Antiandrogen therapy with spironolactone for the treatment of hidradenitis suppurativa

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Background: Hormonal therapy is a potential treatment for hidradenitis suppurativa (HS). However, few data exist describing the efficacy of spironolactone in treatment of HS.

Objective: To assess whether spironolactone treatment improves HS disease severity and patient-reported pain.

Methods: We performed a single-center chart review of female patients with HS who were treated with spironolactone between 2000 and 2017. Primary outcome measurements included the HS Physician's Global Assessment (HS-PGA), Hurley staging, inflammatory lesion count, fistula count, and a numeric rating scale for pain.

Results: On average, subjects were exposed to 75 mg of spironolactone daily over a 7.1-month follow-up period. Patients achieved significant disease improvement with regard to pain (Δ-1.5 [P = .01]), inflammatory lesions (Δ-1.3 [P = .02]), and HS-PGA score (Δ-0.6 [P < .001]). As expected, no change was found for Hurley stage (Δ0 [P = .32]) or fistulas (Δ0 [P = .73]). There was no difference in improvement between subjects who received less than 75 mg of spironolactone daily (n = 25; average dose, 45 mg/d) and those who received more than 100 mg daily (n = 21; average dose, 112 mg/d).

Limitations: Retrospective nature, limited sample size, and variations in severity measures documented were limiting factors.

Conclusions: Management of HS with spironolactone reduces lesion count, HS-PGA score, and pain. Lower doses appear to be effective and may be an appropriate option for patients with tolerability concerns. (J Am Acad Dermatol 2019;80:114-9.)

Key words: antiandrogen; hidradenitis suppurativa; hormonal therapy; spironolactone.

Hidradenitis suppurativa (HS) is a chronic inflammatory disease characterized by nodules, sinus tracts, abscesses, and pain in intertriginous body regions. Although the exact pathophysiology of the disease is unknown, HS is thought to be mediated by follicular occlusion,

Abbreviations used:

HS:	hidradenitis suppurativa
HS-PGA:	Hidradenitis Suppurativa Physician's Global Assessment
SD:	standard deviation

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Ms Golbari and Dr Porter had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis, as well as for drafting of the manuscript and for statistical analysis. Drs Porter and Kimball were responsible for the study concept and design, as well as for critical revision of the manuscript for important intellectual content. Dr Kimball was responsible for study supervision.

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bacterial colonization, and aberrant immune response.[1] Evidence for hormonal influence includes predominance in females, onset in puberty, improvement with menopause, and change in disease severity during menses and pregnancy.[1,2] A few small studies have described antiandrogen treatments as effective therapeutic options for HS.[3-6]

Spironolactone, an androgen antagonist, is used for treatment in hormonally mediated diseases such as hirsutism, acne, and androgenic alopecia. One small published case series examining spironolactone for HS showed improvement in HS Physician's Global Assessment (HS-PGA) score over a 3-month period.[5] We evaluated improvement in HS disease severity and pain in response to longer-term treatment with spironolactone.

CAPSULE SUMMARY

- Antiandrogen therapy has been reported to be an effective treatment for hidradenitis suppurativa.
- This study evaluated both physician- and patient-reported hidradenitis suppurativa severity outcomes for patients treated with spironolactone.
- Antiandrogen therapy with spironolactone may be a useful treatment option for reducing inflammatory lesions and pain for female patients with hidradenitis suppurativa.

METHODS

An institutional board review–approved retrospective review of adult patients with diagnosis of HS (according to *International Classification of Diseases, Ninth Revision,* code 705.83 or *International Classification of Diseases, 10th Revision,* code L73.2) who were treated with spironolactone at Beth Israel Deaconess Medical Center between 2000 and 2017 was performed. The 145 patients identified by the Clinical Data Repository search included 67 female subjects (Fig 1).

Demographic data, baseline HS disease severity, spironolactone dosing, and medication side effects were recorded. HS disease severity was assessed by using the HS-PGA (graded from 0 [clear] to 5 [very severe]), Hurley staging (I-III), lesion count (number of inflammatory lesions defined as inflamed papules, nodules, or abscesses), fistula count (number of draining and nondraining fistulas), and a numeric rating scale for pain (scored on a scale of 0-10). Comparisons were performed by using Student *t* tests for continuous variables. Because not all measures of disease severity were reported at every visit, a listwise deletion of unmatched data was applied to create the data set for analysis. Matched baseline and posttreatment severity scores were available for lesions (n = 32), fistulas (n = 34), pain (n = 15), HS-PGA score (n = 41), and Hurley stage (n = 38).

