

A randomized controlled trial of topical benzoyl peroxide 2.5% gel with a low glycemic load diet versus topical benzoyl peroxide 2.5% gel with a normal diet in acne (grades 1-3)

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Abstract

Background: The improvement in insulin resistance and acne lesions on low glycemic load diets in various studies suggests that diet plays a significant role in acne pathogenesis.

Aims: To compare the efficacy of a low glycemic load diet plus topical benzoyl peroxide 2.5% gel with that of only topical benzoyl peroxide 2.5% gel in grades 1, 2 and 3 of acne vulgaris.

Methods: In a randomized controlled trial, 84 patients with grades 1, 2 and 3 acne vulgaris were divided into two groups, to receive a low glycemic load diet and no dietary intervention respectively. Acne lesions (face) were scored and graded at baseline and 4, 8 and 12 weeks. Homeostasis model assessment of insulin resistance and body mass index were measured during the first and last visits. Statistical analysis was done with Statistical Package for the Social Sciences, version 17.0.

Results: Both groups showed significant reduction in acne counts at 12 weeks ($P = 0.931$) with no statistically significant difference between the groups. The differences in body mass index and homeostasis model assessment of insulin resistance between the groups were statistically significant ($P = 0.0001$). Group 1 showed reductions in body mass index and homeostasis model assessment of insulin resistance values at the end of the study, whereas group 2 did not.

Limitations: Application of mild topical cleanser in both the groups might have contributed to the improvement in epidermal barrier function, and topical application of 2.5% of benzoyl peroxide gel in both groups contributed to the improvement in acne counts.

Conclusions: A low glycemic load diet did not result in any significant improvement in acne counts.

Key words: Acne, benzoyl peroxide, low glycemic load diet

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Introduction

Acne is a very common skin disorder affecting individuals of all age groups.^{1,2} Populations that consume low glycemic load diets, such as the Kitavan islanders of Guinea, Ache hunters, Inuits and rural Brazilians, tend to be acne-free.³ An increase in

the incidence of acne was observed in Inuits, Okinawa islanders and Chinese after they started following a western diet.³ These observations suggest that lifestyle factors like diet may have

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a role in acne pathogenesis. A high glycemic load diet causes hyperinsulinemia, high androgen bioavailability, increased insulin-like growth factor-1 and acne.^{4,5} Increased insulin-like growth factor-1 further increases dihydrotestosterone and dehydroepiandrosterone sulfate, which increase sebum secretion and sebocyte proliferation.^{4,5} Increased insulin levels in blood elevate plasma levels of epidermal growth factor, transforming growth factor- β and free nonesterified fatty acids, thereby causing sebaceous gland inflammation and acne.⁶ We conducted this study to determine the efficacy of a low glycemic load diet in the management of acne vulgaris.

Methods

The study was designed as a randomized controlled investigator-blinded trial. After obtaining institutional ethical committee clearance, a total of 84 patients (male and female, age 14–29 years) with acne of grades 1, 2 and 3 were included randomly from among dermatology outpatients in a tertiary care centre between September 2014 and May 2016. Patients already on topical medication, those on oral retinoid in the last 6 months or oral antibiotics in the last 15 days and pregnant women were excluded.

Patients were randomly assigned to two groups of 42 participants each, using the chit in the box method. Allotment was done by a registrar not involved in the rest of the study. Detailed history was taken from all participants including details of diet, duration of acne, treatment history, family history, personal history, cosmetic use and any specific aggravating factors.

A low glycemic load diet (comprising 45% of energy from low glycemic load carbohydrates, 25% from proteins and 30% from fats) was advised for patients in Group 1.

(Glycemic load = Glycemic index of the food item \times its carbohydrate content (g)/100. Glycemic index values were referred from a reference table,⁷ from the Sydney University's Glycemic index website⁸ and from the National Institute of Nutrition, ICMR, Hyderabad, India.⁹)

Constituents of the low glycemic load diet were: Total calories: 1900 (\pm 300 kcal) Carbohydrates: 47% (\pm 5%). Proteins: 23% (\pm 3%) Fats: 30% (\pm 3%) Table 1.

Every participant in group 1 received an individualized diet plan from the dietitian on the first visit which matched their baseline diet. Group 1 patients maintained a diet chart with a daily menu which was examined during every visit to determine adherence.

