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New Management Lines of Acne Vulgaris: Review Article

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ABSTRACT
Background: The pilosebaceous unit is affected by acne vulgaris (AV), which manifests as open and closed comedones, papules, pustules, and nodules, and variable degrees of scarring. Adolescent onset is the norm for AV, which is otherwise a very rare disorder. Reevaluation of pharmaceutical treatments is suggested after 8 weeks for mostly comedonal or moderate inflammatory acne and 12 weeks for severe disease.
Objective: Review of new management lines of acne vulgaris.
Methods: We scoured scholarly papers and databases including PubMed, Google Scholar, and Science Direct for information on acne vulgaris and management lines. Between January 2001 and November 2022, however, only the latest or most comprehensive study was considered. The authors also assessed the usefulness of references taken from similar books. Documents written in languages other than English have been overlooked because of a lack of funding to translate them. Unpublished articles, oral talks, conference abstracts, and dissertations were all generally agreed upon to not constitute valid scientific investigation.
Conclusion: New therapy approaches and numerous permutations and combinations have been developed as a result of a deeper comprehension of the aetiology of acne. Benzoyl peroxide, antibiotics, retinoids, and other topical medications are the backbone of treatment. They can be administered in any combination. Oral antibiotics, hormone therapy, and isotretinoin are considered examples of systemic options of treatment, although the best option will vary from patient to patient.
Keywords: Acne vulgaris, Management.

INTRODUCTION

More than eighty-five percent of adolescents around the world suffer with acne vulgaris (AV), a skin condition. Although it typically appears and worsens throughout adolescence, research has shown that this most prevalent skin disease can appear at any age [(1)].

Although acne is not fatal, it does cause severe emotional distress and has many co-occurring conditions that must be addressed in order to restore the patient's confidence and appearance [(2)].

The majority of people with active acne put off getting treatment, which increases their risk of developing acne scars. Different types of acne scars have been identified, including those with increased tissue production [(3)].

Management of Acne:

New therapy approaches and numerous permutations and combinations have been developed as a result of a deeper comprehension of the aetiology of acne (Figure 1).

Benzoyl peroxide, antibiotics, retinoids, and other topical medications are the backbone of treatment; they can be administered in any combination. Patients' needs will dictate which systemic therapeutic options, such as oral antibiotics, hormone therapy, or isotretinoin, are used. Lesion excision is one method of physical therapy, and phototherapy is effective for some cases [(1)]. Reevaluation of pharmaceutical treatments is suggested after 8 weeks for mostly comedonal or moderate inflammatory acne and 12 weeks for severe disease [(4)].

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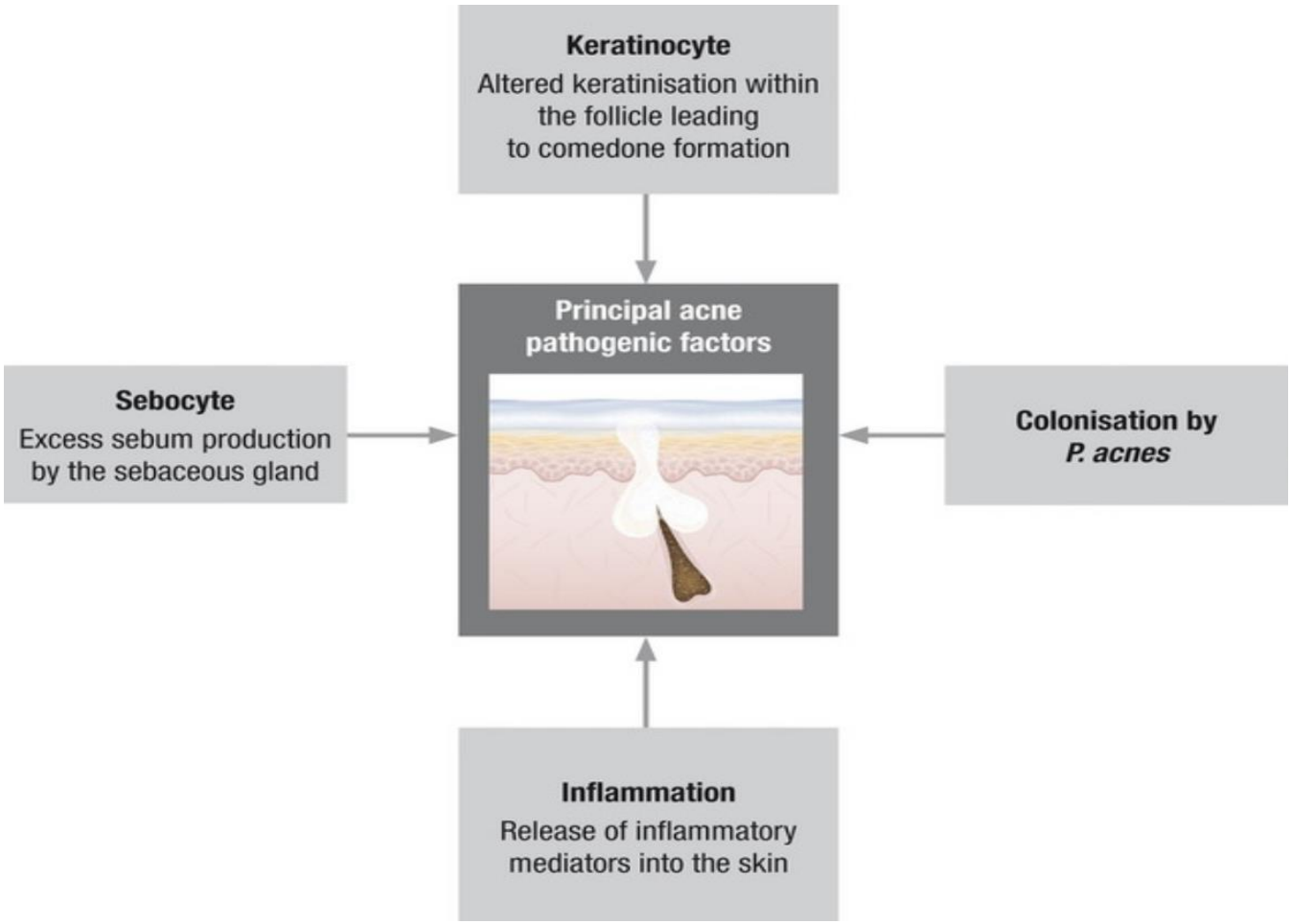

