An Overview About Acne Vulgaris

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Abstract

Background: Acne vulgaris (acne) is a long-term inflammatory skin disease. Typical features of acne that often appear in adolescents on the forehead include visible, clinically recognized blackheads or whiteheads (comedones) that develop into inflammatory red papules or pustules and possible scarring. Acne primarily affects skin with a relatively high number of sebaceous glands including face, neck, chest, and upper back. Acne and postinflammatory hyperpigmentation have a strong negative impact on mental health, including mood disorders, depression, and suicidal thoughts. Also, acne may cause low self-esteem, decrease social interactions, and quality-of-life scores in adolescents. Typical features of acne include increased secretion of sebum by the skin, microcomedones (a structure invisible to the naked eye), comedones, papules, nodules, and pustules, and often result in scarring. It may result in psychological and social problems. Acne lesions are classified into non-inflammatory and inflammatory. Non-inflammatory acne lesions consist of open and closed comedones. Open comedones are clearly obvious in the skin and can be found in the face centrally. Closed comedones, by inspection in a good light room, are slightly hypopigmented, tiny, usually less than 1 mm in size, with no visible opening. Comedones are superficial and can remain with no progress or get inflamed and become deep. Inflammatory acne lesions include papules (red, inflamed, raised lesions of size less than 5 mm), pustules (scattered pus-filled papules) and nodules (lesions, 5 mm or larger in size). These lesions affect deep structures in the skin so their inflammation can lead to formation of scars. Acne vulgaris is a chronic skin disease of the pilosebaceous unit that occurs as a result of the following four factors: increased sebum production (due to increased activity of androgens and IGF-1), excessive deposition of keratin in pilosebaceous follicles leading to comedo formation, colonization of the follicle by P. acnes bacteria, and the local release of pro-inflammatory chemicals in the skin through certain inflammatory mechanisms. Limited evidence supports comedo extraction, but it is an option for comedones that do not improve with standard treatment. Another procedure for immediate relief is the injection of a corticosteroid into an inflamed acne comedo. Electrocautery and electrofulguration are effective alternative treatments for comedones. Inflammatory and non-inflammatory lesions are common in acne vulgaris, which is a complex illness linked to the pilosebaceous follicle. Since inflammation can occur in both the early stages of acne vulgaris and the late stages of the disease, inflammation plays a critical role in the development of acne vulgaris lesions, both inflammatory and non-inflammatory. There are different updated modalities for acne vulgaris treatment.

Keywords: Acne Vulgaris

INTRODUCTION

Acne Vulgaris
Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Acne can present as noninflammatory lesions, inflammatory lesions, or a mixture of both, affecting mostly the face but also the back and chest. Despite the fact that it doesn't shorten a patient's life expectancy, it's thought to have a negative impact on their quality of life, much like diabetes and coronary heart disease do. Low self-esteem and increased incidences of social isolation, unemployment, and depression were seen in adolescents with acne compared to those who had not had acne (1,2).

Epidemiology:
Acne presently affects 9.38 percent of the world's population (3). It's estimated that almost 85% of teenagers will experience acne at some point in their lives. According to recent epidemiological research, developed countries face a greater danger than developing countries (4).

Course:
In most situations, acne is a self-limiting illness that goes away after puberty, but it can last for many years and even into adulthood in certain people (5).

Pathogenesis:
Hyperkeratinization of the follicular epithelium, excessive sebum, Cutibacterium Acnes colonization, and finally inflammatory changes exacerbated by these factors culminate in activation of innate and adaptive immunity as the four main pathogenic events implicated in the pathogenesis of acne vulgaris (6).
Inflammatory changes:
Acne lesions are now known to be primarily driven by inflammatory changes mediated by the host's innate and adaptive immunity, and that inflammation is required for the emergence of acne lesions and is not a coincidental occurrence (7).

Clinical presentation
Acne's primary lesion, microcomedones make up histological changes that aren't visible clinically. The follicle is damaged by sebum buildup, and comedones form, which are non-inflammatory lesions also known as "white heads," or open, also known as "black heads." The dark colour is a result of sebum oxidation, which is why it's black. Papules, pustules, nodules, and cysts are examples of inflammatory lesions. Papules are raised red spots on the skin, whereas pustules are the same but include a little amount of pus in the centre. Nodules are large, hard lesions that are more than 5 cm in diameter and have become firmly indurated as a result of the inflammation (8). Typically, the lesion is painless and itchless, however erythema or pain may accompany it in some situations (9).

