

Pathogenetic Rationale for the Complex Therapy of Acne Vulgaris Based on Clinical and Immunological Studies

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Abstract One of the urgent problems of modern dermatovenereology is acne due to its high prevalence among people of pubertal and active reproductive age, significant material and moral damage to patients, long duration and insufficiently high efficiency of existing treatment methods. Acne is characterized by a chronic, often relapsing course, the formation of open and closed comedones, papules, pustules, superficial or deep, and even cystic formations.

Keywords Dermatovenereology, Acne, Papules, Pustules, Psycho-emotional state of patients

1. Introduction

The urgency of the problem. Acne vulgaris (acne, acne) is one of the most common diseases that affects up to 90-95% of the world's population [2]. The peak incidence occurs between the ages of 12 and 25. However, approximately 7% of patients may develop late acne (adult acne), including after 40 years. In most patients with severe acne, irreversible post-inflammatory skin changes are formed, which disturb patients no less than the manifestations of acne themselves, and require long-term and complex treatment [5]. The presence of cosmetic defects negatively affects the psycho-emotional state of patients, reduces self-esteem, causes depressive disorders, and leads to social maladaptation [4].

In recent years, some progress has been made in the study of the pathogenesis of acne. According to modern concepts, the occurrence of acne occurs against the background of several interrelated pathogenetic mechanisms. The most significant of them are the violation of keratinization processes, pathological follicular hyperkeratosis, hyperproduction of sebaceous secretion accompanied by lipid imbalance and reproduction of microorganisms, among which *Propionibacterium acnes* plays the main role [1]. mediated reactions of the leukocyte system and a dysfunctional state of the humoral immunity [11]. The development of adequate therapy is determined by the pathogenetic mechanisms of acne and includes topical and systemic drugs (antibiotics, synthetic retinoids, antiandrogenic and immunotropic drugs), physiotherapy, peels, etc. However, there is often a need for long-term therapy, which leads to serious side effects and complications, and resistance to applied agents [5]. Given

these problems, it seems interesting to develop an integrated approach to the treatment of the most common forms of acne using topical antibacterial and anti-inflammatory drugs, immunomodulators [13], which prevent the development of resistance and help restore nonspecific defense mechanisms, and antidepressants with a pronounced vegetative-stabilizing effect [7].

Acne vulgaris is characterized by chronic inflammation of the hair follicles and associated sebaceous glands. At the heart of the etiopathogenesis of papular-pustular acne are violations of the keratinization of the epidermis with the development of hyperkeratosis of the mouths of the hair follicles and the formation of comedones against the background of absolute or relative hyperandrogenism with the formation of retention cysts of the sebaceous glands; change in the chemical composition of sebum; inflammation and suppuration of cysts with the participation of *Propionibacterium acnes* with the addition of *Staph. aureus* or *Staph. epidermididis*, fungi of the genus *Malassezia* [1,3].

2. Materials and Methods

Starting in adolescence (14-17 years), papular-pustular acne may spontaneously resolve by 19-22 years, but in some patients (up to 3-5%), papular-pustular acne may occur up to the age of 45-50 and even up to 60 years old [3,4,16]. Among the predisposing factors of acne are immune disorders, changes in the metabolism of hormones and lipids, zinc deficiency in the body, infectious and genetic factors (hereditary predisposition), psychosomatic disorders [1,3,8,16]. It is known that inhibition of personal evaluation in patients with acne causes them to constantly experience acute and chronic stressful situations that lead to autonomic and endocrine disorders, including the release of androgen stress hormones that stimulate the function of the sebaceous glands [3,8,16,17].

The principles of the general treatment of acne involve the appointment of antibiotics (tetracyclines, macrolides, cephalosporins), isotretinoin, hyaluronidase (longidase) preparations, immunocorrective and immunostimulating therapy (staphylococcal toxoid, purified, adsorbed, or polyoxidonium, or immunofan), physiotherapeutic methods (according to indications), local treatment, including topical antibiotics and antiseptics [1,15,16]. According to V.P. Fedotov et al., the simultaneous administration of an antibacterial drug in combination with comedonolytic agents is more effective than local antibiotic treatment in the dosage form [16]. External therapy of acne vulgaris is based mainly on the use of tretinoin, benzoyl peroxide, antibiotics, and, more recently, azelaic acid preparations [1,2,9,13].

