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Research Article

A pilot study to determine the short-term effects of a low glycemic load diet on hormonal markers of acne: A nonrandomized, parallel, controlled feeding trial

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Observational evidence suggests that dietary glycemic load may be one environmental factor contributing to the variation in acne prevalence worldwide. To investigate the effect of a low glycemic load (LGL) diet on endocrine aspects of *acne vulgaris*, 12 male acne sufferers (17.0 ± 0.4 years) completed a parallel, controlled feeding trial involving a 7-day admission to a housing facility. Subjects consumed either an LGL diet (n = 7; 25% energy from protein and 45% from carbohydrates) or a high glycemic load (HGL) diet (n = 5; 15% energy from protein, 55% energy from carbohydrate). Study outcomes included changes in the homeostasis model assessment of insulin resistance (HOMA-IR), sex hormone binding globulin (SHBG), free androgen index (FAI), insulin-like growth factor-I (IGF-I), and its binding proteins (IGFBP-I and IGFBP-3). Changes in HOMA-IR were significantly different between groups at day 7 (–0.57 for LGL *vs.* 0.14 for HGL, p = 0.03). SHBG levels decreased significantly from baseline in the HGL group (p = 0.03), while IGFBP-I and IGFBP-3 significantly increased (p = 0.03 and 0.03, respectively) in the LGL group. These results suggest that increases in dietary glycemic load may augment the biological activity of sex hormones and IGF-I, suggesting that these diets may aggravate potential factors involved in acne development.

Keywords: Acne / Androgens / Glycemic load / Insulin resistance

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1 Introduction

Acne pathogenesis is complex, with strong evidence supporting the involvement of increased sebum production, abnormal differentiation of skin keratinocytes, bacterial colonization, and inflammation [1]. Although scientific research has clarified many of the histological and immunological processes that characterize acne, the fundamental cause of the disease remains unknown. Experimental evidence has shown that androgen hormones are essential for acne development [2, 3], however the relationship between acne severity and circulating androgen levels has been difficult to prove. Variations in the clinical response to androgens suggests that acne development may also be affected by androgen bioavailability, androgenic precursors, and androgen receptor sensitivity [4]. Furthermore, acne development can also be influenced by other biological factors, including growth hormone, insulin-like growth factor-I (IGF-I), and insulin [4].

It is possible that the expression of acne may be affected by endocrine changes which are closely related to the pubertal rise in insulin resistance. The insulin response to glucose loads is increased during normal puberty and adolescence, and insulin sensitivity is decreased compared with adults and prepubertal children [5, 6]. Insulin can affect the entire androgen axis: the pituitary, where it acts as a gonadotrophin amplifier [7]; the gonads where is stimulates androgen syn-

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Abbreviations: FAI, free androgen index; **GI,** glycemic index; **HGL,** high glycemic load; **HOMA-IR,** homeostasis model assessment of insulin resistance; **iAUC,** incremental area under the curve; **IGF-I,** insulin-like growth factor-I; **IGFBP,** insulin-like growth factor binding protein; **LGL,** low glycemic load; **PCOS,** polycystic ovary syndrome; **SHBG,** sex hormone binding globulin; **tAUC,** total area under the curve

thesis [8, 9]; the adrenal glands, where it stimulates production of androgenic precursors [10]; and the liver, where it inhibits sex hormone binding globulin (SHBG) production [11]. Insulin can also have direct effects on sebum production [12], and can amplify the growth promoting effects of IGF-I by inhibiting the production of IGF binding protein-1 (IGFBP-1) [11]. Therefore, it is possible that underlying changes in insulin metabolism may potentiate multiple factors involved in acne development.

