

RESEARCH LETTER

The Efficacy of Doxycycline versus Spironolactone in Treating Acne Among Pediatric and Adult Females: A Retrospective Cohort Study

Justine Galambus, MD¹, Megan Bradley, BS², Alyssa Hansen, MD³, and Michael G. Wilkerson, MD, MS³

¹ Lake Granbury Medical Center, Dallas, Texas, USA

² University of Texas Medical Branch, Galveston, Texas, USA

³ Department of Dermatology, University of Texas Medical Branch, Galveston, Texas, USA

ABSTRACT

Acne is a common complaint prompting referrals to a dermatologist. Many patients follow a stepwise protocol starting with a topical regimen then progressing to oral medications. Recent data from a small randomized controlled trial suggests that spironolactone is more effective than doxycycline at treating acne in adult females. We sought to validate that finding via a retrospective cohort analysis using a national database. Our results suggested that adult women treated with doxycycline were significantly less likely to subsequently be prescribed isotretinoin as compared to patients treated with spironolactone. However, in pediatric females, the reverse was observed. Pediatric females treated with doxycycline were significantly more likely to subsequently be prescribed isotretinoin as compared to patients treated with spironolactone.

INTRODUCTION

Doxycycline and spironolactone are commonly used oral medications in the treatment of acne in pediatric and adult females. Doxycycline is a tetracycline antibiotic that has anti-inflammatory properties^{1, 2} and is used off-label for acne. Spironolactone has been used as an off-label treatment and functions as an aldosterone receptor antagonist that exhibits anti-androgen activity^{2,3}.

To compare the efficacy of these two agents in the treatment of adult female acne, the FASCE trial was performed. This randomized control trial had 133 adult women with moderate acne treated with either

spironolactone or doxycycline⁴. The results from this study suggest spironolactone was superior to doxycycline in both disease control and quality of life in adult patients, though this has not been validated with further comparative studies.

METHODS

To validate and further investigate these findings, a retrospective cohort study was conducted using the US Collaborative Network in TriNetX. Using International Classification of Disease-10 (ICD-10) and RxNorm codes, two cohorts were composed of patients that had either been prescribed doxycycline (RxNorm 3640) or

September 2025 Volume 9 Issue 5

spironolactone (RxNorm 9997) within three years of acne diagnosis, indicated by ICD-10 code L70. Patients were excluded from any usage of the other agent (doxycycline or spironolactone), isotretinoin (RxNorm 6064), or tretinoin (RxNorm 10753) in the past. To approximate treatment failure, we queried for subsequent use of isotretinoin within three months to five years following the use of either doxycycline or spironolactone. Risk difference, odds ratios (OR), and 95% confidence intervals (CI) were calculated among cohorts of pediatric patients aged ≤ 17 years, and adult female patients aged 18 to 45 years.

RESULTS

Pediatric females treated with doxycycline were more than twice as likely to subsequently be prescribed isotretinoin as compared to those treated with spironolactone ($p=0.002$, **Table 1**). In adult females, doxycycline had a lower risk of subsequent use of isotretinoin compared to spironolactone; the difference was milder but remained significant ($p<0.001$, **Table 2**).

DISCUSSION

Because of the use of spironolactone in pediatric female acne is associated with lower subsequent risk of isotretinoin use, androgen agonism may be a significant etiology in pediatric female acne. However, androgens may have less of a role in the pathophysiology of adult female acne as superiority was not seen with spironolactone in this age group. These results contrast with the FASCE trial, which determined that spironolactone was superior to doxycycline in the treatment of adult female acne⁴. The data from this study suggests a greater role for spironolactone in the treatment of female pediatric acne as compared to female adult

acne. While adult females had a statistically significant lower risk of isotretinoin use if they were treated with doxycycline, the risk difference demonstrated only seven more females out of a thousand progress to isotretinoin when treated with spironolactone. Thus, either agent is likely acceptable in adult females.

Our study does have limitations. Most notably, we use subsequent isotretinoin use as a proxy for treatment failure as we are unable to assess for reported treatment failure. There are numerous patient factors (e.g., inability to attend frequent visits, concerns of side effects) that would restrict the decision to use isotretinoin even in the case of treatment failure. Use of spironolactone or doxycycline is not required prior to isotretinoin initiation. We do not have adherence data or data regarding acne severity before or after treatment. Additional studies further investigating these two medications both individually and jointly are needed.

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:

Justine Galambus

2100 Research Row Ste 100

Dallas, TX 75235

Email: justine.galambus@unthsc.edu

References:

1. 050641Orig1s032lbl.pdf. Accessed August 11, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/050641Orig1s032lbl.pdf
2. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74(5):945-973.e33. doi:10.1016/j.jaad.2015.12.037
3. Barbieri JS, Spaccarelli N, Margolis DJ, James WD. Approaches to limit systemic antibiotic use in acne: Systemic alternatives,

Table 1. Risk Difference and Odds Ratio of Subsequent Isotretinoin Use in Pediatric Females with Acne Treated with Doxycycline versus Spironolactone

Cohort	Patients in cohort	Patients subsequently prescribed isotretinoin	Risk	
Doxycycline	391	37	0.095	
Spironolactone	391	15	0.038	
		95% CI	z	p
Risk Difference	0.056	(0.022, 0.091)	3.158	0.002
Odds Ratio	2.620	(1.413, 4.857)	N/A	N/A

Table 2. Risk Difference and Odds Ratio of Subsequent Isotretinoin Use in Adult Females with Acne Treated with Doxycycline versus Spironolactone

Cohort	Patients in cohort	Patients subsequently prescribed isotretinoin	Risk	
Doxycycline	13,449	298	0.022	
Spironolactone	13,449	392	0.029	
		95% CI	z	p
Risk Difference	-0.007	(-0.011, -0.003)	-3.625	<0.001
Odds Ratio	0.755	(0.648, 0.879)	N/A	N/A

emerging topical therapies, dietary modification, and laser and light-based treatments. *J Am Acad Dermatol.* 2019;80(2):538-549.

doi:10.1016/j.jaad.2018.09.055

- DRÉNO B, NGUYEN JM, HAINAUT E, et al. Efficacy of Spironolactone Compared with Doxycycline in Moderate Acne in Adult Females: Results of the Multicentre, Controlled, Randomized, Double-blind Prospective and Parallel Female Acne Spironolactone vs doxyCycline Efficacy (FASCE) Study. *Acta Derm Venereol.* 2024;104:26002. doi:10.2340/actadv.v104.26002