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Research Progress of Skin Barrier and Acne

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Abstract: Acne is a common chronic inflammatory skin disease of hair follicles and sebaceous glands. It usually occurs in teenagers aged between 20 and 30. It can lead to post-inflammatory hyperpigmentation and even permanent scar in severe cases.In recent years, many studies have shown that acne patients have abnormal skin barrier function, including changes in sebum membrane composition, increased transcutaneous water loss (TEWL), increased skin water content, and increased PH value. The severity of acne is positively correlated with the damage of skin barrier function.In this paper, the research progress of the correlation between acne pathogenesis and skin barrier function is summarized as follows.

1. Introduction

Acne is the most common chronic inflammatory hair follicle and sebaceous gland disease in dermatology, with an incidence rate of about 80% in adolescents and up to 64% in adults aged 20-30 years [1]. It is usually caused by acne, pustules, papules, cysts or nodules on the face and chest and back (see figure 1), and leaves pigmentation or scar of varying severity after the skin lesions subside, causing a great burden to patients physically and mentally. At present, it is believed that the onset of this disease is mainly related to the increase of androgen level in adolescence, genetic factors, insulin resistance, enhanced skin sensitivity, high sugar, high fat and irritating food, personal hygiene and other factors.The pathogenesis of this disease is: excessive sebaceous secretion, microbial infection, hair follicle sebaceous duct keratosis, immunological factors, etc.Skin is the largest organ in the human body, located in the outermost layer of the body surface. It has many physiological functions, such as barrier, secretion, absorption, excretion, immunity, metabolism, thermoregulation and sensation, among which the barrier function is the most basic and important one, including physical barrier, immune barrier, osmotic barrier, neural barrier and pigment barrier.The skin barrier commonly referred to clinically refers to the epidermal osmotic

barrier, which can participate in resisting the invasion of antigens, sunlight and microorganisms externally and prevent the loss of nutrients and water in the body internally. Recent studies have shown that acne patients have abnormal skin barrier function, including changes in sebum membrane composition, increased sebum content, increased transepidermal water loss (TEWL), decreased skin water content, and increased pH value [2], and the damage of skin barrier function is positively correlated with the severity of acne. In this paper, the research progress of the correlation between acne pathogenesis and skin barrier function is summarized as follows.

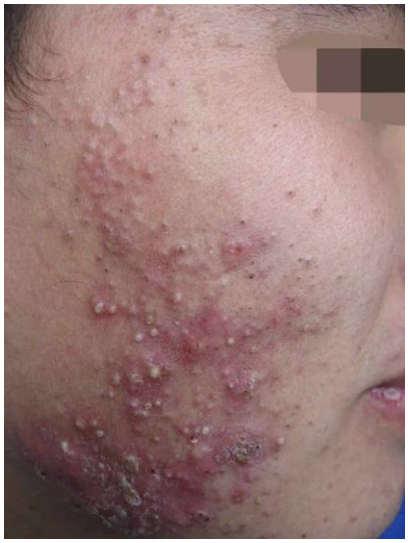

Figure 1. Cheek, jaw dense blackhead, whitehead acne, inflammatory papules, mounds pustular rash

2. Pathogenesis and Skin Barrier of Acne

2.1. Hair Follicles Sebaceous Glands and Skin Barrier

Under the action of androgens, adolescent acne m secretion is one of the important causes of acne (see Figure 2).Chinese Tsou Semen et al. [3] determined the lipid content, cuticle water content, and transepidermal water loss rate (TWEL) of 80 acne patients and found that the sebum content and TWEL value of acne were higher than that of the healthy control group, and the cuticle water content was lower than that of the healthy control group, suggesting that the skin barrier opromotes the proliferation of hair follicle sebaceous gland cells (see table 1), and the significant increase of sebuf acne was damaged. On the one hand, increased sebum secretion will change the composition of sebum. Downing et al. [4] found that the amount of sebum in acne patients was 59% higher than that in normal people, and the increased sebum diluted linoleic acid, resulting in a relative lack of linoleic acid, which plays a certain role in promoting the formation of acne. Adult sebum consists of triacylglycerol and its hydrolysate (57.5%), wax ester (26.0%), squalene (12.0%), cholesterol ester (3.0%) and cholesterol (1.5%).Propionibacterium acnes can decompose glycerol into free fatty acids and cholesterol, free fatty acids in vitro can induce hair follicle sebaceous duct keratinization and acne inflammatory reaction, oxidized squalene can promote keratinocyte secretion of inflammatory factors, resulting in acne. Ceramides, on the other hand, are the main components of human cuticle lipids and are important factors in maintaining normal skin barrier function. At present, various ceramides have been found to participate in the proliferation, differentiation, apoptosis and other processes of keratinocytes [5].In acne patients, the level of ceramide is reduced and the composition is changed, which leads to the defects of the keratinocyte bilayer lipid membrane, indicating that the defects of the intercellular lipid membrane are related to

