JAMA Clinical Guidelines Synopsis

Management of Acne Vulgaris

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GUIDELINE TITLE Guidelines of Care for the Management of Acne Vulgaris

DEVELOPER American Academy of Dermatology (AAD)

RELEASE DATE February 12, 2016

PRIOR VERSION 2007

FUNDING SOURCE AAD

TARGET POPULATIONS Adolescent and adult patients with a diagnosis of acne vulgaris (acne)

MAJOR RECOMMENDATIONS

- Topical retinoids, the fundamental component of topical acne therapy, are recommended as monotherapy for comedonal acne or in combination with topical or oral antimicrobials in patients with mixed or primarily inflammatory acne (level of evidence I).
- Benzoyl peroxide is an effective topical acne treatment (level of evidence I).
- Topical antibiotic therapy (ie, clindamycin or erythromycin) is recommended only in combination with benzoyl peroxide (level of evidence I).
- Systemic antibiotic therapy is recommended for management of moderate and severe inflammatory acne and acne resistant to topical treatments (level of evidence I).
- Systemic antibiotic use should be limited to the shortest possible duration, typically 3 months. Concomitant and ongoing topical therapy with benzoyl peroxide or a topical retinoid is recommended for maintenance (level of evidence I).
- Combined oral contraceptives are effective in treating inflammatory acne in girls and women (level of evidence I).
- Oral isotretinoin is recommended for treatment of severe nodular acne, moderate recalcitrant acne, or acne that produces scarring or psychosocial distress (level of evidence I).

Summary of the Clinical Problem

About 50 million people in the United States have acne.[1] Acne affects 85% of all adolescents and about 12% of adult women.[2,3] Acne is a chronic inflammatory condition presenting as comedones (blackheads and whiteheads), papules, pustules, and nodules. It is caused by androgen-induced sebum production, follicular hyperkeratinization, and colonization of the folliculosebaceous unit by the *Proprionibacterium acnes* bacterium.[4] Follicles become impacted with sebum because of follicular keratinization and then become distended, forming comedones. *Proprionibacterium acnes* growth in the follicle results in cytokine release, causing inflammatory lesions.[5] Although it is a benign condition, acne can have considerable morbidity, including pain and discomfort, permanent scarring, and depression and anxiety resulting in poor self-esteem.[2]

Characteristics of the Guideline Source

The AAD assembled a working group of 17 recognized acne experts, 1 general practitioner, 1 pediatrician, and 1 patient to develop the guideline. The panel conducted a systematic review and developed recommendations from this evidence.[4] In situations for which evidence-based data were not available, inconsistent, or limited, expert opinion was used to generate clinical recommendations. Expert opinion was identified as such within the document, although not in all the tables. The AAD required detailed disclosures of all relevant interests from each work group member. If a potential conflict was noted, the member was recused from participating in the discussion or drafting of that particular topic (Table).

Evidence Base

Clinical trial results strongly support use of anti-inflammatory and comedolytic topical retinoids as the mainstay of acne therapy. Three topical retinoids are available (tretinoin, adapalene, and tazarotene) but no high-quality studies have compared the efficacy of any of these drugs relative to the others.

Benzoyl peroxide use, with or without a topical antibiotic, is also supported by clinical trial outcomes.[4] Benzoyl peroxide is not known to promote development of resistant organisms and is available without a prescription. Use of topical antibiotic therapy is also supported by data from randomized clinical trials (RCTs). Topical antibiotics are not recommended as monotherapy because of the associated increased incidence of bacterial resistance. The guideline describes the evidence regarding other topical agents

Table. Guideline Rating

Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Fair
Guideline development group composition	Fair
Clinical practice guideline–systematic review intersection	Good
Establishing evidence foundations and rating strength for each of the guideline recommendations	Good
Articulation of recommendations	Good
External review	Fair
Updating	Good
Implementation issues	Good

(azelaic acid, dapsone, salicylic acid, sulfur, nicotinamide, resorcinol, sodium sulfacetamide, aluminum chloride, and zinc) marketed by prescription or over the counter for acne as nonexistent or, at best, mildly (azelaic acid 20% cream) to moderately (dapsone 5% gel) effective.

