REVIEW

Acne and diet: truth or myth?

Acne e dieta: verdade ou mito?

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Abstract: Numerous studies were published over the last 50 years to investigate whether diet is associated with the etiology of acne. Although older studies well known by dermatologists that refute the association between acne and diet exist, their scientific foundation is weak. New articles have recently brought to light evidence contrary to previous findings. Therefore, we would like to investigate whether diet, directly or indirectly, influences one or more of the four fundamental etiopathogenic pillars of acne: (1) hyperproliferation of basal keratinocytes, (2) increase of sebaceous production, (3) colonization by Propionibacterium acnes, and (4) inflammation.
Keywords: Acne vulgaris; Diet; Glycemic index

Resumo: Nos últimos 50 anos, foram publicados inúmeros estudos com a finalidade de comprovar se a dieta está relacionada à etiologia da acne. Embora existam estudos antigos, que são bem difundidos entre os dermatologistas e negam a associação entre acne e dieta, seu delineamento científico é pobre. Recentemente, novos artigos demonstraram evidências contrárias às publicações anteriores. Sendo assim, os autores realizaram esta revisão bibliográfica com o intuito de averiguar se a dieta influencia direta ou indiretamente um ou mais dos quatro pilares etiopatogênicos fundamentais da acne: (1) hiperproliferação dos queratinócitos basais, (2) aumento da produção sebácea, (3) colonização pelo Propionibacterium acnes e (4) inflamação.
Palavras-chave: Acne vulgar; Dieta; Índice glicêmico

INTRODUCTION

For many decades, researchers have tried to prove an old theory, surrounded by miths and popular beliefs: the association between acne and diet. [1-3]

Acne vulgaris is a chronic dermatosis. It is a disease of the pilosebaceous follicle with four fundamental etiopathogenic factors: sebaceous hyperproduction, follicular hyperkeratinization, increase of *Propionibacterium acnes* colonization, and periglandular dermal inflammation. It affects all races, although it is less intense in Asians and Blacks. [4-6]

Its overall prevalence varies between 35% and 90% in adolescents; In the West, it affects 79 to 95 % of adolescents. [7] In general, acne affects 95% of sixteen-year-old boys and 83% of sixteen-year-old girls, and it can reach 100% in both genders. [8-10] Its development and prevalence are higher among males, due to androgenic influence. [11,12] Acne is a disease that is highly influenced by genetics since follicular hyperkeratinization and sebaceous secretion are under hormonal control. [12,13]

Regarding the hypothetical association between environmental factors and acne, sebum would probably be the most influenced component. In this case, a possible hyperinsulinemic state, associated with the secondary presence of growth-factor insuline-simile 1 (IGF-1), would stimulate the synthesis of androgens by various tissues of the body, which would then fuel sebum production. [3,14]

Approved by the Editorial Board and accepted for publication on 21.09.2009.
* Work conducted at the Dermatology Service of the Pontifical Catholic University of Campinas (PUCCAMPINAS) - Campinas (SP), Brazil.
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

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Based on data from the literature that relate acne vulgaris with diet, we have written this review to clarify the hypotheses about this topic.

Hypothesis n^0 1: Obesity and acne: it is not how much you eat, but what you eat

Although without clear evidence, many people have the impression that acne and obesity are related. A major study evaluated 2,720 military recruited for obesity and acne and found this association in only two individuals, aged between 20 and 40 years. No association was found among adolescents aged 15-19 years. This suggests that acne, in a younger population, may be associated with other factors besides obesity and insulin resistance. [15]

In a recent study with twins – 458 monozygotic and 1,099 dizygotic – there was no significant difference in the clinical profile of acne among the twins in relation to weight, body mass index, cholesterol, triglycerides and glucose levels in the blood. [16]

The results of the two studies mentioned above show that it is not how much we eat that affects the development and severity of acne, but what we eat may play a role.