Strong support for a link between acne and insulin resistance can be found in the high prevalence of acne in women with polycystic ovary syndrome (PCOS), a condition associated with insulin resistance, hyperinsulinemia and hyperandrogenism [13, 14]. Evidence is accumulating that Western dietary habits contribute to this high risk hormonal profile [15], but the efficacy of dietary change in altering hormone levels has not been sufficiently investigated [16]. Treatments for PCOS now includes insulin-sensitizing drugs or carbohydrate digestion inhibitors, which improve insulin sensitivity, restore fertility and alleviate acne [17, 18].

Dietary glycemic load may be one environmental factor linking acne and hyperinsulinemia. The glycemic load may be interpreted as a measure of the blood glucose and insulin-raising potential of a meal or diet [19]. Unlike the glycemic index (GI), which classifies the glycemic response of carbohydrates on a gram-for-gram basis, the glycemic load also takes into consideration the amount of carbohydrate consumed and is defined as the product of the GI and the carbohydrate content. Cordain *et al.* [20] recently proposed that a high glycemic load (HGL) Western diet may frequently expose adolescents to significant hyperinsulinemia and a hormonal cascade that favors increased keratinocyte growth and androgen-mediated sebum production. This is supported by the observed low rates of acne among cultures existing on low glycemic load (LGL) traditional diets comprised of minimally processed plant foods or low amounts of carbohydrate [20 – 22]. Furthermore, when these societies urbanize and become exposed to an HGL diet, acne becomes a common and sometimes severe problem [21]. However, it remains unknown whether reducing dietary glycemic load can alter clinical or endocrine aspects of acne. Therefore, in a controlled feeding trial, we investigated the short-term effects of altering the dietary glycemic load on endocrine variables associated with acne and insulin resistance.

2 Materials and Methods

2.1 Study design

The experimental protocol followed a parallel, nonrandomized feeding trial involving a 7-day admission to a temporarily assigned research facility at Ballarat University (Ballarat, Victoria, Australia). The research facility consisted of two separate dormitories, each offering a fully equipped kitchen, dining area, and accommodation for the overnight housing of subjects. In a well-controlled feeding environment, seven subjects consumed a LGL diet and five consumed an HGL diet for a period of 7 days. To ensure optimal control of dietary interventions, subjects were housed and fed in separate wards according to their dietary group allocation. At days 0 and 7, a venous blood sample was taken after an overnight fast. In addition, capillary blood samples were obtained on day 3 every hour for the measurement of blood glucose responses to meals.

The primary endpoints of this study were changes in insulin sensitivity and hormonal markers of acne. This study was approved by the Human Ethics Committee of RMIT University and all subjects and guardians (if aged < 18 years) gave informed consent to participate in the study.

2.2 Study subjects

Twelve young males (aged 15 – 20 years) with mild-moderate acne were recruited from primary care physicians, dermatologists, and newspaper advertisements. Participants were classified as having acne based on self-reported history of persistent acne (acne present on most days for the past 6 months). As several patients were recruited from specialists, this study was bound by a duty-of-care to provide nonharmful treatments to patients seeking medical treatment. It was considered unethical to place referred patients on an intervention that could potentially harm or worsen acne severity. For this reason, subjects exhibiting milder forms of the disease, who were not actively seeking treatment, were recruited as controls. This research was intended as a pilot study for the design of a larger, randomized dietary intervention trial.

2.3 Dietary intervention

Dietary glycemic load was manipulated by means of modification to the amount and type of carbohydrate. The LGL diet was achieved by means of a reduction in the amount of carbohydrate and by utilizing carbohydrates with a lower GI. To maintain energy intakes, the percentage of lost energy from carbohydrates was replaced with energy from protein. In contrast, the HGL diet supplied more energy from carbohydrates and less from protein, and included foods with a higher GI. The target macronutrient composition of the LGL diet was 25% energy from protein, 45% energy from carbohydrates, and 30% energy from fats and that of the HGL diet was 15% energy from protein, 55% energy from carbohydrates, and 30% energy from fats. For the average subject (age 17, height 177 cm, weight 69 kg), a 7-day menu plan was calculated to meet each diet's target macronutrient composition, as well as matching for energy (1.16 MJ) and the composition of dietary fats (saturated 8%, polyunsaturated 7%, monounsaturated 13%) between groups. Main meals were prepared and served according to specifications in the planned menu, however subjects were

