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Author

Kazemi, Tiana

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Abstract:

An evidence-based literature review was conducted in order to identify human clinical trials that assess the effect of a low glycemic index diet on facial acne severity (*Acne vulgaris*). Of the twenty-one studies identified, three met the inclusion criteria of randomized-controlled clinical trials (RCTs) with a primary endpoint of changes in number and severity of acne lesions and were included for final analysis.⁷⁻⁹ During the trials, mean glycemic load in control groups ranged from 157 to 207, and mean glycemic load in intervention groups ranged from 102 to 130. In two studies, improvement in acne severity at the end of the trial between the control and intervention groups reached significance. In one trial, the difference between the two groups did not reach significance, however, the intervention group experienced a much greater magnitude of facial acne improvement than the control group. The results of this systematic review of RCTs strongly indicate that a low glycemic index diet improves the severity of facial acne.

Keywords:

Acne vulgaris, acne, glycemic index, glycemic load, diet

You Are What You Eat: RCTs show a low glycemic index diet improves facial acne

INTRODUCTION

Over 85% of adolescents in industrialized countries suffer from *Acne vulgaris*, making it the most prevalent skin disease among this age group.^{1,2} Acne often persists into adulthood and affects around 64% of individuals in their 20's and 43% of individuals in their 30's. It is estimated that in the United States alone, the cost of this disease is over 3 billion dollars in treatment and loss of productivity.³

The relationship between acne and diet has been historically controversial. Between the 1930's and 1960's, it was believed that foods high in sugar or fat, such as chocolate, would exacerbate acne. However, this view lost favor after the publication of two highly influential papers by Fulton in 1969 and Anderson in 1971 that revealed the lack of an association between acne and diet.^{4,5} In 2002, interest was re-ignited after a study by Cordain et al. linked acne to Western diets by demonstrating the lack of acne prevalence in non-Westernized populations who consumed diets low in glycemic index and load.^{1,5} As a result of this finding, several randomized-controlled clinical trials (RCTs) were completed to further explore the relationship between diet and acne pathogenesis. These RCTs are reviewed here and demonstrate a significant positive correlation between improved facial acne and a low glycemic index diet.

To aid better understanding of these studies, the terms glycemic index and glycemic load are briefly defined here. Glycemic index (GI) is an evidence-based system devised to rank the effect of carbohydrates on blood glucose levels. The GI of a food indicates its effects on postprandial glycemia. Glycemic load (GL) is a ranking system that combines the effects of GI and portion size, thereby allowing for the direct comparison of the net effect of a food or meal on blood glucose levels. As an example, the GL of a large portion of a low GI food will be equal to the GL of a small portion of a high GI food.⁶

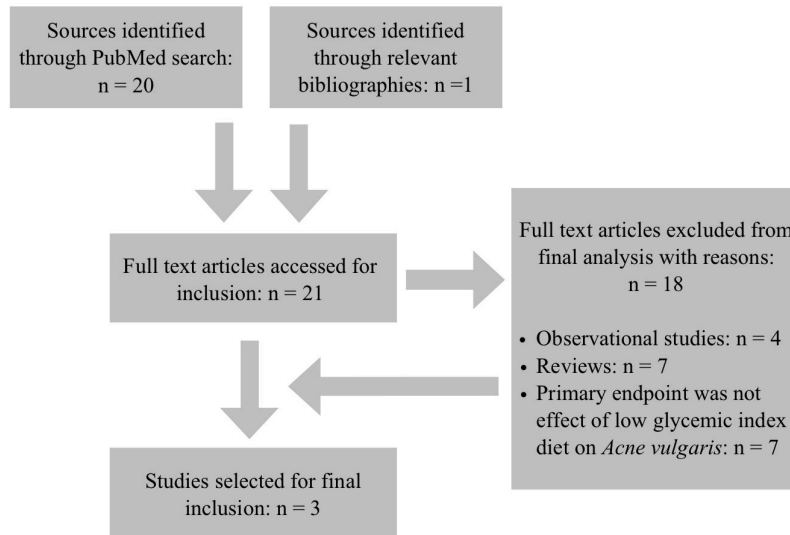
METHODS

PROCEDURE

Relevant studies on the effect of a low glycemic index diet on *Acne vulgaris* were obtained through an electronic search of PubMed using the Medical Subject Headings (MeSH) with the following keyword combination: 'Acne Vulgaris,' 'Glycemic Index,' and 'Humans.' The search was limited to include publications in the English language only. Bibliographies of studies obtained through this search algorithm were also screened for further relevant papers.

