Does prolonged acne treatment of adolescents with tetracycline or tretinoin have any long-term sequelae?

Evidence-based answer
These agents may be used safely in most patients. Topical tretinoin has minimal systemic absorption and has not been shown to be teratogenic. (SOR: C, extrapolated from a cohort study of adolescents and adults.) Oral tetracycline (but not doxycycline) is associated with a 0.5% incidence of hepatotoxicity. (SOR: C, extrapolated from a mixed-age case-control trial.) Also, tetracycline-class agents cause permanent staining of developing teeth and are contraindicated in pregnant adolescents. (SOR: C, based on case reports and expert opinion.)

Evidence summary
Two studies assessed the systemic absorption of topical tretinoin.1 Twenty-eight male volunteers (ages 19–57 years) applied tretinoin 0.05% cream in a 50-cm² area of the forehead and 1 cheek either as a single dose or as repeated once-daily doses for 28 days. Topical absorption (measured by the sum of urinary and fecal excretion) was approximately 2% after a single dose and 2% after 28 days. The second study, including 3 men and 6 women aged 45–62 years, demonstrated 2% absorption after a single dose and 1.1% after 12 months of once-daily applications.

A retrospective cohort study examined the effects of topical tretinoin exposure in the first trimester of pregnancy.2 Data were collected from Group Health Cooperative of Puget Sound (1976–1991) regarding women (ages 15–44 years) exposed to topical tretinoin (either 4 months before becoming pregnant or during the first 3 months of pregnancy) in the first trimester of pregnancy (n=215) and age-matched, nonexposed women (n=430) who delivered live or stillborn infants at the same hospitals. There was no significant difference in the prevalence of major fetal anomalies for live births among women exposed to tretinoin compared with nonexposed women (1.9% vs 2.6%, respectively; RR 0.7; 95% CI, 0.2–2.3).

In 2004, nearly 900,000 prescriptions for tetracycline and 4.8 million prescriptions for doxycycline were written.3 A retrospective, matched, case-control study (July 1999–December 2001) using California Medicaid claims data aimed to quantify the risk of hepatotoxicity (defined as acute and subacute liver necrosis, hepatic coma, and toxic hepatitis) in subjects taking these agents by comparing subjects (n=3,377; mean age 41.2 years) who had at least 1 diagnosis for hepatotoxicity with controls (n=3,377; mean age 39.7 years). Covariates (hepatotoxic drugs, age, renal dysfunction, pregnancy, illicit drug/alcohol use) were taken into account.

Current and past users of tetracycline had a statistically significant increased risk of hepatotoxicity (incidence with tetracycline <0.5%) compared with controls (current user OR 3.7, 95% CI, 1.2–11; past user OR 2.7, 95% CI, 1.3–5.9). Conversely, those using doxycycline did not have an increased risk of hepatotoxicity (current user OR 1.5, 95% CI, 0.61–3.6; past user OR 1.7, 95% CI, 0.99–3.1).3

Case reports have also documented that tetracyclines cause permanent staining of fetal teeth during the period of tooth development. Experts state that tetracyclines are contraindicated during pregnancy and in children up to 8 years of age.4

Evidence You Can Trust
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