allowed to eat *ad libitum* between meals. Foods were weighed before each meal, and any unconsumed portions were also weighed to determine the amount of food consumed. Subjects were instructed to only eat the foods provided or prepared within their housing ward during the 7-day trial period. Dietary intakes were calculated using Australia specific dietary analysis software (Foodworks, Xyris Software, Highgate Hill, Australia).

2.4 Calculation of dietary GI and glycemic load

The dietary GI and glycemic load were calculated using the following equations: dietary GI = Σ(GI for food item × proportion of total carbohydrate contributed by item), and dietary glycemic load = Σ(GI for food item × its carbohydrate content in grams ÷ 100). The GI values used had glucose as the reference food and were taken from reference tables [23], and Sydney University's GI website (The Glycemic Index and GI database is produced by Sydney University and is available at http://www.glycemicindex.com; accessed 2003).

2.5 Diurnal measurement of capillary blood glucose

On day 3, blood glucose was measured every hour between 09:00 and 21:00 to verify differences in glycemic load. Subjects were allowed to engage in light activities (*e.g.*, slow walking, easy physical work, and sitting) during the day of testing, but were restricted from doing any moderate-high intensity activities. Capillary blood glucose was measured using the glucose dehydrogenase method (HemoCue 201+ glucose analyzer, Sweden; intra-assay CV = 1.6%). The postprandial glucose responses were assessed using the incremental (iAUC) and total (tAUC) area under the glucose curve. iAUC and tAUC were geometrically calculated using the trapezoidal method [24].

2.6 Acne scoring

Scaling of acne was performed by a dermatology registrar on day 0 of the study to provide information on subject characteristics at baseline. The registrar assessed facial acne occurrence and severity only, using the Cunliffe-Leeds lesion count technique [25]. Changes in acne severity were not reported as at study outcome due to the short duration of the study and as treatment response usually takes several weeks [26].

2.7 Laboratory analyses

Code labeled serum samples were stored at −20°C for analysis poststudy by an independent laboratory. Day 0 and day 7 samples for each subject were included in the same assay run to avoid interassay variability. Serum insulin was measured using a commercially available microparticle enzyme immunoassay (Abbott Laboratories, Tokyo, Japan; intra-assay CV: 4.0%). SHBG concentrations were assayed with a commercially available RIA (Orion Diagnostica, Espoo, Finland; intra-assay CV = 2.5%). Total testosterone was measured using solid-phase RIA (Diagnostic Products, Los Angeles, USA; intra-assay CV: 2.7%). The free androgen index (FAI) was calculated as testosterone concentration (nmol/L) × 100 ÷ SHBG concentration (nmol/L). Total IGF-I (intra-assay CV: 2.9%) and dehydroepidandrosterone sulfate (DHEAS, intra-assay CV: 8.1%) were measured using semiautomated Immulite technology (Diagnostic Products). IGFBP-1 and IGFBP-3 were assayed with a non-commercial RIA as previously described [27, 28]. An automated Olympus analyzer (Melville, USA) was used to measure total cholesterol, HDL cholesterol, and triglyceride levels (intra-assay CV were 1 – 2% for all tests). Low-density lipoprotein cholesterol was calculated by the Friedewald formula [29].

2.8 Insulin sensitivity

The homeostasis model assessment of insulin resistance (HOMA-IR) was used as a surrogate measure of insulin sensitivity. HOMA-IR was calculated as fasting glucose (mmol/L) × insulin (μU/mL) ÷ 22.5 [30].

