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Review Article

Psoriasis and Nutritional Therapy

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Abstract

The role of nutrition in the treatment of psoriasis has been studied for many years. Recently, comorbidity conditions have been associated with psoriasis. Such observation has fostered an interest in nutrition to improve comorbidity conditions. Many studies have evaluated the role of nutrients in the development of psoriasis. However, few studies have investigated the effect of a healthy diet, such as the Mediterranean one.

The purpose of this study is, to investigate the relationship between adherence to the Mediterranean diet, along with a healthy lifestyle, and the severity of psoriasis.

Keywords: *Psoriasis; Mediterranean Diet; Healthy Lifestyle; Nutrients; Nutrition*

Introduction

Psoriasis is a non-contagious, strongly relapsing chronic inflammatory skin disease mediated by T lymphocytes [1]. Psoriasis occurs at any age, but it is most common in between the 50 - 69 age group [2]. The prevalence of psoriasis varies between 0.91% and 8.5% of the total population, making this pathology a serious global health problem [3].

Psoriasis is defined as a highly complex pathology with regard to the numerous consequences on the quality of life of the patients who suffer from it [4,5]. The treatment of psoriatic patients requires multidisciplinary treatment aimed not only at improving skin symptoms, but also at identifying and managing cardiovascular, metabolic, nutritional, as well as socio-psychological comorbidities that often are associated with this pathology. Given the importance of the multidisciplinary therapeutic approach a Nutrition professional, requires adequate training and updating, in order to provide an adequate nutritional approach to patients suffering from psoriasis.

Psoriasis: pathogenesis and symptoms

Psoriasis is an inflammatory skin disease usually of a chronic relapsing nature. It presents itself clinically with the presence of erythemato-squamous plaques, resulting from a very rapid skin turnover (3 - 4 days compared to 28 days of normal skin).

Autoimmune, genetic and environmental factors are involved in its pathogenesis. The immunological response plays a central role through the activation of T helper lymphocytes and the consequent release of pro-inflammatory cytokines such as IL1β, IL17, IL22, IL23 and TNF-α which determine the proliferation, the incomplete differentiation of keratinocytes and the development of typical lesions characterized by pink plaques with silvery scales on the scalp, elbows, knees and lower back [6].

In addition to genetic factors [7] some environmental factors, considered "triggers", which make manifest what is already genetically determined and favor the onset or aggravation of the disease, may also be important [8].

The most important are: stress; physical trauma (injuries, bruises); infections, not just skin infections; some drugs such as beta-blockers, interferon, lithium, antimalarials and FANS; cigarette smoke; alcohol abuse; obesity.

Among environmental factors, diet plays a central role therefore incorrect nutritional habits, excessive body weight can increase clinical symptoms or even trigger the disease. In addition, clinical evidence indicates that psoriasis is frequently associated with other inflammatory and/or autoimmune diseases such as metabolic syndrome, adult heart disease (CVD), type 2 diabetes mellitus, hypertension, hepatic steatosis, and inflammatory bowel disease [9,10]. Clinical features, in particular the size and dispensation of psoriatic lesions, allow the classification of psoriasis into plaque, guttate, pustular and erythrodermic psoriasis [11].

This disease can occur at any age, but usually appears for the first time between the ages of 20 and 30, while it is rare in children; a second peak of incidence occurs in the age group between 50 and 60 years [12]. In general, an early onset of psoriasis (before the age of 15) is associated with a more severe form. Psoriasis has the same incidence in the two sexes [13]; in a good percentage of cases it tends to regress in summer and then flare up in the winter months.

Among the most commonly used quantitative indices to evaluate the severity and extent of psoriasis, the PASI score (Psoriasis Area Severity Index) is an effective method for assessing psoriatic lesions based on the characteristics of erythema, infiltration and flaking and to the affected surface area [14].

The symptoms that most frequently manifest themselves in psoriasis are [15]: peeling of the skin (92%), itchy skin (72%), erythema of the skin (69%), fatigue-asthenia (27%), swelling of the skin (23%) plaque burning (20%), skin bleeding (20%).