There are two outcomes to acne: it goes away on its own, or it leaves scars that can be either atrophic or hypertrophic but more usually is atrophic, such as erythema, post-inflammatory hypo-or hyperpigmentation, or scarring (10).

Treatment:
General lifestyle changes such as reducing high glycemic diets, avoiding oil-based cleansers that clog pores, and using cleansers no more than twice daily are critical to the effectiveness of medical treatment (11). Alkaline soap (9-10 PH) with various surfactants is recommended for acne patients as well (12).

Topical Therapy:

1. Retinoids:
In acne treatment, retinoids, a class of vitamin A derivatives, are essential. To combat inflammation, they reduce TLR-2 expression on monocytes, while also reducing the production of microcomedones by inhibiting sebocyte hyperproliferation and differentiation. Lastly, they inhibit the manufacture of proinflammatory mediators such transcription factor activator protein (AP), prostaglandins, and proinflammatory cytokines like IL6, IL12, TNF α, and Interferon (IFN) γ by acting as a comedolytic (13).
Retinoids such as tretinoin, adapalene, and tazarotene are among the retinoids that can be used to treat acne. A number of undesirable side effects such as photosensitivity, dryness and exfoliation have been linked to the use of tretinoin. More steady and tolerant than adapalene in terms of adverse effects. Despite being equally effective as adapalene and being photo-stable, tazarotene is less pleasant and must be used daily. While tazarotene falls under pregnancy category X, both tretinoin and adapalene do not (14).

2. Benzoyl peroxide (BP):
When used topically, it has antibacterial properties due to the generation of free nitric oxide, which is bactericidal yet does not lead to antibiotic resistance. Retinoids should be taken in conjunction with this product (15).
It is safe to use during pregnancy since it does not transform into benzoic acid until it reaches the stratum corneum. Bleaching and staining of clothing are two of the most typical negative effects (16).

3. Topical antibiotics:
In the treatment of acne caused by bacteria, the antibiotics erythromycin and clindamycin are the two most commonly prescribed options. They suppress protein synthesis by attaching to the 50s ribosome (17).
Erythema, itching, and exfoliation are the most common side effects. Topical clindamycin use has been linked to a very small number of occurrences of pseudomembranous colitis, so it's best to proceed with caution if you have antibiotic-associated colitis (18). Both medications fall under pregnancy category B, which means they can be taken in conjunction with benzoyl peroxide to treat acne while pregnant if necessary (19).
It is critical to use the correct topical therapeutic combinations to ensure the treatment's success. Combining Retinoids and Benzoyl peroxide is more effective than using them alone as monotherapy. This is the initial line of treatment for comedonal acne, but it's important to leave enough time between applications to avoid benzoyl peroxide inactivating the retinoids. There is also an orange skin discoloration when BP and dapsone are combined (10).

4. Azelaic acid (15% cream or 10% gel):
In addition to its anti-inflammatory and antibacterial properties, azelaic acid is a comedolytic. Additionally, it aids in the reduction of post-acne hyperpigmentation when used as an adjuvant. The most common side effects include stinging, dryness, exfoliation, hypopigmentation, and hypertrichosis, which normally go away after 8 weeks of continuous use because to the acidic qualities that can irritate sensory nerves. Even though it's pregnancy category B, there's no proof that it's safe to use on children just yet (20).

3. Topical dapsone (5% gel):
A synthetic sulphone antibacterial agent, it's used to fight germs. When it comes to inflammatory lesions, it's important to keep this in mind, especially for women with darker skin. G6PD deficiency cannot be detected even in high-risk patients taking the systemic form of the medicine, but a rare instance of hemolysis in a toddler taking trimethoprim antibiotics due to inadvertent methemoglobinemia has been recorded (21).
6. Topical salicylic acid:
A beta-hydroxy acid called salicylic acid has been discovered to have keratolytic and anti-comedogenic effects. It has been given the green light to be utilized in a variety of acne drugs, but it must be used in conjunction with other treatments on a regular basis (12).

