The effect of a high-protein, low glycemic–load diet versus a conventional, high glycemic–load diet on biochemical parameters associated with acne vulgaris: A randomized, investigator-masked, controlled trial

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Background: No previous study has sought to examine the influence of dietary composition on acne vulgaris.

Objective: We sought to compare the effect of an experimental low glycemic–load diet with a conventional high glycemic–load diet on clinical and endocrine aspects of acne vulgaris.

Methods: A total of 43 male patients with acne completed a 12-week, parallel, dietary intervention study with investigator-masked dermatology assessments. Primary outcomes measures were changes in lesion counts, sex hormone binding globulin, free androgen index, insulin-like growth factor-I, and insulin-like growth factor binding proteins.

Results: At 12 weeks, total lesion counts had decreased more in the experimental group (−21.9 [95% confidence interval, −26.8 to −19.0]) compared with the control group (−13.8 [−19.1 to −8.5], $P = .01$). The experimental diet also reduced weight ($P = .001$), reduced the free androgen index ($P = .04$), and increased insulin-like growth factor binding protein-1 ($P = .001$) when compared with a high glycemic–load diet.

Limitations: We could not preclude the role of weight loss in the overall treatment effect.

Conclusion: This suggests nutrition-related lifestyle factors play a role in acne pathogenesis. However, these preliminary findings should be confirmed by similar studies. (J Am Acad Dermatol 2007;57:247-56.)

The pathogenesis of acne is complex, with strong evidence supporting the involvement of sebaceous hyperplasia, follicular hyperkeratinization, bacterial and yeast intrafollicular colonization, and inflammation.[1] Although androgens play an essential role in the development of acne, few studies have demonstrated a direct correlation between acne severity and plasma androgen

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The study was supported by a research grant from Meat and Livestock Australia.

Disclosure: This study was the responsibility of the investigators. Meat and Livestock Australia had no role in data collection, data analysis, data interpretation, or submission for publication. Ms Smith receives a postgraduate scholarship from MINTRAC (National Meat Industry Training Council of Australia). Authors Mann, Braue, Mäkeläinen, and Varigos had no conflicts of interest to disclose.

Presented at the 15th Congress of the European Academy of Dermatology and Venereology Meeting in Rhodes, October 5, 2006, and at the Nutrition Society of Australia Meeting in Melbourne, December 2, 2005.

Accepted for publication January 9, 2007.

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Published online April 20, 2007.
0190-9622/$32.00

doi:10.1016/j.jaad.2007.01.046

Abbreviations used:

BMI:	body mass index
CV:	coefficient of variation
DHEAS:	dehydroepiandrosterone sulfate
FAI:	free androgen index
GI:	glycemic index
HOMA-IR:	homeostasis model assessment of insulin resistance
IGF:	insulin-like growth factor
IGFBP:	insulin-like growth factor binding protein
LGL:	low glycemic load
PCOS:	polycystic ovary syndrome
SHBG:	sex hormone binding globulin

levels.[2] Variations in the clinical response to androgens suggests that the endocrine control of acne is complex.[3] Some studies suggest that acne severity correlates better with sex hormone binding globulin (SHBG) than circulating testosterone levels.[4-6] Elevated dehydroepiandrosterone sulfate (DHEAS), the major adrenal androgen, has also been shown to correlate with acne severity in adolescent girls and with lesion counts in adults.[7,8] Other biologic factors, such as insulin and insulin-like growth factor (IGF)-I, may also augment sebum production, one of the 4 proximate causes of acne. Clinically, IGF-I has been shown to correlate with acne lesion counts in adult women and significantly higher IGF-I levels have been described in women with acne compared with control subjects.[8-10]

Acne is also a common feature of women with polycystic ovary syndrome (PCOS), a condition characterized by hyperandrogenism and hyperinsulinemia.[11] Clinical and experimental evidence suggests that insulin resistance and its compensatory hyperinsulinemia are the underlying disturbance in PCOS, as insulin resistance generally precedes and gives rise to hyperandrogenism.[12] Insulin has been shown to stimulate ovarian androgen production through effects on steroidogenic enzymes and by amplifying gonadotrophin-releasing hormone secretion.[13] Insulin and IGF-I stimulate adrenal androgen synthesis[14] and inhibit hepatic SHBG production,[15] allowing for an increase in androgen bioavailability. Furthermore, insulin has been shown to decrease IGF-binding protein (IGFBP)-1, allowing free IGF-I concentrations to act on target tissues.[16] Treatments aimed at reducing insulin secretion and/or increase insulin sensitivity, such as metformin or acarbose, have been shown to improve clinical symptoms of acne in patients with PCOS.[17-19]

Expression of acne during adolescence may also be affected by endocrine changes, which are closely related to changes in insulin sensitivity. During normal puberty and adolescence, there is a transient decline in insulin sensitivity,[20,21] which is accompanied by a reciprocal decrease in levels of SHBG and IGFBP-1.[22] According to cross-sectional observations, acne begins about the same time as the gradual increase in plasma insulin,[20] the preadolescent increase in body mass index (BMI),[23] and the increase in IGF-I concentrations.[20,21] Acne incidence more closely corresponds to the changing course of insulin and IGF-I levels than to changes in plasma androgens. This is because insulin and IGF-I levels peak during late puberty and gradually decline until the third decade.[20] Acne generally resolves by this time despite circulating androgens remaining unchanged.

