



Review Article

Acne: Etiopathogenesis and its management

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Abstract

Acne vulgaris is one of the commonest skin disorders, which dermatologists have to treat, mainly affect adolescents, though it may present at any age. Acne is chronic inflammatory disease of pilosebaceous units. Clinically it can present as seborrhea, comedones, erythematous papules, pustules and nodules. In recent years, due to better understanding of the etiopathogenesis of acne, new therapeutic modalities are designed. The purpose of this article is to review the etiopathogenesis and treatment options available with us in the present scenario.

Key words

Acne vulgaris, Pilosebaceous units, Seborrhea, Comedones.

Introduction

Acne vulgaris is a most common skin disorder of the pilosebaceous unit [1]. It is generally characterized by seborrhea, comedone formation, inflammatory lesions and increased colonization by propionibacterium spp. staphylococcus spp. and yeast of malassezia spp. within the follicular canal [2]. It is common enough to be called a physiological process. Ninety percent of female and male individuals experience some degree of acne between puberty and thirty years of age. It is better regarded as a disease due to its inflammatory component and physical, psycho-social morbidity and is therefore, in need of systematic

and rational treatment. The disorder can cause significant emotional distress and physical scarring if untreated. Underestimating its importance is of serious consequences [3].

Definition

A precise definition of acne vulgaris is difficult to frame it can be defined as a chronic, self limiting, inflammatory disease of pilosebaceous unit, manifesting generally in adolescence with pleomorphic lesions like comedones, papules, nodules and cysts. Extensive scarring can occur [4].



Etiopathogenesis of acne

Acne vulgaris is multifactorial in origin involving both endogenous and exogenous factors. There are four primary pathogenic factors, which interact in a complex manner to produce acne lesions [5].

- Increased sebum production by the sebaceous gland.
- Alteration in the keratinization process.
- Follicular colonization by propionibacterium spp.
- Release of inflammatory mediators into the skin.

Others contributing factors include hormonal influences from estrogen and androgens, such as DHEAS (dehydro-epiandrosterone sulfate), which increases sebum production in prepubescent children, leading to acne [6, 7].

Seborrhea (increase in sebum secretion) and sebaceous gland hypertrophy and hyperplasia are the hallmarks of acne [8]. The changes in the quality of sebum may cause irritation of the duct epithelium. It is found that high levels of squalene and wax esters are found in sebum of acne patients [9]. Lowered levels of linoleic acid in sebum can lead to acne vulgaris by promoting the accumulation of cornified cells [10, 11].

Ductal hypercornification is seen histologically as microcomedones, which are initial Lesions of acne. The stimulus to the hyperkeratosis of duct epithelium may be androgens, or it may be irritating effect of sebaceous lipids as they pass through the duct. The acceleration in the rate of sebum secretion or its composition may irritate the infundibular keratinocytes, leading to release of inflammatory substance like IL-1 α , this in turn causes reduction of sebaceous linoleic acid and 5 α -reductase enzyme levels. These changes lead to induction of follicular hyperkeratosis [12]. Comedogenesis occurs when abnormally desquamating corneocytes

accumulate within the sebaceous follicle and form a keratinous plug [13]. It blocks the follicular ostium at the skin surface; it becomes visible as closed comedone (white head). An open comedone (black head) occurs if the follicular ostium dilates and filled with debris.

It is widely accepted that propionibacterium species (*P. acne*, *P. granulosum*) etc. are a major factor in the pathogenesis of acne. *P. acne* is a common skin resident and one of the major components of the microbial flora of the pilosebaceous follicle [14]. These resident bacteria produce more lipases which are responsible for hydrolysis of triglycerides to free fatty acids contributing to follicular hyperkeratosis and even rupture of follicle [15].

Inflammatory process is a key component of acne which largely accounts for its morbidity and sequelae. Perifollicular T- cells are involved in the immunological events in genetically predisposed individuals, initiating comedogenesis through release of IL-1 [16]. In addition, ductal corneocytes also produce IL-2, IL-8 and TNF- α which contribute to inflammation. Androgens increase sebum secretion and also cause sebaceous gland hyperplasia [17]. Estrogen, on the other hand, suppresses sebaceous gland activity [18]. There is a negative relationship between acne severity and serum sex hormone binding globulin (SHBG) levels. Peripheral hyper-androgenism in many cases may correlate with severity of acne in women, and can guide appropriate hormone therapy [19].

A hot and humid climate aggravates acne due to increased sweating causing ductal hydration. Emotional stress also plays a significant role in the aggravation of the pre-existing acne [20]. External application of oils, pomades, and other comedogenic chemicals cause acneiform eruptions [21].

A high glycemic diet induces hyper-insulinemia which results in androgen synthesis, similar to polycystic ovarian disease (PCOD) [22]. Diet induced hyper-insulinemia also increases level of IGF-1 (Insulin Like growth factor) and reduce IGF binding proteins. The increased free IGF-1 level results in unregulated growth of follicular epithelium, increased sebum production and synthesis of androgens from gonads [22].

Sequence of events

The microcomedones are the first subclinical lesion. It is caused by blockage of the sebaceous canal due to altered keratinization leading to retention of sebum and initiation of an inflammatory process. An increase in the microbial flora increases inflammation (papules and pustule formation). Further retention of sebum leads to rupture of sebaceous gland and spreads the sebum in the dermis resulting in nodule formation. Confluence of affected glands results in accumulation of pus, fluid and cyst formation. A scar results when such cysts heal after rupture or absorption of fluid [4].

The severity of acne can be graded on clinical grounds as under [4].