2.9 Statistical analysis

All statistical analyses were performed using SPSS 11.0 for Windows (SPSS, Chicago, IL). Baseline data and nutritional characteristics were compared between groups using a Mann – Whitney or an independent-sample *t*-test, depending upon whether or not the data was normally distributed. For the primary endpoints, general linear models were used to test for overall treatment differences with adjustments made for baseline data. Within group comparisons were performed using the paired *t*-test. Changes from baseline are reported as adjusted means and percentages, with statistical analyses done for absolute values. *p*-values less than 0.05 were considered significant.

3 Results

3.1 Subjects

Table 1 shows the baseline characteristics according to group allocation. The groups had similar baseline characteristics with the exception of acne lesion counts. The LGL group had a greater mean number of acne lesions than subjects on the HGL diet.

3.2 Dietary composition

Table 2 shows the composition of the mean baseline diet of all subjects and the LGL and HGL diets during the trial

Table 1. Baseline characteristics of subjects by dietary group

Variable	LGL ($n = 7$)	HGL ($n = 5$)	$p^{a)}$
Age (year)	16.6 ± 0.5	17.6 ± 0.5	0.18
Acne lesion count	34.7 ± 5.0	7.2 ± 2.5	0.001
Weight (kg)	65.4 ± 3.5	75.1 ± 9.3	0.37
BMI (kg/m^2)	20.5 ± 0.6	24.6 ± 2.2	0.15
Waist circumference (cm)	71.8 ± 2.4	81.5 ± 6.1	0.13
Fasting glucose (mmol/L)	4.66 ± 0.38	4.68 ± 0.24	0.94
Fasting insulin (mU/L)	7.91 ± 1.70	8.84 ± 2.01	0.73
HOMA-IR index	1.67 ± 0.39	1.82 ± 0.40	0.80
IGF-I (nmol/L)	42.4 ± 4.3	40.6 ± 5.1	0.80
Testosterone (nmol/L)	20.6 ± 2.1	16.6 ± 2.3	0.23
SHBG (nmol/L)	26.0 ± 4.0	19.4 ± 3.7	0.27

Data are expressed as means ± SEM.
a) *p*-value corresponds with an independent-sample *t*-test or Mann – Whitney for means.

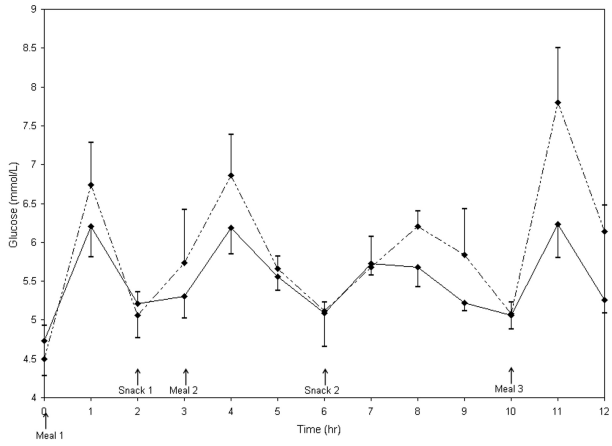

Figure 1. Capillary blood glucose profile for participants on the HGL or LGL diet. Values are mean ± SEM. (–) LGL group ($n = 6$); (- - -) HGL group ($n = 5$).

period. No significant group differences were observed for any dietary variables at baseline. During the trial, both diets were significantly different with regards to the dietary glycemic load and dietary GI. Both diets were also consistent with their target macronutrient composition and the composition of dietary fats was comparable. Although subjects were permitted to eat *ad libitum* between meals, energy intake did not differ significantly between the groups.

3.3 *In vivo* verification of dietary glycemic load

Figure 1 shows the postprandial blood glucose response to meals on day 3. Blood glucose rose to a higher peak in the HGL group after each meal. The calculated iAUC was significantly greater for the HGL group compared to the LGL group ($p = 0.02$; Table 3). However, the total calculated area under the curve was not significantly different between groups.