Figure (1): Acne is caused by four primary reasons [4]

Management of acne vulgaris patients includes the following:

A. General measures.

B. Specific measure (Figure 2).

A. General measures:

1. Reassurance can help to reduce tension.
2. Patient counselling on the nature of his illness, available treatment options, and potential outcomes.
3. Refrain from scratching or squeezing the lesions because doing so might exacerbate acne and raise the possibility of long-term scarring.
4. Examine premenstrual flares and the endocrine system.
5. Refrain from using acne-causing medications, oils, and heavy cosmetic
6. Dietary measures (such as low-glycemic meals and avoiding dairy or skim milk) help in decreasing skin lesions [5].

B. Specific measures: Figure (2).

C. Topical treatment:

Since topical treatments are applied directly to the skin, they have the dual benefits of minimizing the drug's systemic absorption and increasing its localized delivery to the pilosebaceous units. Topical therapies for acne are often effective, although they often cause skin irritation [7].

a. Topical retinoids:

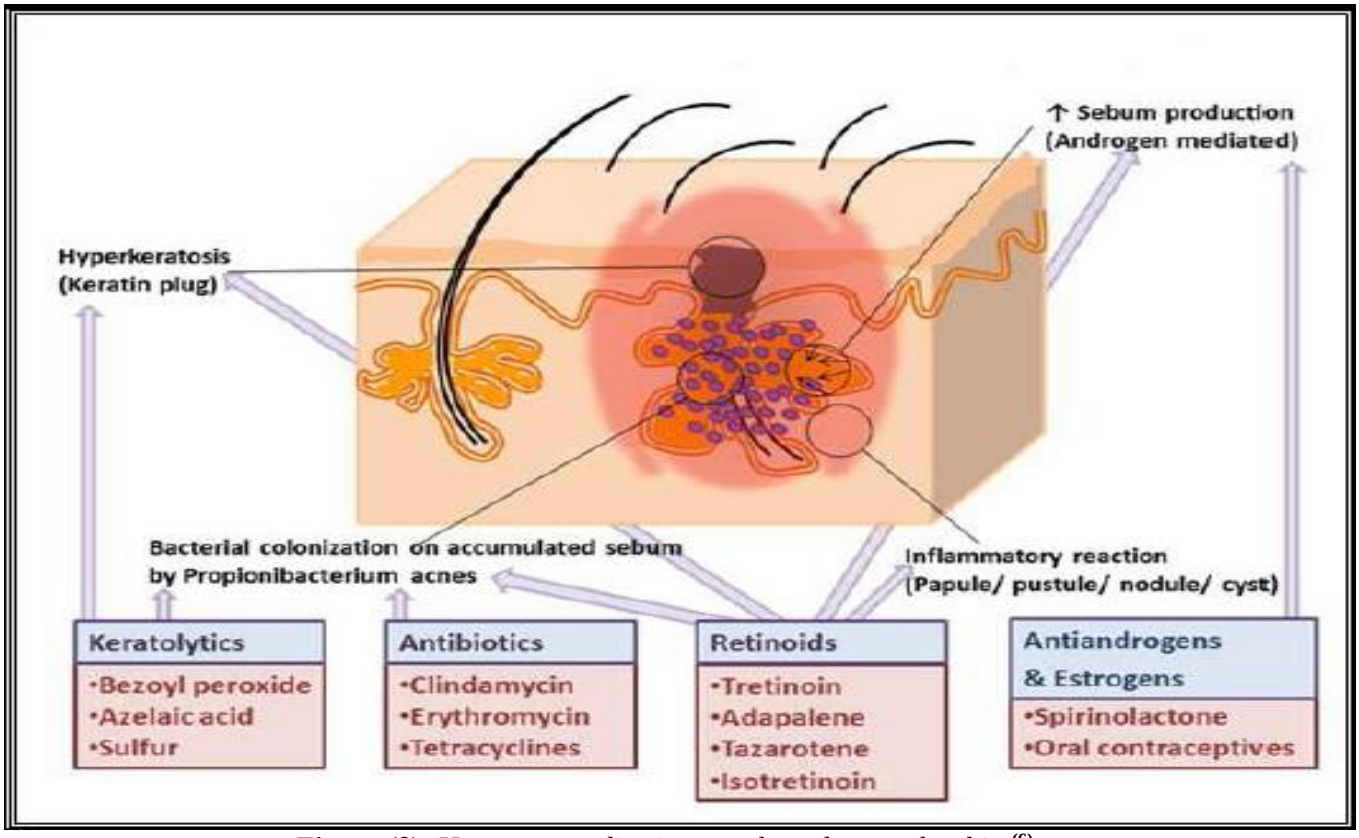

Figure (2): How acne medications work to clear up the skin [6].

It was stated that "retinoids are the core of topical therapy for acne because they are comedolytic, resolve the precursor microcomedone lesion and are anti-inflammatory;" further, they "allow for maintenance of clearance" [8]. There are three different retinoids that can be used topically (tretinoin, adapalene, and tazarotene). Each comes in a variety of forms and strengths. Adapalene and other third-generation medicines are generally more well-tolerated by patients. Common reactions include redness, itching, scaling, and burning [9].

Desquamation can be brought back to normal with the help of retinoids, which inhibit keratinocyte growth and stimulate differentiation. Toll-like receptor expression can also be down regulated by isotretinoin, tretinoin, and tazarotene. Inhibiting cellular inflammation and lowering the production of inflammatory cytokines and nitric oxide are the results of blocking these pathways [8].

