Advances in the Study of Acne in Adult Women

Bi Wang¹, Xiaoning Yan²,*

¹The First Clinical Medical College of Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
²Shaanxi Provincial Hospital of Chinese Medicine, Xi’an 710003, Shaanxi, China
*Correspondence Author

Abstract: The clinical presentation of acne in adult women is different from that of adolescent acne, with a more complex pathogenesis, and treatment along the lines of standard acne treatments is ineffective. Due to the chronicity of the disease course and the involvement of facial lesions, acne has been shown to have a serious negative impact on the quality of life of adult female patients. In this article, we review the clinical manifestations, etiology and pathogenesis, and treatment of acne in adult females in light of the recent advances in acne research in China and abroad, intending to provide a reference for further research on the disease.

Keywords: Acne in adult women, Research advances, Pathogenesis, Treatment.

1. Clinical Manifestation

1.1 Pathogenesis [1]

The first onset of AFA occurs more frequently on the forehead and cheeks, and involves multiple sites on the forehead and back [2]; AFA lesions are mainly located in the lower face in a “surgical mask” pattern, i.e., the mandibular, chin, and perioral regions, and may extend to the front of the neck, with the trunk rarely being involved [5]. Recently, however, the notion that AFA develops more frequently in the lower third of the face has been questioned [6], and a study by Bagatian E et al. [7] showed that the location of acne in 89.8% of women did not significantly correlate with the age of the patient [4].

AFA tends to start with acne, with a wide range of lesions and a rapid progression, ranging from mild inflammatory lesions to severe nodular cysts; AFA tends to be inflammatory papular-pustular lesions, often with a chronic progression, with 61%-80% of mild to moderate lesions [5]. Perhaps related to the long-term recurrence of acne, adult female patients are more prone to hyperpigmentation and scarring [3].

1.2 Accompanying Symptoms

Adult female acne patients are more likely than adolescent acne patients to have secondary disorders such as anxiety, depression, or comorbid endocrine disorders such as obesity, hirsutism, alopecia, and polycystic ovary syndrome [8].

2. Etiology and Pathogenesis

2.1 Key Factors

2.1.1 androgenic hormone

Estrogen may be involved in the development of AFA. This is reflected in three ways: i) increased sensitivity of the sebaceous glands to androgens; ii) increased peripheral hormone conversion: high and abnormal activity of enzymes associated with androgen metabolism converts androgen precursors to active androgens and are less likely to be metabolized to estrogens [9]; and iii) a relative increase in hormones versus active androgens relative to estradiol: 60-70% of women experience acne during the premenstrual period, premenopause, pregnancy, and acne or aggravation of pre-existing symptoms during use of progestogen-based contraceptives [6][7].

2.1.2 genetic predisposition

A study by Dréno B et al [5] showed that the probability of having a first-degree relative with acne is as high as 50-70% in adult female acne patients. Confocal microscopy of adult female acne also showed that the number of follicles and pimplies was higher in the experimental group compared to the control group [10]. These findings point to a genetic susceptibility to AFA. Genetic factors, which can influence the number, size, and activity of sebaceous glands, modulate the action of hormonal factors, promote follicular keratinization, and regulate the innate immune system, play an undeniable role in the pathogenesis of acne in adult women [6].

2.1.3 Loss of skin microbial diversity

Loss of microbial diversity in skin symbiotic communities has recently been shown to frequently accompany inflammatory skin diseases [11]. Loss of diversity in a subset of Chlamydia strains, including IA1, as well as other lineage types, activates the innate immune system leading to skin inflammation [7]. In addition, the gut microbiome, through the interaction of other skin microorganisms, is involved in acne pathogenesis [11]. This finding opens up new possibilities for the treatment of acne, and maintaining a direct balance between the different types of Acinetobacter may be a novel topic and direction for drug development.

