

Inner Connection Between Gut Microbes and Acne

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Abstract. Acne is a common skin disease, which is associated with reduced diversity of intestine flora, intestine flora imbalance, and host-intestine co-metabolite differences. The occurrence of acne is related to microorganisms such as *Propionibacterium acnes*, while the role of intestine flora imbalance and immune system regulatory cells and molecules are also involved. Although the relevant mechanisms are not fully understood, intestine flora plays a role in the occurrence of acne. Therefore, regulating intestine flora can improve digestive system health, enhance immune system, reduce disease risk, and other health-care effects. Intestine flora is the largest microbial environment in the human body, and its microbial ecological balance is crucial for health and immunity. Intestine flora imbalance may lead to changes in the composition of the flora, promote the growth of harmful bacteria, produce metabolites and inflammatory factors, and play a role in the occurrence of acne. This article analyzes the intrinsic link between gut flora and acne and finds that microbial ecological balance is essential for health and immunity. An imbalance in the gut flora may lead to changes in the composition of the flora, promoting the growth of harmful bacteria and the production of metabolites and inflammatory factors that play a role in the development of acne. Based on the comparison of recent treatments and modulation methods, this paper suggests that human microecology can be further improved by traditional Chinese medicine thereby alleviating the symptoms of patients and providing a reference point for future research.

Keywords: Acne, intestine flora, intestine-skin axis, immune system.

1. Introduction

Acne is a common skin disease, and more than half of adolescents are deeply troubled by acne problems. Existing research has shown that the diversity of intestinal flora in patients with acne is often lower than that in normal populations, and there is a significant difference in intestinal flora imbalance and host-intestine co-metabolite production [1]. In essence, acne is an inflammatory reaction, and microorganisms are closely related to the occurrence of this disease. On the level of the skin barrier, *Propionibacterium acnes* is the main microorganism that causes inflammation and induces acne. In the human intestinal immune system, the imbalance of intestinal flora can also lead to inflammation and induce acne.

The intestine is the largest immune organ in humans, with numerous microscopic lymph nodes and capillaries. The microorganisms in the intestine are also the largest microbial environment in the human body. The microbial ecological balance of intestinal flora plays a crucial role in human health and immunity. Dysfunction of intestinal flora can lead to changes in the composition of flora, promote the growth of harmful bacteria, produce metabolic products and inflammatory factors, which may play a role in the occurrence of acne; regulatory cells and regulatory molecules in the intestinal immune system can regulate systemic and skin inflammation by affecting immune response; in addition, the normal function of the intestine is crucial for the absorption and metabolism of nutrients. Deficiency or abnormal metabolism of nutrients may affect skin health and also be related to the occurrence of acne. According to research, there are more than 1,000 known microbial species in the intestine, of which 30-40 are major bacterial species [2]. It can be seen that the microbial ecological environment of intestinal flora is closely related to host health status, and acne has a relatively complex pathogenesis, of which intestinal flora is an important influencing factor.

The intestinal flora is a complex microbial ecosystem in the human body. These microorganisms interact with the human body and affect human health. The intestine plays an important role in the

human immune system. It is not only a place for digestion and absorption of nutrients, but also a concentration of immune cells, symbiotic flora, and immune regulatory molecules. The functions of the intestinal immune system include protecting the body from harmful microorganisms, maintaining the integrity of the intestinal mucosal barrier, regulating immune balance, and suppressing excessive inflammatory responses. Regulating the intestinal flora can improve digestive system health, enhance the immune system, reduce disease risk, and other health-care effects. There is increasing research on the link between the intestine and acne. Although the relevant mechanisms are not fully understood, the intestinal flora may play a role in the occurrence of acne. This article briefly describes the mechanism of intestinal flora factors causing acne to explore how to improve acne through the pathway of intestinal flora.

2. Acne Vulgaris

Acne vulgaris is a common skin disease, and the common types are acne vulgaris and rosacea. The former is more common in adolescents and exists in the face, back, chest, and is a common inflammatory disease of the hair follicle and sebaceous gland. Clinical manifestations include acne, inflammatory papules, pustules, nodules, cysts, etc. While the latter mainly occurs on the face and is more common in middle-aged adult women, its symptoms include persistent facial erythema, vascular dilation, pustules, and papules. Unlike acne vulgaris, rosacea usually does not accompany closed acne and open acne.

