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THE ROLE OF KETOGENIC DIET IN ACNE AND PSORIASIS

Battaglia Alma[1*], Tanzola Rosa[1*], Galdo Giovanna [1,2]

[1]Post Graduate University Course in "Diete e Terapie Nutrizionali Chetogeniche: Integratori e Nutraceutici (NutriKeto)" - Dipartimento di Farmacia, University of Salerno, Via Giovanni Paolo II – Fisciano (SA), Italy
[2]Oncologic Dermatology Unit, IRCCS-CROB, Rionero in Vulture, Potenza, Italy

Email address: alma.battaglia@libero.it; dott.tanzola@gmail.com; nutriketo@unisa.it

Abstract

Diet can affect many dermatological conditions. In some cases, dietary interventions influence the course of skin disease, such as acne; in others, dietary changes can be linked to systemic diseases that can affect health outcomes, such as in psoriasis. (1) Dietary change may also be an important aspect of the prevention of associated systemic diseases, such as CVD and other systemic diseases associated with psoriasis. The role of chronic inflammation that causes metabolic and vascular disorders is increasingly recognized. Pro-inflammatory cytokines contribute to atherogenesis, peripheral insulin resistance and the development of hypertension and type II diabetes. Psoriasis as a chronic inflammatory skin disease is characterized by a variety of immunological and inflammatory changes and can similarly pre-arrange for these disorders (2). Based on data from the literature that relate acne vulgaris and psoriasis with diet, this review clarifies the hypotheses about this topic explaining which way the KD, a low-carbohydrate, high fat caloric diet based above all on protein, reduce the unpleasant effects of these disorders.

Keywords: *ketogenic, diet, very low-calorie diet, weight loss, acne, psoriasis, nutrition, insulin*.

Introduction

Several dermatologists have denied for years a connection between diets and skin diseases. Eating habits in industrialized nations promote diets rich in fat, salt and sugar with an excessive caloric intake that causes obesity, that is a chronic condition characterized by excess body weight due to the increase in energy reserves stored as body fat. [3] There is a link between acne psoriasis and obesity. Andrews (1954) states that acne it is aggravated by excess fat, sweet and starchy foods. [4] The relationship between obesity and psoriasis is bidirectional, with obesity predisposing to psoriasis and psoriasis that favour obesity. Psoriasis is an inflammatory disease of the epidermis based on an immunological mechanism involving Langerhans cells and T lymphocytes that produce pro-inflammatory cytokine. Obese patients have an increased double risk of psoriasis and in epidemiological studies, obesity and a high abdominal fat mass have been shown to lead to a worse clinical outcome for patients with psoriasis [3, 5]. Adipose tissue is an essential endocrine organ that secretes a wide range of soluble mediators involved in immunity, inflammation, metabolic regulation and appetite. Soluble mediators released by white adipose tissue possess pro-inflammatory actions and contribute to low-grade inflammation. White adipose tissue is a crucial site in the formation of pro-inflammatory adipokine [6] underlying dermatological diseases.

Methods

We have reviewed the literature available through research on PubMed, academic articles published in scientific journals and review of bibliographies of selected articles. We used as keywords "ketogenic diet", "very low calorie diet" "psoriasis", "nutrition", "diet", "weight loss", "obesity", "inflammation", "body fat", "acne", "insulin", "metabolic syndrome" . We included in the search reviews, observational study, clinical trial, case report and randomized clinical study.

Acne vulgaris

Acne is a skin disease characterized by the formation of comedones, papules, pustules, nodules, and / or cysts due to obstruction and inflammation of the pilosebaceous units. The prevalence of acne varies among different populations: in non-western countries, where the diet has a low glycemic load, the incidence is lower than in the United States where it affects 80% of the population during puberty and remains in 50% of young people adults. [7] Dermatologists have denied for years a connection between acne and diet. Recent researches have confirmed the role of specific food which play a role in the pathogenesis of acne.

Acne occurs due to the synergy of 4 main factors:

- Excessive sebum production
- Obstruction of the follicle with sebum and keratinocytes
- Colonization of follicles by Propionibacterium acnes (a normal human anaerobic)
- Release of more mediators of inflammation

Many studies highlight that diets with high glycemic load are implicated in the etiology of acne, due to their ability to stimulate insulin secretion and, consequently, to:

-Promote androgen synthesis

-Influence, through the induction of steroidogenic enzymes, the hypothalamic secretion of GnRh and the production of SHBG

- amplify the effects of IGF-1

- increase the proliferation of basal keratinocytes

- Encourage the production of androgen-induced sebum.