Hyperinsulinemia may provide an important link between nutrition-related lifestyle factors and the incidence of acne. Accumulating evidence suggests that low glycemic–load (LGL) diets may play a dual role in the prevention of hyperinsulinemia by lowering the postprandial insulin demand and improving insulin sensitivity.[24-27] Dietary glycemic load may be interpreted as a measure of the blood glucose and insulin-increasing potential, as it represents the rate of carbohydrate absorption (indicated by the glycemic index [GI]) and the quantity of carbohydrate consumed.[28] It has recently been postulated that high intakes of refined, high-GI carbohydrates may be a significant contributor to the high incidence of acne in Western countries.[29] However, the impact of such a dietary change on acne and hormone levels has not been previously investigated. Therefore, the aim of this study was to investigate the effect of a LGL diet, compared with a typical high glycemic–load diet, on acne severity and metabolic and endocrine variables associated with insulin resistance.

METHODS

Study population

Male patients with acne were recruited using flyers posted at a university and newspaper advertisements. Informed consent was obtained from participants and guardians (if age < 18 years) and the study was conducted with the approval of our human ethics committee. This study included only male participants, age 15 to 25 years, with mild-moderate facial acne. Eligible participants were required to have acne for more than 6 months and a severity grade of greater than 0.25 but less than 2.0 as defined by the Leeds acne grading technique.[30] Volunteers were excluded if they were taking medications known to affect acne or glucose metabolism. A washout period of 6 months was required for oral