Tables 3 and 4 show the nutritional characteristics and foods consumed on the day of blood glucose monitoring. The diets were significantly different with regards to glycemic load ($p < 0.001$), dietary GI ($p = 0.001$), percentage energy from carbohydrate ($p = 0.01$), and percentage energy from protein ($p = 0.02$). With regards to relationship of dietary variables and blood glucose profile, the iAUC correlated with dietary GI ($r = 0.60$, $p = 0.04$), but not glycemic load ($p = 0.08$).

Table 2. Dietary composition of the LGL and HGL diets at baseline and during the controlled feeding period

Nutrient	Baseline[a)] ($n = 13$)	Trial period		
		LGL ($n = 7$)	HGL ($n = 5$)	$p^{b)}$
Energy (kJ/day)	9814 ± 542	10278 ± 912	11574 ± 425[c)]	0.30
Dietary GI	58.1 ± 1.0	36.0 ± 0.3[c)]	71.0 ± 1.4[c)]	<0.001
Dietary glycemic load	175.7 ± 11.1	93.5 ± 9.2[c)]	254.9 ± 10.6[d)]	<0.001
Carbohydrate (% of total kJ)	52.1 ± 1.8	44.0 ± 1.0[c)]	54.0 ± 2.4	0.001
Protein (% of total kJ)	16.4 ± 1.0	24.1 ± 0.9[c)]	15.6 ± 0.4	<0.001
Total fat (% of total kJ)	31.4 ± 1.2	31.0 ± 1.4	30.6 ± 1.8	0.85
Fat subgroups (% of total kJ)				
Saturated	13.2 ± 0.6	8.0 ± 0.3[d)]	7.7 ± 0.4[d)]	0.50
Polyunsaturated	4.1 ± 0.3	6.7 ± 0.7[c)]	6.7 ± 0.4[e)]	0.94
Monounsaturated	11.5 ± 0.6	13.6 ± 0.7	13.6 ± 0.9	0.96
Cholesterol (mg/day)	296 ± 28	391 ± 17[c)]	200 ± 9	<0.001
Dietary fiber (g/day)	19.3 ± 1.3	31.6 ± 3.9	22.5 ± 2.1	0.16

Data are expressed as means ± SEM.
a) An independent-sample *t* test revealed no significant group differences at baseline.
b) *p* value corresponds with independent-sample *t*-test.
c) – e) Significant difference from baseline: (c) $p < 0.05$, (d) $p < 0.01$, and (e) $p < 0.001$.

Table 3. Nutritional characteristics and the area under the glucose curve for the day of diurnal blood glucose monitoring

Variable	LGL ($n = 7$)	HGL ($n = 5$)	p
Nutritional characteristics (Day 3)			
Energy (kJ)	9817 ± 660	10400 ± 568	0.54
Dietary glycemic load	88.7 ± 6.7	248.7 ± 20.5	<0.001
Dietary GI	33.1 ± 0.5	71.4 ± 1.4	0.001
Carbohydrate (% of total kJ)	45.0 ± 2.5	56.9 ± 2.8	0.01
Protein (% of total kJ)	22.8 ± 0.9	18.4 ± 1.5	0.02
Fat (% of total kJ)	31.8 ± 3.0	24.2 ± 2.4	0.09
Glycemic profile (Day 3)			
iAUC (mmol.h/L)	10.3 ± 1.5[a)]	16.9 ± 1.9	0.02
tAUC (mmol.h/L)	66.4 ± 2.0[a)]	70.9 ± 2.4	0.18

a) $n = 6$ due to an outlier of more than 3 SDs from the mean. Subject had an undiagnosed myopathy.

