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Review Article

Hypothesis of the Human Microbiome in the Etiopathogenesis of Common Acne

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Abstract

The various studies on the influence of diet and acne carried out for several decades were inconclusive. The objective of this review is to contribute to explaining the pathophysiological mechanisms of acne and the possible improvement with dietary recommendations. With new bacterial DNA sequencing techniques, it has been proven that various pathophysiological mechanisms related to the intestinal microbiota and the skin, related through the intestine-brain-skin axis, can contribute to reducing intestinal permeability, usually related to dysbiosis, bacterial translocation and local inflammation, with clinical improvement of acne. According to several studies and clinical experience, this is achieved with a plant-based diet and/or vegetarian diet. However, more studies are still required to elucidate, among other issues, the influence of conventional acne treatments on the intestinal microbiota and skin.
Keywords: Acne. Gut microbiota. Gut-brain-skin axis. Plant-based diet. Vegetarian diet. Intestinal dysbiosis.

Introduction

The first observation of bacteria in acne lesions was made by the German doctor Paul Gerson Unna in 1896, and they were isolated by Sabouraud in 1897 (1). Of the factors that can contribute to the development of acne, such as excessive sebum production, pore clogging and inflammation, the relationship between the intestinal microbiota (IM) and the skin has recently been re-considered, and may contribute to explaining the pathophysiology and pathogenesis of acne and thus expand the therapeutic offer (2) (3) (4) (5

Empirically, some doctors have provided dietary advice to clients with acne and, in general, the results obtained have been better. In recent years, research has been conducted on the gut-brain-skin axis and the role it plays in the immunopathology of acne. Some time ago it had already been observed that stress worsened acne, possibly due to an increase in intestinal permeability (6).

The gut microbiome appears to influence the skin microbiome through short-chain fatty acids (SCFAs) that are produced when dietary fiber is fermented by the colon microbiota. With this interaction, SCFAs such as propionate, acetate and butyrate are produced, which facilitate the predominance of certain microbial profiles of the skin that would subsequently influence the skin's defense mechanisms (7).

A typical Western diet that includes foods such as red meat and sausages, rich in saturated fatty acids, refined sugars that produce a high glycemic index, dairy, etc., can aggravate acne by increasing levels of insulin-like growth factor (IGF-1) (8). This diet is usually low in fiber which, together with the high amount of fat it contains, produces a particular IM that predisposes to inflammation, cardiometabolic diseases and inflammatory skin conditions, such as acne.

The increase in intestinal permeability, often associated with intestinal dysbiosis, if maintained over time produces chronic low-grade inflammation, which is a predisposing factor for numerous diseases that plague developed countries such as those mentioned above (9). In a context of overweight/obesity, the scenario could be more relevant. It has been observed in recent decades that a plant-based diet reduces inflammation (10). The same phenomenon was also observed with the vegetarian diet a long time ago (11).

Acne pathophysiology

Lactobacillus and Bifidobacterium are common probiotic species that balance IM by fermenting unabsorbed oligosaccharides in the upper intestine. These bacteria strengthen the intestinal barrier, reducing permeability and improving the epithelial resistance of the intestine. Additionally, they stimulate the production of CD4 + Foxp3 (scurfin) + regulatory T cells (Treg) and regulatory dendritic cells, which suppress the response of helper T cells and B cells and cytokine production. Butyricicoccus generates butyrate, which provides energy to cells and prevents damage and inflammation of the intestinal mucosal barrier (12).

The microbiota of sebaceous areas such as the face, back, chest, etc., undergoes changes with the arrival of puberty. The hormones secreted during this period activate the sebaceous glands and greater oil secretion is produced. The skin microbiota is an essential part of human health, and gut dysbiosis is thought to cause or aggravate skin diseases. Advances in sequencing technology, such as 16S ribosomal RNA (16S rRNA) gene sequencing, have provided great insight into the human microbiome. As the main inhabitant of the skin, bacteria are the best studied parts of the skin microbiota, although there are also fungi, mites, viruses, etc. Table number one classifies the skin commensal bacteria according to the different phyla (13).

