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Editorial
Use of antibiotics in acne vulgaris

Zahida Rani

Dermatology Department, Unit II, King Edward Medical University/Mayo Hospital, Lahore

Acne vulgaris is one of the most frequent disorders encountered in dermatology practice. Although the disease affects teenagers, prepubertal onset is not uncommon and many patients present with acne in their thirties. The devastating psychosocial impact of disease especially in teenagers outweighs its physical disability.[1] This necessitates an early and effective treatment.

Although the pathogenesis of acne vulgaris is multifactorial, *Propionibacterium acnes* is believed to play a major role in the formation of inflammatory lesions of acne and possibly comedogenesis.[2] *P. acnes* triggers innate immune response and the inflammatory reaction involving inflammatory cells such as monocytes, macrophages, neutrophils, dendritic cells, and keratinocytes. As evidenced by clinical data, suppressing *P. acnes* with antimicrobial therapy is an important aspect of the management plan in moderate to severe acne vulgaris. Some antibiotics e.g. tetracyclines exhibit anti-inflammatory effects besides their antibiotic properties, which adds to their therapeutic benefit in acne vulgaris.[3]

The primary indication for oral antibiotic therapy in acne vulgaris is moderate to severe inflammatory involvement on the face or trunk.

Address for correspondence
Dr. Zahida Rani,
Assistant Professor,
Department of Dermatology, Unit II,
King Edward Medical University/Mayo Hospital, Lahore
Email: zahidaraffad@yahoo.com

A serious problem with the extended use of oral antibiotic therapy is emergence of strains of *P. acnes* less sensitive/resistant to oral antibiotics e.g. tetracyclines and erythromycin.[4] To overcome this rising problem, various researchers recommend optimal use of oral antibiotics for treating acne vulgaris.[5] Such recommendations include limiting the duration of therapy, using combination therapy regimens with a topical agent from the outset, avoiding unnecessary switching of oral antibiotics, and adding a benzoyl peroxide-containing formulation to reduce emergence of antibiotic-resistant *P. acnes* strains. Adverse drug reactions and interactions associated with specific oral antibiotics are also another important aspect.

Among the conventionally prescribed oral antibiotics for acne vulgaris, the greatest reduction in *P. acnes* has been documented with minocycline, followed in order by doxycycline, tetracycline, and erythromycin. Alternative oral antibiotics useful in the treatment of acne vulgaris are trimethoprim/sulfamethoxazole, trimethoprim alone, azithromycin, clarithromycin, cephalosporins and fluoroquinolones.[6] Many trials reported the efficacy of azithromycin in acne vulgaris; however, considering the utility of azithromycin and other antibiotics in many other systemic infections, these antibiotics should be reserved for short-term use in selected refractory cases of acne to avoid the risk of development of resistant organisms.[5]

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Antibiotic monotherapy should be avoided because of promotion of antibiotic resistance.[5] Oral antibiotic therapy is best used in combination with a topical regimen that includes a benzoyl peroxide (BPO)-containing formulation and a topical retinoid.[7,8] BPO itself is effective in reducing inflammatory acne lesions and moderately reduces noninflammatory acne lesions. It also suppresses preexisting *P. acnes* organisms resistant to multiple antibiotics, including erythromycin, tetracycline, doxycycline, and minocycline and reduces the emergence of antibiotic-resistant strains of *P. acnes* and It may be beneficial to initiate BPO use for 2 to 3 weeks before starting oral antibiotic therapy. A ''leave on'' formulation of BPO (i.e. gel, cream), with or without topical clindamycin, is optimal for facial use. Alternatively, a quality BPO cleanser or wash may be used, especially for truncal skin, in patients less tolerant to ''leave on'' BPO or those who show poor compliance with application of multiple ''leave on'' products.[5,8]