Topical 2.5% benzoyl peroxide gel and a mild noncomedogenic cleanser were advised for all patients in both the groups.

Acne lesions (face) were scored and graded at all visits (baseline, 4, 8 and 12 weeks). Skin evaluation was done by modified Cunliffe–Leeds lesion count technique.¹⁰ Body mass index and homeostasis model assessment of insulin resistance (fasting glucose mg/dl \times fasting insulin μ U/ml/405) were calculated at baseline and 12 weeks.

Statistical Package for the Social Sciences (SPSS) version 17.00 (SPSS Inc. 233, South Walker Drive, Chicago, IL) was used for statistical analysis. Student's unpaired *t*-test was used to analyze mean values of all quantitative variables. *P* < 0.05 was considered significant.

Sample size was determined by the formula: $n = 2(Z_{\alpha} + Z_{\beta})^2 \sigma^2 / d^2$. With the power of study 90% and the confidence level of 95%, substituting in the above formula, the

Table 1: Diet Chart

7AM TO 8 AM, BREAKFAST	Multi grain toast, 1 cup of multigrain dhal & 1 cup tea or coffee, boiled egg white OR 2 small idlis with chutney or sambar, boiled egg white & tea or coffee OR 1 cup of upuma with chutney or sambhar, boiled egg white & tea or coffee
10 AM	1 Fresh fruit like apple or orange or pear or mosambi, 1 cup of butter milk OR 1 cup of fresh juice or orange or mosambi or apple without sugar with 4 or 5 almonds OR 8 almonds and 3 walnuts, cucumber slices 1 cup
12 PM TO 1.30 PM LUNCH	1½ cup of boiled white rice (or 2 chapathis or 2 phulka) with 1 cup of sambhar, 1 cup of rasam, 1 cup of vegetable curry (or chicken curry or fish curry or mutton curry or mushroom curry), 1 small roasted papad
3.30 TO 4.30 PM	1 cup of coffee with any fruits or almonds, peanuts
7 TO 8 PM DINNER	2 chappatis or 2 phulkas or multigrain toast, 1 cup wholegram dhal, 1 cup spinach curry (or fish curry) 1 cup raita with grated cucumber
9.30 PM	1 fresh fruit & milk

There will be at least 2 hours gap between meals and 1 hour gap between snacks. In between the meal they can eat 3 or 4 light digestive biscuits, or fruits or vegetable salads or vegetable soup or mushroom soup or peanuts or lemon juice or soya milk or boiled pulses or boiled lentils or cashew nuts (or any other nuts hand full).

The stomach will be half filled always.

They won't take full stomach instead of that they can take frequent small quantity foods.

FOOD TO AVOID: CORN FLAKES, OATMEAL, JUNKFOODS - All junk foods and roadside foods to be avoided (including pizzas, burgers, sandwiches, chips, ice creams, pastries, all bakery products like bread, buns, canned processed drinks, biscuits especially cream biscuits, chocolates, samosa, museli, coca cola, cocktail juices).

FRUITS: Can be taken only one cup at a time (Kiwi, Pineapple, Jack fruit, Papaya, Cranberry, Cherry, Mango, Banana, Watermelon, Raisins, Apricots, Dates)

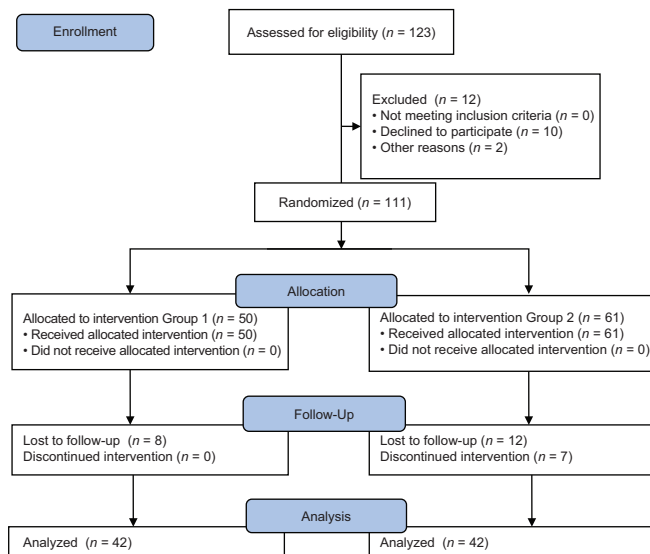
VEGETABLES: Can be taken only one cup at a time (Beetroot, Pumpkins, Potato, Tapioca, Sweet corn)

number of participants required for the study was 84. A total of 111 were enrolled in the study; though some patients were lost to follow-up and some more discontinued the treatment, we retained the required number [CONSORT Flowchart].

