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Acne and nutrition: hypotheses, myths and facts

Authors

JP Claudel[1], N Auffret[2], MT Leccia[3], F Poli[2], B Dréno[4]

Authors Affiliations

[1]Private Practice, Tours, France

[2]Private Practice, Paris, France

[3]Department of Dermatology, Allergology and Photobiology, CHU A Michallon, Grenoble, France

[4]Department of Dermato, CIC 1413, CRCINA Inserm 1232, Nantes University Hospital, Nantes, France

Corresponding author

Brigitte Dréno, Department of Dermato, CIC 1413, CRCINA Inserm 1232 Nantes University Hospital, Place Alexis Ricordeau, 44093 Nantes Cedex, France. Phone: +33 (0) 24.00.83.118, Fax: +33 (0) 24.00.83.117. E-mail: brigitte.dreno@atlanmed.fr

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Abstract

Acne is an inflammatory and multifactorial skin disease. Different external and internal factors including air pollution, aggressive skin care products, medication, mechanical, hormonal, family factors and, more recently, lifestyle and stress, have been suggested as having an impact on acne. Moreover, for many years nutrition was believed to cause or worsen acne. Over the last decades, however, it has become a dermatological doctrine that there is no direct association between diet and acne.

Even if recent research has allowed to identify certain nutritional elements and behaviour that may impact on acne, including the excessive intake of dairy products and hyperglycaemic food, modern lifestyle nutrition, obesity and eating disorders, knowledge about the role of nutrition in the physiopathology of acne still remains sparse and hypotheses and myths continue to dominate the debate.

Thus, further clinical and translational research is necessary to investigate and confirm the association between nutrition and acne.

Introduction

Acne is an inflammatory and multifactorial skin disease.(1) Different external and internal factors including air pollution, aggressive skin care products, medication, mechanical, hormonal and family factors and, more recently, lifestyle and stress have been suggested as having an impact on acne.(2-18)

Even if for many years nutrition was believed to cause or worsen acne, it has become a dermatological doctrine over the last decades that there is no direct association between diet and acne. (19-24) Cordain *et al*. were the first to question this belief, by studying acne-free populations having no hyperglycaemic carbohydrate and no dairy product intake.(25) The authors have shed some new light on this issue through their hypothesis that acne is a typical disease of Western civilization and thus associated with what we eat.(26-29) Indeed, ecological studies suggest that the incidence of acne is low in non-Western societies and increases with the adoption of a Western diet, characterised by a high intake of dairy products, hyperglycaemic food and free fatty acids.(30-34)

However, to date there is still no clinically confirmed link between nutrition and acne, thus continuing to support various hypotheses and myths.(35, 36)

Through the present review we intend to provide an overview of currently available information and on the overall role of nutrition and associated factors in acne.

Methodology

Our group of experts in acne discussed the impact of nutrition on acne, based on currently available sources of literature.

Evidence was obtained through a PubMed search using the key word 'acne', associated with regimen, diet, nutrition, food, chocolate, milk, skimmed milk, dairy products, whey proteins, alcohol, tea, coffee, chocolate, sugar, salt, alcohol consumption, hyperglycaemic food protein and insulin. A preference was given for the most recent articles published.

Results

While published literature provides some evidence that nutrition may be associated with acne, to date no level A articles (double-blind, comparative, randomized clinical studies) have been published. The information collected and reviewed in this study has therefore been exclusively reported through level B (randomized studies with serious limitations or a low number of cases) and level C (case-control or cohort studies) papers, only.

Based on this, we identified the following nutrients that have been reported as potentially playing a role in acne: dairy products, hyperglycaemic food, whey proteins, alcohol, tea, coffee, chocolate and salt.

Of these, three factors currently draw our attention and that of nutritionists and physicians: dairy products, hyperglycaemic food and whey proteins.

Nutrition factors potentially impacting on acne

- *Dairy products*

In 2005, Adebamowo et al. investigated the relationship between dairy products and acne through a level C study.(37) More than 47 000 adult women were asked to recall their high school diet using a validated food frequency questionnaire. Subjects were also asked if they had ever had physician-diagnosed severe acne. As a result, acne was positively associated with milk, particularly skimmed milk. These results were confirmed through two other level B studies in adolescent boys and girls.(38, 39) The authors hypothesized that dairy products influence acne through hormonal mediators by increasing plasma insulin-like growth factor (IGF)-1 levels.