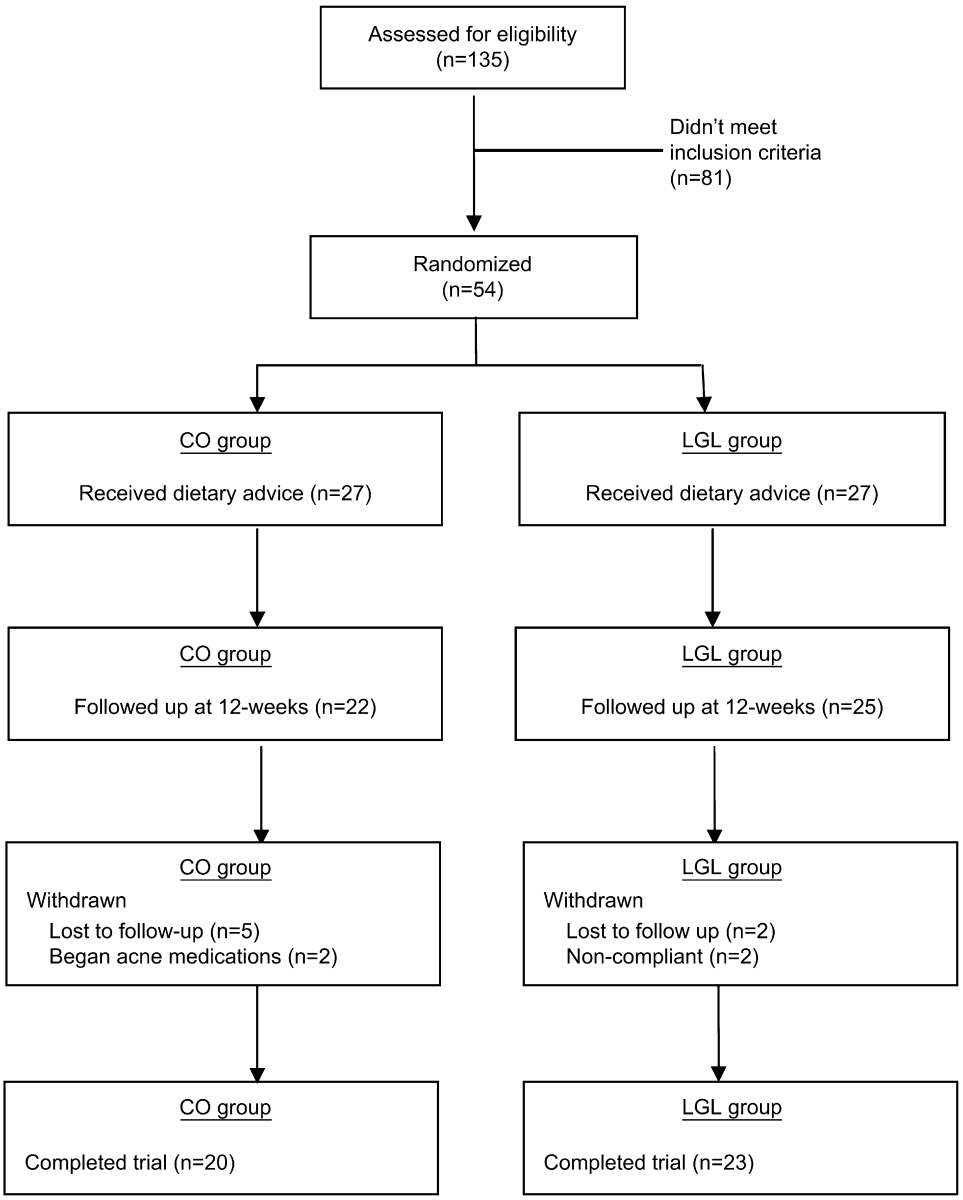

Fig 1. Recruitment to completion of participants in trial.

retinoids or 2 months for oral antibiotics or topical agents.

Study design

It was calculated that 20 participants per group would provide 80% power (at the 2-sided 5% level) to detect a difference of 20% in acne lesion counts, 2.7 μU/mL in fasting insulin, 5.5 nmol/L in SHBG, and 8.3 ng/mL in IGFBP-1. To compensate for expected patient withdrawal, 54 patients were enrolled.

Eligible participants were recruited between June 2003 and June 2004. Approximately 2 to 3 weeks after recruitment, participants attended their baseline appointment and were randomly assigned (1:1) to either the LGL or control group (Fig 1). Randomization was carried out by computer-generated random numbers and allocation to groups was performed by a third party.

This study was designed as a parallel dietary intervention study with investigator-masked dermatology assessments. Topical therapy, in the form of a noncomedogenic cleanser, was standardized for both groups and facial acne was scored at monthly visits (weeks 0, 4, 8, and 12) at the academic research clinic. On all visits, height, weight, percentage body fat, and hip and waist circumferences were measured. All patients were weighed in light clothes and BMI was calculated as: weight (kg)/height $(m)^2$.

Table I. Baseline characteristics of the participants by dietary group for the per protocol population

Variable	LGL (n = 23)	Control (n = 20)	*P*
Age, y	18.2 ± 0.5	18.5 ± 0.5	.66
Body mass index, kg/m^2	22.9 ± 0.6	22.5 ± 0.7	.34
Weight, kg	73.5 ± 2.5	73.3 ± 3.3	.90
Waist circumference, cm	79.2 ± 1.7	79.0 ± 2.2	.81
Total count average	40.6 ± 5.0	34.9 ± 4.3	.40
Inflammatory count average	31.9 ± 3.9	28.4 ± 3.6	.72
Noninflammatory count average	8.8 ± 2.2	6.5 ± 1.6	.62
Fasting glucose, mmol/L	4.76 ± 0.07	4.47 ± 0.09	.02
Fasting insulin, μU/mL	7.37 ± 0.66	7.35 ± 0.74	.99
Testosterone, nmol/L	20.97 ± 1.19	20.36 ± 1.48	.75
SHBG, nmol/L	25.39 ± 1.27	24.75 ± 1.92	.78

LGL, Low glycemic load; *SHBG*, sex hormone binding globulin.

Percentage body fat was measured using a bioelectric impedance analyzer (TBF-521, Tanita Corp, Arlington Heights, Ill). At baseline and 12 weeks, a venous blood sample was taken after an overnight fast.

Dietary intervention

Participants were informed that the study was comparing the carbohydrate to protein ratio in the diet and were not informed of the study's hypothesis. The LGL diet was low in glycemic load, achieved through modifications to the amount and type of carbohydrate. The LGL group members were educated on how to substitute high-GI foods with foods higher in protein (eg, lean meat, poultry, or fish) and lower in GI (eg, whole grain bread, pasta, and fruits). Some staple foods were supplied and participants were urged to consume these or similar foods on a daily basis. Each participant's dietary directions were isocalorically matched with their baseline diet as determined from 7-day weighed/measured food records. The recommended LGL diet consisted of 25% energy from protein, 45% from low GI carbohydrates, and 30% energy from fats. In contrast, the control group received carbohydrate-dense staples and were instructed to eat these or similar foods daily. The foods provided had moderate to high GI values and were typical of their normal diet as evidenced from 7-day weighed/measured food records. The control group were not informed about the GI, but were urged to include carbohydrates as a regular part of their diet. All participants received initial education on how to use foods scales and keep food records. During the study period, nutrient intakes were calculated from 3-day weighed/measured food records each month using Australia-specific dietary analysis software (Foodworks, Xyris Software, Highgate Hill, Australia). Dietary compliance was monitored by regular telephone interviews, assessments of glycemic load per day and 24-hour urine samples (weeks 0 and 12) for an assessment of urea excretion relative to urinary creatinine.