Intralesional corticosteroids:
Large nodules are treated with intralesional injections of corticosteroids, particularly triamcinolone acetonide. It has the advantage of flattening the lesion quickly, however adverse effects including atrophy or telangiectasia can occur. The dosage is typically 3mg/ml (22).

Systemic therapy:
1. Systemic antibiotics:
Antibiotics from the tetracyclins family, such as tetracycline, doxycycline, and minocycline, are widely recommended to treat C. acnes. In mild to moderate inflammatory acne, antibiotics are often the initial line of defence. However, they are no longer utilised as a monotherapy because of their systemic resistance adverse effect (23).

Additionally, tetracyclines have an anti-inflammatory impact because of the inhibition of chemotaxis and the reduction of proinflammatory cytokines, as well as MMP activity (24).

In addition to their inability to be used during pregnancy and in children under 9 years, Tetracyclins have the most commonly reported side effects of photosensitivity and tooth discoloration (25).

Only pregnant women should use azithromycin due to the increased risk of bacterial resistance (26). As a last resort, trimethoprim sulphemethoxazole is used to treat patients when all other treatment options have failed (27).

2. Oral isotretinoin:
There was FDA approval for the use of isotretinoin, a systemic vitamin A derivative, for the treatment of severe recalcitrant acne or acne that was more likely to leave scars. FoxO1 and FoxO3 proteins are activated, which causes sebocyte death and suppresses sebogenesis. It also reduces the expression of TLR2 on monocytes, which inhibits the release of cytokines (28).

Use between 0.5 and 1 mg/kg for a period of 16 to 30 weeks. The most prevalent side effects are dryness of the skin, lips, and eyes, as well as an increase in blood triglycerides and cholesterol (29). Isotretinoin has been linked in certain studies to inflammatory bowel illness, however this has not yet been proven (30).

Depression is a serious side effect of acne, but acne is also linked to depression, particularly in adolescents. So, it's still up for debate, and it's not recommended for use in patients who are depressed (31).

Hormonal Therapy:
Females exhibiting indications of hyperandrogenism, flares before menstruation, or deep nodules on the neck or face are candidates for hormone therapy. The majority of therapeutic options target androgen production suppression or androgen receptor blockade (32).

1. Oral contraceptive pills (OCPs):
Antiandrogenic actions of oestrogen are well-known. Oral contraceptive pills authorised by the FDA as a second-line medication in adolescent or adult females include: There are three types of ethinyl estradiol available: ethinyl estradiol-norgestimate, ethinyl estradospirenone, and norethindrone acetate (33). A low-androgen progesterone was introduced to minimize the risk of malignancies linked to oestrogen. (34). They are naturally antiandrogenic in their effects. Additionally, they raise the production of sex hormone binding globulin (SHBG), which binds to free testosterone, lowering the total amount of testosterone in the body. In addition, they inhibit 5-alpha reductase activity, and ultimately, they inhibit androgen receptors (35).

Side effects include lower libido, gas, increased risk of DVT and pulmonary embolism, myocardial infarction, and estrogen-induced malignancies such as breast and endometrial, which is why it is not recommended for anyone in any of the preceding groups: men, women, or children (25).

2. Oral spironolactone:
In females with hormonal acne when OCPs fail to manage it, especially in the setting of PCO, spiro lactone is an off-label potassium sparing diuretic given. As a result of inhibiting 5 reductase activity and increasing SHBG levels, androgen levels drop (36).

2. Cyproterone acetate (CPA):
In terms of acne severity, this antiandrogen and progestin worked wonders. Combining it with oral contraceptives maximises its effectiveness. Inhibition of androstenedione synthesis from DHEA by CPA leads to a reduction in sebum production (25).

4. Metformin:
Diabetes, insulin resistance and acne associated with PCO can all be improved with metformin, an anti-diabetic drug. It does this without causing hypoglycemia. It increases the P53 pathway, which in turn decreases the amount of insulin-induced mTORC1. Acne lesion development is mediated by mTORC1 (29).