Industrial cow's milk has been reported to be spiked with anabolic steroids and other growth factors, such as progestin testosterone precursors.(40-42) Testosterone precursors and 5α-reduced molecules are thought to contribute to the comedogenicity of milk by stimulating sebum production and hyperkeratinisation of the pilosebaceous unit.(37, 40, 43)

Commonly, cow's milk is available at different fat levels: whole milk, containing about 3.5% of fat, reduced-fat milk containing about 2% of fat and fat-free or skimmed milk. Of those, skimmed milk was associated with higher plasma IGF-1 levels. (44-47) IGF-1 stimulates the synthesis of androgens in both ovarian and testicular tissues and inhibits hepatic synthesis of sex hormone-binding globulin resulting in increased bioavailability of androgens. Adebamowo et al. confirmed that only skimmed milk significantly correlates with acne.(37) The authors hypothesized that the bioavailability of comedogenic triggers of milk may be increased by skimmed milk processing. In addition, skimmed milk may be more acnegenic because, in comparison with whole milk, as it contains less oestrogen, which is known to reduce acne.(12, 48) A level C case-control study, conducted by LaRosa et al. paralleled these findings, reporting that skimmed milk rather than full-fat milk triggers acne and a level B longitudinal study performed by Ulvestad et al. showed that intake of full-fat dairy products was associated with moderate to severe acne.(49, 50)

Recent translational research evidenced that Western diet (hyperglycaemic carbohydrates and milk consumption) reduces the activity of transcription factor p53, which has been identified being involved in the pathogenesis of acne and prostate cancer.(51) Moreover, epidemiological findings underlined a correlation between acne in late adolescence and increased risk of prostate cancer which may potentially improve translational evidence for a relationship between dairy products and acne.(52)

But, even though there are more and more elements confirming the relationship between acne and dairy products, to date there is no consensus concerning the role of fat levels in dairy products in the physiopathology of acne.

- *Whey proteins*

Whey proteins are milk serum proteins used as oral supplements to increase muscle mass.(53) Several articles report the potential association of these proteins and acne.(54, 55)

Whey protein extracts from cow milk contain six growth factors: tumour growth factor (TGF), insulin growth factor- (IGF)-I and -II, platelet-derived growth factor (PDGF) and fibroblast growth factor 1 and 2 (FGF-1 and -2).(56) They all are potent inducers of glucose-dependent insulinotropic polypeptides stimulating insulin secretion of pancreatic β-cells and may be related to acne.(56, 57)

- *Hyperglycaemic food*

Chronic and acute hyperinsulinemia activates a hormonal cascade that favours unregulated tissue growth by simultaneously elevating the free insulin-like growth factor 1 (IGF-1) level and reducing levels of insulin-like growth factor binding protein 3 (IGFBP-3).(58-60) Free IGF-1 is a potent mitogen.(61) Elevated concentrations of free growth factor have the potential for stimulating growth in tissues, including the follicle, thus potentially leading to acne.(62)

A level B study showed that a low-glycaemic-load diet improved acne severity and insulin sensitivity, as expressed by the homeostasis model assessment of insulin resistance (HOMA-IR). This suggests that nutrition-related lifestyle factors may also play a role in the pathogenesis of acne.(63) The adipocyte-derived hormone adiponectin is mainly produced by subcutaneous fat; it exhibits important anti-inflammatory, antioxidant properties, inhibits pro-inflammatory cytokines and has antidiabetic effects.(64-67) A high dietary glycaemic index and glycaemic load have been shown to be inversely associated with adiponectin concentrations.(68, 69) Thus, adiponectin may be a pathogenic cofactor contributing to the development of the disease.(67)

Table 1 provides an overview of nutrients that may have metabolic and nutrigenomic effects in acne.

The impact of the following three nutrient factors may be considered with caution as no reliable clinical data are currently available to confirm or reject their role in the pathogenesis of acne.

- *Alcohol*

Level C studies showed that testosterone levels had increased in men both after acute and habitual alcohol consumption.(70, 71) Several hypotheses have been raised.

Androgens, including testosterone, are an important acne trigger, and are present in both males and females.(72) After alcohol consumption, some alcohol is secreted through the sweat, thus possibly acting as a nutritive for *Cutibacterium acnes*.(73) Moreover, it has been hypothesized that the by-product acetaldehydes may also exacerbate acne.(73) Furthermore, alcohol may worsen acne by influencing the immune system. Frequent and long-term alcohol use is known to suppress the immune system, which in turn allows bacteria to grow and multiply, leading to an unbalanced skin microbiota and to acne.(73, 74) And finally, chronic consumption of alcohol has been suggested to increase cytokine release which may influence acne.(75, 76)

- *Tea, coffee and chocolate*

To date, there is no clinical evidence that products containing coffee or caffeine-cause or worsen acne.