the damage of the epidermal osmotic barrier [2].Studies have found that ceramide deficiency is common in patients with acne vulgaris, and ceramide supplementation can increase treatment tolerance and thus improve clinical efficacy. Reduce the secretion of skin oil and the intake of high-sugar and high-fat foods as much as possible. Add ceramide, squalene, hyaluronic acid and other ingredients into skin care products to regulate the secretion of skin oil and reduce the damage of acne skin barrier.

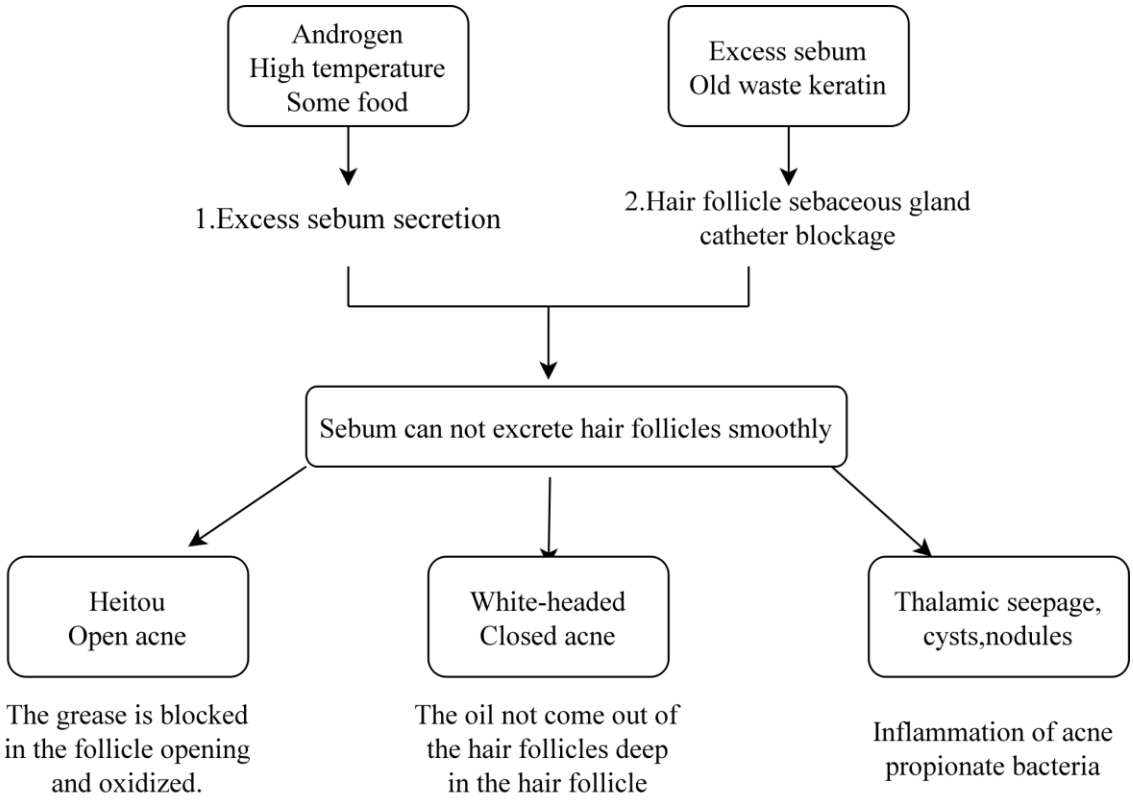

Figure 2. Simple acne formation mechanism

Table 1. Comparison of cortical content, cuticle water content and TWEL between acne and healthy human