INCLUSION CRITERIA

Only randomized-controlled clinical trials (RCTs) with a primary endpoint of changes in number and severity of acne lesions were included in this evidence-based literature review. Of the 20 published studies compiled through this search algorithm, only three papers met these criteria and therefore selected for final inclusion (see figure below). A fourth RCT study was excluded because the study represented a subset of a larger RCT already included in this review and its primary endpoint was the effect of a low GI diet on the fatty acid composition of skin surface triglycerides. Of the relevant studies identified through the bibliography screen, none were RCTs and were thus excluded from the final analysis.



DATA EXTRACTION

The following data were extracted from studies selected for final inclusion: study location, study population, study design, study duration, primary endpoint, baseline and trial glycemic load, assessment of *Acne vulgaris*, and changes in acne severity at the conclusion of each study.

RESULTS

The literature search identified three randomized-controlled clinical trials with a primary endpoint of changes in number and severity of acne lesions as a result of a low glycemic index diet. Of these three studies, two reported statistically significant improvements in facial acne between the control and intervention groups after the intervention period. The third study found no significant difference in acne improvement between the intervention and control groups, however, both groups demonstrated a significant difference in number and severity of acne lesions at the end of the study as compared to respective baseline assessments.

Kwon et al., and Smith et al., both report a significant positive correlation between a low glycemic index diet and improvement in the severity of *Acne vulgaris*.^{7,8} Kwon et al. randomly divided 32 males and females (24 males, 8 females) between the ages of 20-27 with mild to moderate acne into two groups: low glycemic load diet (LGLD) and control diet. The two groups completed a 10-week parallel dietary intervention trial with a primary endpoint of assessing clinical and histological effects of a low glycemic load diet on both inflammatory and non-inflammatory acne lesions. Throughout the intervention period, the LGLD group replaced high glycemic index foods with lower glycemic index foods with the energy lost due to reduced carbohydrate intake replaced by protein energy. The control group was instructed to maintain their normal diet and continue eating carbohydrate-rich foods on a daily basis. The number and severity of acne lesions were assessed blindly by two independent dermatologists using the Leeds Revised Acne Grading System. At the start of the trial, the mean baseline acne scores for the control and LGLD groups were 2.08 and 2.18, respectively. The differences in baseline number of inflammatory and non-inflammatory lesion counts between the two groups were not statistically significant ($p = 0.34$, $p = 0.45$). Outcomes were reported as changes to acne score. After the dietary intervention period, the two groups demonstrated a statistically significant

difference in acne score ($p = 0.02$). Specifically, the mean acne score for the LGLD group decreased to 1.60 ($p = 0.02$) while the control group mean acne score decreased to 1.85 (estimated from graph, not statistically significant). In addition, the authors report a significant decrease in the overall size of sebaceous glands in the LGLD group at the end of the intervention compared with baseline measurements. Sebaceous gland changes within the control diet group are not reported.⁷

Similarly, Smith et al. randomly assigned 43 males between the ages of 15-25 with mild to moderate acne to two groups: low glycemic load (LGL) group and control group. The two groups completed a 12-week parallel dietary intervention trial with a primary endpoint of assessing changes in the number of inflammatory and total acne lesion counts. Throughout the intervention period, the LGL group was instructed to replace high glycemic index foods with foods either lower in glycemic index or higher in protein value. The control group was encouraged to consume carbohydrate-rich foods as a regular part of their daily diet. Number and severity of acne lesions were determined using a modified Cunliffe-Leeds Lesion Count Technique by a dermatology registrar who was blinded to group assignment. At the start of the trial, the control group and LGL group had baseline mean total acne lesion counts of 34.9 (± 4.3) and 40.6 (± 5.0), respectively ($p = 0.4$). Mean inflammatory lesion counts for the control and LGL groups at baseline were 28.4 (± 3.6) and 31.9 (± 3.9), respectively ($p = 0.72$). Outcomes were reported as decreases in lesion counts. At the conclusion of the study, the two groups demonstrated a statistically significant difference in mean total lesion count decrease. Specifically, the control group exhibited a 12.0 (± 3.5) count decrease in mean number of total lesions while the LGL group demonstrated a 23.5 (± 3.9) count decrease ($p = 0.03$). A similar, significant decrease in inflammatory lesion counts between the two groups was also observed with the control group inflammatory lesion count dropping by 7.5 and the LGL group inflammatory lesion count decreasing by 17.0 ($p = 0.02$).⁸