Diet-induced insulin / IGF-1 secretion: i) suppresses the FOXO1 pathway which, when active, inhibits the expression of the androgen receptor, PPARγ and sterol response element binding protein-1c (SREBP-1c), transcriptional factors crucial for sebaceous lipogenesis; ii) activates the mTOR / mTORC1 pathway key regulator of anabolism and lipogenesis. Activates PPARγ, and SREBP-1c and promotes sebum secretion. [8]

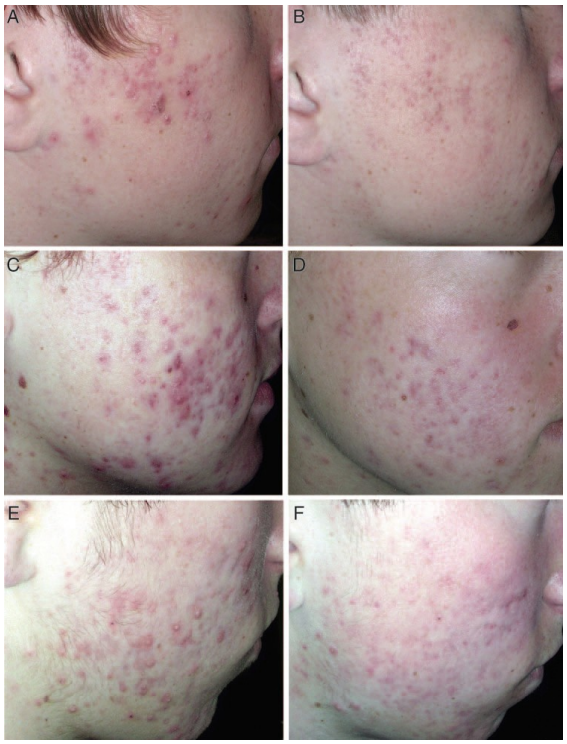
The aberrations of the quantity and quality of sebum promote overgrowth of Propionibacterium acnes and therefore the transformation of the biofilm which becomes rich in: free palmitate, that induces TLR2-mediated activation of inflamosome

with the consequent release of IL-1β and IL-1 and free oleate that stimulates adhesion of P.acnes, keratinocyte proliferation and comedogenesis via IL-1-α. [8]

In a study [9]: Sample: 54 males diagnosed with acne. Age between 15 and 25 years old. 43 subjects completed the study. Control diet (CHO 50%, P 17.4%) normocaloric. Low-Glycemic-Load LGL diet (45% low-GI CHO, 25% P, 30% L) normocaloric. Duration: 12 weeks. Blind dermatological checks: 1 per month

Reduction of inflammatory injuries:
- LGL: 45% reduction
- Control: 23% reduction

Reduction of total injuries
- LGL: 51% reduction
- Control: 31% reduction [10]



Smith RN et al, The American journal of clinical nutrition, 2007. [10]

KDs influence numerous inflammatory markers and improve insulin levels, with a consequent effect on the IGF-1 pathway, and could be effective in reducing the severity and progression of acne. Therefore, physiological and biochemical bases exist to support the use, for a limited period of 30-60 days, of KDs with the aim of acting on the pathogenic mechanisms underlying acne vulgaris and restoring a correct hormonal status. [11]

Psoriasis

Psoriasis is a chronic immune mediated inflammatory skin disease affecting 2-4% of the world population. [13] Psoriasis is currently considered a multifactorial disease caused by interaction between genetic and environmental triggers. [3,5]

Both adaptive and innate immune systems are thought to be responsible for psoriasis pathogenesis. Environmental factors such as emotional stress and smoking can negatively influence the onset of symptoms and the severity of the disease. An environmental factor of high interest to patients is the influence of diet; improper nutrition, inadequate body weight, and metabolic diseases may increase the clinical symptoms or even trigger the disease. The immunological response is primarily driven by activated T helper 1 cells, and the consequent release of cytokines results in proliferation of keratinocytes. [3]

Psoriasis is characterized by well-demarcated, erythematous plaques covered by silvery-white scales, typically occurring in a symmetric distribution involving the elbows, knees, trunk and scalp. Psoriasis onset is triggered when genetic and/or environmental factors activate plasmacytoid dendritic cells, resulting in the production of numerous pro-inflammatory cytokines, including tumour necrosis factor (TNF)-α, interferon (IFN)-γ, interleukin (IL)-17, IL-22, IL-23 and IL-1β. Many of these cytokines stimulate keratinocyte hyperproliferation, which perpetuates a cycle of chronic inflammation. Systemic elevations in these cytokines promote chronic subclinical inflammation associated with comorbidities that disproportionately affect patients with psoriasis, including psoriatic arthritis (PsA), cardiovascular disease (CVD), diabetes mellitus, obesity, inflammatory bowel disease (IBD) and non-alcoholic fatty liver disease (NAFLD)' certain malignancies, infections, and mood disorders. An higher prevalence of cardiovascular risk factors, such as dyslipidemia and obesity, has been reported in psoriatic patients. [14,15]