Results

The study included 42 individuals in group 1 who followed a low glycemic load diet and 42 patients in group 2 with no dietary intervention. Fifty-four (64.2%) of patients were in the age group of 20–24 years and a majority (57,67.8%) were women [Table 2]. No significant differences were seen between the two groups in age distribution ($P = 0.443$) or sex distribution. Both groups had higher female populations ($P = 0.815$). A majority (68, 80.9%) in both the groups had grade 3 acne, with no significant difference in the grade of acne between the 2 groups ($P = 0.581$).

There was also no significant difference in the duration of acne between two groups. Duration of acne in most patients in our study was between 1 month and 5 years ($P = 0.430$). Thirty-eight (90.4%) patients in group 2 had a family history of acne, compared to 18 (42.8%) patients in group 1 ($P = 0.0001$). Thirty one (73.8%) patients in group 2 had a history of usage of cosmetics compared to 28.5% of patients in group 1 ($P = 0.0001$).



Flowchart: Patient allocation of the present study in a CONSORT flow diagram

Adherence to the low glycemic load diet in group 1 as determined from their daily diet chart was up to 75%.

Even though there was a significant reduction in acne counts at the end of the study in both the groups, [Figures 1 and 2] there was no significant difference [Table 3] between the two groups ($P = 0.931$). The difference between group 1 and group 2 in respect to reduction of body mass index [Table 4] during the study period was statistically significant ($P = 0.0001$). The difference in homeostasis model assessment of insulin resistance [Table 5] during the study period between the two groups was also statistically significant ($P = 0.0001$).

Discussion

Nearly all individuals of 15-17 years age suffer from acne¹¹⁻¹³ and in 15–20% of young individuals, acne is moderate to severe.^{11,14,15} Smith *et al.*, in a randomized controlled trial on 43 male participants aged up to 25 years with mild to moderate facial acne, found that acne was a common problem faced by that age group.¹⁶ The severity of acne vulgaris increases with maturity, and prepubertal girls with severe acne have higher dehydroepiandrosterone sulfate levels.^{17,18} In a German study, the authors found that 64% of people in the age group of 20-29 years and 43% of those in the age group of 30-39 years had acne.^{19,20}

A large Chinese study conducted among undergraduate students found that 78% of first-degree relatives had acne, which was heritable in nature.²¹ Many retrospective studies have identified the genetic basis and clustering of familial cases in acne.²²⁻²⁶

In a cross-sectional study including Kitavan and Ache hunters, Cordain *et al.* observed that there was no acne in these populations consuming low glycemic load diets.² They proposed that a high glycemic load diet is a major factor contributing to acne in Western populations.² Kim *et al.* observed that consumption of fermented milk with lactoferrin decreases the total non-inflammatory and inflammatory lesion counts.²⁷ Kwon *et al.* also found that patients consuming low glycemic load diets showed decrease in the number of acne lesions after 5 weeks.²⁸ Di Landro *et al.* found that there was a positive association between acne and frequent consumption of milk and

Table 2: Demography of analyzed patients and allocated patients

Characteristics	Group 1		Group 2	
	Analyzed	Allocated	Analyzed	Allocated
Baseline characteristics				
Women	28	33	30	44
Men	14	17	12	17
Age	21.71±3.04	21.36±3.14	22.19±3.19	22.37±2.88
Gender ratio	Women: Men=2:1	Women: Men=1.94:1	Women: Men=5:2	Women: Men=2.58:1
Lesion count	Week 0=15.04±7.98	15.380±7.65	Week 0=16.30±8.28	16.27±7.77
Duration of acne (mean±SD)	5.047±2.879	4.8200±2.79	5.787±4.021	5.721±3.87
BMI	Week 0=21.5090±2.3826	21.532±2.300	Week 0=21.384±2.411	21.154±2.307
	Week 12=21.1717±2.2563		Week 12=21.668±2.565	

