Review Article

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Acne vulgaris management: what's new and what's still true?

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ABSTRACT

Acne vulgaris is one of the commonest skin disorders that can affect individuals from childhood to adulthood, most often occurring in the teenage years. Regarding its management, what's still true is that a wide range of treatment options are available, ranging from the commonly used topical treatments like benzoyl peroxide, azelaic acid, sulfur, antibiotics, retinoids and superficial chemical peels while the systemic treatments available include the use of systemic antibiotics, retinoids, and antiandrogens. What's new in the management of acne vulgaris is the use of laser and light devices and other newer technologies. The present article reviews the use of above mentioned agents in the current scenario.

Keywords: Acne, Pimples, Tretinoin, Benzoyl peroxide, Antibiotics, Retinoids

INTRODUCTION

Acne vulgaris is the most common disorder of human skin that affects up to 80% of adolescents. Acne by definition is multifactorial chronic inflammatory disease of pilosebaceous unit. 2

Various clinical presentations include seborrhea, comedones, erythematous papules and pustules, less frequently nodules, deep pustules or pseudocysts and ultimate scarring in few of them. Acne has a negative effect on the quality of life; although this can be improved with effective treatment.³

Acne has four main pathogenic mechanisms: increased sebum production, hyperkeratinization, propionibacterium acne colononization and the inflammatory reaction.⁴ Therapeutic modalities are designed now due to better understanding of the pathogenesis of acne (Figure 1).⁵

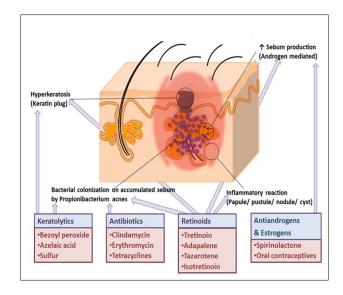


Figure 1: Pathogenesis of acne vulgaris and mechanism of action of drugs used in this condition.

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The present review article discusses what's still true in the successful management of acne vulgaris is the use of keratolytics (including sulfur used since Egyptian times), antibiotics, retinoids and antiandrogens. What's new in the management of acne vulgaris is the new forms of treatment with lasers, lights and vaccines.

SULFUR

Sulfur has been used for acne since the time of Cleopatra. It is available in washes, leave-on lotions, creams, foam formulations and as masks. It is useful as a drying and antibacterial agent. Sulfur could be more useful in patients also having acne rosacea and seborrheic dermatitis. Sodium sulfacetamide is often combined with sulfur and has anti-inflammatory properties.

BENZOYL PEROXIDE

Benzoyl peroxide has long been the main agent in the treatment of acne. It is one of the most effective and widely used drug, present in many over-the-counter preparations; as a wash (soap or face wash) or leave-on product (gel or cream). Benzoyl peroxide acts because of its comedolytic (keratolytic) as well as antibacterial properties. Adding a topical antibiotic like clindamycin or erythromycin could add to its efficacy, as in many cases monotherapy is often less successful. Benzoyl peroxide could also be an effective addition to the oral antibiotics, as it is shown to reduce the number of antibiotic resistant organisms. In treatment of mild acne vulgaris, generally benzoyl peroxide along with topical antibiotic or a retinoid is recommended. For moderate cases of acne, however, an oral antibiotic is to be added.

Common side effects of benzoyl peroxide include contact sensitivity, irritation, excessive dryness, scaling, erythema and bleaching of skin. One should avoid contact with eyes, lips, mucous membranes and denuded skin.