- **Grade 1 (mild):** Comedones, occasional papules.
- **Grade 2 (moderate):** Comedones, many papules, few pustules.
- **Grade 3 (severe):** Predominantly pustules, nodules and abscesses.
- **Grade 4 (cystic):** Mainly cysts or abscess, widespread scarring.

The grading is arbitrary and is used as one of the parameters for treatment and follow up.

Management of acne vulgaris patients [4]

- General measures.
- Specific measure.

General measures

- Eliminate stress by reassurance.
- Counseling of the patient regarding nature of illness, treatment modalities and its outcome.
- Advice to avoid scratching of lesions.
- Assess the endocrinal status and premenstrual flares.
- Advise to avoid the use of acnegenic drugs, oils, pomades and heavy cosmetics.
- Balanced diet should be advised. Avoid high glycemic diet.
- Regular washing of face with soap and water.

Specific measures

The general principles of treatment are based upon four strategies that may be combined according to the clinical aspect of acne patient.

- Decreasing the sebaceous gland secretion.
- Correcting the ductal hypercornification.
- Decreasing P. acne population and associated flora.
- Producing an anti-inflammatory effect.

Keep in mind "one treatment does not fit all" [23].

Topical therapy

Numerous topical preparations are in use for their anti-comedogenic, anti-seborrheic and antibacterial properties.

Topical Retinoids

Various topical retinoid preparations available are

- Tretinoin: 0.025%, 0.05%, 0.1% gel /cream.
- Isotretinoin: 0.05% gel.
- Adaplene: 0.03%, 0.1% gel.
- Tazarotene: 0.1% and 0.05% gel.



Mechanisms of action include restoration of the disturbed keratinization, increase in cell turnover and regulation of prostaglandin synthesis. Topical retinoids reduce the number and formation of precursor lesions; reduce mature comedones and inflammatory lesions. The main adverse effect with these agents is primary irritant dermatitis which can present as erythema, scaling, and burning sensation and can vary depending on the skin type, sensitivity and formulation [24].

- **Benzoyl Peroxide:** It is as effective as topical retinoids and used in gel, cream or lotion in a strength varying from 2.5 to 10%. It is a broad-spectrum antimicrobial agent effective via its oxidizing activity. It has anti-inflammatory, keratolytic and comedolytic activities. It is indicated in mild to moderate acne. Its main side effects are excessive dryness, irritation, allergic contact dermatitis and bleaching of clothes, hair and bed linen [25].
- **Topical antibiotics:** These are used in inflammatory acne. Topical erythromycin and clindamycin are the most popular [26], used in 1-4% formulation either alone or in combination with benzoyl peroxide or adaplene. Side effects are minor including erythema, peeling, itching, dryness, burning and development of resistance.
- **Other topical agents are mentioned as below.**
 - Azelaic acid available 10-20% cream and effective in inflammatory and comedonal acne [27, 28].
 - Salicylic acid used as comedolytic agent, but is less potent than topical retinoid [29].

- Lactic acid is found useful in reducing acne lesions [30].
- Tea-tree oil 5% [31]
- Picolinic acid gel 10% [32]
- Dapsone gel 5% [33]
- Topical 5-fluorouracil [34]

Systemic therapy

- **Tetracyclines [35]**
 - Tetracyclines - 500mg - 1gm per day.
 - Doxycycline - 50-200mg per day.
 - Minocycline - 50-200mg per day.
 - Lymecycline - 150-300mg per day.
- **Sulpha drugs [36]**
 - Cotrimoxazoles (80 mg trimethoprim + 400 mg sulphamethoxazole).
 - Dapsone – 50 – 200 mg per day.
- **Macrolides [36]**
 - Erythromycin – 250-500 mg qid
 - Azithromycin – 500 mg once a day for three days in a week
- **Hormonal therapy [37]**
 - Estrogen – ethynyl estradiol 30 micro gm with progesterone.
 - Antiandrogens: Cyproterone acetate – 50-200 mg, Spironolactone – 50-100 mg per day
 - Corticosteroids: Prednisolone – 2.5-5 mg per day [38].
- **Oral zinc therapy** – 200 mg per day [39].
- **Oral retinoids** - isotretinoin 0.1-2 mg per kg per day [40].



- **Phototherapy** – the efficacy of UV radiation in acne is because of presence of porphyrins in p-acne [41].

Chemical peeling with 10-50% glycolic acid or 10-30 % salicylic acid leads to significant resolution of comedones, papules and pustules. Repeated glycolic acid peeling is necessary for acne scars and cystic lesions [42].

Conclusion

Various topical and systemic drugs are available to treat acne. A summary of the approach to treatment of acne as per the severity is as follows [43].

A. Mild involvement (only comedones)

- benzoyl peroxide gel
- salicylic acid as cleanser
- azelaic acid

B. Mild to moderate involvement (comedone, few papules and or pustules)

- benzoyl peroxide gel or
- topical retinoids and
- topical antibiotics.

C. Moderate to severe involvement (many inflammatory papules, pustules, 1-2 nodules and or scarring)

- Oral antibiotics
- Sebostatic agent - hormonal therapy, Isotretinoin.

D. Cystic acne (more than 2 nodules, cysts abscess, scar)

- Aspiration of the cysts and intra-lesional steroid and
- Systemic antibiotics and
- Dapsone or sebostatic agent
- Adjunctive therapy - comedone expression, chemical peels, micro-derma-abrasion.
- Laser and light therapy - blue light, UV light, pulsed dye laser.

- Acne surgery - draining of cysts and punch grafts for scars, skin resurfacing with laser, cryosurgery, derma-abrasion and fillers.

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