Hypothesis n^0 2: The Westernization of dietary patterns and the development of acne

In a study in which more than 1,200 individuals from two non-Western societies (natives of Kitava Island, Papua New Guinea, and the Ache Indians of Paraguay) were evaluated, the absence of acne in these populations was attributed to their diet. There is a substantially low glycemic index in their diet as compared to that of Western diets. [7] In epidemiological studies with the Inuit Eskimo population, it was observed that they had not presented this dermatosis until the introduction of Westernized food habits. [17]

Other studies with populations from rural villages, such as those living in Kenya, Zambia, and Bantu, in South Africa, concluded that these people had significantly less acne than their descendants who migrated to the United States; in other words, those that became Westernized. [18-20]

With these epidemiological findings, we can postulate that, contrary to the food habits of these non-Western populations, the frequent consumption of carbohydrates with a high glycemic index can expose adolescents to the risk of acute hyperinsulinemia. This, in turn, influences follicular epithelial growth, keratinization, and sebaceous secretion. [7]

Hypothesis n^0 3: Nutrition as a triggering factor of sexual maturation and acne

Nutrition improvement has been associated with early sexual maturity and the development of acne in young individuals. Studies show that adolescents that regularly eat food with a low glycemic index have delayed menarche, similar to what occurs with athletes and ballerinas. [21] In 1970, menarche occurred around 12 years of age and in 1835, it occurred around 16 years of age. [22]

In a longitudinal cohort study that lasted for 5 years in which 871 girls were included, the authors concluded that a severe comedonal condition was more prevalent in girls with early menarche and with high levels of dihydroepiandrosterone.[23] The study also showed that the precocity of the development of comedonal acne may be the best indicator of the severity of the disease in the future. The prevalence and the prognosis of acne are correlated with sexual maturity. Although Cordain et al. [7] have not reported anything about sexual maturation, this factor might play a key role in the fact that natives of Kitavan Island or Ache Indians do not have acne. [24]

Hypothesis n^0 4: Influence of hyperinsulin in the concentration of androgens and sebum production

Hyperinsulin, through an increase in androgen levels, stimulates sebum production, which plays a fundamental role in the development of acne. Extreme calorie restriction drastically reduces the level of sebum excretion. This can be reverted with the adoption of a normal diet. [25]

Hyperinsulin influences the circulating concentration of IGF-1 and of insulin- like growth factor binding protein 3 (IGFBP-3), which act directly on the proliferation of keratinocytes and on apoptosis. In a hyperinsulinic state, levels of IGF-1 increase, whereas levels of IGFBP-3 drop, leading to an imbalance that culminates in the hyperproliferation of keratinocytes. [26] IGF-1 appears to mediate comedogenic factors, such as androgens, growth hormone, and glucorticoids. In a study with humans, it was shown that endogenous androgen increases IGF-1 serum levels, and levels of IGF-1 increase androgen levels; a vicious circle is established and it ultimately increases sebum production. [27,28]

Hypothesis n^0 5: Milk as a cause for acne outbreaks

An exception to the evidence of the high glycemic index diet is the ingestion of milk derivatives. They have a low glycemic index, but paradoxically increase the levels of IGF-1, leading to the development or aggravation of acne. This is more severe when fat free milk is ingested, showing that this association is not due to the fat content of milk, which strengthens the theory of IGF-1 levels. [27,28]

In addition to the comedogenic effect of IGF-1, milk contains strogen, progesterone, androgen precursors (androstenedione and dihydroepiandros-

terone sulphate), and 5α-recdutase steroids (such as 5?-androstenedione, 5α-pregnonadione and dihydrotestosterone), some of which are implicated in comedogenesis. [29]

Milk is enriched with other bioactive molecules that act on the pilosebaceous unit, such as glucocorticoids, transforming growth factor –β (TGF-β), hormone peptides similar to thyrotropin and compounds similar to opiates. It is thought that the processing of fat free milk changes the bioavailability of these bioactive molecules or their interaction with binding proteins. Therefore, it is possible that the hormonal balance of fat free milk is altered, culminating in greater comedogenesis. [29] Moreover, to simulate the consistence of whole milk, whey proteins, especially α-lactoalbumine, are added to the formula of fat free and reduced fat milk. This also appears to play a role in comedogenesis. [27,28]