In a similar design to the above two studies, Reynolds et al. alternately allocated 43 males between the ages of 15.5-17.5 with mild to severe acne to either a high glycemic index (HGI) or low glycemic index (LGI) diet group for an 8-week parallel dietary intervention trial. The primary endpoint of the study was to assess the changes in number and severity of acne lesions. Two dermatologists blinded to group assignment assessed the number and severity of acne lesions and assigned a grade of 0-3 with 0 indicating no acne, 1 indicating mild, 2 indicating moderate, and 3 indicating severe acne. Throughout the intervention period, the LGI group was instructed to replace high glycemic index carbohydrates with low glycemic index carbohydrates while the HGI group was instructed to consume high glycemic index carbohydrates on a daily basis. At the start of the trial, the mean baseline acne scores for the HGI and LGI groups were 1.9 (± 0.2) and 2.1 (± 0.1), respectively ($p = 0.3$). Outcomes were reported as changes to acne score. At the conclusion of the intervention period, both groups demonstrated a statistically significant improvement in facial acne with the HGI group exhibiting a mean acne score decrease of 0.40 (± 0.14 , $p = 0.01$) and the LGI group exhibiting a mean acne score decrease of 0.61 (± 0.13 , $p = 0.0004$). The difference in acne scores between the two groups did not reach significance. As a result, the authors report that a low glycemic index diet does not correlate with significant improvements in facial acne severity compared with a macronutrient-matched high glycemic index diet. However, it should be noted that the study's finding that facial acne scores decreased to a larger extent in the LGI group (26% decrease, $p = 0.0004$) compared with the HGI

Table 1: Randomized-Controlled Trials Assessing the Relationship Between Facial Acne Severity and Low Glycemic Index Diet

Author & Year	Location	Study Demographics	N	Study Design	Duration (weeks)	Baseline GL	Trial GL	Significant Difference Between C & I Glycemic Load?	Baseline Acne Score	Final Acne Score Change	Baseline Total Lesion Count	Final Total Lesion Count Change	Significant Difference Between C & I at end of trial?	How is Acne vulgaris Assessed?
Kwon et al. 2012	South Korea	24 males, 8 females, age range 20-27 years, with mild to moderate acne	32	RCT, parallel dietary intervention trial	10	C: 190.5±33.1 I: 177.2±41.5	C: 207.2±23.2 I: 129.5±22.2	Yes <i>p</i> < 0.05	C: 2.08 ^a I: 2.18	C: -0.23 ^c I: -0.58***			Yes <i>p</i> < 0.05	Leeds Revised Acne Grading System
Smith et al. 2007	Australia	Male, age range 15-25 years, with mild to moderate acne	43	RCT, parallel dietary intervention trial	12	C: 181.5±11.5 I: 174.7±9.1	C: 174.3±10.7 I: 101.5±6.1	Yes <i>p</i> < 0.001			C: 34.9±4.3 I: 40.6±5.0	C: -12.0±3.5 ^d I: -23.5±3.9 ^d	Yes <i>p</i> = 0.03	Modified Cunliffe-Leeds Lesion Count Technique
Reynolds et al. 2010	Australia	Male adolescents age range 15.5-17.5 years, with mild to severe acne	43	Alternate allocation based on recruitment order, parallel dietary intervention trial	8	Not reported	C: 157±18 I: 102±9	Yes <i>p</i> < 0.01	C: 1.9±0.2 ^b I: 2.1±0.1	C: -0.40±0.14** I: -0.61±0.13***			No <i>p</i> = 0.28	Assigned a grade of 0-3