Apart from one recent level C epidemiological study, there were no data about the potential relationship between the consumption of tea and the onset or worsening of acne.(36) Even though this study reports recent epidemiological data about factors triggering acne, other factors, including diet, may be concomitantly responsible for the evolution of acne in the population studied, such as sugar added to beverages containing tea. Conversely, there is some evidence through level C studies that green tea polyphenols may be beneficial in reducing sebum secretion, while also showing some antimicrobial properties, thus being potentially beneficial in acne.(77, 78)

Vongraviopap and Asawanonda reported that 99% dark chocolate, when consumed in normal amounts for four weeks, exacerbated acne in male subjects with acne-prone skin, potentially due to the presence of saturated fatty acids.(79) In a crossover, randomized, level B study, the impact of chocolate bars and jelly beans on the worsening or onset of acne showed that chocolate bar intake resulted in a worsening of acne.(80) However, these data should be considered with caution, as

chocolate was administered as a chocolate bar also containing sugar and milk: both are considered as potentially playing a role in acne.

- *Salt (Sodium Chloride)*

Only very few level C data about the role of salt or sodium chloride consumption in acne are available. While until recently there was no evidence that a diet containing high loads of sodium chloride triggers acne, a recent clinical level C study showed that consumption of salty foods was significantly higher among patients with acne compared to acne free subjects, making the consumption of salty food a possible participating factor in the development of acne.(81-83) Advanced investigations still have to be performed to determine the role of salt in acne.

Associated factors

In addition to nutrients, we identified uncontrolled food intake (nibbling, modern life-style nutrition), obesity and eating disorders as potentially impacting acne:

- *Uncontrolled food intake*

Several level C papers reported that modern lifestyle, consisting in sedentary leisure, such as watching TV, playing video games and working for several hours on a computer may result in uncontrolled food intake, especially of high calorie, high glycaemic-or high-fat-load and high meat intake.(25, 31, 32, 84, 85)

- *Obesity*

Level C data provide evidence that high glycaemic food intake, excessive consumption of milk and dairy products as well as of saturated fatty acids is a characteristic feature of the Western diet.(31, 32) Thus overweight, obesity and, consequently, increased body mass index (BMI) resulting from this type of diet have been reported as being associated with acne.(15, 86, 87)

- *Eating disorders*

Eating disorders such as *anorexia nervosa* and *bulimia nervosa* may result in significant medical complications in all of the primary human organ systems, including the skin.(88-90) Among a large spectrum of skin diseases, level C information provided evidence that acne may be associated with eating disorders.(91)

To date, only a small amount of empirical level B and C data about the relationship between acne and the Western diet, obesity and eating disorders is available. Epidemiological and long-term observational studies are necessary to assess the impact of these co-factors on acne.

Nutrients which are potentially beneficial in acne

Acne is a rare condition in non-Westernized societies with higher ratios of n-3 to n-6 polyunsaturated fatty acids (PUFA) from dietary intake, as reported through level C papers.(32, 92)

Regular fish and vegetable consumption have been reported to reduce acne. Melnik reported that populations in Papua-New Guinea and Inuits, who have no milk or cereal intake, do not develop acne while in those individuals who changed their nutrition habits, an increase of acne prevalence was observed.(32) The author suggests that a palaeontological nutrition regimen, consisting of fish, vegetables and fruits with a low glycaemic, lipid and transfatty acid load may help to reduce the risk of acne. These observations were confirmed by level C data generated by Grossi et al. in 2016.(93)

- *Fish products*

Lower n-3 PUFA content of the Western diet is an important dietary modulator of inflammatory mediators.(25, 33, 94, 95) A Korean level B study found that individuals with acne consumed significantly less fish and more junk food than the control individuals.(96) A similar level C study conducted in Italy reported that consumption of fish was associated with a protective effect against moderate to severe acne.(15) This inverse association between fish consumption and acne severity may be due to the fact that fish contains high levels of n-3 eicosapentaenoic acid (EPA) that acts as a competitive inhibitor of arachidonic acid (AA) conversion to inflammatory mediators, prostaglandin E2 (PGE_2) and leukotriene B4 (LTB_4), reducing inflammation in acne.(97)

A pilot level C study conducted by Khayef et al. provided some evidence that fish oil supplements may improve overall acne severity, especially of moderate to severe acne.(92) Conversely, Burris et al. reported through his level C paper that fish intake may impact or aggravate acne.(98)

Based on the available data, no conclusion on the impact of fish food on acne can be drawn.

- *Vegetables and fruits*

Plant-based approaches have been practiced in multiple medical perspectives, including Chinese medicine and Ayurveda.(99)

Several level C papers reported that a low intake of fruit or vegetables triggers acne, especially in the female population, while the Mediterranean diet, rich of vegetables and fruits and unsaturated fatty acids,positively impacts acne.(100, 101)

Nutrition and potential targets in acne

- *Keratinocytes*

Abnormal follicular keratinization is important for comedone formation in acne. Diet-induced changes in sebum quantity and composition may not only induce the inflammation of acne but may also drive the process of comedogenesis.(32)

IGF-1 was reported to stimulate keratinocyte proliferation via the activation of the IGF-1 receptor.(102-106) Thus, diet may increase comedogenicity.(32, 39, 107, 108)