Despite the lack of proof for considerable systemic absorption of topical retinoids, it is nonetheless advised that adult females avoid becoming pregnant if they are using this treatment. This is because of the teratogenicity of oral retinoids [10].

b. Topical Antibacterial Agents:

In addition to benzoyl peroxide, topical antibiotics such as 1% clindamycin and 2% erythromycin are often used to treat mild to moderate acne. Depending on the type of antibiotic, topical medicines can either reduce inflammation or kill bacteria. Due of erythromycin's diminishing efficacy, which is probably related to developing resistance of C. acnes, clindamycin is preferred over erythromycin. To lessen the likelihood of antibiotic resistance, topical antibiotics should not be used as monotherapy or maintenance therapy, and treatment should last no longer than 12 weeks at most [11].

c. Benzoyl peroxide:

One of the most powerful oxidizers is benzoyl peroxide (Bp). The reactive oxygen species it produces have a bactericidal effect, making it useful against P. acnes in the acne vulgaris pathogenesis [12]. BP's keratolytic actions are the second way by which it fights acne [13].

c. Azelaic acid:

Azelaic acid inhibits bacterial growth, reduces keratinization of skin cells, and soothes inflammation. Acne of both the inflammatory and non-inflammatory varieties benefit from its use. In the treatment of mild to moderate acne, it is as effective as other topical therapies. It's well-liked and well-tolerated by patients. Azelaic acid's antityrosinase activity makes it useful for treating post-inflammatory hyperpigmentation [14].

d. Topical Dapsone:

Dapsone is a synthetic sulfone that can kill bacteria and reduce inflammation. Its anti-inflammatory properties make it an ideal acne therapy. When paired with a topical retinoid, its effectiveness is increased [15].

e. Metronidazole gel:

Acne that is mild in severity can be treated with metronidazole gel (2 percent), which is effective, safe,

and well-tolerated. The anti-inflammatory, immunosuppressive, and antibacterial effects may all contribute to its mechanism of action [16].

