IAA Consensus Document

Oral antibiotics

There is more experience and data for antibiotics in acne than any other therapy.[1] Antibiotics target *P. acnes* and inflammation.[1] They reduce the number of *P. acnes* and *Staphylococcus epidermidis*.[1] The anti-inflammatory effect is manifested through inhibition of neutrophil chemotaxis, cytokine production, and macrophage function. [1] They are usually used in low dosage and for prolonged periods. They are indicated in moderate to severe inflammatory acne.[1] They are best used in combination with topical retinoids and BPO.[1] Over the years practice patterns have changed owing to emergence of resistant *P. acnes*,[2,3] and resistant Streptococcus pyogenes in the upper respiratory tract. [4,5] Global Alliance recommends that oral antibiotics be used till inflammatory lesions cease to erupt and existing lesions resolve. [1] Ideally they should be used for 12 weeks or under.

The preferred antibiotics are minocycline, doxycycline, and lymecycline. Lymecycline is not available in India. Oral antibiotic options for our country are listed in table 10. The recommended initial dosage for both minocycline and doxycycline is 50–100 mg b.i.d. A sustained release formulation of minocycline is now available in India that permits o.d. dosing. Suboptimal antimicrobial dosage (20 mg b.i.d.) of doxycycline has been reported to be effective in acne. [6] This concept is yet to gain currency. Minocycline being lipophilic achieves greater tissue concentration, and is thought to be more effective than doxycycline in acne. That is the view held by the Global Alliance. However, many acne experts, including some in the IAA, dispute this claim and assert that the two antibiotics are equal in efficacy. Market data from Europe and USA favor popularity of minocycline. In India, perhaps because of cost difference, doxycycline is more prescribed by the dermatologists. Minocycline is best given empty stomach when the absorption is 90–100% of the administered dose. [7] When administered with food, especially dairy products, the absorption decreases by about 20%. [7] Oral minocycline has the lowest risk for bacterial resistance over time. [8] Most tetracycline resistant bacteria are sensitive to minocycline at the dose of 100 mg b.i.d.[8] Doxycycline and minocycline are equally effective provided *P. acnes* are not resistant to doxycycline.[8]

The adverse effect profile of doxycycline and minocycline is also comparable with the exception of a few unique differences. Minocycline produces a blue-black pigmentation in a dose-dependent manner, which in its severe form is generalized with involvement of the mucosae, sclerae, and nails, and with a predilection for sun-exposed areas, scars (acne and nonacne), and active inflammatory acne lesions in the mild form. [9] Minocycline pigmentation represents dermal deposition of melanin-drug complexes, which takes months to clear after cessation of therapy. [9] Doxycycline causes photosensitivity, also in a dose-dependent manner. [9] Long-term minocycline treatment (over two years) has been associated with more serious adverse effects such as autoimmune hepatitis, drug-induced lupus, serum-sickness like reactions, and ANCA positivity. [8,10]

Some dermatologists regard older tetracyclines (TCN)

Table 10: Oral antibiotics for acne vulgaris

Drugs	Usual daily dosage (mg)	Comments/side effects
Tetracycline	250–500	Dental staining <9 years, dairy products decrease absorption, GI upset, photosensitivity, teratogenic, vulvovaginal candidosis
Minocycline	100–200	Dental staining <9 years, GI upset, blue-gray skin pigmentation, drug/lupus-like reactions, hepatitis, teratogenic
Doxycycline	100–200	Dental staining <9 years, photosensitivity, teratogenic
Erythromycin	250–500	GI upset
Trimethoprim/ Sulfamethoxazole	80/400	Severe drug reactions, bone marrow suppression, hepatitis, GI upset
	160/800	
Clindamycin	75–150	*Pseudomembranous colitis*, GI upset, drug reactions
Azithromycin	250–500	GI upset, drug reactions
Roxithromycin	150–300	GI upset
Clarithromycin	250–500	*Pseudomembranous colitis*, GI upset

as more effective and continue to use them, especially in high doses in nodulocystic acne. The preferred TCN is oxytetracycline, and it is used in a dose of 500 mg q.i.d. for 2–3 weeks, tapering to 500 mg o.d., and continuing for 12–24 weeks according to clinical response. Tetracycline achieves high concentration in sebaceous follicles, especially in the presence of inflammation.[8] The absorption of oxytetracycline is affected by certain foods (dairy products) and medications (antacids containing aluminum, calcium, and magnesium, and iron preparations). Common drug interactions are with oral contraceptives, and anticoagulants. All tetracyclines, including doxycycline and minocycline, are best avoided in pregnancy, during lactation, and in children below 12 years of age, as they cause dental staining, hypoplasia of the enamel, and bone abnormalities. Older drugs like erythromycin and trimethoprim-sulfamethoxazole are no longer used because of poor performance (bacterial resistance in case of erythromycin), and undesirable side effects. Macrolides, however, are safe in pregnancy.

Azithromycin is the newest oral antibiotic in the treatment of acne. It has the advantage of better absorption, convenient dosing, less drug resistance, and cost-effectiveness. Its main appeal is in pulse dosing of which there are several variations – 250 mg b.i.d. or 500 mg o.d. for 3, 4, 5, or 6 days per month, or 500 mg od for 4 days every 15 days (twice monthly). Comparative clinical studies have shown efficacy similar to daily doxycycline.[11,12]

ORAL ANTIBIOTICS

- Target *P. acnes* and inflammation.
- Used in low dosage for prolonged periods.
- Indicated in moderate to severe acne.
- Best used in combination with benzoyl peroxide and topical retinoids.
- Are continued till inflammatory lesions cease to erupt.

In summary, oral antibiotics are no longer the mainstay of acne treatment, but retain an important place in combination treatment of moderate to severe acne. The new thinking[1] is to use them for shorter duration, intermittently if required, linked to occurrence of inflammatory lesions, and where topical antibiotics are required to combine them with same or similar antibiotics. Oral antibiotics can be advantageously combined with oral isotretinoin but the risk of intracranial hypertension (pseudotumor cerebri) increases with tetracyclines, and the contraceptive properties may be compromised when combined with oral antiandrogens (Diane 35).

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