Phyla	Families	Bacteria (s)	Percentage
Actinobacterias	Corynebacterineae Propionibacterineae	Corynebacterium acnes	90%
Proteobacteria			
Firmicutes	Staphylococcaceae		
Bacteroidetes			

Table 1. Commensal skin bacteria (13)

The bacterial composition differs from person to person and varies depending on the site of the body. Environmental factors such as the use of soaps, cosmetics, antibiotics, occupation, temperature, humidity and exposure to ultraviolet rays, among others, influence microbial colonization. It also varies according to sex, age, ethnicity, etc. Corynebacterium acnes is the most abundant bacteria in the pilosebaceous unit and represents up to 90% of the skin microbiota.

The gut-brain-skin axis

The skin and intestine have certain similarities such as barrier function, being well vascularized and innervated, and have similar neuroendocrine and immune functions. Research in recent years has shown a bidirectional connection between these two organs. Numerous studies relate intestinal health to general homeostasis and allostasis and, therefore, skin health. Recent advances in metagenomics have expanded the understanding of IM and its influence on human health and disease. IM performs metabolic and immune functions, playing a fundamental role in maintaining homeostasis. Table number two shows some functions performed by IM according to Allaire and collaborators (14).

Breaks down indigestible fiber	Production of short chain fatty acids (butyrate, propionate, etc.)
Synthesize vitamins	B12, biotin, K
Role in the immune system	Allows tolerance against food and environmental antigens. Defense against pathogenic germs

Table 2. IM functions

In the intestine, dendritic cells control the mechanisms of immunological tolerance against dietary antigens and/or commensal flora, while they are capable of initiating an active immune response in the presence of an invading pathogen (15).

The organism's detection of an immense amount of antigens, a product of the enormous diversity of genes contained in the IM, has an important function in the immunotolerance of the microbiota with the organism, avoiding bacterial translocation, superinfection and local inflammation. This constant and varied exposure provides the immune system with the opportunity to learn a large number of antigens, expand the functionality of immunological memory and strengthen innate and adaptive responses. This wide variety of antibodies that are generated with the microbiota-organism interaction can present cross-reaction with microorganisms, including parasitic or viral types (16).

Stimulation of plasma cells increases the production and class switching of IgA, which promotes the maturation of Peyer's patches. These interactions become relevant from birth; it has been seen that the type of early colonization that a baby presents during vaginal delivery favors a downregulation of interleukin-1 associated receptor kinase (IRAK-1), which is translates into an immunoprotective function for the individual. This type of modulation does not occur only locally. Several studies have detected the presence of bacterial metabolites in peripheral tissues, which enter the circulation by unknown mechanisms (17).

Currently, there are studies that indicate that IM plays a mediating role between skin inflammation and emotion. Although it is not yet fully understood, the mechanism by which IM influences skin homeostasis seems to come from its modulatory effect on systemic immunity. Additionally, evidence suggests that IM may affect the skin more directly, by transporting IM to the skin (translocation). When the intestinal barrier is broken, IM and its metabolites quickly enter the bloodstream, accumulate in the skin and disrupt the balance of the skin (18).

IM influences acne, possibly by interacting with the mammalian Target of rapamycin (mTOR) signaling pathway. IM metabolites can constitutively control cell expansion, fat metabolism and other metabolic functions through the mTOR pathway. This pathway may affect IM itself by controlling the intestinal barrier. In case of intestinal dysbiosis with alteration of the intestinal barrier, a positive feedback loop can form, which can amplify the host's metabolism and inflammation. The connection between acne and gastrointestinal dysfunction may originate in the brain. This hypothesis may explain the aggravation of acne induced by stress. Human studies have shown that stress affects normal IM, especially Lactobacillus and Bifidobacterium species (19).

It has long been known that probiotics modify the pathophysiological factors that contribute to acne and do so through antimicrobial proteins that directly inhibit Corynebacterium acnes (20).

Despite all these advances and their implementation in the clinic, more studies still need to be done to identify the IM of acne patients and see what changes have occurred in the IM after treatment of acne with oral antibiotics and isotretinoin.

Conclusions

1) The connection between the intestinal and skin microbiota, as well as the fluctuation in the composition of the skin microbiome, can induce, in cases of dysbiosis, the appearance of inflammatory diseases such as acne.

2) A plant-based and/or vegetarian diet can contribute to reducing inflammation in the context of acne

3) Dietary fiber contributes, through the production of short-chain fatty acids, to the clinical improvement of acne

4) Lactobacillus-type probiotics, by fermenting unabsorbed oligosaccharides, reduce intestinal permeability

5) The detection by the intestinal immune system of an immense amount of antigens and the tolerance it shows with them, prevents bacterial translocation, superinfection and local inflammation

There are no conflicts of interest

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