Generally speaking, the clinical manifestations are characterized by papules, pustules, nodules, and other polymorphous lesions formed in the hair follicles and sebaceous glands of the face, chest, and back. [3]. When the degree is severe, it seriously affects the patient's appearance, and often leaves scars and pigmentation after healing, which causes great psychological pressure to the patient and often affects aspects such as personal work, study, life, and interpersonal communication, even leading to anxiety, depression, autism, and other psychological disorders [4].

The external causes of acne include diet, mood, genetics, endocrine, and many other factors. The main cause of acne is excessive secretion of sebaceous glands, excessive keratinization of the epithelium leading to obstruction of the hair follicle and sebaceous gland ducts, immune inflammation in the presence of acne propionibacterium, and the influence of hormonal changes in the body [5].

3. Intestine and Skin

3.1. Intestinal Flora

The intestinal flora refers to various microorganisms living in the human intestine. These microorganisms live with humans day and night, accompanying them through the physiological processes of growth, development, and aging from the embryonic stage. The human intestine provides a suitable living environment for these microorganisms, while also participating in the digestion and absorption of nutrients in humans. It can be described as a symbiotic relationship in which both are mutually beneficial. These microorganisms include bacteria, fungi, and viruses, mainly bacteria. This paper will mainly study the main bacteria among them.

According to the interaction between bacteria and humans, there are three types: beneficial, harmful, and neither harmful nor beneficial.

(1) Symbiotic type is a low-immunogenicity obligate anaerobe, which is the absolute dominant flora in the intestine and is beneficial to the host, such as bifidobacteria, bacteroides, eubacteria, and digestive cocci;

(2) Conditionally pathogenic bacteria are dominated by facultative anaerobic bacteria, which are harmless and necessary for maintaining the balance of intestinal flora. Under certain conditions, they can become invasive and harmful to humans, such as *Enterococcus* and *Escherichia coli*;

(3) Pathogenic bacteria: Most are transient bacteria, which are bacteria that are ingested through the mouth and pass through the gastrointestinal tract, consisting of non-pathogenic and potentially

pathogenic bacteria. If the normal flora is disrupted, transient bacteria will multiply rapidly, causing disease. Transient bacteria have a low chance of long-term colonization, and when the ecological balance is maintained, the number of such bacteria is low and does not cause disease. However, when the number exceeds normal levels, it can cause disease, such as *Proteus*, *Pseudomonas*, and *Clostridium* [6].

The factors that affect intestinal flora are complex and diverse, which are closely related to the lifestyle, dietary habits, and food intake of human hosts, as well as the external environment, such as staying up late, unhealthy diet, alcohol consumption, medication, and even antibiotic use, altitude sickness, surgery, diseases, and so on.

3.2. Intestine-Skin Axis

In previous understanding, there is often no clear correlation between intestine flora and acne, but this is not the case. Currently, research on the skin-intestine axis is an academic hotspot. The intestine and skin share many similarities in structure, function, and other aspects, such as having similar embryonic differentiation origins, similar immune functions, similar neural pathways, and abundant symbiotic microbial colonization. This is the theoretical basis for the "intestine-skin axis" [7].

The intestine and skin are both important parts of the immune system, and they communicate and regulate each other through immune cells, immune factors, and regulatory cells. Immune cells and regulatory molecules in the intestine can affect the inflammatory response and immune balance of the skin through blood circulation and the lymphatic system.

In addition, the intestine plays an important role in the absorption and metabolism of nutrients, and proper nutrient intake can maintain the health of the skin. The regulation of intestinal flora and the disturbance of nutrient absorption may affect the skin's nutrient supply and metabolism, thereby affecting the function and appearance of the skin. For example, unhealthy dietary habits such as high-fat diets can directly lead to the imbalance of intestinal flora, which can increase the permeability of the intestine, resulting in systemic low-level inflammation, the production of endotoxins and inflammatory factors, accompanied by a decrease in anti-inflammatory factors. This can stimulate the hyperplasia and hypertrophy of sebaceous glands, [8] increase oil secretion, and induce acne.