RESULTS

Baseline characteristics

A total of 67 female patients for whom spironolactone had been prescribed for treatment of HS were identified. A total of 21 patients were lost to follow-up after the initial visit. The baseline data were similar between the groups with and without follow-up. The average age at initial presentation of the 46 patients with at least 1 follow-up was 35.1 years (standard deviation [SD], 10.3). The mean age was 21.4 years (SD, 10.1) at disease onset and 31.1 years at diagnosis (SD, 9.4). Self-reported subject race was White (50%), Black (35%), Hispanic (7%), other or unknown (6%), and Asian (2%). The subjects' average body mass index was 34.8 (SD, 8.0). The most common comorbidities included psychiatric disease (33%), acne (22%), and polycystic ovarian syndrome (PCOS) (17%). Six patients (13%) reported a family history of HS.

At baseline, patients had a mean HS-PGA score of 2.6 (SD, 0.9), with 7% categorized as being at Hurley stage I, 74% at Hurley stage II, and 11% at Hurley stage III. Before treatment initiation, 38 patients (83%) had previously received other systemic treatment, including antibiotics (83%), biologic agents (4%), and retinoids (2%).

Response to spironolactone

The average follow-up time for patients undergoing spironolactone therapy was 7.1 months (range, 0.75-28 months). The average dose received by patients at the start of therapy was 71.7 mg/d (range, 25-200 mg). Over the treatment course, the spironolactone dose was increased for 10 patients (average increase of 57.5 mg/d) and reduced for 2 patients (average reduction of 37.5 mg/d). Accounting for dose changes, the average dose of spironolactone was 75 mg/d over the study period.

Disease improvement was significant in terms of pain (P = .01), lesion count (P = .02), and HS-PGA score (P < .001). No significant change was found for Hurley stage (P = .32) or fistula count (P = .73) (Table I and Fig 2). Subanalyses of groups stratified by race, body mass index, or comorbidities did not show significant differences in disease response.