Obesity and psoriasis

The dietary habits in industrialized nations promote high-fat, high-salt, high-sugar diets with excess caloric intake resulting in an obesity epidemic. Obesity is a chronic condition characterized by excess body weight due to increased energy deposits stored as body fat. [3] The relationship between obesity and psoriasis is bidirectional, with obesity predisposing to psoriasis and psoriasis favouring obesity. In a research organized by Zuccotti and others, conducted in the MEDLINE electronic databases for articles published in English between 1 January 1990 and September 2018 from which only controlled clinical trials were selected, emerged that psoriasis patients are more likely to be overweight or obese. Statistically significant association exists between increased psoriasis severity and higher body mass index (BMI). Obese patients have a two-fold increased risk of psoriasis. Epidemiological studies have shown that obesity and high abdominal fat mass lead to a poorer clinical outcome for psoriasis patients. [3,5] Adipose tissue is an essential endocrine organ secreting a wide range of soluble mediators involved in immunity, inflammation, and metabolic and appetite regulation. The soluble mediators released from white adipose tissue possess pro-inflammatory actions and contribute to the low-grade inflammatory state in obese individuals.

Several studies have demonstrated that white adipose tissue is a crucial site in the formation of pro-inflammatory adipokines, which include the classical cytokines such as IL-6, TNF-α, and the specific molecules leptin, adiponectin, and resistin. Adiposity may lead to induction of T-helper 17 cells (Th17). Th17 cells secrete IL-17 and are recognized for the involvement in the pathogenesis of autoimmune diseases including psoriasis. Psoriasis is characterized by proliferation of Th1, Th17, and Th22 cells resulting in the production of the pro-inflammatory mediators interferon-γ, TNF-α, IL-6, and IL-22. Therefore, TNF-α and IL-6 secreted by adipose tissue may contribute to the inflammatory state in psoriasis. Furthermore, patients with psoriasis have higher levels of leptin compared to persons without psoriasis; both resistin and leptin promote the secretion of TNF-α and IL-8 which are involved in the pathogenesis of psoriasis. [6]

Diet and psoriasis

Researchers underline the important role that nutrition plays in the management of psoriatic disease and patients are often very interested to know what dietary and lifestyle changes may improve the disease. [12,13,16] Several studies have examined the various nutritional strategies for the treatment of psoriasis. In a review of the literature published by Hammam A Alotaibi, it shows that diet and exercise are an important support for the treatment and management of psoriasis, improving not only the patient's general health, but also contrasting oxidative stress factors. So they have a positive impact on Psoriasis Area and Severity Index (PASI) scores. [17,18] Body weight reduction with a low-calorie diet can help patients with overweight or obese psoriasis, leading to an improvement in psoriasis severity. [3] The adherence to low-calorie dietary regimens can enhance the efficacy of treatment therapy but also improve response to them. [5]

A 2015 clinical case by Castaldo et al. reported a patient treated with biological therapy who restored his response to the systemic treatment of psoriasis after a 4-week intensive ketogenic low calorie diet based on protein without carbohydrates. [5]

This nutritional therapy, that led to rapid weight loss, resulted in a reduction of the inflammation associated with the loss of visceral adipose tissue (which is particularly characteristic of psoriasis patients), responsible for insulin resistance and other metabolic complications. VLC diet regimens involve rapid weight loss and visceral fat, especially when adequate amounts of protein are administered.

Through rapid and consistent weight loss, a very low calorie ketogenic diet can help restore a rapid response to systemic therapy in recurrent plaque psoriasis. [5,19] The same authors reported that in drug-naïve adult overweight patients with stable chronic plaque psoriasis, an aggressive ketogenic weight loss program consisting of a VLCKD, followed by a balanced, hypocaloric, Mediterranean-like diet, appeared to be an effective first-line strategy to reduce disease severity. [20] In another clinical study, 30 psoriasis patients were subjected

to a ketogenic nutritional regimen and monitored for 4 weeks by evaluating the clinical data, biochemical and clinical parameters, NMR metabolomic profile, and IL-2, IL-1β, TNF-α, IFN-γ, and IL-4 concentrations before and after the nutritional regimen. The results showed that a VLCKD can be considered a successful strategy and therapeutic option to gain an improvement in psoriasis-related dysmetabolism, with significant correction of the full metabolic and inflammatory status. [21]

Conclusions

The role of diet in the management of dermatological diseases is multifactorial. Dietary manipulation may not be intended as primary treatment for psoriasis or acne, but there is potential to incorporate it with other first line treatments to synergistically promote successful treatment outcomes and reduce incidence of life change including cardiovascular disease.

A ketogenic diet based on a drastic, almost total, reduction of carbohydrate and relative increase in protein and fat, induce a rapid weight loss that influence efficacy of therapy. Ketosis reduces several markers of inflammation and by reducing insulinemia, which also affects the IGF-I pathway, it could be effective in reducing the severity and progression of acne. [11]

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