AZELAIC ACID

Azelaic acid is useful in the treatment of acne as well as in post-inflammatory pigment changes. Patients often report local burning or stinging sensation but it generally resolves in one to four weeks. Azelaic acid is applied once or twice a day and has been shown to be effective especially in combination with benzoyl peroxide, tretinoin, erythromycin and clindamycin.⁹

TOPICAL ANTIBIOTICS

Clindamycin, erythromycin and tetracyclines are appropriate for inflamed papules rather than non-inflamed comedones. These agents inhibit propionibacterium acne by inhibiting their protein synthesis. These antibiotics may be lesser effective than benzoyl peroxide but have the advantage of not causing skin irritation. Antibiotics may also be combined with

benzoyl peroxide for better response, especially for tackling resistant bacteria. Choosing a formulation depends on the skin type of the individual such as gels are better suited for oily skin and ointments are better suited for drier skin. Nadifloxacin is a newer topical quinolone broad spectrum antibiotic which has exerted therapeutic benefit in inflamed acne and folliculitis.

SYSTEMIC ANTIBIOTICS

Tetracyclines (doxycycline and minocycline) and erythromycin have been used orally for treating moderate to severe acne, though other antibiotics e.g. cephalexin, azithromycin, trimethoprim/sulfamthoxazole could also be effective. The widespread and long term use of antibiotics has unfortunately led to serious auto-immune reactions and the emergence of resistant bacteria. Long term therapy with oral antibiotic is not only a threat to resistance of propionibacterium acne, but also to coagulase negative staphylococci on the skin and streptococci in the oral cavity, and upper respiratory tract infections. ¹³

Doxycycline is prescribed generally 100 mg daily but recently a sub-MIC (minimal inhibitory concentration) dose of 20 mg twice a day has been tried. Standard treatment for moderate acne consisted of doxycycline 100 mg, clindamycin 1% and adapalence 0.1%, as the initial therapy.

TOPICAL RETINOIDS

The topical retinoids used in the treatment of acne include tretinoin, adapalene, and tazarotene. They act by their keratolytic (comedolytic), antibacterial and anti-inflammatory properties. Because of their multiple mechanisms, retinoids are considered important in long term maintenance therapy of acne. The main side-effect is irritation, which is lesser with adapalene among the three.⁶ Pharmaceuticals are making different topical formulations to decrease the irritation and therefore increasing compliance. ^{15,16} With topical retinoids, besides local irritation, there is concern about systemic adverse effects like intracranial hypertension ¹⁷ and teratogenicity.

The combination of adapalene with oral or topical antibiotics has been shown to release a faster response than an antibiotic alone. 18 Clinical studies have shown some success with a combination of doxycycline and adapalene. 19 There is a significant in-vitro evidence suggesting a possible pathogenetic role for staphylococcus aureus (S. aureus) in acne vulgaris. 20

SYSTEMIC RETINOIDS

The systemic retinoid available is isotretinoin which is used mainly in case of severe acne. It principally acts by reducing sebum production and correcting abnormal keratinization. A twenty week course of 0.5-1 mg/kg daily brings about remission in most cases of

nodulocystic acne. Side effects are frequent-cheilitis, dryness of skin, eyes, nose and mouth, epistaxis, pruritus, conjunctivitis, paronychia, rise in serum lipids, increased intracranial tension and musculoskeletal symptoms. Depression and suicidal tendencies have been reported but a causal relationship has not been established. ²¹

Isotretinoin is highly teratogenic; upto 25% exposed fetuses had birth defects- craniofacial, heart and CNS abnormalities.²² It is contraindicated in women likely to become pregnant during therapy and one month after. Its half-life is 18 hours and is not accumulated like other retinoids used in psoroiasis.

ANTIANDROGENS AND ESTROGENS

Use of hormones in the treatment of acne came to the forefront in the early 1990s. In the United States there are three oral contraceptive pills approved for the treatment of acne in women. These include ethinyl estradiol and norgestimate, norethindrone acetate and ethinyl estradiol and ethinyl estradiol/drosperinone. In some countries, cyproterone acetate is also used for the treatment of acne. Although using hormones would help many patients with acne, it is important to look for endocrinopathies such as polycystic ovarian syndrome (PCOS). For patients with PCOS and acne, the ethinylestradiol/drosperinone combination pill can help with both conditions. ²³

As an antiandrogen, spironolactone has produced good results in the patient who has menstrual acne flares and deep cystic acne. Spironolactone should not be given to those who have renal insufficiency. Since this drug is potassium retaining, it should never be prescribed concurrently with other potassium retaining drugs like ACE inhibitors and nonsteroidal anti-inflammatory drugs. Also, it should not be prescribed in pregnancy. Dosage ranges for spironolactone are 50-200 mg daily starting usually at 50-100 mg a day.