2.1.4 Other factors

Deficiency of epidermal barrier function has now also been reported as a possible trigger for acne. Disruption of the barrier and the consequent excessive loss of epidermal water may be responsible for the development of inflammation, and the inflammatory response constitutes the central lesion in the pathogenesis of acne [12]. Chronic stimulation of the innate immune system by drug-resistant bacteria has also been reported as a trigger for acne [5]. Long duration of acne as well as prolonged use of antibiotics leads to the colonization of Propionibacterium acnes with drug-resistant bacteria, which provide chronic stimulation of the skin's innate immune...
2.2 Push Factors

2.2.1 dietary preference

A study by Rocha MA [12] and others suggests that the Western diet may be associated with acne flare-ups in adult women. The Western diet is a high-calorie, high-glycemic, high-fat, milk-consuming diet. This type of diet increases insulin and IGFI secretion, which in turn induces cell proliferation, inhibits sebocyte and keratinocyte apoptosis and stimulates sebum secretion, which ultimately leads to the development of acne [13].

2.2.2 stresses

Some studies have reported [14] that emotional stress is a predisposing factor for acne in 25.7%-71% of adult women: i) stress stimulates the release of pro-inflammatory cytokines and corticotropin-releasing hormone (CRH), which leads to an increase in cortisol levels, and binding of CRH, cortisol, and other glucocorticoids to skin receptors, which can contribute to the development of acne damage by regulating lipid synthesis in sebocytes and promoting a low concentration of lipid content increase, which can exacerbate acne damage; (ii) Substance P (SP), a neuropeptide associated with stress and pain, stimulates an immune response to IL-1, IL-6, and TNF-α, which affects the production of inflammatory mediators; and (iii) sleep deprivation also acts as a stressor, stimulating the hypothalamic-pituitary-adrenal axis, and promoting an increased secretion of stress-related hormones, such as dehydroepiandrosterone sulfate, and free testosterone, which can lead to the exacerbation of acne [14].

2.2.3 seasonality

The role of seasonal factors in triggering acne is still being observed. Some cases have been reported in which acne improves in summer and worsens in winter. However, cases triggered after sun exposure and during the summer months have also been reported [3]. In addition to inflammatory effects, UV radiation may also lead to an increase in squalene peroxidase, which has acneogenic properties. This triggering factor is still under clinical observation and the mechanism of triggering is not clear and still needs to be followed up.

2.3 Chemical Factors

Chemical factors such as cosmetics, tobacco, and drugs have also been reported to be associated with the development of AFA [15]. In one study [3], 22% of adult women reported that their acne was caused by cosmetics. Cosmetic ingredients such as lanolin, isopropyl myristate, cetyl alcohol, and stearic acid have acne-causing properties that trigger closed lesions of acne in adult females, which are mainly manifested as large numbers of pimples on the checks and forehead [16]. Isoniazid, testosterone, lithium, and certain anticancer drugs have also been reported to be associated with pharmacologic acne [3]. Nicotine, a major component of cigarettes, acts on acetylcholine receptors, leading to hyperkeratosis triggering skin peroxidation, which causes changes in sebum composition and ultimately induces acne [17]. There are also studies that cast doubt on these chemical factors inducing the development of AFA, with the onset of acne in adolescence showing a small correlation and a strong correlation with the prevalence of acne in adult females, and determining the exact effect of cigarettes on the occurrence and severity of the two types of acne will also require further research.

3. Treatment of Acne in Adult Women

3.1 Pre-treatment Assessment

The treatment of acne in adult women should take into account the different characteristics and circumstances of each patient, and factors that may influence treatment decisions should be evaluated. These include acne severity and duration, response to prior treatment, psychosocial influences, pregnancy status, skin sensitivity, tendency to scarring and hyperpigmentation, concomitant symptoms, and personal preference and cost of treatment [18].

3.2 Topical Treatments

Topical treatments are the most effective option for the treatment of mild-to-moderate AFA and maintenance therapy for AFA [19]. Available topical preparations include topical retinoids, antibiotics, benzoyl peroxide, azelaic acid, and amiloride and various fixed-dose combinations of these agents.

3.2.1 Retinoids.

Topical retinoic acid alone can be used as a first-line agent for mild AFA or as part of a combination regimen for moderate-to-severe AFA.A randomized controlled trial by Poinas A et al [20] demonstrated that adapalene gel at 0.3% was more effective and better tolerated than the placebo group, with inhibitory effects on both inflammatory and non-inflammatory lesions. Salavasta R C [21] et al. demonstrated the effectiveness and tolerability of adapalene gel at a concentration of 0.1% concentration of adapalene gel was also well tolerated. However, due to its teratogenicity, it should be avoided by women during pregnancy. The results of a Meta-analysis [19] indicated that 0.1 % adapalene gel in combination with 2.5 % benzoyl peroxide gel was more effective and safe compared to monotherapy. The combination of retinoic acid-clindamycin has been used in the treatment of acne, and the combination has been shown to be more effective than retinoic acid or clindamycin alone in reducing inflammatory and non-inflammatory lesions [22].

