to-height ratio, or percent body fat) between treatment groups.
Fabbrocini et al. (1)	2016	Italy	Randomized controlled trial	6 months	Age 17–24 years, male sex and presence of acne for at least 1 year that was resistant to common therapies.	Metformin plus a hypocaloric LGLD	Case: n=10 Control: n=10	17–24	100	Decrease in GAGS,BMI,WHR, HOMA-IR, Fasting glucose, Fasting insulin, oGTT, Total cholesterol, HDL in LGLD group
Kwon et al. (11)	2012	Korea	Randomized controlled trial.	10 weeks	Participants with mild to moderate acne	LGLD consisted of 25% energy from protein, 45% from low-GI carbohydrates, and 30% energy from fats	Case: n=17 Control: n=15	20–27	75	Decrease in acne grades, total number of acne lesions, size of the sebaceous gland, H & E, SREBP-1, IL-8. No statistically significant changes in the BMI.
Reynolds RC et al. (12)	2010	Australia	Randomized controlled trial.	8 weeks	Acne severity grade 1, 2 or 3, stable weight over the past three months	Assigned to the high or low GI diet	Case: n=23 Control: n=20	16.5±1.0	100	No significant differences in subject characteristics, baseline acne severity or blood biochemistry between the two diet groups
Smith R et al. (13)	2008	Australia	Non-randomized, parallel controlled feeding trial	7 day	Having acne based on self-reported history of persistent acne (acne present on most days for the past 6 months)	LGLD (25% energy from protein and 45% from carbohydrates) or a HGL diet (15% energy from protein, 55% energy from carbohydrate)	Case: n=7 Control: n=5	17.0±0.4	100	The LGL group: increased insulin sensitivity, IGFBP-1, IGFBP-3 and decreased triglycerides, no change in FAI while the HGL group: Increased insulin resistance, FAI and decreased SHBG, HDL. Both groups demonstrated significant decreases from baseline in total cholesterol and LDL
Smith R et al. (25)	2008	Australia	Randomized controlled trial	12 weeks	Had acne for longer than 6 months prior to recruitment	LGLD, comprised of 25% energy from protein and 45% from low GI carbohydrates	Case: n=16 Control: n=15	15-25	100	LGLD reduced weight and total lesion counts and increases in the ratio of saturated to monounsaturated fatty acids of skin surface triglycerides when compared to controls

BMI: Body mass index, GI: Glycemic Index, GL: Glycemic Load, IGF-1: insulin-like growth factor-1, LGLD: low glycemic load diet, IGFBP: insulin-like growth factor binding protein, GAGS: Global Acne Grading System, WHR: waist to hip ratio, HOMA-IR: Homeostasis Model Assessment of Insulin Resistance, oGTT: oral glucose tolerance test, HDL: high-density lipoprotein, H&E: hematoxylin and eosin, SREBP: sterol regulatory element-binding protein, IL-8: interleukin-8, HGL: high glycemic load, FAI: free androgen index, SHBG: sex hormone binding globulin, LDL: low-density lipoprotein composition modifications when comparing groups and illustrated no differences in waist circumference, waist-to-height ratio, BMI, or percent body fat, between groups (4). Therefore, the findings of low glycemic load diet intervention on acne lesions is verified.

Low Glycemic Load Diet and Acne Lesions

The mean number of lesions declined representing a significant correlation between the alterations in total number of acne lesions and a decrease in the glycemic load (11). A significant decline in the overall size of the sebaceous glands was seen in the LGLD group when compared to the baseline values (11). Only in one clinical trial, no significant differences was noted regarding subject characteristics, baseline acne severity or blood biochemistry between the two diet groups (12). This review summarized the literatures on the effect of low glycemic load diet on acne lesions and parameters in relation to it and the possible mechanisms. All clinical trials indicated a decline in acne lesions in the LGLD group (1, 4, 11, 13, 25). Only one by Reynolds et al. displayed no significant differences in relation to subject characteristics, baseline acne severity or blood biochemistry between the two groups (12). GI and GL were invloved in acne pathogenesis because of diet-induced hyperinsulinemia, stimulating a rise in IGF-1 levels and androgen hormones and consequently, amplifying acne-promoting pathways (31, 32). Table 1 demonstrates the effects of glycemic control on acne based on different human studies.

Conclusion

In patients with acne resistant to common treatments, a possible diagnostic/therapeutic algorithm would be as follows: Evaluating the serum glucose and insulin levels, then HOMA-IR, and finally OGTT. If metabolic variables were altered, an endocrinological consultation could be undertaken to assess the prescription of a low glycaemic diet.

Conflict of Interest

None declared.

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