Standardized topical cleanser

All patients were provided with a topical cleanser (Cetaphil gentle skin cleanser, Galderma, Forrests Hill, Australia) and were advised to use it in place of their normal wash, soap, or cleanser. The cleanser provided contained no active agents for acne and its formulation is identical to that which is currently available overseas. Participants began using the topical cleanser 2 weeks before baseline and were asked to maintain a standard level of use during the trial. Compliance was determined from self-report at each visit.

Dermatology assessment

Scaling of the acne was performed by a dermatology registrar who was masked to the group assignment of the participants. The registrar assessed facial acne occurrence and severity using a modified lesion count technique (Leeds) form Burke and Cunliffe.[30] To ensure all acne lesions were counted, located, and graded by size and severity, lesions were mapped by placing a transparent plastic film with a laser-printed grid gently against the skin. Facial anatomic landmarks, such as the ear, chin, and tip of nose, were used to ensure consistency between assessments. Each side of the face was assessed separately. Where necessary, the registrar palpated the skin to determine the lesion type. All assessments were performed under fluorescent background lighting and with a halogen lamp, which could be easily moved to illuminate both sides of the patient's face. To maintain reproducibility of the above method, one physician performed all the dermatology assessments. A small group of volunteers (n = 4) was counted 1 week apart to evaluate the reproducibility by the same physician (9.5% coefficient of variation [CV]).

Biochemical measurements

Code-labelled samples were stored at −80°C for analysis poststudy by an independent laboratory. Baseline and 12-week samples for each participant were included in the same assay run to avoid interassay variability. Serum insulin was measured using a commercially available microparticle

Table II. Dietary composition of the low glycemic load and control diets before randomization and during the trial period

Nutrient	Before randomization (n = 43)	Trial period		P
		LGL (n = 23)	Control (n = 20)	
Energy, kJ/d	10,585	9320*	10,620	.06
Dietary glycemic index†	57	43*	56	<.001
Dietary glycemic load‡	178	101*	174	<.001
Carbohydrate, % total kJ	49	44*	50	<.001
Protein, % total kJ	17	23*	17	<.001
Total fat, % total kJ	32	31	32	<.74
Fat subgroups, % total kJ				
Saturated	13.2	9.0*	12.6	<.001
Polyunsaturated	4.5	6.8*	4.8	<.001
Monounsaturated	11.7	12.4	11.9	<.51
Cholesterol, mg/d	296	309	304	<.93
Dietary fiber, g/d	25.3	36.9*	26.2	<.001

P value corresponds with 1-way analysis of variance or Mann-Whitney.
LGL, Low glycemic load.
*Significantly different from baseline ($P < .05$).
†Calculated as the weighted average glycemic index of all carbohydrate-containing foods in the diet.
‡Calculated as the food's carbohydrate amount (grams) × the respective glycemic index value and divided by 100, then totalled for all foods each day.

enzyme immunoassay (Abbott Laboratories, Tokyo, Japan) (intra-assay CV 4.0%). Capillary blood glucose was measured using a glucose analyzer (201+, HemoCue, Ängelholm, Sweden) (intra-assay CV 1.6%). The homeostasis model assessment of insulin resistance (HOMA-IR) was used as a surrogate measure of insulin sensitivity, calculated as: fasting glucose (mmol/L) × insulin (μU/mL)/22.5.[31] SHBG concentrations were assayed with a commercially available radioimmunoassay (Orion Diagnostica, Espoo, Finland) (intra-assay CV 2.5%). Total testosterone was measured using solid-phase radioimmunoassay (Diagnostic Products, Los Angeles, Calif) (intra-assay CV 2.7%). The free androgen index (FAI) was calculated as: testosterone concentration (nmol/L) × 100/SHBG concentration (nmol/L). IGF-I (intra-assay CV 2.9%) and DHEAS (intra-assay CV 8.1%) were measured using semi-automated technology (Immulite, Diagnostic Products). IGFBP-1 and IGFBP-3 were assayed with a noncommercial radioimmunoassay as previously described.[32,33] An automated analyzer (Olympus, Melville, NY) was used to measure total cholesterol, high density lipoprotein cholesterol, and triglyceride levels (intra-assay CV were 1%-2% for all tests). Low-density lipoprotein cholesterol was calculated by the formula of Friedewald et al.[34]