skimmed milk.²⁹ In our study, patients who consumed a low glycemic load diet showed decrease in body weight after a period of 12 weeks while those on a regular diet did not. Consuming high glycemic index and carbohydrate-rich foods repeatedly causes acute hyperinsulinemia in adolescents. Hyperinsulinemia has been implicated in acne pathogenesis due to its association with high a bioavailability of androgens and high concentrations of free insulin-like growth factor I.^{4,5} Rapid increase in insulin levels results in a rapid lowering of blood sugar. In turn, androgen released by the adrenal glands signals the liver to secrete glycogen from its storage

to increase blood sugar towards normal. Decrease in blood sugar also stimulate food cravings. Finally, these cycles continue in a chronic manner. Frequent hyperinsulinemia increases appetite and then body weight and body mass index.³⁰

Nagpal *et al.* conducted a cross-sectional study to determine the prevalence of insulin resistance and metabolic syndrome in men affected by acne and found that post-adolescent males with acne and higher body mass index more commonly have high insulin resistance.³¹



Figure 1: Patient in Group 1 at 0 and 12 weeks

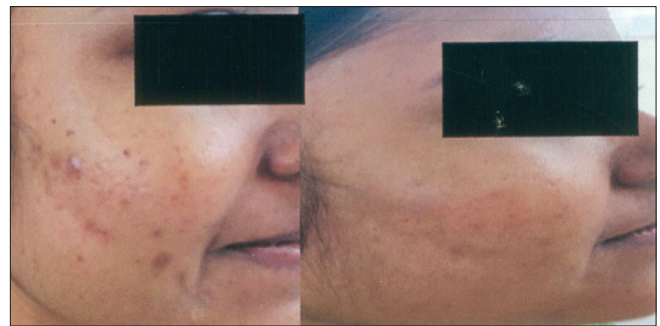


Figure 2: Patient in Group 2 at 0 and 12 weeks

Table 3: Acne counts of the analyzed patients and allocated patients

Group	Number of patients who showed improvement in acne counts at 12 weeks	Mean difference	SD of difference	P
Analyzed patients				
Group 1	42/42	12.262	7.382	0.931 (not significant)
Group 2	42/42	12.405	7.645	
Allocated patients				
Group 1	50/50	1.2600	7.102	0.000 (S)
Group 2	61/61	1.2360	7.1810	

SD: Standard deviation, S: Significant

Table 4: Body mass index of analyzed patients and allocated patients

Group	Number of patients showed improvement in BMI at 12 weeks	Mean difference	SD of difference	P
Analyzed patients				
Group 1	32/42	0.338	0.486	0.0001 (HS)
Group 2	16/42	0.296	0.368	
Allocated patients				
Group 1	10/50	0.323	0.494	0.0001 (HS)
Group 2	16/61	-0.230	0.370	

SD: Standard deviation, HS: High significant, BMI: Body mass index

Table 5: Homeostasis model assessment of insulin resistance of analyzed patients and allocated patients

Group	Number of patients showed improvement in HOMA-IR at 12 weeks	Mean difference	SD of difference	P
Analyzed patients				
Group 1	31/42	0.179	0.278	0.0001 (HS)
Group 2	19/42	0.161	0.385	
Allocated patients				
Group 1	43/50	0.1606	0.3109	0.001
Group 2	18/61	-0.1278	0.346	

SD: Standard deviation, HS: High significant, HOMA-IR: Homeostasis model assessment of insulin resistance

These studies indicate correlations between insulin resistance, body mass index and acne. In our study too, only group 1 patients had significant improvements in homeostasis model assessment of insulin resistance values, indicating that a low glycemic load diet helps decrease insulin resistance. However insulin resistance and body mass index values did not correlate with the number of acne lesions in our study .

Limitation of our study is application of mild topical cleanser in patients of both groups. Topical cleanser improves the normal skin barrier along with topical application of 2.5% of benzoyl peroxide gel in both groups. Topical benzoyl peroxide itself is a potent topical agent against acne. These might be the main factors responsible for significant reduction in acne counts in group 1 and group 2, so no significant difference in acne counts in between the two groups was observed. So a study on the effect of low glycemic load diet alone on acne may help us to overcome this limitation. Even the adherence to diet chart was only 75% in group 1 and this might be a limitation of the study. The other limitation would be that no specific diet chart was given to the group 2, so it is possible that some/many of them paid more attention to their diets once they were a part of the study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the forms the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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