1. Systemic treatment:

However, not every acne can be treated with over-the-counter creams. Acne that persists or is severe typically requires oral drugs to manage [1].

a. Antibiotics:

For many years, systemic antibiotics have been the gold standard in treating acne. They work well in tandem with a topical retinoid and BP for patients with moderate to severe inflammatory acne [17]. In patients with moderate to severe inflammatory acne, tetracycline therapies are regarded first-line therapy unless contraindicated by factors such as pregnancy, age 8 years, or a proven allergy [18].

If you suffer from acne but are unable to take doxycycline, you may have success with oral azithromycin pulse treatment instead. Excellent patient compliance and few adverse effects make azithromycin 500 mg three times weekly for 12 weeks a safe and effective treatment for acne vulgaris [18].

b. Isotretinoin:

The vitamin A derivative isotretinoin is thought to intervene in acne at every stage of its development. Isotretinoin reduces sebum production and stimulates comedolysis by directly inhibiting the function of sebaceous glands. Reduced chemotactic inflammatory modulator release and decreased C. acnes proliferation lead to less redness and swelling of the skin [19].

By binding its metabolites, endogenous retinoic acid receptor (RAR) and retinoid X receptor, 13-cis-retinoic acid exerts its impact (RXR). Next, the retinoid ligand binds to the RAR, RXR heterodimer, which subsequently regulates the transcription of genes involved in anti-inflammatory responses, follicular keratinocyte differentiation, and reduced sebaceous gland activity. Acne scarring and tissue devastation-inducing MMP activation can be reduced thanks to RAR and RXR's ability to inhibit activator protein-1 [20].

Traditional recommendations for isotretinoin dosing range from 0.5 to 1.0 mg/kg per day up to a maximum cumulative dose of 120 to 150 mg/kg. The effectiveness of this regimen is matched by its various side effects, most of which are dose-dependent. For a long time, acne of moderate to severe severity was treated with a low dose of isotretinoin (10-20 mg daily). This is prescribed to make acne therapy more bearable by decreasing dose-dependent adverse effects [21]. Isotretinoin has many dose-dependent side effects, including xerosis, cheilitis, acne flare-ups, dry eyes, headaches, and elevated lipid and hepatic enzyme levels. Isotretinoin has been linked to IBD, depression, and suicidal thoughts, although these hypotheses have not been verified [22]. Dermatologists should routinely check for pregnancy in women of reproductive age since isotretinoin has the potential to cause birth defects. It's advised that people using isotretinoin keep a close eye out for any adverse reactions or toxicities it may cause [9].

Antihistamine plus isotretinoin:

Inflammatory indicators, irritation caused by Propionibacterium acne, squalene and sebum levels in sebocytes, anxiety, hormonal imbalance, and scarring caused by mast cells are all reduced by antihistamine treatment. When paired with the azithromycin and isotretinoin treatment, oral desloratadine has been shown to considerably improve severe acne lesions while also reducing their associated side effects [23].

c. Inhibitors Of Ovarian Androgen Production:

By preventing the pituitary gland's cyclical release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), a class of drugs known as gonadotropin-releasing hormone (GnRH) analogues reduces ovarian androgen production [24].

Combined oral contraceptive pills (COCs):

High doses of estrogens are the only ones that have been shown to be sebosuppressive (lower sebum production). Most modern COCs, however, contain lower levels of estrogens (20-50 g), which are not sebosuppressive but can block androgens via numerous routes:

- Reduce androgen production by the ovaries by preventing ovulation and pituitary gonadotropin secretion.
- Prevent androgen receptors from working.
- Suppressing testosterone levels in the blood via increasing sex hormone binding globulin (SHBG) synthesis in the liver.
- The COCs' progestins inhibit the enzyme 5-reductase, preventing the production of strong androgens [25].

There are currently three different forms of oral contraceptives available: those that include both oestrogen and progesterone, those that contain solely progesterone, and the continuous or extended use pill. The FDA has legally authorised certain brands of combination acne tablets for use. Hormonal contraception not only improves the cosmetic condition, but also decreases the risks associated with hyperandrogenemia in cases of hormonal disorders [26]. The usage of the combined oral contraceptive (drospirenone + ethinylestradiol) significantly reduced TLR-2 expression in the skin of adult females with facial acne. Modulation of this receptor may account for the anti-inflammatory impact of oral contraceptives in adult female acne (AFA) [27].

d. Inhibitors of Adrenal Androgen Production Glucocorticoids:

In situations of late congenital adrenal hyperplasia and acute inflammatory lesions in adult female acne, prednisone (2.5 or 5 mg) and comparable corticosteroids are suitable for the short-term therapy of very severe acne (AFA) [28].