Statistical analysis

All statistical analyses were performed for the per protocol population using software (SPSS 11.0 for Windows, SPSS Inc, Chicago, Ill) and significance was set at *P* less than .05. Baseline variables were analyzed for between group significance using Mann-Whitney U test or 1-way analysis of variance, depending on whether the data was normally distributed. General linear regression models were used to test for overall treatment differences, with adjustments made for potential cofounders, including age, ethnicity, and baseline data. Secondary analyses of acne end points and hormone variables were performed adjusting for changes in BMI. All covariates were individually entered into the models to determine whether there was an interaction between the covariate and the treatment. Bivariate linear regression analysis was also conducted, pooling data from both groups, to explore relationships between endocrine variables and the change in lesion counts.

RESULTS

Patients

In all, 43 patients completed the study per protocol (Fig 1). Seven participants did not complete the study (5 in control and two in LGL groups) and 4 were removed from data set (two were noncompliant; two began medications known to affect acne, an exclusion criterion). Baseline characteristics are shown in Table I.

Diet composition

Table II lists the diet composition of the LGL and control groups before randomization and during the trial. No significant group differences were observed

Table III. Mean change in outcome variables for the per protocol population at 12 weeks according to dietary group

Variable	Adjusted means (95% CI)*		*P*
	LGL group (n = 23)	Control group (n = 20)	
Total lesion counts	−21.9 (−26.8, −19.0)	−13.8 (−19.1, −8.5)	.01
Inflammatory lesion counts	−16.0 (−20.3, −11.8)	−8.4 (−13.0, −3.8)	.02
Weight, kg	−2.9 (−4.0, −1.7)	0.4 (−0.8, 1.7)	<.001
BMI, kg/m^2	−0.89 (−1.25, −0.54)	−0.02 (−0.41, 0.36)	.002
Percentage body fat (%)	−2.2 (−3.0, −1.4)	−0.5 (−1.3, 0.4)	.006
Waist circumference, cm	−2.2 (−3.6, −0.9)	−0.2 (−1.6, 1.2)	.04

BMI, Body mass index; *CI*, confidence interval; *LGL*, low glycemic load.
*Means are adjusted for differences in baseline values, age and ethnicity.

Table IV. Mean change in hormone concentrations and plasma lipids for the per protocol population at 12 weeks according to dietary group

	Adjusted means* (95% CI)		*P*
	LGL (n = 23)	Control (n = 20)	
Fasting insulin, μU/mL†	−0.90 (−2.59, 0.79)	1.96 (0.15, 3.77)	.03
Log(HOMA-IR)	−0.05 (−0.13, 0.03)	0.09 (0.01, 0.18)	.02
Testosterone, nmol/L	−1.32 (−2.75, 0.12)	−1.20 (2.74, 0.34)	.91
SHBG, nmol/L	0.27 (−1.56, 2.09)	−2.71 (−4.67, −0.74)‡	.03
FAI, nmol/L	−8.73 (−17.34, −0.12)‡	4.51 (−4.74, 13.75)	.04
DHEAS, μmol/L	−0.68 (−1.30, −0.06)‡	−0.12 (−0.79, 0.55)	.22
IGF-I, nmol/L	−2.93 (−6.21, 0.35)	−2.79 (−6.31, 0.73)	.95
Log(IGFBP-1), ng/mL§	0.14 (0.05, 0.22)‡	−0.09 (−0.18, 0.03)	.001
IGFBP-3, mg/mL	0.11 (−0.10, 0.32)	0.16 (−0.06, 0.38)	.75
Total cholesterol, mmol/L	−0.42 (−0.63, −0.21)‡	−0.05 (−0.27, 0.17)	.02
LDL cholesterol, mmol/L	−0.32 (−0.51, −0.13)‡	−0.04 (−0.25, 0.16)	.06
HDL cholesterol, mmol/L	−0.04 (−0.10, 0.10)	−0.05 (−0.11, 0.01)	.92
Log(triglycerides), mmol/L	−0.06 (−0.13, 0.08)	0.03 (−0.05, 0.10)	.10

CI, Confidence interval; *DHEAS*, dehydroepiandrosterone sulfate; *FAI*, free androgen index; *HDL*, high-density lipoprotein; *HOMA-IR*, homeostasis model assessment of insulin resistance; *IGF*, insulin-like growth factor; *IGFBP*, IGF binding protein; *LDL*, low-density lipoprotein; *LGL*, low glycemic load; *SHBG*, sex hormone binding globulin.
*Means are adjusted for differences in baseline values, age, and ethnicity.
†n = 42 As a result of an outlier of more than 3 SD from the mean.
‡Significant difference from baseline to 12 weeks ($P < .05$).
§Analysis was performed on log-transformed variable as the data was log-normally distributed.