It is known that iodine ingestion can exacerbate acne. Another argument that strengthens the association between milk consumption and acne is that the iodine in milk may be involved in the etiology of this dermatosis. [30] The iodine found in milk is due to supplementation of the diet offered to animals and the use of iodine solutions in milking equipment. [31]

The results of a study help to support the association between iodine present in milk and acne. In this study, 1,006 adolescents were evaluated through a questionnaire. The objective was to determine if iodine levels, found in water and salt, could influence the prevalence or severity of acne. The sample population lived in three distinct regions of North Carolina: the costal region, the mountainous region and one in between the two. The authors concluded that in patients who lived in the costal region, with greater salt comsumption, the prevalence of severe acne (cystic and with scarring) was higher. [32]

Threfore, it is advisable to recommend as a fundamental step in the treatment of acne to avoid the ingestion of dairy and carbohydrates with a high glycemic index to reduce the levels of IGF-1, which acts synergically with dihydrotestosterone on the pilosebaceous unit of genetically predisposed individuals. [33]

Hypothesis n^0 6: Corroborating evidence of the association between insulin metabolism and acne

Acne is one of the clinical characteristics of polycystic ovary syndrome (POS). Obesity, hyperinsulinemia, insulin resistance, and hyperandrogenism are also frequently present. These patients show high levels of androgens, IGF-1, and low concentration of sex hormone binding globulins (SHBG). [3]

Both insulin and IGF-1 stimulate the synthesis of ovarian and testicular androgens. In addition, insulin and IGF-1 inhibit the hepatic synthesis of SHBG and increase the bioavailability of circulating androgens. High concentration of androgens, insulin, and IGF-1 may be associated with female adult acne. [3]

Androgen levels may drop with the reduction of insulin resistance, either by weight loss or use of medicine. Metformin and pioglitazone not only reduce insulin resistance, but also decrease the levels of the adrenocorticotropical hormone, which stimulates androgen production in women with POS. The correction of these physiological alterations may be therapeutic in patients with acne. [33,34]

Hypothesis n^0 7: Clinical benefit of a low glycemic index diet for patients with acne

The precise mechanism through which glycemic index influences sebum composition is unknown. It is accepted that to synthesize lipids, sebaceous glands need energy that may be acquired through the betaoxidation of fatty acids and/or glucose catabolism. [35] According to Downine and Kaealey, the pattern of lipid synthesis is maintained by the endogenous glycogen, an important NADPH supplier, for the synthesis of triglycerides. Therefore, it is possible that the ingestion of food with a low glycemic index may alter the stock of glycogen in sebaceous glands, and this may be a limiting factor in sebaceous lipogenesis. [35,36]

It is suggested that food with a low glycemic index influences sebum composition by means of metabolic effects and/or, secondarily, levels of free testosterone and androgens. Evidence shows that a low glycemic index diet can lower glycogen stocks in the tissues of the body (muscle and liver), thus limiting sebaceous lipogenesis. In addition, this diet may reduce the bioavailability of testosterone and the concentration of dihydroepiandrosterone sulphate. Since sebum production is controlled by androgens, their reduction may change sebum composition. [37]

As we will see in hypothesis no. 8, it is suggested that a low glycemic index diet alters the relationship between monounsaturated fatty acids (MUFAs) and saturated fatty acids (SFAs), creating a protective mechanism against acne. [37]

Based on what has been described above, it is thought that low glycemic index food can influence sebum production by means of a synchronized modulation of androgens and of glycogen stocks, as shown in the diagram below (Figure 1). [7, 35-41]

A single study published by Kayamak [42] refuted this theory by showing that the glycemic index of a diet, glycemic weight, and insulin levels do not play a role in the pathogenesis of acne presented by young patients. However, this study is heavily criticized for being the only one that goes against common knowledge among experts in the issue.

