Spironolactone and breast cancer: Fear not!

Warren R. Heymann, MD
Marlton, New Jersey

Key words: acne; alopecia; androgen; breast cancer; hirsutism; spironolactone.

One of the challenges of modern practice is allaying fears from easily accessed information. Off-label use of spironolactone offers potential benefit for disorders where androgens are involved in the pathophysiology—notably acne vulgaris and androgenetic alopecia (AGA). Spironolactone inhibits 5α-reductase, thereby blocking the conversion of testosterone to dihydrotestosterone; it also inhibits binding of testosterone to androgen receptors. Patients may be leery of spironolactone when they read "Tumorigenic: Shown to be a tumorigen in chronic toxicity animal studies. Avoid unnecessary use" in the "Warnings/Precautions" section of Lexicomp (accessed July 23, 2020) (Wolters Kluwer N.V., Alphen aan den Rijn, Netherlands). This is particularly worrisome for women at risk or who have a history of breast cancer (BC).

The concern for antibiotic resistance has contributed to the spironolactone renaissance for acne. A total of 395 patients (median age, 32 years) received a median spironolactone dose of 100 mg daily. Approximately two-thirds of patients (66.1%) had a complete response, and 85.1% had a complete response or partial response greater than 50%. Median times to initial response and maximum response were 3 and 5 months. Only few adverse effects were observed.[1]

Spironolactone is the most commonly used, off-label antiandrogen for the treatment of female AGA and hirsutism, although studies that support the efficacy of spironolactone are limited.[2] Spironolactone, a diuretic, is well tolerated, especially at lower doses. Common adverse effects include menstrual irregularities, breast tenderness, breast enlargement, and central nervous system symptoms (fatigue, dizziness, and headaches).

Abbreviations used:

AGA: androgenetic alopecia
BC: breast cancer

Despite animal studies linking spironolactone to numerous benign and malignant tumors, large retrospective cohort studies have not revealed any association with breast, uterine, cervical, or ovarian cancers.[3] Rozner et al,[4] in their systematic review, concluded that there are no data to support that spironolactone interacts with endocrine therapies used for BC, nor is spironolactone linked to an increased incidence of BC.

Understandably, patients with a history of BC may be concerned about recurrence of the malignancy should they opt to use spironolactone for AGA. In this issue of the *Journal of the American Academy of Dermatology*, Wei et al[5] report the results of a retrospective analysis of patients with a history of BC stratified by spironolactone prescription matched 1:1 using propensity score analysis. Both cohorts were compared and analyzed. A total of 123 patients (16.5%) prescribed spironolactone developed BC recurrence compared with 3649 (12.8%) patients who developed BC recurrence without spironolactone being prescribed (P = .004). After propensity matching, adjusted Cox regression analysis showed no association between spironolactone and increased BC recurrence (adjusted hazard ratio, 0.966). The major limitation of this study was that surveillance was limited to 2 years. The authors concluded that spironolactone was not independently associated with increased BC

From the Division of Dermatology, Cooper Medical School of Rowan University, Marlton.
Funding sources: None.
Conflicts of interest: None disclosed.
IRB approval status: Not applicable.
Reprints not available from the author.

Correspondence to: Warren R. Heymann, MD, 100 Brick Rd, Ste 306, Marlton, NJ 08053. E-mail: wrheymann@gmail.com.
J Am Acad Dermatol 2020;83:1008-9.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2020.07.104

recurrence and may be considered for treating alopecia [and presumably acne] in BC survivors.

Marie Curie stated, "Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less." Wei et al[5] have provided BC survivors a thoughtful analysis that may bring comfort to women who are struggling with the fear of using spironolactone for their AGA.

REFERENCES

1. Roberts EE, Nowsheen S, Davis MDP, et al. Treatment of acne with spironolactone: a retrospective review of 395 adult patients at Mayo Clinic, 2007-2017 [e-pub ahead of print]. *J Eur Acad Dermatol Venereol*. 2020. https://doi.org/10.1111/jdv.16302. Accessed July 24, 2020.
2. Fabbrocini G, Cantelli M, Masarà Annunziata MC, et al. Female pattern hair loss: a clinical, pathophysiologic, and therapeutic review. *Int J Womens Dermatol*. 2018;4:203-211.
3. Marson JW, Baldwin HE. An overview of acne therapy, part 2: hormonal therapy and isotretinoin. *Dermatol Clin*. 2019:195-203.
4. Rozner RN, Freites-Martinez A, Shapiro J, et al. Safety of 5α-reductase inhibitors and spironolactone in breast cancer patients receiving endocrine therapies. *Breast Cancer Res Treat*. 2019;174:15-26.
5. Wei C, Bovonratwet P, Gu A, et al. Spironolactone use does not increase the risk of female breast cancer recurrence: a retrospective analysis. *J Am Acad Dermatol*. 2020;83:1021-1027.