Manifestations of rosacea (rosacea) are localized mainly on the face, less often on the neck and chest, represented by erythema, nodular-pustular elements, telangiectasias, and nodes in the formation of rhinophyma [1]. Clinical experience shows that in recent years the proportion of the incidence of rosacea has increased. Ukrainian colleagues also speak about this - according to their data, in Ukraine, rosacea already accounts for 5% of all dermatological diagnoses [5]. The pathogenesis of rosacea is diverse, the pathology of the gastrointestinal tract, vascular and psychosomatic disorders, consumption of alcoholic beverages, weather conditions play a certain role, the role of mites of the genus *Demodex folliculorum* is also discussed [14]. The main contingent is women from 30 to 50 years old, men get sick less often, but such a complication as rhinophyma occurs almost exclusively in men [1,7]. There are several working classifications for rosacea. In the classification set out in the monograph by V.P. Adaskevich, 3 stages of rosacea are distinguished: erythematous-telangiectatic, papular-pustular and infiltrative-nodular (phymatous).

Treatment of patients with rosacea is carried out taking into account the stage of the pathological process. Since *Helicobacter pylori* infection is often diagnosed in such patients, a course of anti-*Helicobacter* therapy is recommended in these cases. In more than half of patients with rosacea, in scrapings from the affected skin, in the tires of pustules, the mite *Demodex folliculorum* is found, therefore, sulfur preparations, a 10% suspension of benzyl benzoate, spregal, Yam ointment, ointments and creams with metronidazole are used for local treatment [1,9,11]. Systemic therapy for rosacea is often based on the use of antibiotics (tetracyclines, macrolides), isotretinoin, metronidazole [1,5]. For external therapy, a gel or cream with metronidazole, antibiotics (erythromycin, clindamycin), and azelaic acid was successfully used [2,5,9,12]. One of the goals of this publication is to increase knowledge about the use of azelaic acid preparations for the external treatment of patients with acne vulgaris and rosacea.

Initially, azelaic acid was used in dermatology for the treatment of hyperpigmentation and malignant melanoma without the development of depigmentation of normal skin [13]. Subsequently, it began to be used as a 20% cream, first

for the treatment of acne [1-4,10], and then as a 15% gel for rosacea [6,7,9,12]. Azelaic acid is a naturally occurring straight chain saturated 9-carboxylic dicarboxylic acid. It is a product of the oxidation of unsaturated dicarboxylic acids; in the human body, it is an intermediate product of lipid metabolism; it is formed in a small amount [6,14]. Azelaic acid is safe for the human body, non-toxic, does not have mutagenic properties, so pregnancy and lactation are not a contraindication for the external use of this acid preparations [13,14]. The antimicrobial properties of azelaic acid are associated with the ability to inhibit the mitochondrial activity of cells, it is a competitive inhibitor of various oxygen-reducing enzymes, exhibits antioxidant activity, selectively penetrating into inflamed and neoplastic cells [10,12,13,20]. According to Professor N. N. Potekaev, the clinical efficacy of topical preparations of azelaic acid in rosacea is also associated with its anti-inflammatory effect due to inhibition of the oxidoreductase enzyme and the formation of hydroxyl radicals by neutrophils [12]. Along with anti-inflammatory and antimicrobial action, azelaic acid has the ability to normalize the processes of keratinization in the follicles, that is, it has an anticomedogenic effect [13]. Thus, Skinoren cream containing 20% azelaic acid can be considered as an alternative to topical acne therapy with macrolide antibiotics [16]. The main indications for the use of azelaic acid preparations (20% Skinoren cream or 15% Skinoren gel) are papular-pustular acne vulgaris and papular-pustular form of rosacea. Experimental studies conducted by ScheringPlow employees on skin biopsies of hairless mice showed the advantages of the gel base, which provided a more effective concentration of azelaic acid and its rapid penetration into the skin [10]. Skinoren-gel does not contain alcohol and fats, has a pH of 4.8, is non-toxic, odorless, does not cause photosensitivity, and has a cooling effect. Skinoren-gel turned out to be more acceptable for the external treatment of rosacea than skinoren-cream, since the gel contains only 15% azelaic acid, while the cream has 20%. The clinical efficacy of skinoren-gel in acne vulgaris and rosacea has been shown in many publications by foreign and Russian dermatologists [9].