The consequences and diseases associated with psoriasis can influence the quality of life causing decreased work productivity, extended physical disability, and impaired social relations [16].

Psoriasis and gluten: Highlighted correlations between psoriasis and celiac disease

Among patients with psoriasis there is a higher prevalence of autoimmune diseases, including celiac disease [17,18]: a meta-analysis demonstrated an approximately 3-fold increased risk of CD among patients with psoriasis [19]. Several studies suggest common genetic and inflammatory pathways between psoriasis and celiac disease [20]: they, in fact, have similar anomalies in the release of pro-inflammatory cytokines [21-24] and both present a genetic susceptibility at the base [25] First, the association between CD and several autoimmune diseases, such as type I diabetes mellitus and autoimmune thyroid disease, is well documented [26,27]. It is assumed that shared genes (at-risk human leukocyte antigen [HLA] haplotypes) might be responsible for this association. For example, type I diabetes mellitus and CD share multiple familiar genetic loci such as HLA-DR3, HLA-DQ2, and HLA-DQ8 [28]. The shared genes may play a homogeneous role in the association between psoriasis and CD. Second, the hyperproliferated keratinocytes found in patients with psoriasis are known to produce an excessive amount of interleukin (IL)-1 and IL-18, the essential signals for the induction of Th1 (T helper 1) response. Interestingly, mucosal inflammation in patients with CD is also caused by activation of Th1 in response to dietary gluten [21]. 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. Interleukins such as IL1β, IL17, IL22 IL23, and TNF-α are involved [21] in the immunological response. During inflammation, regulatory T (Treg) cells play an important role, due to their ability to inhibit the immunological response and maintain the cutaneous immune homeostasis [22]. Therefore, it is possible that those ILs might predispose patients to CD. Third, it is also possible that, in fact, CD increases the risk of psoriasis, but diagnosis of CD is often delayed or missed as its clinical manifestation could be subtle and nonspecific. Intestinal barrier dysfunction associated with undiagnosed or untreated CD may allow increased passage of immune triggers resulting in increased risk of autoimmune diseases including psoriasis [29]. Given the possible mechanistic links between the two diseases, gluten-free diet, the cornerstone for the management of CD, may also have a role in the management of psoriasis. In two studies, a positive correlation was found between celiac disease antibody positivity and severity of psoriasis or psoriatic arthritis [30,31]. In a case-only study of 130 psoriasis patients, a significantly higher proportion of patients with elevated celiac disease markers required systemic immunosuppressants or PUVA phototherapy, indicating that elevated celiac disease markers correlated with increased psoriasis disease severity [30]. Interestingly, in these psoriasis patients elevated celiac disease antibodies did not necessarily correspond to a biopsy-confirmed diagnosis of celiac disease, suggesting that psoriasis may be associated with gluten sensitivity (marked by antibody positivity) but not necessarily gluten enteropathy [32-34]. Regarding the benefit of a gluten-free diet (GFD) in psoriasis patients, two small clinical trials showed a decrease in serological markers of celiac disease after GFD and one showed a significant reduction in the PASI (Psoriasis Area Severity Index). Three case reports also documented resolution of psoriasis after GFD. Based on the available evidence, we recommend that providers verbally screen their psoriasis patients for symptoms of gluten sensitivity such as diarrhea, flatulence, fatigue, and history of iron-deficiency anemia. Positive symptoms should be followed up with antibody testing, with IgA EMA or IgA tTG recommended as the most sensitive and specific tests [35]. Based on some studies, a gluten-free diet may potentially be beneficial in celiac antibody positive psoriasis patients, but additional more well-powered studies are needed to confirm this.