Currently, clinical treatment is mainly based on drugs, such as topical tretinoin cream to promote skin cell renewal and oral tetracycline antibiotics (such as doxycycline) to treat infection and inflammation. The intestinal flora is an influencing factor of acne, and the regulation of intestinal flora has a direct impact on the physiological condition of the skin. Therefore, taking this as a key point, using the regulation of intestinal flora to treat acne has become a new idea beyond traditional treatment methods.

4. Specific Mechanism of Intestinal Flora on Acne

There are two mechanisms involved in the role of intestine flora in acne. First, bacteria in the intestine produce harmful substances, which stimulate the skin to produce inflammatory reactions, thereby inducing the occurrence of acne. Second, a dysfunctional immune system caused by an imbalance in intestine flora reduces resistance to harmful bacteria, leading to the occurrence of acne.

Taking common acne as an example, research has confirmed the phenomenon of intestinal flora imbalance in patients with common acne; among the 242 kinds of intestinal flora analyzed in the diseased group and the control group, there are 38 different bacteria, and the abundance of 35 flora in the common acne group is reduced; the abundance of Bacteroidetes in the intestinal flora of patients with common acne increases, while that of Firmicutes decreases; a non-parametric test analysis of the differences in 145 metabolites between the common acne group and the normal control group found that 24 metabolites were significantly different [9].

SCFAs (short-chain fatty acids) are a class of organic compounds produced by intestinal flora fermenting dietary fiber in the human intestine. They are short-chain fatty acids composed of 2-6 carbon atoms, including acetic acid, propionic acid, and butyric acid. *Clostridium*, *Bifidobacterium*,

Lactobacillus, and Veillonella are the main bacteria that produce SCFAs. SCFAs are the main metabolites of intestinal flora, and their levels play an important role in the pathogenesis of acne [10]. SCFAs can not only reduce inflammation infiltration through cytokine effects in the immune regulatory pathway, affecting the occurrence and development of acne. In addition, SCFAs also have the ability to regulate signaling factors to alter signaling pathways to inhibit sebaceous gland secretion, ultimately affecting the progression of acne.

SP is a neuropeptide composed of amino acids that has biological activities such as affecting lymphocyte proliferation and cytokine synthesis, regulating immune cells, and is a key mediator connecting the brain and the hair follicle skin. The mechanism of SP action is that the absence of bifidobacteria affects the permeability of the intestine, resulting in the production of endotoxins, causing endotoxemia, exacerbating oxidative stress and inflammatory reactions, and promoting the release of SP from the nervous system [11]. The increase in SP not only can promote the proliferation of sebaceous gland precursor cells, increase the volume of sebaceous gland cells, but also can mediate the inflammatory response of the skin through the secretion of inflammatory cytokines such as interleukin (IL)-1 β , IL-6, tumor necrosis factor- α (TNF- α) by monocytes, which further exacerbates the development of acne [12].

5. Adjustment Methods

Now it is found that increasing the SCFAs-producing flora in the intestine is a mechanism that is beneficial to the improvement of intestinal flora. Differences in diet will inevitably affect the balance of intestinal flora. According to a survey, college students who have a drinking habit, high learning and living pressure, constipation, sweet food cravings, spicy, hot, high protein, high salt, high fat and fried foods have a higher incidence of acne [13]. This shows that a healthy diet is very important for regulating intestinal flora, and these situations should be avoided as much as possible. In addition, new research in the field of traditional Chinese medicine has found that Chinese herbal ingredients such as Pueraria lobata, Evodiamine, Atractylodes polysaccharide, Chrysanthemum polysaccharide, Echinacea purpurea glycoside, Shenlingbaizhu Powder, Schisandra chinensis extract can increase the abundance and diversity of SCFAs-producing flora in the intestine [14].

