



Mini Review

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The Role of Microbiota in Psoriasis. An Update

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Abstract

Psoriasis is an entity with high morbidity in the population, whose chronic course requires the knowledge of all the factors that could be involved in the pathophysiology of the disease, in order to seek therapeutic options that would have a positive impact on the quality of life of patients. The objective of this review is to point out how the role of the microbiota can modify the course of the disease and thus be considered as an object of study to obtain fundamental therapeutic targets in the future.

Keywords: Microbiota; Microbiome; Psoriasis; Skin; Inflammatory Disease; Probiotics; Bacteria

Introduction

Psoriasis is an inflammatory, chronic and immune-mediated disease that affects both men and women, it has a bimodal presentation, with most of the prevalence between 20 and 30 years and between 50 and 60 years [1]. It is characterized by scaly lesioned plaques with defined borders, mainly located on the scalp and extremities. Commensal bacteria play an important role in the immune responses of the skin, for example *Staphylococcus epidermidis* one of the most abundant skin commensal can suppress TLR3-dependent inflammation [2], it is therefore, any imbalance in the skin microbiota can result in a chronic inflammatory disorder such as psoriasis; the impact of these microbial community constituents upon the epidermal barrier condition, and upon the immune system functioning, is being intensely scrutinized. Other inflammatory conditions described to be related to a microbiota imbalance are acne, atopic dermatitis and rosácea [3]. Current evidence shows that the intestinal microbiome also plays a crucial role, due to the fact that the bacterial profile is responsible for innate and adaptive immune responses at this level, so that, any alteration in its composition can result in an increased intestinal permeability which leads to bacterial translocation and in consequence the output of microbial agents and their metabolites into systemic circulation, which can trigger an immune activation [4]. Many factors are described to be involved in the profile of the

microbiota's gut and skin, for example the place of residence, body area, age, comorbidities, medications, hygiene and dietary habits [5].

Microbiota Profile in Patients with Psoriasis

Skin microbiota is made up four main bacterial phyla *Actinobacteria*, *Firmicutes*, *Proteobacteria*, and *Bacteroidetes* [6]. Today it is well known that there are significant differences in the variability in the microbiota of patients with psoriasis compared to those with healthy skin, psoriatic plaques have a greater number of bacteria, among the most frequent are *Corynebacterium spp*, *Propionibacterium spp*, *Staphylococcus spp* and *Streptococcus spp* [7]. Any alteration in the balance of the skin microbiota is called dysbiosis and it is the responsible of the dysregulation in the host skin's immune responses, leading to a pro-inflammatory condition. But it is important to know that fungi also play an important role in the course of psoriasis, for example *Malassezia spp* is increased in active lesions in the period of exacerbations [7], its contribution to the inflammatory process is considered to be attributed to the production of unsaturated free fatty acids, causing abnormal keratinization [8]. Several studies have also examined the oral microbiota where it has been found a greater presence of *Candida spp* in patients with psoriasis [9]. Without forgetting the crucial role of the intestinal microbiota, patients with psoriasis have

shown a profile characterized by a reduction at the family level in Lachnospiraceae, and an increased population of *Veillonellaceae* and *Ruminococaceae*, this profile had shown some similarities with Sjögren's syndrome and Crohn's disease [10].

Immunological Mechanisms Triggered by Alteration of the Microbiome

All the changes in the microbiological profile of psoriasis patients have been correlated to the ability to increase the expression of cytokines such as TGF-beta, also integrins and HSP 70, resulting in the recruitment and migration of immune cells. The important link between skin diseases and an unbalanced intestinal microbiome, has been attributed as the responsible for triggering immune disorders through the activation of cells, mainly with the participation of T lymphocytes [10]. It is known that there is a constant interaction between microbiota and Toll-like receptors, peptidoglycan recognition proteins, cytokines and antimicrobial peptides, therefore any disturbance of this balance poses the risk of promoting a proinflammatory environment and the release of interferon-gamma, tumor necrosis factor- α , IL 17, IL 1-beta, IL-23 as a consequence of the activation of cells of innate and adaptive immunity, with mostly with a central role in T cells and dendritic cells. Intestinal microbes cells also have the ability to activate complement, represented by higher levels of C3 and C4 reported in psoriasis patients [10], the importance lies in the fact that the upregulation of these cytokines causes hyperproliferation and inflammation of the skin, resulting in the characteristic psoriatic plaque.

Usefulness of probiotics

The prescription of probiotics has shown countless benefits among them the regulation of the immune response, thanks to its ability to promote a physical barrier with increased mucus production which blocks the entry of pathogens into epithelial cells by overexpression of cell binding proteins [11]. Even though the use of probiotics has not been shown to achieve a significant change in the microbiota profile of the patients, they have been associated with clinical improvement demonstrated by a reduction in the severity of the disease and exacerbations, documented by obtaining a lower PASI score compared to placebo⁹, this is attributed to a decrease in the migration of inflammatory cells in the dermis and reduced levels of proinflammatory cytokines, such as IL-17, IL-19 and IL-23 [12].

Few studies have demonstrated the beneficial role of probiotics, the oral administration for 8 weeks of *Bifidobacterium* infants, show to decrease levels of C reactive protein and tumor necrosis factor- α , *Lactobacillus pentosus* has been related to reduce tumor necrosis factor- α , IL-23, IL-17, and consequently a decrease in psoriasis plaques [13]. Navarro-López et al compared a probiotic mixture composed of *Bifidobacterium longum*, *Bifidobacterium lactis* and *Lactobacillus rhamnosus* versus placebo

for 12 weeks, the results of the study showed that the 66.7% of the probiotic group reached a PASI75, versus 41.9% by the placebo group. Nowadays, in the clinical practice, the most widely used probiotics are *Lactobacillus spp*, which can be used via orally or by topical application.

Role of diet in the microbiota

As previously mentioned, microbiota depends on different factors and one of the most important is diet, dietary habits has been shown to play a very important role in the microbial composition, it is one of the most effective ways of altering the biodiversity of the microbiota, changes in dietary habits can alter the bacterial profile of patients in 24 to 48 hours. Therefore, the diet of patients may lead to an altered composition of their microbiota that explains the outbreaks related to the consumption of sugar, alcohol, nightshades or gluten.

Psoriasis comorbidities

Psoriasis has been associated with multiple comorbidities, the main one is metabolic syndrome. It is here that the role of the microbiota also influences indirectly through the regulation of *miRNA* expression in adipocytes, thus controlling adiposity and insulin resistance [14]. This patients show a reduction in the population of *Akkermansia muciniphila*, which contribute to the concomitance of Psoriasis and its comorbidities [15]. It has been reported also a relationship between the gut microbiota profile and the body mass index, with an increase in *Ruminococcus* and *Megasphaera*, this might be a confounding or ever a contributing factor in the intestinal dysbiosis in psoriasis.

Conclusion

The mechanisms by which the microbiota induces and prevent some diseases have many applications to the skin. Although there are several reviews of the literature that indicate the important role of the microbiota in the pathogenesis of patients with psoriasis, there are few studies that demonstrate the benefits of using probiotics as an adjuvant in the treatment of the disease. And there is still no consensus on which microorganisms can be used for this purpose. Understanding the interaction between the microbiota and the pathogenesis of psoriasis may lead to intensified research to find other treatment options for patients with psoriasis.

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