Psoriasis and vitamin D

Current data on the relationship between hypovitaminosis D and psoriasis confirm the hypothesis that Vitamin D affects the proliferation and regeneration of keratinocytes; therefore, its deficiency is a possible risk factor; however, there is still no definite evidence [18,36]. There are also several reports on the association between hypovitaminosis D and autoimmune skin conditions. Vitamin D may have an essential role in modulating dendritic cell function and regulating keratinocytes and T-cell proliferation that can lead to skin pathology. Moreover, some studies have identified an association between polymorphisms of vitamin D receptor (VDR) and the severity of psoriasis disease, believing it affects the alteration of the cutaneous barrier.

Vitamin D also acts as a pluripotent immunomodulator that can inhibit proliferation of T-cell lymphocyte and induce regeneration of CD25+/CD4+ regulatory T-cell that preserves/controls immunological homeostasis and prevents autoimmune response against self-antigens.

Vitamin D also has a vital role in inflammatory function. Its metabolite is responsible for down-regulating the production and expression of TNF-α, IL-1β, IL-6, IL-8 and inflammatory profile of human monocytes/macrophages. Finally, vitamin D also helps to protect skin from opportunistic infections by inducing autophagy in macrophages and normalize innate response of skin barrier integrity and permeability [37]. A high daily dose of vitamin D supplement improved PASI scores significantly in patients with psoriasis. However, it is unclear whether low vitamin D level is a pathophysiologic cause of psoriasis [18,36]. The etiology of psoriasis remains unclear and is likely multifactorial. Several studies showed that circulating 25 hydroxyvitamin D (25(OH)D) levels were significantly lower among patients with psoriasis than healthy controls [38]. Current studies demonstrate the improvement of mild psoriasis with oral vitamin D2 supplementation, an increase in serum 25(OH)D concentrations, a reduced rate of vitamin D deficiency, and good tolerability. It suggests vitamin D2 is

a good adjunctive treatment to the standard therapy. Additional studies should examine the efficacy of higher doses and longer duration of vitamin D2 in moderately severe and severe psoriasis to determine whether vitamin D would be a suitable adjunct treatment.

Psoriasis and dietary supplementation of fish oil, zinc, selenium, curcumin and tryptophan

In the literature, the possible therapeutic effects of the supplementation of fish oil, tryptophan, selenium, zinc and curcumin have been analyzed [18,39]. The use of fish oil, especially omega 3 fatty acids, has led to a clinical improvement in psoriasis patients. This integration has positive effects at different dosages; the average estimated dose of eicosapentaenoic acid (EPA) was 4 g/day while that of docosahexaenoic acid (DHA) 2.6 g/day [40]. Although adding fish oil to the diet has been shown to improve the severity of psoriasis, the results are mixed showing positive results in some studies and negative results in others make it difficult to have clear conclusions [41-43].

A decrease in serum selenium levels, an essential element with antiproliferative and immune regulatory properties, has been associated with an improvement in psoriasis.

A study [44] has shown that psoriasis treated with selenium in combination with coenzyme Q10 and vitamin E has had positive effects on disease progression.

In a further study [45] the integration of selenium in combination with folic acid, magnesium, iron, zinc, copper, manganese, chromium, iodine and vitamins A, D, E, K, C, of group B and low-dose methotrexate confirmed a clinical improvement of psoriasis.

However, the data in the literature concerning the integration of selenium and zinc are conflicting [46].

Finally, a possible role of curcumin was analyzed which with its antioxidant and anti-inflammatory properties could have beneficial effects and improve skin lesions caused by psoriasis [18].

Correlations between psoriasis and obesity

A 2008 study [47] showed that the prevalence of obesity in psoriatic patients is higher than that observed in the general population. Controversy still exists, particularly whether obesity is a risk factor for the development of psoriasis or is only a consequence of it. Some authors suggest that overweight and obesity occur after the onset of psoriasis [48], others have found that overweight and obesity represent, however, a risk factor for the psoriatic pathology [49,50]. A recent review conducted in 2016 [51] underlined that overweight/obesity represent behave as a trigger for the manifestation of the psoriatic pathology in genetically predisposed subjects, due to the continuous inflammatory state (low grade inflammation) given by the release of pro-inflammatory cytokines from adipocytes [51].