Group	Cases	Cortical content(ug/cm2)	Cuticle water content%	TWEL(g/m2h)
acne	80	185.22±22.11	23.73±7.44	20.33±6.45
Ahealthy person	80	65.22±13.22	43.34±12.12	7.23±2.24
P		<0.01	<0.01	<0.01

2.2. Propionibacterium Acnes and Skin Barrier

Skin is the largest organ in the human body, and the colonization of beneficial microorganisms can act as an effective physical barrier to pathogen invasion. Existing data show that propionibacterium acnes induces immune and non-immune cells to participate in the inflammatory response. In recent years, studies have confirmed that propionibacterium acne activates toll-like receptors (TLR) to release cytokines and cause inflammation. The cell wall, enzymes and metabolites of propionibacterium acne have strong pro-inflammatory properties, which can lead to the amplification of inflammation cascade. Propionibacterium acnes can secrete lipase to decompose sebum into free fatty acids, which can induce abnormal keratinocyte keratinization and

destroy the skin barrier [6] (see Figure 3). Propionibacterium acnes is one of the components of biofilm. Studies have shown that there is an imbalance of bacterial flora in the skin lesions of acne patients, which can lead to the reduction or even disappearance of Staphylococcus epidermidis [7].An increase in harmful microbes and a decrease in beneficial ones lead to an imbalance in the skin's surface flora, which in turn leads to a breakdown of the skin barrier.Therefore, it is necessary to select reasonable antibiotics according to the inflammatory situation of skin lesions to reduce the harmful microorganisms on the skin surface.

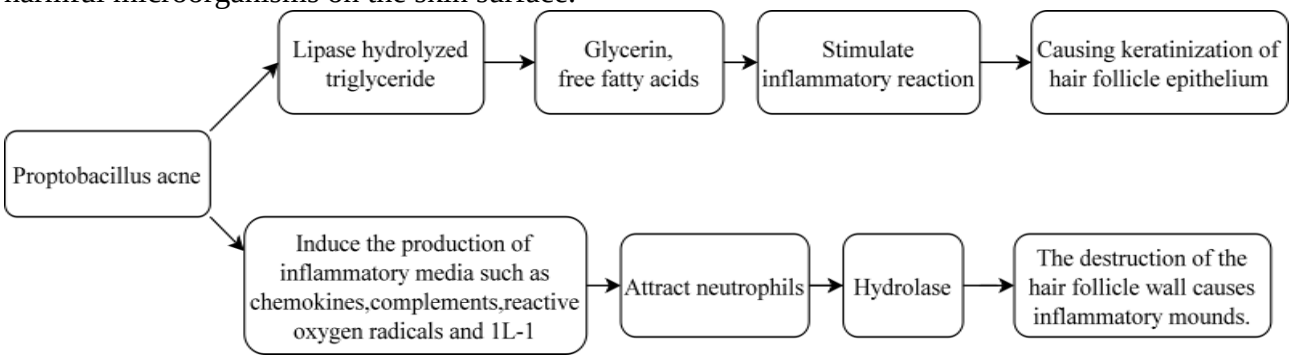

Figure 3. The inflammatory process of Proptobacillus acne

2.3. Inflammatory Response and Skin Barrier

Acne is one of the most common inflammatory skin diseases, and the inflammatory response of acne may be related to the damage of skin barrier function [8].Studies have shown that the expression levels of IL-1α, IL-6, IL-8, TNF-α and IGF-1 in skin lesions of acne patients are higher than those in adjacent normal skin [9].Jeremy et al. [10] used acne patients' micro-acne as the research object, and found that hair follicle sebaceglands had significant inflammatory reactions, and the expressions of macrophages, CD4+ lymphocytes, IL-1α and epidermal α-integration number were significantly up-regulated, and these inflammatory transducers were all important components of the inflammatory response. Inflammatory transmitters can activate and chemotactic inflammatory cells to gather in the skin lesions, seriously kill keratinocytes, and further aggravate the damage to the skin barrier function.IL-1α is the most strongly expressed inflammatory factor in the pathogenesis of acne. Kurokawa et al. [11] believed that IL-1α directly acts on receptors or induces the release of related cytokines to promote keratinocyte keratinization. At the same time, IL-1α can also induce keratin 16(K16) to participate in the activation of regulatory pathways. Stimulates keratinocyte excessive proliferation and epidermal inflammation, leading to the formation of micro acne. In addition, various inflammatory mediators can also make keratinocytes edema and cell gap widening through inflammatory response, weakening the skin barrier function against the invasion of external substances. Therefore, anti-inflammatory is essential in the treatment of acne patients.

