Acne and Nutrition: A Systematic Review

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Few well-defined, evidence-based nutritional recommendations for people with skin diseases have been published in the scientific literature and standard dermatological textbooks. Using a systematic review of acne vulgaris as an example, the aim of this study was to determine whether there are systematic studies on the topic and, if so, of what quality. Four evidence levels were defined: (A) double-blind randomized study; (B) randomized study with serious limitations/low number of cases; (C) case-control or cohort study; and (D) expert opinion/case report. PubMed and Cochrane searches were performed using combinations of the terms "diet", "nutrition", "meal" and "food" with "acne". Foodstuffs mentioned in relevant articles were subdivided by evidence level and recorded as having a beneficial (+), neutral (0) or adverse (–) effect. However, only a small proportion of studies met sufficiently high scientific standards that would enable therapeutic recommendations to be made in practice.

Key words: nutrition; acne; evidence level; overview.

Accepted Apr 28, 2016; Epub ahead of print May 3, 2016

Acta Derm Venereol 2017; 97: 7–9.

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Patients often ask about the effects of nutrition on acne, but current research into this topic is very limited compared with that of high-quality drug studies. One of the main reasons for lack of research into nutrition and acne is the high cost of appropriate studies, since, unlike for medications, the expected efficacy is low and there is a lack of options for increasing the price of foods to finance research. Nonetheless, several nutritional studies of various qualities have been published during the past few decades. However, very few high-quality studies meeting modern standards have been performed, and those that have involve only a small proportion of the wide range of foods available (1, 2). Some studies were performed several years ago and, from today's viewpoint, have design flaws that would not allow dietary recommendations to be made (3). The number of food items that could be included in a meta-analysis is limited because there is no, or not good enough, evidence about many food items (1). An overview of all the foods that influence a specific disease, stratified by evidence level, could support clinicians as well as researchers. Using a systematic review of acne vulgaris as an example, the aim of this study was to determine whether there are systematic studies on the topic and, if so, of what quality.

METHODS

PubMed and Cochrane searches were performed with the search terms "nutrition", "diet", "meal", "food", each in combination with "acne". The hits were then examined for relevant articles using pre-defined criteria. Initially, the timeframe for the sample search was limited to 11 years (Cochrane; 2004–2014) and 6 years (PubMed; 2004–2009)[1], respectively. Articles were classed as relevant if foodstuffs, vitamins, trace elements, certain diets, food forms, alcohol and nicotine were studied, or at least mentioned, as influencing factors in the skin disease, and an effect was rated beneficial/neutral/adverse. Furthermore, only studies of per os administration in humans, but no studies of topical application, cell culture or animal experiments were considered. All foods with the respective effect reported were listed alphabetically in a table and assessed by evidence level. The evidence level in the Atkins and Bigby system (4, 5) was expanded to a search for usually non-randomized studies by evidence Level D with expert opinion or mention of the food. Otherwise, Level A corresponds to randomized double-blind studies with a high number of cases, Level B to randomized studies with serious limitations or a low number of cases, and Level C to case-control or cohort studies. Within each of the 4 evidence levels, adverse (–), neutral (0) or beneficial (+) effects were differentiated into a corresponding total of 12 groups. The results are summarized for each food as a row in a table and illustrated by a graphical presentation with respect to the results/evidence.

RESULTS

A total of 162/21 (PubMed/Cochrane) hits for acne were found in the study timeframe, of which 58/6 relevant articles on acne could be assessed based on the selection criteria (for a complete reference list in alphabetical order, see Appendix S1[2]). Higher grade studies (evidence Levels A and B) were rarely found, while mentions of foods (evidence Level D) formed a clear majority.

[1]This study was part of FF's medical doctoral thesis and thus has to reflect its results. The addition of PubMed listed papers for a further 5 years (2010–2014) would exceed the space limitations of the medical faculty rules for medical doctor theses; thus, only the Cochrane database search was expanded (2004–2014).
[2]https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-2450

doi: 10.2340/00015555-2450

For acne there were 370 mentions of 146 influencing foods. Evidence assessment showed none of Level A, 4 of Level B, 45 of Level C and 321 of Level D (**Table I**).

While several foods were mentioned only once in connection with acne within the study timeframe, other foods or diets were mentioned up to 22 times within various evidence levels, sometimes with contradictory influence (**Table II**).