A common agreement between the authors is that the overweight/obese subject may exhibit an exacerbation of psoriatic symptoms compared to a normal weight subject [52]. The results of a meta-analysis that involved 15939 psoriasis patients and 103984 controls support the fact that psoriasis patients have a higher incidence of metabolic syndrome. This study recommends that psoriasis patients should be regularly monitored for metabolic syndrome complications and its associated risk factors such as hypertension, raised triglyceride, lowered HDL Cholesterol, increased fasting plasma glucose, and waist circumference [53]. In fact, many studies correlate psoriasis with an increased risk of cardiovascular disease [54], dislipidemia [55], high blood pressure [56]. A careful evaluation of the nutritionist and the proposal of a low-calorie diet (LCD) aimed at the loss of fat mass is beneficial for the improvement of psoriatic symptoms [57]. Calorie restriction causes insufficient arachidonic acid conversion to leukotriene and decreases oxidative stress, thereby explaining the efficacy of an LCD. Calorie restriction improves PASI scores and DLQI for 16 weeks but difficulty complying to a strict diet can be a barrier to patient outcome [18].

Correlations between psoriasis and microbiome

The microbiota is the set of microorganisms or bacteria present in the intestine; instead the set of genes of the microorganisms themselves form the microbiome. The human microbiota plays an important role for our health in different ways, helps us a digester, absorb energy, defend us against pathogens, produce precious nutrients and modulate the immune system [58]. The alteration of the composition of the microbiota, called dysbiosis, is associated with the development of autoimmune, inflammatory and systemic diseases such as type 1 diabetes mellitus, rheumatoid arthritis, inflammatory bowel disease or psoriasis. Antibiotics, prebiotics, probiotics and faecal transplantation could represent a therapeutic target for people with psoriasis as they reduce pathogenic bacterial species however further studies defined by this hypothesis.

Studies of the cutaneous microbiome have revealed interesting compositional trends in the microbiome of psoriatic skin. Lowered relative abundance of *Propionibacterium* in psoriatic lesional skin was seen in 3 out of 4 studies. *Propionibacterium* are a major component of normal skin microflora as well as prolific producers of the SCFA, propionate, which modulates the immune system. Loss of *Propionibacterium* can therefore lead to decreased immune tolerance and increased propensity for psoriatic inflammation. These studies have also found increased levels of *Streptococcus* on psoriasis lesions [58]. The observed increase in *Streptococcus* may play a pathogenic role in psoriasis as streptococcal infections have been associated with the later development of guttate psoriasis and the worsening of chronic plaque psoriasis. Modifications in the abundance of *Staphylococcus* in psoriatic skin are less consistent. In addition, *Staphylococcus* is a diverse genus in which some species, such as *S. epidermidis* appear to have a commensal role enhancing the innate immune barrier [58] while others, like *S. aureus* evoke a pathogenic Th17 response. Scher., *et al*. found that psoriatic arthritis patients had a gut microbiome composition that differed significantly from that of patients with skin limited disease [58,59]. Other changes observed in gut microbiome studies include a decrease in *Actinobacteria* [58]. This may suggest a protective role of *Actinobacteria*, a phylum which includes *Bifidobacterium* species that have been shown to reduce intestinal inflammation, suppress autoimmunity. Perturbations in the balance of *Firmicutes* and *Bacteroidetes* were also noticed in psoriasis and psoriatic arthritis. Also an imbalance in the *Firmicutes/Bacteroidetes* ratio in the psoriatic gut microbiome may reflect the relationship between psoriasis and its cardiovascular and metabolic comorbidities.

To date, there are few evidences about Psoryatic mycobiome: Takemoto and colleagues [60] found that psoriatic skin had higher fungal diversity and decreased abundance of *Malassezia* compared to controls, although *Malassezia* was the most abundant phylum in both groups. In addition, the ratio of *M. globosa* to *M. restricta* was lower in psoriatic patients relative to control [60]. Other two studies by Paulino., *et al.* found that *Malassezia restricta, globosa* and *sympodialis*, were not significantly different between healthy and psoriatic skin [61,62].