Moreover, saturated fatty acids, a main compound of the Western diet, increase the release of toll-like receptor2/interleukin-1β (TLR2/IL-1β) signalling of dendritic cells, promoting Th17 cell differentiation and an increased secretion of IL-17A. Increased local levels of IL-1β and IL-17A have been detected in acne lesions .(109) IL-17 contributes to keratinocyte hyperproliferation and

decreases keratinocyte differentiation.(110) As a result, follicular keratinocyte homeostasis in acne is disturbed, a mechanism comparable to that drives keratinocyte hyperproliferation in psoriasis.(111)

- *Sebocytes*

An *in vitro* study showed that forkhead box transcription factor (FoxO)1 activity was reduced in sebaceous glands through an increase of insulin and IGF-1 levels in SZ95 sebocytes proposing that FoxO1 principally might be involved in the regulation of growth-factor-stimulatory effects on sebaceous lipogenesis and inflammation in the pathological condition of acne.(112) Moreover, insulin and IGF-1, both stimulated by milk products and whey protein intake, have been shown activating the PI3K-Akt pathway which plays a key role in the sebaceous lipogenesis being of critical importance in the pathogenesis of acne. (112, 113) FoxO transcription factors are inhibitors of mTORC1 activity.(57) Agamia et al. demonstrated a relationship of reduced FoxO1 levels associated with upregulation of mTORC1 activity and high-glycaemic diet.(114, 115)

Moreover, increased Akt/mTORC1 signalling pathway was shown enhancing sebocyte survival, growth and lipogenesis, thus promoting hyperseborrhoea and dysseborrhoea with an exaggerated release of sebum-free fatty acids promoting inflammation.(32, 116)

Management of acne through the nutrition facet: practical aspects

To verify if nutrition may potentially play a role in acne, patients should be questioned during their first visit about their daily food habits, potential family acne history, lifestyle or eating disorders. Moreover, if considered necessary, BMI should be calculated to verify if the patient is at risk of being overweight or obese, thus facing an increased risk of acne.

Should nutrition be an issue, then patients may be advised to change their food habits or, if necessary, seek the help of a nutritionist in addition to a pharmacological treatment of their acne, according to the severity of the condition and current treatment guidelines.(117, 118) Moreover, in male patients with moderate to severe acne, not responding to acne treatments or with a fast relapse, metformin combined with a low glycaemic diet may be indicated to improve their disease.(119)

Conclusion

Recent research has shed some new light on the relationship of nutrition and acne, allowing the identification of a certain number of potential triggers, such as dairy products, mainly skimmed milk, hyperglycaemic load and the excessive intake of whey proteins. However, evidence is still mainly based on epidemiological studies, questionnaires and basic or translational research, reported through level B and C publications. Currently, no clinical data generated through controlled level A clinical trials allow the association between nutrition and acne to be confirmed.

Nevertheless, several indicators may allow nutrition factors that potentially have an impact on acne to be identified. Their identification may therefore allow the better management of acne in certain patients, thus making nutrition control an additional element in the armamentarium of acne care.

Further clinical and translational research remains necessary to investigate and confirm the association between nutrition and acne.

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Table 1 Nutrients and their metabolic and nutrigenomic effects in patients with acne according to Melnik 2015(32)

Nutrients	Metabolic and nutrigenomic effects	Sources
Hyperglycemic carbohydrates	Postprandial hyperinsulinemia	Sugar
	Insulin-mediated hepatic IGF-1 synthesis	Sweets
	Reduction of IGFBP3	Soft drinks
	Increased bioavailability of free circulating IGF-1	Pizza
	Reduction of SHBG	Pasta
	Increased bioavailability of free circulating testosterone	Wheat bread
	Reduced nuclear activity of FoxO1	Wheat rolls
	Increased expression of sebocyte SReBP-1c Activation of mTORC1 Glucose-mediated microRNA-21 expression	Cornflakes
Milk, dairy and whey products	Postprandial hyperinsulinemia	Whole and skim milk
	Increased levels of circulating IGF-1	Pasteurized fresh milk
	Leucine-mediated activation of mTORC1	Yogurt
	Glutamine-mediated activation of mTORC1	Ice cream
	Palmitate-mediated activation of mTORC1	Whey and casein supplements
	Milk-microRNA-21-mediated proliferation and inflammation	Cheese
Saturated and trans fats	Palmitate-mediated activation of mTORC1	Butter
	Palmitate-driven inflammasome activation	Cream
	Possible mTORC1 activation	Fast food
	Proinflammatory signaling	French fries

Abbreviations: IGF-1, insulin-like growth factor 1; IGFBP3, IGF binding protein 3; SHBG, sex hormone binding globulin; FoxO1, forkhead box O1; SReBP-1c, sterol response element binding protein 1c; mTORC1, mechanistic target of rapamycin complex 1.