DISCUSSION

There are polarizing, often speculative, opinions concerning the efficacy or non-efficacy of diets and foods as part of the treatment of diseases, especially in dermatology. This study systematically assessed the available scientific literature with respect to the influence of food, using acne as an example.

In comparison with drug testing, studies on the effect of nutrition on skin diseases have rarely been performed at evidence Levels A or B. High-quality studies are expensive and medication studies are usually amortized with the selling price later on, which is not possible in the case of foods. Randomizing and controlling human subjects and diet is extremely difficult. There are many confounders in nutrition studies, but less so in drug studies. Double-blind testing is very difficult because of the shape and the taste of the food. The best way to test would be a double-blind placebo-controlled food challenge (DBPCFC) including blinding of colour, shape and taste, as used in food allergy testing, but this would substantially increase overall expenditure.

In order to include the results of survey articles on knowledge of foods, as well as those used as remedies in natural medicines, and older articles cited currently during the study period, the arrangement of evidence levels as proposed by Atkins (4) and Bigby (5) was modified and expanded by a Level D for citations/expert opinion/case reports. The results presented here, using acne as an example, were selected because a connection to nutrition is, or was, considered relatively certain by both dermatologists and patients. In this respect, there are a number of articles in the defined publication timeframe that addressed the corresponding connections.

Only human studies were taken into account for the assessment of relevance. *In vitro* studies were excluded in order to limit our topic to practical relevance in nutrition.

Table I. Assessed foods mentions arranged by evidence level[a]

	Level A Σ/–/0/+	Level B Σ/–/0/+	Level C Σ/–/0/+	Level D Σ/–/0/+
Acne vulgaris	**0**/0/0/0	**4**/0/1/3	**45**/15/28/2	**321**/163/70/88

[a]Level A corresponds to randomized double-blind studies with a high number of cases, Level B to randomized studies with serious limitations or a low number of cases, Level C to case-control or cohort studies, and Level D to usually non-randomized studies expressing expert opinion or mention of the food. Within each of the evidence levels, adverse (–), neutral (0) or beneficial (+) effects were differentiated in a corresponding total of 12 groups. The results are summarized for each item (**bold** figures).

Table II. The 10 most-frequently studied/mentioned foods (and smoking) in the examined time-frame

Food	Total Σ/–/0/+	Level A –/0/+	Level B –/0/+	Level C –/0/+	Level D –/0/+
Milk	**22**/17/5/0	0/0/0	0/0/0	2/0/0	15/5/0
Chocolate	**17**/7/10/0	0/0/0	0/0/0	2/0/0	6/10/0
Milk products	**17**/13/3/1	0/0/0	0/0/0	0/1/0	13/2/1
Western diet	**14**/14/0/0	0/0/0	0/0/0	0/0/0	14/0/0
Low glycaemic load	**12**/0/0/12	0/0/0	0/0/2	0/0/1	0/0/9
High glycaemic load	**12**/11/1/0	0/0/0	0/0/0	1/0/0	10/1/0
High glycaemic index	**11**/9/2/0	0/0/0	0/0/0	0/0/0	9/2/0
Low-fat milk	**9**/8/1/0	0/0/0	0/0/0	2/1/0	6/0/0
Smoking	**7**/1/4/2	0/0/0	0/0/0	0/2/0	1/2/2
Pizza	**6**/1/5/0	0/0/0	0/0/0	0/2/0	1/3/0

For explanation of evidence levels see Table I and Methods.

As for other topics, the number of studies on individual foods reveals a focus of scientific interest of often limited timeframe. This, of course, limits the screened publication period, but, on the other hand, expanding the study time period to 50 years or more would mean including a number of older articles, which have serious limitations in study structure (3, 6) according to today's standards. This expansion would be necessary to obtain the most complete overview possible, but it is not appropriate in establishing a prototype and in defining the analysis algorithm because of the considerable effort and costs involved.

Multiple studies or mentions of a particular food in the various evidence levels and with differing influence in a text often limit the clarity of presentation of the result for the reader. Thus, a graphical presentation is provided in addition to the tabular presentation. This enables a visual overview based on colour and distribution between right and left over the study situation within the 12 possible degrees of influence (evidence Levels A–D each with 3 categories: adverse/neutral/beneficial). Like a scale, evidence Level A, with the highest quality, is always positioned at the edge comparable to the greatest leverage. An identical distance right or left from the middle of the chart thus corresponds to the same evidence level, but results with contradictory influence (left adverse and right beneficial). The colours were borrowed from a traffic light: red for adverse (–), yellow for neutral (0) and green for beneficial (+) influence. Since graded assignment of the evidence level with neutral relationship causes neither positive nor negative lateral shift in the results, the neutral results were entered vertically in yellow. Using milk in acne as an example (**Fig. 1**), an adverse influence can be observed with entered numbers only in the left horizontal arm. In this, many results were near the centre of the chart at the lowest evidence, Level D; but there are also 2 corresponding results at Level C. Another 5 citations at Level D are shown in the lower middle, which did not cause any shift between beneficial and adverse.