in any of the dietary variables at baseline. During the trial period, dietary glycemic load was significantly lower in the LGL group compared with the control group and this was achieved by a reduction in carbohydrate intake and by means of low-GI foods (as indicated by a reduction in the calculated dietary GI) (Table II). Protein intake increased in the LGL compared with the control group ($P < .001$), indicating that some carbohydrates were replaced with foods higher in protein. This was substantiated by a 15.4% increase in urinary urea/creatinine ratio at 12 weeks for the LGL group compared with a 12.3% decrease for the control group ($P = .009$), indicating good dietary compliance. Although the LGL group received isocaloric dietary advice, energy intake decreased relative to their baseline diet ($P = .02$).

Compliance with topical nonacne cleanser

There was no discontinuation of the topical nonacne therapy among the study completers.

Study outcomes

Table III shows the mean change in lesion counts and anthropometric measures at 12 weeks according to dietary group. After adjusting for age, ethnicity, and baseline counts, the reduction in total lesion counts was significantly greater in the LGL group compared with the control group ($P = .01$). Similar results were observed for the mean decrease in inflammatory counts ($P = .02$). Figure 3 shows examples of acne improvement in the LGL group. The LGL group also showed significantly greater reductions in weight ($P < .001$), BMI ($P = .001$), body

fat percentage (P = .006), and waist circumference (P = .04) when compared with the control group. Statistical adjustment of the mean change in acne scores for changes in BMI altered the outcome for total lesion counts (−21.6 [95% confidence interval −28.9 to 14.4] vs −14.1 [−21.9 to −6.2], P = .07), but not inflammatory counts (−16.0 [95% confidence interval −20.6 to −11.4] vs −8.5 [−13.4 to −3.5], P = .04). However, we found no significant interaction effect of dietary treatment and the change in BMI on acne end points.

Table IV shows the mean change in hormonal variables and plasma lipids at 12 weeks according to dietary group. The mean change in fasting insulin levels (P = .03) and log-transformed HOMA-IR (P = .02) was significantly different between groups with the LGL group showing a trend for improved insulin sensitivity and the control group showing a trend for increasing insulin resistance. SHBG levels decreased in the control group compared with the LGL group (P = .031). The effect of dietary treatment on FAI (P = .041) was marginally significant, with the LGL group showing a decrease in testosterone bioavailability compared with the control group. IGFBP-1 increased significantly in the LGL group relative to baseline (P = .001) and this was significantly different from the mean change in the control group. Statistical adjustment for changes in BMI was found to affect the results for HOMA-IR (−0.04 for the LGL group vs 0.08 for the control group, P = .08), SHBG (−0.04 for the LGL group vs −2.35 for the control group, P = .13), and FAI (−8.8 for the LGL group vs 4.6 for the control group, P = .07), but not IGFBP-1 (0.14 for the control group vs −0.09 for the control group, P = .003).

Hormonal variables as predictors of acne improvement

Fig 2 depicts the results from bivariate linear regression analysis. A positive relationship was observed between the change in total lesion counts and the change in insulin sensitivity as determined by HOMA-IR (r = 0.38, P = .01). A change in SHBG levels was also shown to correlate negatively with a change in lesion counts (r = −0.38, P = .01). In contrast, a change in FAI was not significantly associated with the change in lesion counts (r = 0.10, P = .50).