It is suggested that oral antibiotic therapy for acne vulgaris be administered over a minimum of 6 to 8 weeks and over a maximum of 12 weeks to 6 months.[8] At 6 to 8 weeks after therapy, if there is no improvement in spite of an adequate compliance, oral antibiotic therapy may be changed. However, if partial improvement is observed, the current regimen be continued for another 6 to 8 weeks and then reevaluated. Once reasonable control of acne i.e. no new lesion or a marked decrease in inflammatory lesions, is observed, oral antibiotic therapy should be discontinued while the topical regimen be continued for another 3 to 6 months. No consensus exists on whether oral antibiotic therapy should be discontinued abruptly or tapered.[8]

Overall, the long-term use of oral antibiotic therapy in acne vulgaris is not generally recommended.[3] Individual patients may experience marked flares after discontinuing oral antibiotic therapy, despite the use of a rational topical maintenance program. In such cases, the previously effective oral antibiotic be continued in combination with the topical regimen to sustain acceptable remission. Alternatively, subantimicrobial therapy with doxycycline i.e. 50mg/day, shown to exhibit anti-inflammatory activity without antibiotic effects, may be a ''step down'' option after discontinuing oral antibiotic therapy.[3]

Another recommendation suggests that concomitant use of oral and topical antibiotics that are chemically different be avoided because of risk of development of multidrug-resistant bacterial strains.[9] Instead, concomitant use of BPO would also reduce emergence of *P. acnes* resistance.

Oral antibiotics used for treating acne vulgaris may be associated with a plethora of side effects which may range from mild gastrointestinal upset to life threatening Stevens-Johnson syndrome, toxic epidermal necrolysis and drug hypersensitivity syndrome.[5] Consideration of potential adverse reactions may also influence oral antibiotic selection. Hence, before prescribing an oral antibiotic, a complete medical history is mandatory with special reference to history of hepatitis or renal insufficiency, which may necessitate avoidance of specific antibiotics because of relative contraindications or potential side effects. Similarly, trimethoprim/sulfamethoxazole should be avoided in patients having folate deficiency or megaloblastic anemia. A complete drug history, including prescription and over-the-counter medications, is also important to assess any food-drug or drug-drug interactions, which may lead to a poor therapeutic response

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or side effects, respectively.

To reduce the risk of gastrointestinal upset, erythromycin, doxycycline and minocycline are administered with food; however, concomitant use of iron supplements may decrease gastrointestinal absorption of doxycycline and minocycline. Reduced gastrointestinal absorption of the antibiotic may cause a diminished therapeutic response. In contrast, absorption of tetracycline and azithromycin may be reduced and delayed with food. Concomitant ingestion of metal ions, such as calcium, magnesium, and aluminum found in many vitamin-mineral supplements and antacids, may also significantly reduce gastrointestinal absorption of tetracycline. To avoid gastrointestinal upset and esophagitis, erythromycin and doxycycline, should be ingested when the patient is upright for at least a few hours, and not before anticipated reclining, such as before bedtime. An enteric-coated formulation of doxycycline reduces the potential for gastrointestinal upset and allows for once daily administration.

Erythromycin may inhibit hepatic enzymes involved in the metabolism of other drugs, such as carbamazepine, cyclosporine, and some cholesterol lowering agents, such as lovastatin, simvastatin, and atorvastatin.[3] As a result, toxicity may result from significant elevations in serum level of the inhibited drug. Similarly, trimethoprim/sulfamethoxazole should not be prescribed for patients on methotrexate because of an increased risk for serious hematologic reactions.

Patients should be followed-up at 6 to 8 weeks for response to treatment, compliance, patient feedback on ease of use and degree of satisfaction, tolerability and potential adverse effects, and determine whether to continue the current regimen or make changes. Unless a definite poor response, adverse reactions, or major compliance issues are noted, the treatment regimen should not be changed. Prolonged intervals in follow-up and interaction frequently lead to decreased patient compliance. Patients should be informed to discontinue oral antibiotic therapy and report if they develop a skin eruption or flu-like symptoms, such as fever, malaise, and sore throat. Baseline or periodic laboratory testing is generally not recommended with oral antibiotics for acne vulgaris; however, complete blood counts be performed at baseline and periodically if trimethoprim/sulfamethoxazole is used.

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