3.2.2 Azelaic acid

Azelaic acid (20% cream or 15% gel) is also a first-line agent for the treatment of mild-to-moderate adult acne in women, and clinical studies have demonstrated that its efficacy is similar to that of benzoyl peroxide, retinoic acid, tetracycline, and erythromycin, with mild adverse effects, and that it can be used as the first choice of medication in women during pregnancy [23].

3.2.3 Antibiotics.

Due to the significant increase in clindamycin-
erythromycin-resistant strains of Propionibacterium acnes, the use of these drugs alone is contraindicated [24]. A viable option for the treatment of mild adult female acne is ketoconazole monotherapy, a topical antifungal agent with anti-inflammatory and antiandrogenic effects that has expressed inhibitory effects against antibiotic-resistant strains in in vitro experiments [25]. In a randomized controlled trial [26], topical 2% ketoconazole cream was shown to be superior to a placebo group in terms of efficacy and safety.

3.2.4 Benzoyl peroxide

Benzoyl peroxide has antiseptic, anti-inflammatory, and antikeratinizing properties and is recommended for monotherapy in mild to moderate acne [21]. However, in adult females, it can cause skin irritation or dryness, and concentrations >5% are not recommended for use in this specific population. The results of a coadministration study of 3.75% benzoyl peroxide + 1.2% clindamycin [27] indicated that there was a significant improvement in inflammatory lesions and inflammatory lesions in the lungs, and that no serious adverse effects occurred.

3.2.5 Other:

Clarithromycin, was recently approved by the FDA for topical treatment of acne. It is the first topical androgen antagonist for the treatment of acne in women with favorable efficacy, safety, and tolerability [28].

3.3 Systemic Therapy

3.3.1 Isotretinoin

Isotretinoin is a very effective non-hormonal oral agent for the treatment of acne in adult women [29]. It is used as a first-line treatment for severe nodular cystic acne, and as a second-line treatment for severe acne where topical or oral combination therapy has failed [30]. It has significant dose-related side effects, the most serious and irreversible of which is teratogenicity. Therefore, pregnancy and breastfeeding are absolute contraindications to its use, and highly effective forms of contraception must be used during its administration [7].

3.3.2 Oral antibiotics

Systemic antibiotics should not be used alone considering the increased incidence of antibiotic resistance [31]. It is recommended to combine systemic antibiotics with topical medications, which have a synergistic effect that accelerates the response and reduces the duration of treatment. The combination of systemic antibiotics with benzoyl peroxide prevents the colonization of drug-resistant bacteria, while the combination with retinoids is effective in targeting most of the causative agents [18]. Tetracycline and its derivatives are the antibiotics of choice for the treatment of AFA, with better absorption with food and high patient compliance. Due to teratogenicity, tetracyclines and retinoids are avoided during pregnancy. Erythromycin has greater bacterial resistance but can be used as the drug of choice during pregnancy and lactation.

3.3.3 Hormone therapy

Hormone therapy, including anti-androgens and third/fourth generation oral contraceptives. Adult female patients with moderate-to-severe acne who also have high androgen levels or significant premenstrual acne exacerbation should be promptly treated with estrogen and progesterone, in addition, hormone therapy can even be used in female patients with normal hormone levels but resistant to other treatments [32]. Cyproterone acetate, an androgen receptor inhibitor that also reduces gonadotropin secretion, can be used in combination with ethinyl estradiol and is recommended for the treatment of mild-to-moderate adult female acne [7]. A recent study [33] demonstrated the efficacy of a combination of topical benzoyl peroxide and low-dose spironolactone (50 mg/day) in improving all subtypes of moderate adult female acne, including patients with papulopustular and nodular acne. Low-dose corticosteroids, such as prednisone (2.5 or 5 mg), inhibit adrenal androgen production and are recommended in the short-term treatment of advanced congenital adrenocortical hyperplasia, acute inflammatory lesions of AFA, and very severe acne [24].

