Efficacy and Safety of Spironolactone in Acne Management

Nikita Menta, BA; Savanna I. Vidal, BS; Lawrence J. Green, MD

Spironolactone is an aldosterone antagonist that first was used as a potassium-sparing diuretic to treat heart failure and hypertension. It also possesses antiandrogenic mechanisms including competitively inhibiting androgen receptors, increasing steroid hormone–binding globulin production, and decreasing 5α-reductase activity.[1] These properties have been leveraged in off-label use for dermatologic conditions including acne, hidradenitis suppurativa, androgenic alopecia, and hirsutism.[1,2] Despite being used off-label to treat acne for more than 40 years, spironolactone has not received US Food and Drug Administration approval for this indication.[3] Herein, we review the current evidence for use of spironolactone in acne management.

Spironolactone Efficacy

Spironolactone is efficacious for facial and truncal acne in adult females; it cannot be used in males given its anti-androgenic effects.[4,5] In 2 large studies, spironolactone completely or partially cleared facial acne in 75.5% to 85.1% of patients.[4,5] In the first study, which included 395 patients on a median dose of 100 mg/d (range, 25-200 mg/d), clearance of comedonal, papulopustular, and nodulocystic acne was observed.[4] The second study included 403 patients, most of whom started on spironolactone at 100 mg/d (range, 25-200 mg/d). In addition to facial clearance, patients in this study demonstrated similar rates of partial or complete clearance of acne on the chest (84.0%) and back (80.2%) assessed via a comprehensive acne severity scale.[5] In both studies, doses of 100 mg/d or higher were most effective, and the median time to initial acne improvement was 3 months, with peak effects occurring after 4 to 6 months of treatment.[4,5] Most patients were using spironolactone monotherapy or spironolactone in combination with topical therapies; however, a minority used it concurrently with oral antibiotics and/or combined oral contraceptives.

Spironolactone has demonstrated comparable efficacy to tetracycline antibiotics. A study comparing the rate of switching to another systemic therapy within 1 year of treatment initiation identified similar rates in patients started on spironolactone (n=962) and those started on tetracyclines (n=4236)(14.4% vs 13.4%, respectively). As switching may indicate treatment failure due to insufficient efficacy, adverse effects, or other causes, these findings may suggest similar effectiveness for spironolactone and tetracyclines.[6] These treatments also were compared in a randomized controlled trial of 133 patients receiving topical benzoyl peroxide 5% for 6 months and either spironolactone 150 mg/d for 6 months or doxycycline 100 mg/d for 3 months followed by oral placebo for 3 months. At 4 months, spironolactone performed better than doxycycline as assessed using the Adult Female Acne Scoring Tool.[3] Although doxycycline was stopped after 3 months and only topical therapy was continued, this finding is notable because guidelines from the American Academy of Dermatology recommend limiting tetracycline use to 3 to 4 months, whereas spironolactone may be continued for prolonged durations.[1,4]

From the Department of Dermatology, The George Washington University School of Medicine and Health Sciences, Washington, DC.
Nikita Menta has received independent research grants from Incyte and Johnson & Johnson. Savanna I. Vidal has received an independent research grant from Galderma. Dr. Green is an investigator, speaker, or advisor for Alumis, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, HighlightLL Pharma, Incyte, Janssen, Ortho Dermatologics, Revance, Takeda Pharmaceutical Company, UCB, Verrica Pharmaceuticals, and VYNE Therapeutics.
Correspondence: Lawrence J. Green, MD, 9601 Blackwell Road, Ste 260, Rockville, MD 20850 (drgreen@aederm.com).
Cutis. 2025 April;115(4):108-109, 124. doi:10.12788/cutis.1189

While most studies have evaluated the efficacy of spironolactone in adult females, it is increasingly being prescribed in adolescents.[7] In a study that included 80 females aged 14 to 20 years, 80% (64/80) experienced acne improvement on a median dose of 100 mg/d.[8] Additionally, in the study evaluating treatment switching rates, more than 80% of 1139 adolescents who were started on spironolactone were not switched to a different systemic therapy within the first year of treatment, demonstrating the efficacy of spironolactone in this demographic.[6] However, treatment switching was more common among adolescents started on spironolactone compared with those who started on tetracyclines. As noted for adults, the treatment switching rates were the same for spironolactone and tetracycline users; the difference in adolescents may be due to lower influence of hormonal factors or higher therapeutic expectations in this population.[6]