In contrast, Jagielski., *et al*. detected *M. furfur* only in psoriatic skin compared to atopic dermatitis (AD) and healthy skin [60]. Interestingly, *M. sympodialis* was the predominant species in all patients, but was more prevalent in AD and normal skin than psoriatic skin [60].

These results reveal potential differences in the composition of the skin microbiota in psoriatic disease, further impartial studies are needed to know the profiling of the entire skin mybibiome and significance the importance of these changes in psoriatic disease.

The Mediterranean diet: A protective role towards the most serious forms of psoriasis

A recent study by Phan., *et al*. [63] showed that patients following the Mediterranean diet (MD) are less likely to develop psoriasis than patients not adhering to the Mediterranean diet. This study also confirms the association between the severity of psoriasis and other factors including body mass index (BMI), physical activity levels, heart disease, high triglyceride levels, hypertension, and type II diabetes mellitus. A recent systematic review of the literature [64] recommends the Mediterranean diet as a useful nutritional approach in the psoriatic patient.

A crucial element of the MD is represented by the quality of the lipids, which should come mainly from the consumption of blue fish (rich in eicosapentaenoic acid and docosahexaenoic acid), tree nuts (walnuts, hazelnuts, almonds, pine nuts, cashews, pistachios, pine nuts) and extra virgin olive oil (rich in oleic acid and vitamin E). The reduction in the intake of red meat, processed meat and cured meat, rich in polyunsaturated fatty acids of the Omega 6 series (especially Arachidonic Acid) with pro-inflammatory action, is another cornerstone of the Mediterranean diet. The reduction of simple sugars and the increased supply of complex carbohydrates with medium/low glycemic index (bread, pasta, preferably whole-meal rice, spelt, barley) also produces a modest impact on blood sugar and a reduced stimulus on insulin secretion, moderating synthesis growth factors Epidermal Growth Factor (EGF) and Insulin-like Growth Factor-1 (EGF-1), which are altered in the psoriatic patient [65,66]. The supply of high biological value proteins- preferably white meat, fish, eggs, cheeses - must be adequate for maintaining lean body mass. The presence of an adequate amount of fiber from seasonal fruits and vegetables - preferably of biological origin - rich in water, mineral salts, vitamins and polyphenols with an antioxidant action is important.

Psoriasis patients also have a greater risk of high blood pressure. It is a good dietary rule to avoid adding table salt in the preparation of food and to use as flavor enhancers spices and herbs that are very rich in polyphenolic antioxidants but do not contain sodium chloride [64].

Psoriasis and lifestyle

In addition to pharmaceutical therapies, psoriasis is affected by lifestyle. Patients suffering from serious forms of psoriasis, in addition to following a high-calorie diet particularly rich in fats, simple sugars and processed meat, tend to be alcoholic beverage consumers and heavy smokers [49,50,51,67]. Cigarette smoking and alcohol aggravate psoriatic forms, causing infiltration and extension of psoriatic plaques with exacerbation of the local inflammatory reaction.

Increased usage of any of the substance further affects disease severity, while cessation can improve psoriasis over time [67].

Conclusion

Dietary manipulation may not be intended as primary treatment for psoriasis, but it can synergistically promote successful treatment outcomes and reduce incidence of life changing comorbidities including DM and CVD.

Given the scientific evidence of the decisive contribution of nutrition in the therapy of psoriasis, the role of the nutritionist in the care and involvement of the patient is fundamental.

Although it has not been demonstrated that the adoption of a correct diet excludes the risk of the onset of psoriasis, it is evident that an appropriate dietary habit based on the Mediterranean diet (a balanced diet rich in fruits and vegetables, with a greater intake of blue fish and a lower consumption of red meats and cured meats) improves its clinical expression. The intake of some foods can, on the contrary, aggravate the disease or act as a trigger.

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