3.4 Study outcomes

Table 5 shows the mean change in hormonal variables and plasma lipids at day 7 according to dietary group. The mean change in fasting insulin levels ($p = 0.05$) and HOMA-IR ($p = 0.03$) was significantly different between groups with the LGL group showing a trend for improved insulin sensitivity and the HGL group showing a trend for increasing insulin resistance. At day 7, SHBG levels decreased by 9% ($p = 0.03$) from baseline in the HGL group and the FAI increased by 19% ($p = 0.03$). In contrast, no change in androgen levels or the FAI were observed in the LGL group. However, the LGL group demonstrated a 28% increase in IGFBP-1 levels ($p = 0.03$) and a 27% increase in IGFBP-3 concentrations ($p = 0.03$) when contrasted to the pretreatment values. Both groups also demonstrated significant decreases from baseline in plasma total cholesterol ($p = 0.004$ for LGL group and $p = 0.03$ for HGL group) and LDL-cholesterol ($p = 0.002$ for LGL group and $p = 0.04$ for HGL group). In addition, the HGL group demonstrated a 10% decrease in HDL cholesterol ($p = 0.01$), while the LGL group showed a 32% decrease in plasma triglycerides ($p < 0.001$).

4 Discussion

This study showed that altering the dietary glycemic load may have important effects on insulin sensitivity and factors related to acne. In a well-controlled feeding environment, subjects on the LGL diet demonstrated improvements in insulin sensitivity when compared to the HGL group. In addition, this study found that the HGL diet significantly increased androgen bioavailability, while increases in IGF-I binding proteins in the LGL group suggest a reduction in IGF-I activity. These results are concordant with the known relationship of insulin and the actions of androgens and IGF-I, and suggest that HGL diets may promote underlying causal factors associated with acne development.

The acute physiologic responses to feeding were also demonstrated in the marked between diet differences in

Table 4. Experimental meals during the day of blood glucose monitoring

	LGL group ($n = 6$)		HGL group ($n = 5$)	
Meal 1	Bran based cereal or muesli	40 g	Corn or rice based cereal	50 g
	Milk, low fat	160 g	Milk, skinny	200 g
	Bacon, fat removed, fried	35 g	Bread, white, increased fiber	1 slice
	Egg, whole, fried	35 g	Honey/Jam	1 tsp
	Bread, mixed grain	2 slice	Margarine, polyunsaturated	7 g
	Margarine, canola	7 g	Fruit juice	225 mL
	Honey	1 tsp		
	Apple juice	225 mL		
Snack 1	Yoghurt, low fat	200 g	Yoghurt, low fat	200 g
			Lamington	1 piece
Meal 2	Bread, mixed grain	4 slice	Bread, white, increased fiber	4 slice
	Beef, silverside, lean	150 g	Ham, lean	42 g
	Salad, mixed	60 g	Cheese, low fat	45 g
	Water	500 mL	Salad, mixed	110 g
			Water	500 mL
Snack 2	Milk, low fat	200 mL	Cordial beverage	225 mL
	Chocolate beverage base	2 tsp	Cereal bar	30 g
	Dried fruit and nuts	100 g		
Meal 3	Beef, rump, lean, raw	195 g	Fish, raw	150 g
	Vegetables, raw	170 g	Potato chips, baked	225 g
	Olive oil	1 ½ tsp	Salad, raw	80 g
	Honey	½ tsp	Fruit	1 piece
	Soy sauce, light	1 ½ tsp	Ice-cream, low fat	100 g
	Noodles, mung bean, cooked	75 g	Orange flavored soft drink	225 mL
	Frozen fruit dessert	85 g		

