ORIGINAL ARTICLE

The use of oral antibiotics before isotretinoin therapy in patients with acne

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Background: Systemic antibiotics are used widely to treat moderate to severe acne, but increasing antibiotic resistance makes appropriate use a priority.

Objective: We sought to determine the duration of systemic antibiotic use in patients with inflammatory/nodulocystic acne who eventually required isotretinoin.

Methods: We performed a retrospective, single-site chart review of patients with acne diagnostic codes evaluated January 1, 2005 to December 31, 2014, at a dermatology practice in an academic medical center. Included patients were prescribed isotretinoin during the study period and received 30 days or more of antibiotics.

Results: The average duration of antibiotic use was 331.3 days. In all, 21 patients (15.3%) were prescribed antibiotics for 3 months or less, 88 patients (64.2%) for 6 months or more, and 46 patients (33.6%) for 1 year or longer. Patients treated only at the study site had a mean duration of antibiotic treatment of 283.1 days whereas patients who also received antibiotics from another institution had a mean duration of 380.2 days. This difference approached statistical significance (P = .054).

Limitations: This study was limited to a single center.

Conclusion: Expert guidelines recommend responsible use of antibiotics in acne in light of emerging resistance. We found that patients who eventually received isotretinoin had extended exposure to antibiotics, exceeding recommendations. Early recognition of antibiotic failure and the need for isotretinoin can curtail antibiotic use. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2015.09.046.)

Key words: acne; antimicrobial resistance; isotretinoin; systemic antibiotics.

Acne affects approximately 85% of adolescents and is increasingly recognized in adults.[1,2] Acne is associated with significant psychological and physical morbidity.

Acne treatment is largely dependent on disease severity. Inflammatory and nodulocystic acne often require systemic treatment, including antibiotics. Antibiotic efficacy depends on its ability to reduce the *Propionibacterium acnes* burden and to modulate host inflammation.[3] Antibiotics such as doxycycline, minocycline, tetracycline, and sulfamethoxazole/trimethoprim have become common treatments for severe acne.[4] "Cyclines" (eg, minocycline) are typically first-line treatments.[5]

Despite the efficacy of antibiotics, there have been calls to limit their use in acne because of concerns for bacterial resistance.[6,7] In 2003 and 2009, the Global Alliance to Improve Acne Outcomes published recommendations for acne treatment and suggested limiting the use of systemic antibiotics to 3 months if a patient demonstrates limited clinical improvement.[8,9] Similarly, European consensus statements published in 2004 and 2012 also explicitly recommended limiting antibiotic use to 3 months.[3,5]

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Other expert committees have also recommended limiting antibiotic use more generally.[10,11]

An alternative to long-term systemic antibiotic therapy for acne is isotretinoin (13-*cis*-retinoic acid). Isotretinoin is approved by the Food and Drug Administration for the treatment of nodulocystic acne in patients who have failed systemic antibiotics. However, many published guidelines recommend isotretinoin as first-line therapy for the treatment of severe, nodulocystic acne.[3,9] Unlike antibiotics, isotretinoin can provide a durable remission. In spite of isotretinoin's benefits, its use has been limited by the iPLEDGE system, its severe teratogenicity, and controversies including its association with inflammatory bowel disease and psychiatric disturbances.[12]

CAPSULE SUMMARY

- Although antibiotics are commonly used to treat inflammatory/nodulocystic acne, antibiotic resistance is becoming an increasingly important problem.
- Durations of antibiotic therapy in patients with severe acne exceed recommendations.
- Early recognition of patients who fail to respond to systemic antibiotics and early prescription of isotretinoin would help curtail antibiotic use.

Despite concerns regarding long-term use of antibiotics, few published studies have investigated the duration of antibiotic use for acne. A study by Leyden et al[13] in 1983 reported a mean duration of antibiotic use of 21 months. In 2003, a study by Levy et al,[14] not specifically designed to address antibiotic duration, reported a mean duration of 11.5 months. Most recently, in 2014, Lee et al[4] published data regarding the duration of antibiotic use for acne. In this study, examining the average duration of antibiotic courses between 2008 and 2010 from MarketScan Commercial Claims and Encounters database and defining an antibiotic course as at least 60 days, the authors found a mean course duration of 129 days.

Beyond these studies, little is known about total antibiotic treatment lengths among patients with acne. In particular, duration of antibiotic use in patients who eventually are treated with isotretinoin has not been studied. The current study was designed to examine the duration of oral antibiotic therapy in patients with acne who were ultimately treated with isotretinoin. Our results highlight a potential practice gap in the use of antibiotics and the transition to isotretinoin.

METHODS

We conducted a single-site, retrospective chart review of patients with acne diagnostic billing codes who were seen in the faculty group practice of the Ronald O. Perelman Department of Dermatology at New York University Langone Medical Center, a large academic medical center.

Data were collected for patients seen between 2005 and 2014 inclusive. Included patients were 12 years of age or older, demonstrated a clinical description that was consistent with inflammatory or nodulocystic acne, and had a history of at least 2 visits to the study site. Included patients had a history of isotretinoin use during the study period and systemic antibiotic use 30 days or longer. Acne type was classified based on the patient's most severe phenotype. Patients with a clinical description or diagnosis consistent with comedonal acne exclusively or a history of isotretinoin use at another institution or before 2005 were excluded. Patients with known endocrinologic abnormalities (polycystic ovarian syndrome or congenital adrenal hyperplasia) and those considered ineligible for isotretinoin (pregnant patients, those who refused to comply with iPLEDGE) were excluded. Finally, patients using medications known to cause or exacerbate acne (steroids, lithium, phenobarbital, phenytoin, isoniazid, and epidermal growth factor inhibitors) or with diagnoses that entail treatment with systemic antibiotics (folliculitis, rosacea, Lyme disease, syphilis) were also excluded. Of note, patients with a history of or active depression, anxiety, suicidal ideation, psychiatric medication use (other than lithium), or inflammatory bowel disease were not excluded.

The primary end point, antibiotic duration before isotretinoin, was determined by a detailed review of prescription records and clinical notes. Patients with unclear antibiotic histories were excluded. Moreover, any estimates of antibiotic durations were conservative. Prescriptions noted in the chart without specific documentation of the duration were assumed to be 30 days in duration, which is likely an underestimate. When patients had received antibiotics outside of the study site, the patients were only included if they had a complete and detailed prescription history.

Descriptive statistical analysis was performed using software (SPSS, IBM Corp, Armonk, NY).

RESULTS

A total of 5053 patient charts were reviewed with a billing code for acne during the study period. Of the charts evaluated, 4916 were excluded because they failed to meet inclusion criteria or there were insufficient data on the patient's antibiotic history.