Spironolactone Safety

Spironolactone is well tolerated at doses of 25 to 200 mg/d for acne management. Common adverse effects include diuresis (29% [26/90]), menstrual irregularities (22% [20/90]), fatigue (17% [15/90]), headache (14% [13/90]), and dizziness (12% [11/90]), but they infrequently lead to treatment discontinuation.[4,9] Rates of adverse effects are lower in adolescents compared to adults, although the effects of spironolactone on early endocrine development in adolescents are unknown.[7] Spironolactone should not be used during pregnancy, and concurrent contraception use is advised because spironolactone has caused feminization of male fetuses in animal studies.[1,10-11]

While concerns about potentially severe adverse effects including hypotension, hyperkalemia, and tumorigenicity have been raised, their occurrence in the literature is rare.[5,12-18] In a study evaluating hypotension in 2084 patients taking spironolactone 50 to 200 mg/day for acne, hair loss, and/or hirsutism, 3.1% experienced absolute hypotension, and only 0.26% required dose reduction or discontinuation.[12] Another study of 403 patients taking spironolactone for acne reported a statistically significant but clinically insignificant mean reduction in systolic blood pressure of 3.5 mm Hg.[5] While clinically relevant hypotension is unlikely to occur, some authors still recommend measuring baseline blood pressure before spironolactone initiation.[12]

Many large studies have demonstrated that hyperkalemia with spironolactone use is rare in young healthy women.[13-15] In one study of patients aged 18 to 45 years treated with spironolactone for acne, only 0.72% of 1802 serum potassium measurements fell within the range of mild hyperkalemia.[13] Another study found a significantly greater incidence of hyperkalemia in healthy women aged 46 to 65 years compared with women younger than 45 years (16.7% vs <1%; P=.0245).[14] Additionally, among 27 patients taking spironolactone and oral contraceptives containing drospirenone (a spironolactone analog), none had elevated potassium levels.[15] Given these findings, American Academy of Dermatology guidelines suggest that monitoring potassium in young healthy women has low utility but should be considered in those with risk factors including older age; renal and cardiovascular disease; and concurrent medications that interfere with renal, adrenal, and hepatic function.[1] If performed, monitoring should be done within the first few weeks of initiating spironolactone for early detection of hyperkalemia.[16]

Spironolactone has a US Food and Drug Administration warning for tumorigenicity based on studies in rats that were given up to 150 times the amount for human therapeutic doses and subsequently developed thyroid, hepatic, testicular, and breast adenomas.[1] However, several large studies in humans have not found an association between spironolactone and breast cancer (BC) development.[1,17,18] Furthermore, a large retrospective study found no increased risk for recurrence in BC survivors treated with spironolactone.[2] Most carcinogenicity studies include older women, which may limit generalizability of the findings to younger women, who comprise the majority of patients being treated for acne. Recently, however, a retrospective study evaluating healthy females aged 9 to 40 years with acne identified no significant increased risk for BC in patients treated with spironolactone.[17] When compared to tetracyclines, there was a slightly decreased BC risk with spironolactone, providing further support for the latter's safety. Finally, a large systematic review identified no association between spironolactone and ovarian, bladder, kidney, gastric, or esophageal cancers.[18]

Final Thoughts

Over the past several years, an ever-expanding body of literature supporting the efficacy and safety of spironolactone has emerged. While spironolactone has been used off label for decades to treat acne in healthy adult females, there are now strong data to support its efficacy in adolescent females. Notably, spironolactone consistently demonstrates similar effectiveness to first-line tetracycline antibiotics. Additionally, data suggest that spironolactone is safe in patients with a history of BC. Overall, spironolactone is a safe, comparable, and promising alternative to antibiotics for acne management in adult and adolescent females.