Table 5. Mean change in study endpoints after 7 days on experimental diets

	Adjusted means[a]		
	LGL ($n = 7$)	HGL ($n = 5$)	p[b]
Fasting glucose (mmol/L)	−0.12 ± 0.11	0.10 ± 0.13	0.22
Fasting insulin (mU/L)	−2.58 ± 0.88	−0.59 ± 1.04	0.05
HOMA-IR index	−0.57 ± 0.18	0.14 ± 0.22	0.03
Testosterone (nmol/L)	−1.21 ± 0.76	1.00 ± 0.92	0.11
SHBG (nmol/L)	−1.18 ± 0.75	−2.14 ± 0.89[c]	0.44
FAI (nmol/L)	−2.37 ± 5.91	19.39 ± 7.03[c]	0.04
DHEA-S (mmol/L)	0.32 ± 0.39	−0.11 ± 0.46	0.50
IGF-I (nmol/L)	−4.51 ± 1.95	−7.23 ± 2.31	0.39
IGFBP-1 (ng/L)	8.65 ± 3.23[c]	0.38 ± 3.85	0.14
IGFBP-3 (mg/L)	0.73 ± 0.28[c]	0.23 ± 0.34	0.30
T-Chol (mmol/L)	−0.81 ± 0.15[d]	−0.63 ± 0.17[c]	0.45
LDL-Chol (mmol/L)	−0.85 ± 0.14[d]	−0.51 ± 0.16[c]	0.16
HDL-Chol (mmol/L)	0.03 ± 0.04	−0.10 ± 0.05[d]	0.06
Triglycerides (mmol/L)	−0.24 ± 0.34[e]	0.46 ± 0.41	0.25

DHEA-S, dehydroepiandrosterone sulfate

a) Means are adjusted for baseline values.

b) General linear models were used to test for overall treatment differences.

c) – e) Significant difference from baseline: (c) $p < 0.05$, (d) $p < 0.01$, and (e) $p < 0.001$.

day-long blood glucose responses. By maximizing differences in glycemic load, this study demonstrated a ~60% higher iAUC for glucose with the HGL diet when compared to the LGL diet. However, iAUC for glucose did not correlate with dietary glycemic load possibly due to the small number of subjects and the frequency of blood glucose sampling in the early postprandial phase (<1 h). Instead, this study found that the calculated dietary GI predicted the day-long iAUC for glucose, suggesting that the GI of relative carbohydrate foods was an important determinant in postprandial glycaemia. This is consistent with previous mixed meal studies which found that blood glucose responses can be predicted from the weighted GI of constituent foods [24, 31]. Although the coingestion of protein and fat can reduce postprandial glycaemia [32, 33], Wolever and Bolognesi [34] observed that the amount and type of carbohydrate in mixed meals accounts for 90% of the variability in the blood glucose response. As seen in our study and others [24, 31], variations in the protein and fat content of mixed meals did not appear to obscure the accumulative effect of component carbohydrates. This is supported by the observation that the glycemic load can be used to predict day-long blood glucose and insulin responses for whole diets, independent of increases in protein consumption [35].

One of the important findings of the present study was the rapid and significant effect of dietary intervention on fasting insulin and HOMA-IR. These findings are consistent with previous intervention studies which suggest that LGL diets can improve insulin sensitivity, independently of changes in caloric intake [36, 37]. However, clamping for total energy may limit the full benefit of LGL diets because of the influence of low GI foods on satiety and decreasing food intake [38, 39]. Accumulating evidence suggests that LGL interventions may facilitate weight loss in overweight and obese adolescents, without the need for an imposed energy restriction [40, 41]. Although both diets in the present study were essentially designed to prevent changes in body weight, the voluntary intake of food between meals allowed some degree of variability in energy consumption. However, we suspect that the difference in energy of the two diets was not sufficient in magnitude and/or duration to significantly impact on insulin resistance *via* changes in body fat distribution. Although the underlying mechanisms are yet to be fully defined, HGL diets may influence insulin sensitivity, independently of changes in weight or caloric intake, through elevations in: (i) plasma insulin [42, 43]; (ii) free fatty acids [44]; (iii) counter-regulatory hormones (*e.g.*, cortisol and growth hormone) [45]; and (iv) adipocyte diameter [46].