3. Dietary Habits and Skin Barrier

The onset of acne is closely related to dietary factors, among which carbohydrate, dairy products, saturated fat and so on can induce or aggravate acne. Studies have shown that high-carbohydrate or high-fat diets may increase insulin resistance and the release of androgens and IGF-1, and alter the retinoic acid signaling pathway [12]. IGF-1 and androgens stimulate key factors in acne pathogenesis, such as keratinocyte proliferation, sebaceous gland cell proliferation, and sebum secretion. So regular consumption of foods high in carbohydrates or fat may worsen acne. Ulvestad et al. [13] found that high intake of whole milk (≥2 cups /d) was associated with moderate and

severe acne. Milk whey protein (20%) can promote insulin secretion, casein (80%) can promote IGF-1 secretion, intake of milk can increase the ratio of IGF-1/IGFBP-3, and the increase of free IGF-1 can aggravate acne lesions [14]. ElDarouti et al. [15] conducted a detailed questionnaire survey on 200 acne patients and 200 healthy people matched by age and gender, and found that the daily intake of sodium chloride in acne patients (median 3367.54mg) was significantly higher than that in the control group (median 2271.8mg) by using the "24h information recall" method. Patients with acne and acne lesions were negatively correlated with salt intake (r=-0.216, P=0.031), suggesting that high salt diet may affect keratinocyte calcium iono4 concentration. The effect of diet on acne can be achieved by changing the diet and reducing the damage to the skin barrier.

4. Improper Care and Skin Barrier

The skin barrier function of acne patients is easy to be damaged, so the right way of care is conducive to acne treatment. The first is facial cleansing, which removes excess oil, bacteria and dirt from the skin. It also removes apoptotic keratinocytes and facilitates the absorption of topical drugs/medical skincare products. However, excessive cleansing results in further weakening of the skin barrier function. Most acne patients believe that acne is related to poor hygiene conditions, so they often use alkaline soap or harsh cleanser to clean their skin frequently. Long-term use will damage the skin barrier and lead to skin erythema, itching, tingling and so on. The PH value of normal skin surface is weakly acidic, but many surfactants and soap are alkaline. Using soap to clean the face can increase the skin pH value by 1.5~2.0 units and last for 4~8h. The change of skin pH value from acidic to alkaline increases the sensitivity of skin external irritants. An increase in pH levels causes dry and tight skin. In addition, the damage of UVB to the skin barrier of acne patients should not be ignored. UVB can induce inflammatory response, increase sebum secretion and promote the proliferation of keratinocytes, thus aggravating acne lesions. Incorrect nursing methods directly affect the optimal molar ratio of sebum in the skin barrier biofilm. Sebum is mainly composed of ceramide (50%), cholesterol (25%) and free fatty acids (about 20%). The optimal molar ratio of ceramide, free fatty acids and cholesterol in the distribution of lipid in the cuticle is 3:1:1.Ceramides, linolenic acid and linoleic acid play an important role in maintaining the integrity of the skin barrier and effectively preventing the formation of acne. Therefore, when acne patients choose skin care products, emollients containing ceramides, linoleic acid, linolenic acid and mild and acidic cleaners have better auxiliary treatment for acne. Studies have confirmed that mild cleansers and moisturizers can improve skin lesions in patients with mild acne [16].

5. Drug Damage and Skin Barrier

Some acne drugs may also lead to the damage of skin barrier, such as long-term topical antibiotics or oral administration of some antibiotics may cause changes in the ecology of skin microflora and even produce drug-resistant bacteria [17].Studies have found that oral doxycycline, minocycline and other treatments have little effect on skin barrier function, while topical antibiotics mainly affect the microbial flora. Topical antibiotics can cause the colonization of Staphylococcus epidermidis. Topical benzoyl peroxide or retinoic acid may lead to decreased sebum secretion, accelerated epidermal replacement, thinner cuticle, obvious barrier damage, increased skin TEWL and decreased water content. The most common adverse reactions are erythema, desquamate, dryness, burning, pruritus and tingling of the skin mucosa. In addition, some topical drugs, such as hormones, can cause 5 skin irritation reactions and aggravate the damage of barrier function. Studies have shown that the effect of glucocorticoids on skin barrier function is negative, and topical glucocorticoids can inhibit the synthesis of surface sebulides. Inhibit the formation and secretion of lamellar bodies, resulting in the formation of lamellar structures, delay the recovery of

skin barrier function, and increase the skin water loss through the epidermis. Although medication is an important part of the treatment of propionibacterium acnes, the damage to the skin barrier and adverse reactions it causes cannot be ignored, as it can reduce the compliance of acne patients to the treatment.