Through direct oral probiotics: probiotics can affect the pathogenesis of acne through antibacterial, anti-inflammatory effects and immune regulation. Studies have found that in acne patients supplemented with probiotics of Lactobacillus acidophilus and Lactobacillus bulgaricus, 80% of the patients' symptoms improved, and the improvement was more pronounced in patients with inflammatory lesions. Probiotics can inhibit the growth of acne bacilli by secreting antibacterial substances, and also exert anti-inflammatory effects through immune regulation [15].

Experiments have shown that oral probiotics can increase the level of anti-inflammatory cytokines in the serum of patients with acne vulgaris. The subjects in the study measured the serum level of IL-10 before and after taking oral probiotics for 30 days. The serum IL-10 level before taking oral probiotics was 5.27 \pm 1.49 pg/ml, while the serum IL-10 level after taking oral probiotics was 6.19 \pm 1.68 pg/ml. This indicates that the level of interleukin-10 in the serum of patients with acne vulgaris significantly increased after taking oral probiotics for one month. The only side effect in this experiment was abdominal distension, which occurred in two subjects during the first week of taking oral probiotics. This suggests that oral probiotics can be used as a complementary treatment for acne vulgaris to regulate inflammatory responses, so oral probiotics can be used as an adjuvant treatment for acne vulgaris, and its side effects are also very safe and tolerable [16].

In addition, probiotics can be considered as a treatment option or adjuvant drug for common acne, which can produce synergistic anti-inflammatory effects with systemic antibiotics, resulting in better combined therapeutic effects. According to experimental data, in the case of minocycline use, the total lesion count of all patients significantly improved. However, in the subsequent weeks, compared with the group that did not receive probiotics as an adjuvant treatment, the group that received

antibiotic and probiotics as an adjuvant combination treatment had a significant reduction in the total lesion count. It can also reduce the potential side effects caused by long-term use of antibiotics [17].

This suggests that oral probiotics can be used as an adjuvant treatment for acne vulgaris by regulating inflammatory responses. However, although oral probiotics may help improve the symptoms of acne, these studies are small in size, with inconsistent results and a lack of consistent evidence. Therefore, it remains to be investigated whether oral probiotics directly improve the symptoms of acne in individual patients.

6. Conclusion

Research has shown that although there is a potential link between the intestine and acne, more research is needed to further explore the exact mechanism of the intestine's role in the occurrence of acne. The phenomenon is that people with acne often have abnormalities in the diversity and balance of intestine flora. For example, compared to healthy individuals, people with acne may have more harmful bacteria and fewer beneficial bacteria in their intestine flora, and the diversity of flora may be lower. This imbalance in flora may lead to chronic inflammation and abnormal immune system response, which in turn promotes the development of acne. Secondly, the occurrence of acne is an inflammatory response, and intestine flora can affect skin health by regulating the function of the immune system and inflammatory response. Some studies have shown that certain species in the intestine flora can produce beneficial metabolites, inhibit inflammatory responses, and help maintain the health of the skin. Conversely, flora imbalance and overgrowth of harmful bacteria, which produce harmful substances that cause acne, may lead to abnormal activation of the immune system and excessive inflammation, which can induce and exacerbate symptoms of acne.

At present, the traditional treatment methods commonly used for acne have acceptable effects in most patients, but there are side effects such as recurrence, antibiotic resistance, and imbalance of skin microbiota, which "treat the symptoms but not the root cause". The therapeutic method of regulating intestinal flora aims to directly intervene in the pathogenesis of acne through immunomodulatory therapy, which can avoid the adverse effects of traditional drug treatment. Current research has also shown that oral probiotics can be used as an adjuvant therapy for acne vulgaris. This has given new significance to the study of this new treatment method for acne.

At present, various effective components of traditional Chinese medicine have been found to have inhibitory effects on the pathogenesis of acne. Linking the regulation of intestinal flora with acne treatment is mainly in the field of traditional Chinese medicine. Studying the regulation of intestinal flora related to acne and the pathogenesis of acne provides new ideas for the treatment of acne in clinical practice. Unfortunately, due to the large number of microbial species in the intestine, this article only discusses some of them and their relationship with the pathogenesis of acne, which has certain limitations. Moreover, there are no cases of treating acne by directly regulating intestinal flora in clinical practice, which needs further clinical trials.

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