Hypothesis n^0 8: Anti-acgenicity through dietary modulation of fatty acid metabolism

Human sebum is primarily composed by triglycerides (40%-60%), cerides (19%-26%), scalene (11%-15%), and a small amount of cholesterol and cholesterol ester. [43-45] The triglyceride fraction of sebum is presumably responsible for the development of acne. [46,47] Bacteria may hydrolize sebaceous triglycerides [48] and release fatty acids that can enter the follicular wall and be incorporated into the metabolism of the surrounding epidermis. Nevertheless, the hyperkeratotic effect may not be a characteristic of all fatty acids – recent evidence suggests that only MUFAs stimulate morphological changes, and this is not observed in SFAs. [37]

MUFAs are mainly composed by sapienic acid (16:1 Δ6), which comes from the Δ6 desaturation of palmitic acid (16:0), an SFA acid. [49] The expression of Δ6-desaturase and the consequent accumulation of sapienic acid in sebum appear to be important factors in sebaceous lipogenesis. [50,51] Evidence for this association came from the observation that rats with deficiency in the expression of Δ9 desaturase, which is equivalent to Δ6desaturase in humans, presented hypoplasia of the sebaceous glands. [52]

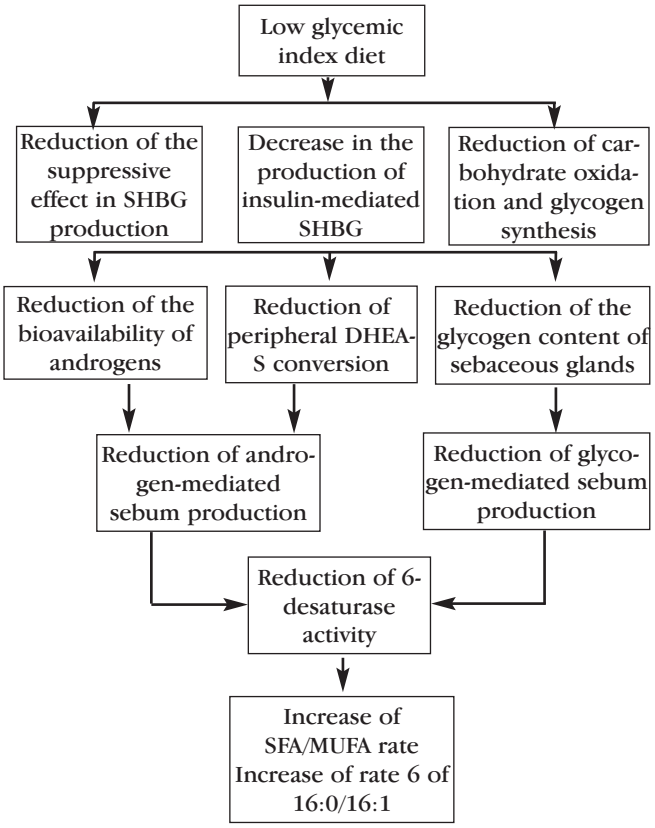

Figure 1: Anti-acgenicity of a low glycemic index diet

Adapted and translated from Smith RN, Braue A, Varigos GA, Mann NJ. The effect of a low glycemic load diet on acne vulgaris and the fatty acid composition of skin surface triglycerides. J Dermatol Sci. 2008;50(1):41-52.

Recently, it was shown that the topical application of unsaturated fatty acids induces abnormal keratinization and hyperplasia of the epidermis. In contrast, triglycerides and SFAs did not alter skin morphology. Moreover, unsaturated fatty acids also increased calcium concentration in keratinocytes, both *in vivo* and *in vitro*. [46] These results suggest that unsaturated fatty acids may increase the concentration of calcium in keratinocytes, leading to abnormal follicular keratinization. [46]

Later, a study confirmed that the fatty acids responsible for the abnormal keratinization and hyperplasia of the epidermis are indeed MUFAs. Clinical volunteers were divided into two groups: one adopted a low glycemic index diet and the other was instructed to include carbohydrates in their regular meals. The first group showed a greater significant improvement of the total number of lesions when compared to the control group. Although an effect of diet intervention in sebum release or in the individual composition of fatty acids was not observed, an increase in the association between SFAs/MUFAs was identified. Interestingly, these changes are correlated with the improvement of acne, suggesting that the desaturation of fatty acids may play role in the development of this disorder. [37]