REFERENCES

1. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2024;90:1006.e1-1006.e30. doi:10.1016/j.jaad.2023.12.017
2. 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. doi:10.1016/j.jaad.2020.05.081
3. 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:adv26002. doi:10.2340/actadv.v104.26002
4. 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. *J Eur Acad Dermatol Venereol*. 2020;34:2106-2110. doi:10.1111/jdv.16302

CONTINUED ON PAGE 124

CONTINUED FROM PAGE 109

5. Garg V, Choi JK, James WD, et al. Long-term use of spironolactone for acne in women: a case series of 403 patients. *J Am Acad Dermatol*. 2021;84:1348-1355. doi:10.1016/j.jaad.2020.12.071
6. Barbieri JS, Choi JK, Mitra N, et al. Frequency of treatment switching for spironolactone compared to oral tetracycline-class antibiotics for women with acne: a retrospective cohort study 2010-2016. *J Drugs Dermatol*. 2018;17:632-638.
7. Horissian M, Maczuga S, Barbieri JS, et al. Trends in the prescribing pattern of spironolactone for acne and hidradenitis suppurativa in adolescents. *J Am Acad Dermatol*. 2022;87:684-686. doi:10.1016/j.jaad.2021.12.005
8. Roberts EE, Nowsheen S, Davis DMR, et al. Use of spironolactone to treat acne in adolescent females. *Pediatr Dermatol*. 2021;38:72-76. doi:10.1111/pde.14391
9. Shaw JC, White LE. Long-term safety of spironolactone in acne: results of an 8-year follow-up study. *J Cutan Med Surg*. 2002;6:541-545. doi:10.1007/s10227-001-0152-4
10. Hecker A, Hasan SH, Neumann F. Disturbances in sexual differentiation of rat foetuses following spironolactone treatment. *Acta Endocrinol (Copenh)*. 1980;95:540-545. doi:10.1530/acta.0.0950540
11. Jaussan V, Lemarchand-Béraud T, Gómez F. Modifications of the gonadal function in the adult rat after fetal exposure to spironolactone. *Biol Reprod*. 1985;32:1051-1061. doi:10.1095/biolreprod32.5.1051
12. Hill RC, Wang Y, Shaikh B, et al. Spironolactone treatment for dermatologic indications is not associated with hypotension in a single-center retrospective study. *J Am Acad Dermatol*. 2024;90:1245-1247. doi:10.1016/j.jaad.2024.01.057
13. Plovanich M, Weng QY, Mostaghimi A. Low usefulness of potassium monitoring among healthy young women taking spironolactone for acne. *JAMA Dermatol*. 2015;151:941-944. doi:10.1001/jamadermatol.2015.34
14. Thiede RM, Rastogi S, Nardone B, et al. Hyperkalemia in women with acne exposed to oral spironolactone: a retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program. *Int J Womens Dermatol*. 2019;5:155-157. doi:10.1016/j.ijwd.2019.04.024
15. Krunic A, Ciurea A, Scheman A. Efficacy and tolerance of acne treatment using both spironolactone and a combined contraceptive containing drospirenone. *J Am Acad Dermatol*. 2008;58:60-62. doi:10.1016/j.jaad.2007.09.024
16. Lai J, Zaenglein AL, Barbieri JS. Timing of potassium monitoring in females treated for acne with spironolactone is not optimal: a retrospective cohort study. *J Am Acad Dermatol*. 2024;91:982-984. doi:10.1016/j.jaad.2024.07.1446
17. Garate D, Thang CJ, Golovko G, et al. A matched cohort study evaluating whether spironolactone or tetracycline-class antibiotic use among female acne patients is associated with breast cancer development risk. *Arch Dermatol Res*. 2024;316:196. doi:10.1007/s00403-024-02936-y
18. Bommareddy K, Hamade H, Lopez-Olivo MA, et al. Association of spironolactone use with risk of cancer: a systematic review and meta-analysis. *JAMA Dermatol*. 2022;158:275-282. doi:10.1001/jamadermatol.2021.5866