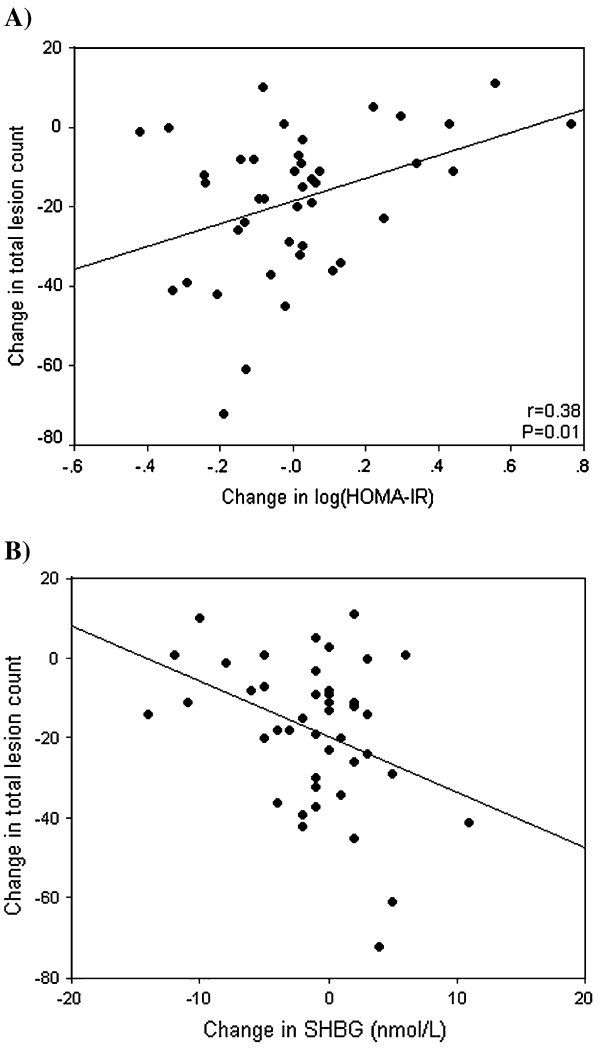

Fig 2. Relationships between acne improvement and hormone variables homeostasis model assessment of insulin resistance (**A**) and sex hormone binding globulin (**B**).

DISCUSSION

This pilot study investigated the independent effects of an experimental LGL diet versus a conventional high glycemic—load diet, combined with a standardized noncomedogenic cleanser. Although both groups showed improvements in acne, the LGL group showed significantly greater reductions in the clinical and endocrine assessments of acne. In addition, participants in the LGL group showed reductions in weight and measures of adiposity, despite receiving dietary advice that was isocalorically matched with diets at baseline. In contrast, participants on the conventional, high glycemic load—diet showed no change in weight or body composition.

This study found a positive effect of a LGL diet on insulin sensitivity when compared with a conventional high glycemic load—diet. The improvement in insulin sensitivity may be attributable not only to the decrease in glycemic load,[35] but also to the decrease in total energy intake and subsequent body weight loss.[36] It has been hypothesized that a decrease in insulin may mediate a reduction in underlying pathological aspects of acne.[29] In accordance with this hypothesis, we observed a moderate relationship

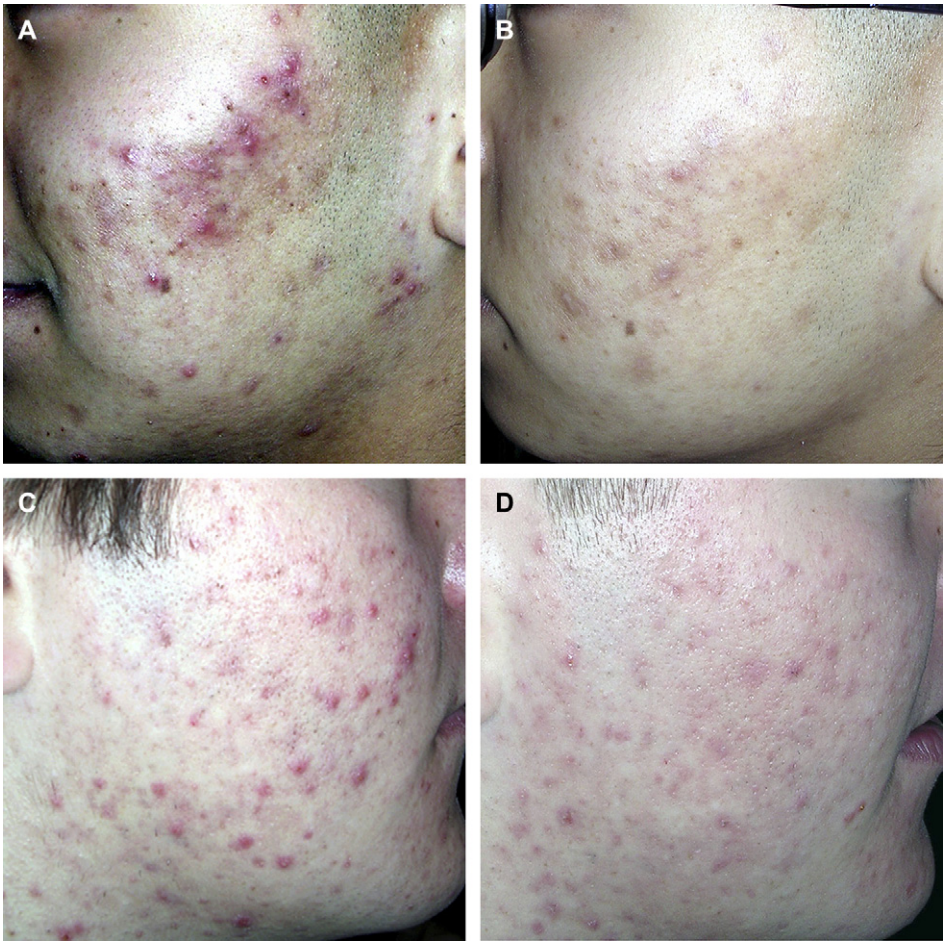

Fig 3. Photographs of acne improvement in low glycemic load group. Patient A at baseline (**A**) and 12 weeks (**B**). Patient B at baseline (**C**) and 12 weeks (**D**).