Acne fulminans-like eruptions can be avoided when first starting isotretinoin, and it is also advised for

people with adrenal hyperandrogenism and severe nodulocystic acne during pregnancy (after the first trimester). Injections of triamcinolone intralesionally reduce the inflammation and pain caused by nodulocystic acne [19].

e. Androgen Receptor (AR) Blockers:

Spironolactone (an aldosterone receptor antagonist) has been shown to be useful in a number of studies for treating acne [29].

Spironolactone:

By preventing androgen-induced sebocyte growth and preventing dihydrotestosterone from binding to the androgen receptor in sebocytes, one can reduce sebum production. Although improbable at therapeutic levels, spironolactone's systemic effects on adrenal production of androgen precursors may also contribute to clinical efficacy. Spironolactone's diuretic effect may help ladies whose premenstrual acne flare is accompanied by fluid retention. There is a low risk of hyperkalemia and other short-term adverse effects, making this an attractive second-line treatment choice for acne in adults [30].

3. Chemical peeling:

Acne may be alleviated by chemical peels because they weaken keratinocyte adhesion and unclog pores. The most often used peeling agents in acne treatment include alpha-hydroxy acids (such as glycolic acid, mandelic acid, etc.), beta-hydroxy acids (such as salicylic acid), and Trichloroacetic acid [31].

4. Mechanical procedures:

Dermabrasion, hyfrecation, comedone extraction, and steroid intralesional injection are all examples of mechanical techniques. Dermabrasion, alone or in conjunction with chemical peels, can improve the appearance of atrophic acne scars in individuals on isotretinoin. Manual extraction of comedones can temporarily enhance the look of the skin, but only around 10% of extractions are successful, and 90% of excised black heads refill over 2-6 weeks, thus monthly treatments are recommended. Individual nodulocystic acne lesions can be reduced with intralesional steroid injection using triamcinolone acetonide if quick resolution is desired. When using this method of treatment, it's important to take precautions to prevent telangiectasias and local skin atrophy [32].

5. Laser and Light-Based Modalities:

Intense pulsed light, narrowband blue light, narrowband red light, combined blue-red light, and lasers are all supported by preliminary study for use in the treatment of acne. Inflammatory acne may respond better to these treatments than non-inflammatory acne does. It is uncertain how effectively they inhibit keratinocyte inflammation, if they kill P. acnes, or whether they trigger the bacterium's native porphyrins [33].

Intensed pulsed light (IPL):

Light with a broad spectrum (400–1200 nm) that is not a laser induces a photodynamic effect in which porphyrins produced by Propionibacterium acne are absorbed by ultraviolet and visible light, which then generates reactive oxygen species with successive bactericidal effects. Inflammatory cytokines including IL-1a, as well as inflammatory infiltration and sebaceous gland size, are reduced, leading to a greater reduction in the percentage of inflammatory lesions than comedones [33].

a. Pulsed-dye lasers (PDL):

The pulsed dye laser (PDL) produces yellow light with a coherent wavelength of 585 to 595 nm. Inflammatory acne lesions are where its benefits really shine. It also aids in the treatment of acne scars by promoting skin remodeling and collagen production. Increased levels of transforming growth factor (TGF)- are associated with anti-inflammatory and neocollagenesis benefits. PDL has a greater photothermal effect than IPL, leading to increased expression of transforming growth factor-b after treatment [34].

b. ND-YAG laser:

Acne treatment with long-pulsed 1064nm neodymium:yttrium-aluminum-garnet (Nd:YAG) laser is effective because it induces sebum reduction by destroying sebaceous glands, modulates inflammation by reducing cytokines like interleukin-8 (associated with epidermal hyperplasia) and Toll-like receptors-2, and stimulates the production of elastin and collagen (activated by Propionibacterium acnes) [35].

CONCLUSION

New therapy approaches and numerous permutations and combinations have been developed as a result of a deeper comprehension of the aetiology of acne. Benzoyl peroxide, antibiotics, retinoids, and other topical medications are the backbone of treatment. They can be administered in any combination. Oral antibiotics, hormone therapy, and isotretinoin are considered examples of systemic options of treatment, although the best option will vary from patient to patient.

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