Although essential fatty acids (EFA), especially linoleic acid, are important in the physiopathogeny of acne, a pilot study in which the patients' diet was supplemented with 3 daily grams of EFA (linoleic, linolenic, and gamma-linolenic acids) for three months did not result in the clinical improvement of acne. However, there was a quantitative reduction of the size of sebaceous glands, seen through *punch* biopsies, three months after continuous use of the product, suggesting a possible benefit of these products with dose adjustment and duration of treatment. [53]

Strong evidence for the adoption of a diet rich in fatty acids is the fact that food is well known for being a modulator of the systemic inflammatory response. One of the most important dietary factors that influence inflammation is the relative ingestion of the polyunsaturated fatty acids (PUFAs) ω-6 and ω-3.[54] The typical Western diet has a significantly greater concentration of ω-6 and a lower concentration of ω-3, due to the predominance of ω-6 in most vegetable oils and processed foods cooked with these oils.[54]

Based on this evidence, Kris-Etherton observed that the ratio ω-6/ω-3 is 10:1 in Western diets and 2:1 to 3:1 in non-Western ones. [55,56] The comsumption of a diet with PUFA ω-3 may be therapeutic due to its ability to suppress the production of inflammatory

cytokines. This is seen with the supplementary ingestion of ω-3 fatty acids, which appear to suppress IL-1β,[57-60] IL-1α,[57-62], tumoral necrosis factor-α,[57-62] IL-6,[58,60,62] and IL-8.[62] The suppression of IL-1α through a diet with ω-3 may positively influence the differentiation of corneocytes by means of the prevention or attenuation of the hypercornification that occurs during microcomedogenesis. [59]

Hypothesis n^0 9: Protective role of a diet rich in zinc and vitamin A

For a long time, vitamin A and zinc had their use widely recommended and defended by various authors to treat acne due to their inhibiting effects on comedogenesis.[63] Such benefit was disputed by others until Michaëlsson[64] conducted a study to show the beneficial effect of vitamin A and zinc in the treatment of acne. The author conducted an analysis of the blood concentration of retinol binding protein (retinol ultimately comes from the tissue metabolism of vitamin A from the diet) and of zinc in 173 patients with acne and a control group. The patients with acne showed lower levels of both, and in those with severe acne these levels were even lower. This finding confirms the importance of vitamin A and zinc in the etiology of acne.

Another relevant aspect that supports this association is the fact that a low-zinc diet worsens or activates acne, especially with pustulous reactions. This is seen in several reports of acne aggravation with the administration of a parenteral low-zinc diet.[65]

Hypothesis n^0 10: Chocolate – an innocent unduly blamed?

Chocolate has always been blamed as an aggravating factor of acne. Patients often report the development of pustulae a few days after the ingestion of this food. [44] For this reason, many patients ask us for a scientific position on this subject. Detailed below is what we know so far.

In 1969, 65 individuals ingested a chocolate bar (112g) daily, rich in chocolate licqueur and cocoa butter, for 4 weeks; after this period, the regimen was changed and patients ingested a control-bar, with the same weight, without chocolate licqueur and cocoa butter, for 4 more weeks. Lesions were classified at the start and end of the study into three different categories: aggravated (lesions increased by 30% at the end of the study), improved (lesions reduced by 30% at the end of the study), and unaltered (lesions changed less than 30%). Since there was no significant difference between the ingestion of chocolate and control bars in the three categories of classification, the authors concluded that " the ingestion of a great amount of chocolate does not interfere in the course of acne vulgaris or in sebum composition."