6. Photoelectric Therapy and Skin Barrier

In recent years several lights and lasers have been used to treat acne, including red and blue light, long-pulsed dye lasers, and diode lasers. Phototherapy is recognized to treat acne by bactericidal and anti-inflammatory, reducing the production of macrophage cytokines. Although photoelectric therapy solves intractable skin diseases, the skin barrier function is inevitably damaged in the process of acne treatment. The histological effects of photoelectric therapy mainly include photothermal effects, photomechanical effects and photochemical effects, which can affect the skin barrier function. The photochemical effect will hinder the synthesis of intercellular lipids in the cuticle, reduce the adhesion between keratinocytes and affect the "brick wall" structure. T hermal damage caused by the photothermal effect can lead to the denaturation of keratin and damage the normal structure of the cuticle, thus affecting the defense ability of the skin barrier. Photomechanical effects lead to increased mechanical stress between cells and damage the integrity of keratinocytes, thus affecting the functioning of various skin barrier functions. Kimura et al. [18] found that Er:YSGG laser treatment could improve facial acne depression scar to a certain extent after one time, and the skin elasticity increased by more than 30% after one month of treatment. Therefore, they believed that Er:YSGG laser had certain curative effect on acne scar. At the same time, they found that TEWL increased and skin hydration decreased significantly on day 3 after treatment, hydration returned to normal level after 1 week, and epidermal moisture returned to normal level after 4 weeks. Therefore, it is recommended that Er:YSGG laser treatment be at least 1 month interval, so that the skin has enough time to recover its normal barrier function. The effect of photoelectric therapy on the damage of the skin barrier can promote the better repair of the skin barrier through the correct use of postoperative repair products.

7. Summary

Acne is closely related to skin barrier, and the severity of acne is positively correlated with the damage of skin barrier. Skin barrier damage can be caused by excessive secretion of sebaceous glands in hair follicles, excessive keratosis of follicular sebaceous duct epithelium, colonization of pathogenic propionibacterium acnes, inflammatory response, poor diet, improper nursing, drugs, and photoelectric therapy. Therefore, in the treatment of acne, in addition to the treatment for the pathogenesis, it is also necessary to pay attention to the repair of skin barrier function (see Figure 4), such as choosing appropriate cleansers, reducing the frequency of cleansing, and rational use of emollients containing ceramides, hyaluronic acid and other components. The repair of the skin barrier can not only alleviate acne from the pathogenesis of acne, but also increase the compliance of acne patients to the treatment and reduce the recurrence rate, so as to achieve a good therapeutic effect.

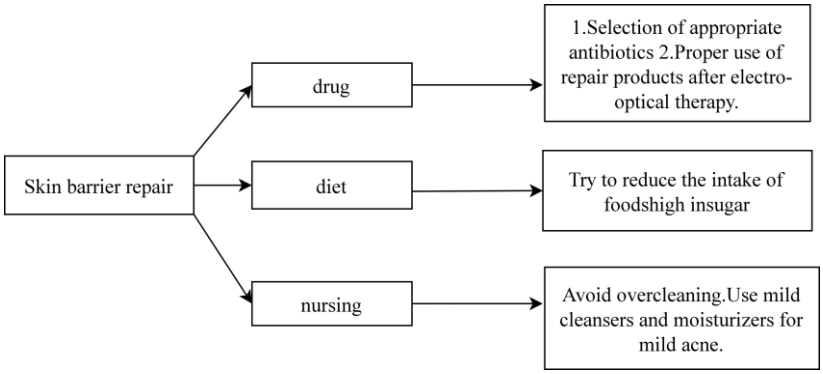

Figure 4. Treatment

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Data Availability

The datasets used during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

The author states that this article has no conflict of interest.

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