CHEMICAL PEELING OF THE SKIN

Superficial chemical peeling has long been used in the treatment of acne. Superficial peels generally treat the epidermis. The chemical solution used during a superficial peel damages the outermost lavers of the epidermis, which causes them to peel away. The peelings are usually performed using Alpha-Hydroxy Acids (AHA), and in some instances Beta-Hydroxy Acids (BHA). Alpha-hydroxy acids are naturally occurring acids which include glycolic acid, lactic acid, and fruit acids, while beta-hydroxy acids include salicylic acid.²⁵ Although the concentration of acid may vary depending on the extent of treatment, the acids used to perform superficial peels are not as harsh as other chemical peels. In fact, low concentrations of AHA are often mixed with facial creams or washes that can be used as part of a daily facial care routine to maintain a youthful appearance. The chemical peels are useful for post-acne pigmentation and scars.²⁶ Although, both alpha-hydroxy (30% glycolic

acid) and beta-hydroxy (30% salicylic acid) peels were found to be equally effective, there were more adverse effects after the initial treatment with glycolic acid peel. (Kessler E, Flanagan K, Chia C, et al. comparison of alpha- and beta-hydroxy acid chemical peels in the treatment of mild to moderately severe facial acne vulgaris. Dermatol Surg. 2008;34:45-50.) Different chemical peeling regimens have their own pros and cons.²⁷

LASER AND LIGHT DEVICES

There are two main mechanisms that laser/light treatments may help acne. Firstly, by destroying propionibacterium acnes through photodynamic therapy reaction. Secondly, by destroying the sebaceous glands/entire pilosebaceous unit.

These therapies work best when combined with traditional therapies. Photodynamic therapy is the treatment of skin with aminolevulinic acid followed by photo activation of the compound. It has been shown to help treat acne. Rarely photodynamic therapy has been associated with a painful pustular reaction, though most patients tolerate it well. Red and blue light therapy is also used to treat acne, with the most recent advances being portable handy devices that allow the patient to deliver the light therapy at home. ^{29,30}

There have been many studies showing early promise, with improvements in the 50-75% range. However, it is difficult to decide where lasers/lights will eventually fit in the overall management of acne as very few comparative studies have been made with conventional medical treatment.

VACCINES

The vaccines are targeted against the P. acnes bacteria.³¹ Since acne is a multifactorial disease, therefore targeting one area may not result in eradication of the condition. However, P. acnes is involved in diseases other than acne including infectious conditions such as endocarditis, endophthalmitis, osteomyelitis and post-surgery infections, and this has lead researchers to develop vaccines.

CONCLUSION

Acne vulgaris, one of the commonest disorder of skin, has four main pathogenic mechanisms: increased sebum production, hyperkeratinization, propionibacterium acne colononization and the inflammatory reaction. What's still true for the successful management of acne vulgaris is the use of keratolytics, antibiotics, retinoids and antiandrogens. What's new in the management of acne vulgaris is the new forms of treatment with lasers, lights and vaccines. As the pathology of acne is multifactorial, a combination of drugs gives a better response. For example, in mild acne vulgaris, benzoyl peroxide along

with topical antibiotic like clindamycin or a retinoid like adapalene is recommended, whereas, for moderate cases of acne, an oral antibiotic like doxycycline is to be added. In severe cases of acne, consider adding oral isotretinoin. Successful management of acne needs careful selection of anti-acne agents according to clinical presentation and individual patient needs.

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