Since IGF signalling affects inflammatory acne lesions more than non-inflammatory ones, metformin improves them more than non-inflammatory ones. Women with PCO may take up to 2000 mg of this medication daily (19).

5. Corticosteroids:
Only severe cases of fulminant acne or acne-associated diseases warrant the use of low-dose short-term corticosteroids due to the potential for flare-ups from elevated androgens. It works by preventing the release of adrenal androgen (37).
Acne and light assisted therapy:
Light therapy works by generating oxygen free radicals, suppressing the release of inflammatory cytokines, and shrinking the sebaceous glands' size and activity (38).

1. Photodynamic therapy (PDT):
With the advent of photodynamic therapy, a photosensitizing chemical is applied topically before being exposed to light. It creates reactive oxygen species upon activation by light, destroying the cells it comes into contact with Menezes et al. (39)
The blue light appeared to have some bactericidal properties when tested on the bacteria C. acnes. Additionally, C. acnes creates a rare porphyrin molecule capable of absorbing blue light (415 nm). This porphyrin molecule releases free radical molecules when it absorbs blue light, which can kill bacteria (40).

2. Intense pulsed light (IPL) (400nm-1200nm):
Cutibacterium Acnes' porphyrin degradation is activated by polychromatic high-intensity pulsed light. Endogenous chromophores absorb light in a way that damages the blood vessels that supply the gland, which in turn reduces sebaceous gland activity (41).
Tumor necrosis factor alpha (TNF-α) is believed to be lowered by IPL, while transforming growth factor beta (TGF-β) is increased as a result. (42).

3. Pulsed Dye Laser (PDL):
It's used to treat acne rashes caused by an inflammatory condition. This drug's chromophore, which is oxyhemoglobin, causes dilated blood vessels to selectively photothermolyze and targets cutaneous immune activation (43).
When used to heal acne scars, it causes dermal remodelling. As an added benefit, it works by causing new collagen to be synthesised via the stimulation of transforming growth factor B (TGF-β) (44).

4. Ablative laser for scarring:
Post acne scars can be successfully treated with fractional CO2 laser resurfacing (10,600 nm wavelength). Water is the chromophore's target for energy absorption, and the laser energy is then absorbed by it. Microthermal zones are coagulation and dermal remodelling zones bordered by ablated, vaporised tissue columns (MTZ) (45).
Resurfacing with ER: YAG (Fractional Ablative Erbium:Yttrium–Aluminum Garnet) (2,940 nm) is possible. It has fewer adverse effects than CO2 laser resurfacing, and you have more control over how deep the laser penetrates. A second method of Er:YAG resurfacing procedure is known as dual-mode. Short-pulsed Er:YAG lasers and Er:YAG lasers produce the best outcomes for people with darker skin tones (30).

5. Non ablative laser for scarring:
There is only a 40-50 percent efficacy after numerous treatment sessions for non-ablative lasers such as the Nd YAG at 1064 nm and the 1450 nm diode laser at 1450 nm. (46).
Acne and peeling:
Reduce inflammation, reduce lesion count, and enhance skin texture are all goals in treating aggressive acne. In comedonal and papulopustular acne, superficial peels can be used as adjuvant treatment; however, they cannot be utilised on nodulocystic types of acne. For acne, some peels contain 20-30% salicylic acid (SA), 70 percent glycolic acid (GA), 40-60% pyruvic acid (PA), 20-25% mandelic acid (MA), Jessener's solution (JS), and 10% trichloroacetic acid (TCA) (47).

Chemical Reconstruction of Skin Scars (CROSS technique):
Focused treatment of high-concentration trichloroacetic acid has shown significant improvement in ice pick scars (TCA CROSS) (48).
When used on scars of all types, including severe boxcar scars, 70% TCA CROSS shows remarkable improvement. Dark-skinned persons with ice pick scars can benefit from TCA CROSS as an effective treatment option. Hydroquinone and tretinoin can help prevent problems by priming the skin beforehand. It was discovered that CO2 pinpoint radiotherapy was better than TCA CROSS for the treatment of ice pick scars (49).