According to Cordain et al., [3] the study mentioned above comes to a wrong conclusion. In the control bar, cocoa, in the form of butter and licqueur, was substituted by hydrogenated vegetable fat (28% of the weight). Moreover, both the modified and the chocolate bar had a high sucrose concentration (53% and 44.3% of the weight, respectively), which predisposed the individual to hyperglycemia and insulinemia, factors that are involved in the development of acne. Therefore, to Cordain et al. [3] the results from the study cannot be generalized to assume that chocolate is not associated with acne, since other ingredients that may be involved in the etiology of acne are used in its manufacture.

In another study, conducted by Anderson, [2] patients who said they did not tolerate chocolate because it aggravated their acne were selected. These patients ingested a great amount of chocolate for seven consecutive days, and no alteration in the number or severity of lesions was observed. Unfortunately, pre or post-experimental lesions were not considered, and there was no control group or statistical analysis of the study. Compared with the reference study, the analysis period of chocolate ingestion was very short (one and four weeks, respectively).

Although with mixed conclusions, the theory of the association between acne and chocolate is almost entirely confirmed by clinical findings from well-designed studies that have been conducted with competence by study groups in nutrition and nutrology.

A study carried out by a group of Australian scientists compared the plasmatic profile of patients after the ingestion of food with and without chocolate. Interestingly, an increase of post-prandial insulinemia in slim young adults who ingested chocolate products (average 28% higher) was observed; the highest levels occurred with the ingestion of chocolate milk (average 48% higher as compared with plain milk) and milk enriched with dark chocolate as compared to white (13% higher). [66]

An explanation for the findings of the Australian group may be that chocolate is rich in biologically active compounds, such as caffeine, teobromine, serotonine, phenylethylamine, triglycerides, and cannabinoid-like fatty acids, which increase secretion of and peripheral resistance to insulin. [67,68] Moreover, the aminoacids present in chocolate (such as arginine, leucine, and phenylalanine) are extremely insulinotropic when ingested with carbohydrates; [69,70] other aminoacids (valine, lysine, and isoleucine), found in other types of food, especially those rich in lactose, can also cause this plasmatic behavior. [71]

Based on what has been described so far, it would not be impertinent to suggest that the inges-

tion of chocolate-based food products may be associated with the development or aggravation of acne vulgaris. It is important to stress that commercial chocolate bars, especially those with a high milk content, have a great amount of carbohydrates (refined sugars, so they have a high glycemic index), which increase the post-prandial plasmatic levels of IGF and IGF binding protein (IGFBP), having an insulinotropic profile. [3,26-29,33,71,72] This is worth considering if you have been convinced of the comedogenic effect of a high glycemic index diet.

CONCLUSION

Over the last 37 years, many studies were conducted about the influence of diet in the pathogenesis of acne, with indication that food may indeed influence this dermatosis. [73] However, the publication of interventionist, randomized, double blind studies, with a control group, is needed, with the evaluation of multiple nutritional factors.

As a starting point, to detect the influence of dietary habits in acne vulgaris, there is a tendency to investigate the food habits of non-Western populations since they do not have acne. [17-20,32] In their diet, there are no processed foods, dairy, sugars and refined oils. Instead, they eat mainly fresh food, fruit, vegetables, meat, chicken, and grilled seafood. [17-20,32]

Based on recent scientific reports, a statement has become more and more accepted: there is a lower incidence of acne in non-Western populations. This incidence increases when a Western dietary pattern is adopted. Therefore, ethnicity is not the only important factor in the etiology of acne, and this reinforces the diet-acne relationship hypothesis. [7] ❑

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How to cite this article/*Como citar este artigo*: Costa A, Lage D, Moisés TA. Acne and diet: truth or myth? An Bras Dermatol. 2010;85(3):346-53.

Erratum

Errata

This erratum refers to the article Acne and diet: truth or myth? An Bras Dermatol. 2010;85(3):346-53. Figure 1 was published without the subtitle. Follows the missing information:

Adapted and translated from Smith RN, Braue A, Varigos GA, Mann NJ. The effect of a low glycemic load diet on acne vulgaris and the fatty acid composition of skin surface triglycerides. J Dermatol Sci. 2008;50(1):41-52.