between the change in insulin sensitivity and the change in acne lesion counts. This suggests that the therapeutic effect may be a factor of the change in insulin sensitivity, or simply that improved insulin sensitivity is another manifestation of a LGL diet. An association between acne and mild peripheral insulin resistance has been previously described in healthy eumenorrheic women.[37] The authors found that patients with acne exhibited significant hyperinsulinemia during an oral glucose tolerance test compared with age-matched control subjects. This relationship was also found to be independent of obesity, as BMI was similar in both groups.

Our results suggest that the improvement in insulin sensitivity may be linked to reductions in androgenicity. We observed a reduction in testosterone bioavailability and DHEAS concentrations in the LGL group and this may help to explain the lessening of acne severity. The observed reduction in free testosterone was probably related to the dual effect of insulin on androgen production in testicular tissues[38] and the hepatic production of SHBG.[15] Plasma concentrations of DHEAS, the major adrenal androgen, also decreased in the LGL group, possibly owing to insulin's effect on the expression of adrenal steroidogenic enzymes.[14] In contrast, the control group showed a decline in insulin sensitivity and SHBG concentrations. Why acne improved in the control group despite no significant change in androgen levels remains unanswered, but the possible direct effect of the topical cleansing agent should be considered.[39] As SHBG correlates inversely with insulin, it was not surprising to find that acne also correlated with the change in SHBG. Our results also corroborate previous evidence that SHBG may be a marker of acne.[5,6,40] However, we observed no relationship between acne severity and free testosterone levels, an association that has been demonstrated in some[7,41] but not all studies.[3,42]

Normal sebaceous gland growth is also influenced by factors other than androgens, such as IGF-I.[9] Therefore, increased expression of IGF-I or

a reduction in the level of its carrier proteins could influence acne. In the current study, IGFBP-1 levels increased significantly in the LGL group compared with the control group and we speculate that this is a compensatory adaptation to the improvement in insulin sensitivity and the reduction in basal insulin. Insulin is the principle determinant of plasma IGFBP-1 levels and low basal IGFBP-1 levels have been observed in insulin-resistant individuals, possibly as a result of increased portal insulin overnight.[43] Therefore, it is possible that the LGL diet may also induce changes to the IGF system that may be clinically relevant to events involved in acne pathogenesis.

There are some limitations regarding the study design and intervention that should be addressed. Firstly, as participants in the LGL group lost weight, we cannot preclude the change in BMI to the overall treatment effect. When we statistically adjusted the data for changes in BMI, the effect of the LGL diet on several clinical and endocrine parameters was lost. However, this does not necessarily imply that acne is influenced by weight loss per se. Weight loss trials, involving women with PCOS, have consistently shown increased SHBG levels[44,45] and decreased FAI.[44,45] However, low-fat dietary interventions in nonobese women have shown no change in SHBG levels after weight loss.[46,47] Currently, there is a paucity of evidence to indicate that acne is more prevalent or severe in overweight adolescents. One study revealed a relationship between weight and acne in men age 20 to 40 years, but this was not true for young males aged 15 to 19 years.[48] Although we cannot determine an aspecific effect of weight loss on acne, one could speculate that a reduction in hyperinsulinemia, either through weight loss or dietary composition, may reduce precipitating factors involved in acne. Another limitation of this study was the use of a fasting index to quantitatively estimate hyperinsulinemia and insulin resistance. Although this index correlates with the euglycemic clamp technique and has proven to be useful in large studies, its applicability to small intervention trials remains uncertain.[49] Furthermore, this test reflects insulin action in a basal state, whereas in life much of insulin action is postprandial. Therefore, it is possible that this index may provide an underestimation or overestimation of the relationship between acne and the extent of hyperinsulinemia.

To our knowledge, this is the first study to demonstrate a therapeutic effect of dietary intervention on acne. The results of this study open the prospect that nutrition-related lifestyle factors may affect the pathogenesis of acne. After 12 weeks, a LGL diet was shown to reduce weight, acne severity, and hormonal aspects of acne (eg, testosterone bioavailability, IGFBP-1, and HOMA-IR) when compared with a conventional high glycemic—load diet. Although we could not determine an aspecific effect of diet from that of weight loss, the finding that insulin sensitivity correlated with acne suggests that both may be involved. Therefore, these results should be considered preliminary and larger-scale studies are needed to confirm the effect of dietary intervention on acne.

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