3. Result and Discussion

The increase in the prevalence and expansion of the age limits of this pathology, its significant impact on the psycho-emotional sphere, social status and social adaptation of patients determine the relevance of this problem and the need for further study of the causes of acne development, as well as new approaches to treatment [1,2].

As noted by numerous authors, among adolescents aged 15-18 years, 80% suffer from acne [3,4].

The main factors in the pathogenesis of acne are:

- hyperproduction by the sebaceous glands of sebum of a changed chemical composition;
- microbial colonization of sebaceous hair follicles.

A change in the composition of sebum increases the

permeability of the epithelium of the follicles and contributes to its hyperkeratization, which leads to the formation of microcomedones - the precursors of all elements in acne - and the development of inflammation. Staphylococci, propionic bacteria, and Malassezia fungi are microorganisms that make up up to 99% of the microflora of healthy skin [5,6]. In connection with acne, *Propionibacterium acnes* is most often mentioned, although data on their etiological role are contradictory: the frequency of occurrence and contamination do not always correlate with the presence and severity of the disease. The results of the study of the skin microflora, obtained using any one method, vary significantly, especially in relation to the assessment of the total population [7,8].

Under the influence of lipases produced by *P. acnes*, hydrolysis of sebum triglycerides occurs with the formation of free fatty acids and their accumulation intrafollicularly. Free fatty acids give a comedogenic effect that can cause severe inflammation when administered intradermally. During the vital activity of *P. acnes*, lipases and a number of other substances are formed that cause neutrophil chemotaxis, which leads to the development of a pronounced inflammatory reaction [9,10].

A significant place in the pathogenesis of acne is given to sex steroid hormones, which is confirmed by the usual development of the disease in the pubertal period. In women suffering from acne, ovulation disorders were found in 60% of cases [11,12]. The skin is an important link in the metabolism of androgens, under the influence of which mitotic activity and intracellular lipid synthesis are enhanced, the volume of the sebaceous gland, the thickness of the epidermis, hair growth, etc. are regulated.

Many authors noted in patients with acne disorders of the digestive organs, hepatobiliary system, lipid metabolism, intestinal dysbacteriosis. In these patients, hyperlipidemia was often recorded, there was a high index of somatic burden, earlier onset of skin diseases [13,14].

4. Conclusions

Treatment of patients with acne, as a rule, is aimed at eliminating pathogenetic factors. It is advisable to prescribe antibiotics, which ensures high efficiency of therapy. A special role in acne is given to lipid metabolism disorders, which indicates the expediency of prescribing drugs containing essential phospholipids, especially when taking antibiotics at the same time. Phospholipids are the main component of biological membranes of human cells. The main biological role of phospholipids is:

- maintaining the fluidity of cell membranes;
- ensuring homeostasis of membrane and lysosomal enzyme systems;
- participation in carrying out information impulses;
- participation in the processes of blood coagulation;
- participation in providing and maintaining immunological reactions;

- participation in cell differentiation, proliferation and tissue regeneration.

Phospholipids play a special role in the formation of lipoprotein complexes and the generation of pathochemical reactions that occur during cell and tissue hypoxia [15,16]. When choosing a dosage form of skinoren for the external treatment of acne vulgaris or rosacea, one should take into account the duration of the course of the disease, the prevalence of the rash and constitutional features - brunettes tolerated cream and gel applications better, blondes prefer the appointment of the gel form of skinoren.

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