For acne, 146 different foods were recorded a total of 370 times in 60 relevant articles. There were only 49 studies with evidence Levels A–C. In these, none corresponded to evidence Level A, 4 cases corresponded to

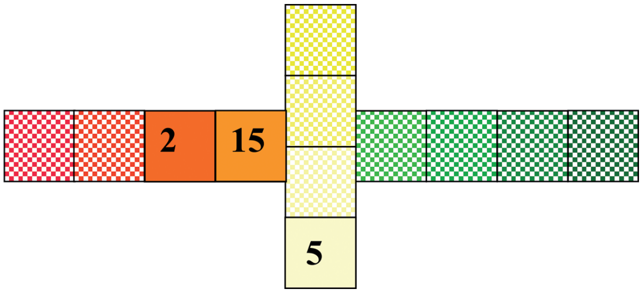

Fig. 1. Example: milk in acne. A total of 22 mentions include mostly adverse effect (red/left horizontal arm), of these 2 at evidence Level C and 15 at Level D. Five articles reported no effect (Level D) (yellow/vertical arm). No beneficial influence (green/right horizontal arm) of milk drinking on acne was found.

Level B and 45 cases to Level C. The majority (86.7%) corresponded to evidence Level D (assessed mention without own study). The main impact of adverse food effects relevant for the industrial countries in the literature studied was seen in the western diet, since the introduction of this diet in populations whose traditional nutrition had been different (7) resulted in a marked increase in the incidence of acne. The main components of the western diet are hyperglycaemic carbohydrates, (cow's) milk and saturated fats (8). The pathogenetic effect of the western diet is mostly ascribed to the high glycaemic load and high glycaemic index, hormonal effects in cow's milk and the shift in the omega-3-FA/omega-6-FA ratio in favour of omega-6-FA (7, 9, 10). The adverse effect of milk and glycaemic load or glycaemic index finds broad consensus (1, 2). The role of androgen hormones in acne is well defined. Hyperinsulinaemia and an increased insulin growth factor 1 (IGF-1) as a result of high glycaemic load and dairy food intake cause an increased production of androgen hormones and sebum associated with acne (1, 2). Overactivated nutrient- and growth factor sensitive kinase mechanistic target of rapamycin complex 1 (mTORC1) and downregulation of nuclear transcription factor FoxO1 levels induced by a western diet increase inflammation and comedogenesis (8). High glycaemic load and hyperinsulinaemia decrease insulin growth factor binding protein 3 (IGFBP-3), which controls cellular growth (1). The resulting stimulation of cellular growth leads to acne.

Some older studies (3) are repeatedly cited anecdotally because of their methodological weaknesses. No well-designed study has been performed to address the belief still deep-rooted in the population that chocolate has an adverse effect on acne.

There are fewer reports on the beneficial effects of foods (n=63, 17.0%) and adverse effects of avoidance (n=8, 2.2%) on acne than reports on foodstuffs with adverse effects when consumed (n=165, 44.6 %) or beneficial withdrawal (n=28, 7.6%). Hence, it can be concluded that acne is more likely.

CONCLUSION AND FUTURE WORK

The current system of collecting evidence on the effects of nutrition on skin diseases could be improved. While in modern drug testing many disruptive factors, such as age, gender etc., are taken into account, confounders caused by variation in the diets of study subjects are usually not considered. However, in reviewing recent scientific literature, there is evidence that foods can influence skin diseases in various ways. In summary, in the example of acne, according to the literature, milk and foods with a high glycaemic burden are the best candidates for food-triggered influence. However, it is not currently possible to set out evidence-based nutritional recommendations in many cases (2). This database linking various skin diseases with an alphabetical list of foods may be help practitioners in making recommendations for dermatological patients concerning nutritional guidance to support healing. Moreover, the results of this collection may indicate suitable candidates for more detailed testing, as long as the potential for beneficial influence on the disease by the food is particularly high or promising.

The authors declare no conflict of interest.

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