The results of the present study suggest that HGL diets may be associated with increases in androgen activity. This study found that the HGL diet increased androgen bioavailability by 19% and decreased SHBG levels by 9% when compared to pretreatment values. These changes may be partly explained by the ability of insulin to suppress SHBG synthesis at the hepatic level [47], thereby increasing the bioavailability of circulating androgens to tissues. In addition, insulin can further promote androgen bioavailability, by acting at the pituitary [7] and gonads [8, 9] to increase androgen synthesis. These findings suggest that dietary glycemic load may have important implications for acne and other clinical manifestation of androgen activity (*e.g.*, hirsuitism, alopecia). Indirect support for this notion comes from evidence of the therapeutic effect of pharmacotherapies aimed at slowing the rate of carbohydrate absorption. Ciotta *et al*. [17] recently demonstrated a 46% reduction in the acne/seborrhea score in PCOS patients treated with an α-glucosidase inhibitor. The clinical improvement was associated with a significant reduction in the insulin response to an oral glucose load, a decrease in androgen concentrations, with a significant rise in SHBG levels [17]. This suggests that reducing the postprandial rise in blood glucose concentrations *per se* may have a therapeutic effect on clinical and endocrine assessments of acne.

This study also suggests that LGL diets can influence IGF-I activity *via* changes in the level of IGF-binding proteins (IGFBPs). The LGL diet increased concentrations of IGFBP-1 by 28% and IGFBP-3 by 27% when compared to the pretreatment values. These changes may be explained by the changes in the metabolic milieu associated with the consumption of an LGL diet. Insulin is the principle determinant of plasma IGFBP-1 levels and low basal IGFBP-1 levels have been observed in insulin resistant individuals, possibly due to increased portal insulin overnight [48]. IGFBP-3, on the other hand, may be affected by postpran-

dial hyperglycemia as demonstrated by the significant reduction in IGFBP-3 concentrations after the consumption of a high GI meal when compared to a low GI meal [49]. Given that IGF-I is a potent stimulator of sebocyte [12] and keratinocyte [50] proliferation, it is possible that LGL diets may induce changes to the IGF-I system which may be clinically relevant to acne development.

Several methodological issues pertaining to this study warrant further consideration. Firstly, as participants were not formally randomized to groups (for reasons previously outlined), we cannot underestimate the influence of selection bias. Nevertheless, our results are consistent with other randomized trials which report that LGL diets reduce androgen bioavailability and increase SHBG levels, while improving insulin metabolism [51, 52]. The use of HOMA-IR as a surrogate measure of insulin sensitivity also warrants consideration. This index reflects hepatic insulin sensitivity and is based on the assumption that insulin sensitivity of the liver and peripheral tissues are equivalent [53]. Although this index has been found to correlate with clamp-derived insulin sensitivity in large studies, its utility in small intervention trials remains uncertain. Furthermore, given the nature of the dietary intervention in this study, it is possible that the compensatory changes in other nutrients (*e. g*., increased meat intake, micronutrients, *etc*.) may have influenced study endpoint measurements.

On the other hand, this study also had several strengths, including the precise control in the composition of foods provided and the accurate recording of dietary intakes. As participants were absolved from outside influences, dietary compliance could be achieved with minimal deviation from the dietary protocol. In nutrition research, knowledge of the level of dietary adherence is crucial when assessing an impact of dietary manipulations on physiologic processes [54]. By eliminating the variability associated with food selection and discrepancies in dietary compliance, this study was able to be performed with fewer numbers and under a shorter time frame.

In summary, these results suggest that LGL diets may have a therapeutic potential in the treatment of acne because of the beneficial endocrine effects of these diets. When compared to a typical HGL Western diet, an LGL diet was shown to reduce postprandial glycemia, while improving insulin sensitivity and decreasing androgen bioavailability. However, as this study only evaluated the short-term effects of dietary intervention under ideal conditions, these suggestive findings will need to be substantiated by larger-scale experiments carried out under real life conditions.

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