GL = Glycemic Load

C = Control group

I = Intervention Group

*: *p* = 0.05 versus baseline

** : *p* < 0.05 versus baseline

***: *p* < 0.01 versus baseline

a: score is calculated using Leeds Revised Acne Grading System

b: score is calculated using 0-3 grading system

c: value estimated from graph

d: *p* values versus baseline not reported

group (16% decrease, $p = 0.01$), does support the authors' hypothesis that a low glycemic index diet is correlated with improvements in facial acne severity.⁹

DISCUSSION

The randomized-controlled trials evaluated in this evidence-based review demonstrate a strong association between facial acne improvement and a reduced glycemic index diet. However, the complex and multifactorial pathophysiology of facial acne warrants an analysis of confounding factors and limitations of each of the above studies.

All three studies included in this review relied upon self-reported food diary entries in order to calculate glycemic index levels of participants throughout the duration of the trial, which may have prevented accurate nutritional composition calculations especially as under-reporting of food quantity is a well-known source of error in adolescent diet assessment.⁸ Moreover, due to the inherent design of each study protocol, subjects were not blinded to treatment or the purpose of the study. Last, all three studies used different systems for assessing facial acne severity, making direct comparisons difficult.

In addition to the above limitations, each of the studies contains additional confounding factors and limitations that should be further analyzed. In Kwon et al., the authors did not adjust for dietary differences between the two groups (such as saturated fat, fiber, zinc, and iodine intake) that may confound the relationship between diet and acne severity. Furthermore, the study did not control for milk and other dairy product intake, which may have further confounded the final results as these foods are known to be nutrient-derived acne-aggravating risk factors by increasing the signaling activity of insulin and IGF-I.⁷

The Smith et al. study protocol included the use of a mild topical skin cleanser for both groups that may have led to improved facial acne severity regardless of changes in dietary glycemic index values. In addition, the authors did not control for the confounding effect of differences in nutritional profiles (such as protein, fiber, zinc, and vitamin A intake) of the high glycemic index versus low glycemic index foods. Furthermore, since the study demographic is exclusively confined to males between the ages of 15-25, the validity of extending these results to both genders and all age groups is limited. Last, it should be noted that although the LGL group exhibited a significant decrease in both weight ($p < 0.001$) and BMI ($p < 0.001$) compared with the control group at the end of the trial period, the study authors report that they found no significant interaction between the dietary treatment and associated change in BMI on acne lesion counts.⁸

The Reynolds study relied upon a novel acne grading system that is not internationally validated and incapable of detecting smaller changes in facial acne severity. As a result, less obvious changes in acne lesions may have been missed. Moreover, this is the only study that included an unknown number of participants with "severe" facial acne, an inclusion that may have made it more difficult to notice changes in facial acne during the trial period. Furthermore, the non-randomized allocation of study participants to the intervention and control groups may have led to selection bias. Study participants also only completed food diaries on weekends, which represents a further source of error in nutritional composition calculations. In addition, the difference in glycemic load between the two diets may not have been significantly large enough to exhibit an effect on male adolescent postprandial glycemic and insulin responses, and

therefore, affect facial acne severity. Like the Smith et al. study, the validity of extending these results to both genders and all age groups is also limited as the study population consisted exclusively of adolescent males in boarding school. Last, the shorter duration of this study (8 weeks compared to 10 and 12 weeks) may have been too short to allow for the observation of significant changes in acne severity.⁹

In summary, the three randomized-controlled clinical trials reviewed here strongly demonstrate that a low glycemic index diet is positively correlated with a reduction in inflammatory acne lesions, non-inflammatory acne lesions, and total acne lesion count. Diets rich in high glycemic index foods induce hyperinsulinemia, which in turn increases blood insulin-like growth factor 1 (IGF-1) and free androgen levels, two factors that are known to aggravate facial acne severity by increasing sebaceous gland activity. A low glycemic index diet inhibits this increase in sebaceous gland activity by preventing postprandial blood insulin and IGF-1 concentration peaks, and therefore, contributes to improvements in facial acne.^{5,7,8} As a result, dermatologists should strongly consider patients' dietary glycemic index and load when treating facial acne.

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