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Q/Which oral antibiotics are best for acne?

EVIDENCE-BASED ANSWER

A/DOXYCYCLINE IS EFFECTIVE (strength of recommendation [SOR]: **B**, randomized controlled trial) and the antibiotic of choice (SOR: **C**, expert opinion) for moderate to severe inflammatory acne requiring oral treatment. Limiting side effects include photosensitivity and gastrointestinal (GI) disturbance.

Other members of the tetracycline family are considered second-line agents because of their side-effect profile and are contraindicated in pregnancy and for children younger than 12 years (SOR: **A**, meta-analysis, and **C**, expert opin-

ion). For these patients, erythromycin is effective and better studied than azithromycin (SOR: **C**, expert opinion). Otherwise, emerging resistance and GI disturbances make erythromycin a third-line treatment.

The use of oral antibiotics should be limited to moderate to severe inflammatory acne unresponsive to topical therapies, including retinoids and antibiotics (SOR: **C**, expert opinion). Oral antibiotics should be used for at least 6 to 8 weeks and discontinued after 12 to 18 weeks of therapy (SOR: **C**, expert opinion).

Evidence summary

Acne vulgaris is an extremely common disorder affecting up to 95% of adolescents.¹ Doxycycline improves inflammatory lesions and has a tolerable side-effect profile.

Doxycycline:

Fewer lesions, few side effects

A 2003 randomized, double-blind, controlled trial of 51 patients demonstrated that a sub-antimicrobial dose of doxycycline (20 mg orally twice a day) reduced comedonal lesions by 53.2% (from 31 to 16; $P=.04$) and inflammatory lesions by 50.1% (from 55 to 25; $P<.01$), whereas placebo decreased comedonal lesions by 10.6% (from 51 to 46; $P=.4$) and inflammatory lesions by 30.2% (from 27 to 19; $P<.01$).²

The most commonly reported adverse effects of doxycycline are GI disturbance and sensitivity to ultraviolet radiation (sunlight). A recent systematic review found an adverse event rate of 13 per 1 million prescriptions written.³

Minocycline: Probably effective, but not the first choice

A 2003 Cochrane review examined 27 randomized trials that compared oral minocycline with placebo or other active treatments, including topical and systemic antibiotics, in a total of 3031 patients with acne vulgaris on the face or upper trunk.⁴ The review determined that minocycline is *probably* an effective treatment for moderate acne vulgaris. However, no reliable evidence from randomized controlled trials (RCTs) justifies its use as a first-line agent, especially given its higher cost relative to other treatments.

Drug resistance weakens macrolides' "punch"

Macrolide antibiotics, primarily erythromycin, were at one time considered first-line treatment for acne, but have fallen out of favor because of emerging drug resistance. Nevertheless, erythromycin's price and safety in pregnant women and young children has

TABLE 1

Estimated cost of oral acne medications

Medication	Dose, formulation, and frequency	Cost of 30-day supply*
Doxycycline hyclate	100 mg capsule daily	\$12.99
Doxycycline hyclate	100 mg tablet daily	\$20.99
Extended-release minocycline	45 mg tablet daily	\$450.97
Minocycline	100 mg capsule twice a day	\$45.98
Minocycline	100 mg tablet twice a day	\$227.98
Erythromycin base	250 mg enteric-coated capsule 4 times a day	\$154.62
Erythromycin base	250 mg tablet 4 times a day	\$114.62
Azithromycin	500 mg tablet daily, 3 days/wk	\$175.20

*<http://www.drugstore.com>. Accessed April 10, 2011.

TABLE 2

Safety and adverse-effect profiles of acne medications⁸

Medication	Adverse effects	Pregnancy category	Lactation safety	Appropriate age range
Doxycycline hyclate	Photosensitivity, GI disturbance, elevated BUN	D	Avoid	>12 y
Minocycline	Tooth discoloration, dizziness, hypersensitivity syndrome	D	Avoid; milk effects possible	>12 y
Erythromycin base	GI disturbance, nausea	B	Safe	FDA-approved for children
Azithromycin	Abdominal pain, GI disturbance	B	Minimal risk	Extended-release formula not FDA-approved for children

BUN, blood urea nitrogen; GI, gastrointestinal.

maintained its standing in acne therapy. A 1986 RCT that compared erythromycin with tetracycline found comparable efficacy: a 65% reduction in papules, from 21 to 12 lesions, for erythromycin and a 62% reduction, from 17 to 10 lesions, for tetracycline ($P<.0001$).⁵ The main side effect of macrolide antibiotics is GI disturbance.

A 2006 RCT randomized 290 patients to the macrolide azithromycin (500 mg daily for 3 consecutive days a week in the first month,

then 250 mg every other day for 2 months) or tetracycline (1 g daily for 1 month, then 500 mg daily for 2 months). The drugs produced comparable results: an 84.7% improvement with azithromycin and a 79.7% improvement with tetracycline ($P<.05$).⁶ Compared with other macrolides and tetracycline, azithromycin has a more tolerable side-effect profile with fewer GI disturbances.

Lack of sufficient data on trimethoprim ± sulfamethoxazole, fluoroquinolones, and

>
Doxycycline is the antibiotic of choice for moderate to severe inflammatory acne requiring oral treatment.

CLINICAL INQUIRIES

cephalosporins precludes their inclusion in routine acne treatment.

Recommendations

The American Academy of Pediatrics (AAP) recommends topical retinoids as the foundation of treatment for most acne patients, and a topical microbial agent for additional therapy. Oral antibiotics should be reserved for moderate to severe inflammatory acne; tetracyclines are the standard first-line choice in most cases. The AAP warns against giving tetracyclines

to children younger than 10 years because of the risk of permanent discoloration of teeth and abnormal skeletal development.^{7,8}

The American Academy of Dermatology also recommends topical retinoids as first-line therapy for acne followed by oral doxycycline or minocycline if needed. Erythromycin is recommended for patients who can't use tetracyclines, but with a warning about possible bacterial resistance.⁹

TABLE 1 shows the cost of various acne medications. TABLE 2 outlines their safety and risk profiles. **JFP**

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