The guideline recommends oral antibiotic therapy for moderate and severe acne and acne that does not respond to topical treatment. The strongest evidence supports use of tetracyclines and macrolides. Doxycycline and minocycline are preferred based on efficacy trials, a few comparison trials, and their notable anti-inflammatory effects (inhibition of chemotaxis and metalloproteinase activity), but neither agent is considered better.[6] To minimize risk of bacterial resistance and adverse reactions, the guideline suggests that systemic antibiotics be used for the shortest effective duration. A treatment course of 3 months is recommended, but data comparing longer or shorter courses are not available.

The guideline cites several RCTs and a 2012 Cochrane review of 31 trials involving more than 12 000 patients demonstrating the effectiveness of estrogen and progestin combined oral contraceptives for acne management.[7] These drugs are recommended for treatment of inflammatory acne in women and girls with or without signs of hyperandrogenism. No single combined oral contraceptive has been shown to be better than any other for treating acne. Four combined oral contraceptives have been approved by the US Food and Drug Administration (FDA) for treatment of acne in girls and women aged 14 years or older. The evidence does not support the use of other antiandrogen therapies, such as spironolactone and flutamide, in patients with acne.

The guideline supports oral isotretinoin as therapy for severe or recalcitrant acne or management of acne that produces permanent scarring. Isotretinoin decreases sebum production and development of new acne lesions and acne scarring. Prevention of acne relapse is best achieved with a cumulative dose of 120 to 150 mg/kg of isotretinoin.

Benefits and Harms

The benefits of treating acne include reducing discomfort, psychological morbidity, and scarring. The clinical response to therapy usually occurs within 8 to 12 weeks after initiating treatment. All topical acne treatments can result in skin irritation and dryness that may compromise adherence. Retinoids may cause skin dryness, erythema, irritation, and peeling, which can be minimized by decreasing the application frequency from daily to every other or every third day. Benzoyl peroxide can cause concentration-dependent irritation, contact dermatitis, and bleaching of fabrics. Topical antibiotic therapy can cause pruritus, erythema, and peeling.

Severe adverse reactions to systemic antibiotics used for treating acne are rare. Doxycycline may cause photosensitivity and gastrointestinal disturbances, while minocycline may cause tinnitus, dizziness, and pigment deposit in the skin, mucous membranes, and teeth. In addition to improving acne, oral contraceptives can lessen menorrhagia and dysmenorrhea and reduce the formation of benign ovarian tumors. Estrogen-containing contraceptives are associated with a small increase in hypercoagulability and may have effects on cancer risk, both positive and negative (protective effect against ovarian, colorectal, and endometrial cancers and possible increased risk of breast and ovarian cancers).

Isotretinoin use is associated with mucocutaneous and ophthalmic dryness and occasional musculoskeletal pain. Elevations of serum cholesterol, triglycerides, and transaminases are occasionally observed; thus, monitoring at baseline and during therapy is recommended. Despite concerns, a causative relationship between isotretinoin use and inflammatory bowel disease or psychiatric disease (depression, anxiety, mood changes, or suicidal ideation) has not been shown. Isotretinoin is a teratogen causing embryopathy affecting the central nervous system, craniofacial, and cardiac structures. A risk management program, iPLEDGE, is used to prevent isotretinoin exposure during pregnancy. The FDA requires that patients and prescribers enroll in and adhere to iPLEDGE requirements while isotretinoin is administered.

Discussion

Successful acne management depends on accurately assessing acne morphology and severity and developing an appropriate treatment regimen. Topical therapy must be used continuously to maintain a satisfactory clinical response. Numerous topical vehicles are available; formulation choice can affect efficacy, tolerance, and adherence. For acne resistant to topical management alone, combined oral contraceptives, isotretinoin, and systemic antibiotics should be considered. Systemic antibiotics should be used for the shortest duration needed to achieve disease control. Effective acne treatment can improve associated depression, anxiety, and poor self-image. Adherence to complicated or time-intensive regimens can be challenging.

Areas in Need of Future Study or Ongoing Research

The efficacy of other therapies such as chemical peels, light therapy, and laser therapy have not been shown effective. There is limited evidence supporting the idea that a high glycemic index diet supplemented with dairy products, particularly skim milk, may influence or be associated with acne. At this time, no specific dietary changes are recommended for acne management.[4]

ARTICLE INFORMATION

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Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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