Physical methods:
Liquid nitrogen is used in cryotherapy, which means it's superficial. Large chronic nodules can be treated with two 15-30 second freeze-thaw cycles (50). Devices that use Selective Cryolysis came next. The sebaceous glands' output was shown to be reduced in just two weeks after being exposed to temperatures as low as -20 C for 20-minute cycles. Due to the possibility of concomitant hypopigmentation, this approach has not yet been studied (51).
Subcision: It is a method in which a needle is repeatedly inserted under the skin in various directions. Fibrotic strands under the scar are severed and released as a mechanism for scar treatment. The best way to use it is to roll acne scars, although treating boxcar and ice pick scars isn't as successful (52).

Novel agents for acne management:

New Topical Agents for acne management:
1. Triaforte
Triaforte is a fourth-generation retinoid that has shown promise in the treatment of acne on the face and in the trunk. It is a retinoic acid receptor (RAR) agonist that is selective (53).
2. Nitric oxide gels:
Antimicrobial activity against Cutibacterium Acnes is provided by the NVN1000 gel, as is immune modulation by inhibition of proinflammatory cytokines such as IL-1β, TNF-alpha, interleukin 8 (IL-8) and interleukin 6 (IL-6)
ocyclin and other tetracyclins, although minocyclin has a lower resistance rate. For the treatment of cystic acne, there is a new topical tetracycline called Minocyclin Foam, which is equally effective as systemic tetracyclins but has none of the adverse effects. It doesn’t cause allergic reactions or inflammation, and it’s also not phototoxic (55).

4. Omiganon pentachloride: It’s an antibacterial peptide cationic in nature. An antibacterial and antifungal spectrum is provided by this topical bovine indolicidin derivative. In anti-acne trials, it was found to be effective because it breaks the cell membrane, causing depolarization and the death of nearby cells (56).

5. Epigallocatechin gallate (EGCG): Green tea polyphenol is the active ingredient in this topical solution. It blocks sebogenesis by preventing the mTORC1 kinase from responding to IGF-1 stimulation. It reduces the amount of IL-1 α and downregulates the NF-B and activator protein pathways to control hyperproliferation. Additionally, it prevents the enzyme 5- reductase from working. (57).

6. Olumacostat glasaretil (OG): In studies on acne vulgaris, it was found to be an effective inhibitor of the acetyl coA carboxylase (ACC) enzyme. The denovo fatty acid synthesis is inhibited when ACC is inhibited, and this prevents excessive sebum production. C. acnes proliferation and biofilm formation could be inhibited by it, too (29).

7. Topical nicotinamide gel: The amide form of niacin is made from a vitamin B3 derivative. It reduces acne through a number of processes. It reduces sebum production and enhances the barrier function of the epidermis against C. acnes by increasing ceramide synthesis in the skin (58).

8. Topical Corticosterone 17α-propionate (C17AP) 1% cream: It is a synthetic steroid antiandrogen that reduces androgen-induced sebum production by inhibiting androgen-to-androgen receptor peripheral binding. Because of its antiandrogenic qualities, this compound shows promise and should only be used by women (59).

9. Topical probiotics: Lactobacillus genus species Enterococcus faecalis SL-5 was isolated from human faeces and used in lotion form. It works against C. acnes as a bacteriocin (60).

10. Lupeol: Solanum melongena L. produces the triterpene, a pentacyclic compound. As a result of the research results, researchers found that taking Lupeol twice a day reduced the expression of several genes including SREBP-1 and keratin 16 in mice. It was found that this can inhibit lipogenesis and Interleukin 1 driven comedone development (62).

11. Vitamin C loaded adapalene: Vitamin C is well-known for its ability to speed up collagen production. Post-acne hyperpigmentation may be helped by this because it is an antioxidant and depigmenting agent. New adapalene-enriched vitamin C compositions have emerged, and they perform better than pure adapalene (63).

12. Next science acne gel (NAG): new gel containing isopropyl alcohol and a surfactant that solubilizes extracellular polysaccharide (EPS) polymers encapsulated in biofilms reduces the risk of antibiotic resistance while having no negative effects on the skin of patients. It is a promising agent that reduces the likelihood of resistance to antibiotics while having no negative effects on skin of patients (64).

REFERENCES