3.3.4 Others

The herbal medicine tanoshinone has been reported to have anti-Propionibacterium acnes and mild anti-androgenic activity, and has been shown to be effective in both inflammatory and non-inflammatory acne with fewer adverse effects. This finding, if confirmed, might be useful as an alternative treatment to hormo.

3.4 Physical Therapy

Physical therapy may be used for patients who do not respond to or tolerate traditional treatments. Commonly used physical therapies include photodynamic therapy, laser therapy, and fruit acid therapy. Certain guidelines have recommended red and blue light therapy as an alternative treatment for acne [34]. Clinical observations have confirmed the efficacy of these treatments in reducing acne lesions, but there is a lack of evidence to support the use of these interventions [34]. 1 450-nm lasers, intense pulsed light (IPL), pulsed dye lasers, and fractional lasers are among the effective treatments for acne and acne scarring currently available, and may also be used in combination with medications [35]. Fruit acid therapy has adjuvant efficacy in mild to moderate acne, but its side effects are also very obvious, which can damage the skin stratum corneum and cause a lack of skin barrier effect, and more research data are needed for clinical use [32]. Glucocorticoids are effective in rapidly treating deep inflammatory nodules [36]; mechanical procedures (e.g., acne picking, cyst drainage) help to reduce non-inflammatory lesions and improve atrophic scars.

3.5 Complementary Treatments

3.5.1 Cosmetics and skin care products [37]

The use of appropriate cosmetics can improve the quality of life by reducing the possibility of lesions and improving the visibility of scarring and can reduce the patient's psychological stress, thereby reducing stress-induced lesions.
or lesion aggravation. Selection of products should be based on skin type, and lesion characteristics: oily skin selection to oil control, and repair the skin barrier ingredients; mixed skin for zoning care: T-zone oil control ingredients, cheeks to repair the skin barrier ingredients; sensitive skin selection to repair the skin barrier, anti-inflammatory ingredients based on localized acne spot-coating keratolytic or exfoliative ingredients based on inflammatory papules spot-coating anti-inflammatory, anti-acne Propionibacterium acneus ingredients mainly [37]. Sun exposure may trigger or exacerbate acne and produce pimples, and sunscreen products are recommended; sunscreens used for this purpose should be noncomedogenic, oil-free, easy to remove, and not close pores.

3.5.2 Dietary and lifestyle interventions [38]

Evidence from several studies [39] suggests that diets high in sugar have a role in exacerbating acne. Milk and dairy products have also been shown to be a possible aggravating factor for acne. The American Acne Clinic Guidelines also indicate that low-fat and low-sugar diets may reduce the number of lesions in acne patients and that milk may be associated with an increased rate of acne outbreaks [38]. Therefore, a low-sugar, low-fat, and low-dairy diet may be considered as a precautionary measure to prevent and maintain AFA treatment. Poor lifestyle habits such as staying up late, irregular sleep, sedentary lifestyle, and frequent use of computers are also associated with acne exacerbation.

3.5.3 Psychological interventions

Acne has been shown to have a serious negative impact on the quality of life of adult female patients, including the development of signs and symptoms of depression and anxiety, such as anger and low self-esteem. Physician care of the patient and the establishment of a good healthcare relationship can have a positive impact on the patient's quality of life.

3.6 Maintenance Therapy

Given the recurrent nature of the disease, maintenance therapy is necessary. Topical retinoids such as 0.1% adapalene or 0.1% tazarotene are recommended as first-line maintenance therapy, with 15% or 20% azelaic acid as a viable alternative [24].

4. Summary

The incidence of acne in adult women is increasing year by year, and the clinical manifestations, pathogenesis, and causative factors differ significantly from those of adolescent acne, making standard treatments for this condition less targeted. The authors suggest that the treatment of this patient group should be individualized, taking into account the complexity of the etiological factors and the high social and psychological impact of the disease. The aim of treatment should not only be to improve the clinical symptoms of the disease but also to reduce psychological stress and improve the quality of life of the patients. Finally, the pathogenesis of AFA has not yet been fully elucidated, and there is a lack of data on the development of targeted drugs. The protective mechanisms for the low incidence of acne in adult males have also been little studied, and these may be something to be looked at in the future.

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