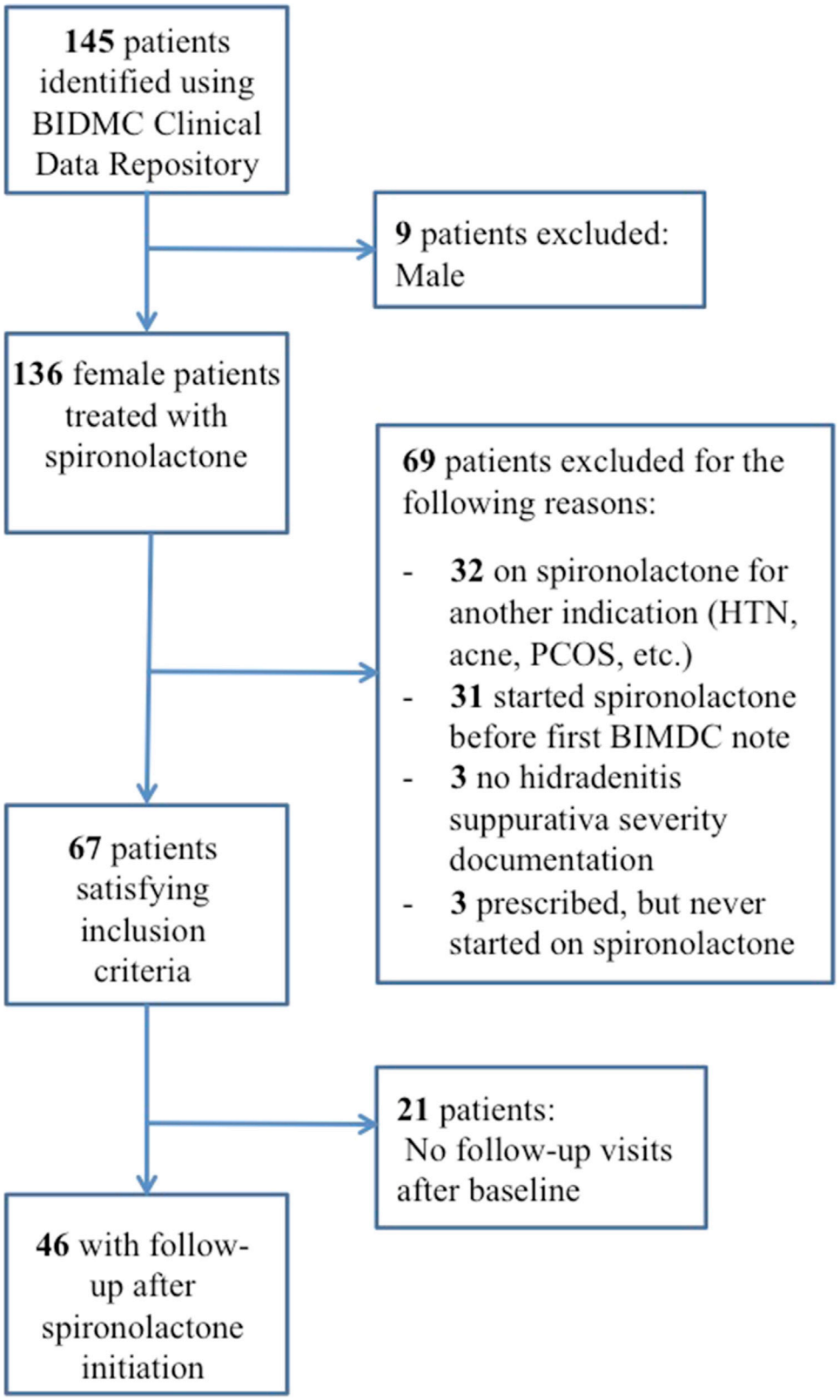

Fig 1. Flowchart of selection of patients with hidradenitis suppurativa. *BIDMC*, Beth Israel Deaconess Medical Center; *HTN*, hypertension; *PCOS*, polycystic ovarian syndrome.

Table I. Improvement in HS disease severity after treatment with spironolactone

Metric	At baseline visit, mean (SD)	At final visit, mean (SD)	*P* value
Pain score (0-10)	2.7 (2.4)	1.2 (1.6)	.01
Lesion count	3.4 (3.3)	2.1 (2.4)	.02
Fistula count	0.7 (1.2)	0.7 (1.3)	1.0
HS PGA score	2.6 (0.9)	2.0 (1.0)	.0001
Hurley stage	2.0 (0.4)	2.0 (0.4)	.32

HS, Hidradenitis suppurativa; *HS-PGA*, Hidradenitis Suppurativa Physician's Global Assessment; *SD*, standard deviation.

Patients who had a visit within 3 months of initiation of spironolactone (n = 21, average 2-month follow-up) achieved a significant reduction in lesions (4.2 vs 2.9 [P = .01]) and HS-PGA score (2.8 vs 2.5 [P = .01]) but did not achieve a significant reduction in pain. Those who had follow-up within 6 months (n = 37, average 4-month follow-up) achieved significant improvement in lesion count (3.4 vs 2.0 [P = .02]), HS-PGA score (2.6 vs 2.2 [P = .005]), and pain (3.2 vs 1.4 [P = .02]).

Disease response to spironolactone was also stratified by dose. There was no difference in change in pain (Δ-1.5 vs Δ-1.3 [P = .91]), fistulas (Δ-0.2 vs Δ+0.1 [P = .52]), lesion count (Δ-2.2 vs Δ-0.3 [P = .09]), HS-PGA score (Δ-0.7 vs Δ-0.4 [P = .25]), or Hurley stage (Δ-0.1 vs Δ0 [P = .38]), between patients who received less than 75 mg daily over the study period (n = 25 [average, 45 mg/d over average follow-up of 6.8 months]) and those who received more than 100 mg daily (n = 21 [average, 112 mg/d over average follow-up of 7 months]), respectively.

In addition to spironolactone, patients received concurrent therapy with antibiotics (37%) (including tetracyclines [n = 14], clindamycin and rifampin [n = 1], clindamycin [n = 1], and an unknown antibiotic for treatment of *Helicobacter pylori* infection [n = 1]), hormonal contraceptives (30%), retinoids (2%), biologic agents (2%), and systemic steroids (2%). No differences in outcomes were detected by sensitivity analysis between patients receiving concurrent therapy and those receiving spironolactone monotherapy (pain, Δ-2.5 vs Δ-0.7 [P = .13]; fistulas, Δ-0.2 vs Δ-0.1 [P = .53]; lesion count, Δ-0.9 vs Δ-2.2 [P = .25]; HS-PGA score, Δ-0.6 vs Δ-0.6 [P = .97]; and Hurley stage, Δ-0.1 vs Δ-0.1 [P = .88]).

Spironolactone was well tolerated. Seven subjects (15%) reported side effects, including nausea (7%), dizziness (4%), breast tenderness (2%), and changes in urination (2%). Only 2 discontinued spironolactone therapy because of side effects.

DISCUSSION

The patients in this study who were treated for HS with spironolactone achieved significant decreases in lesion count, HS-PGA score, and pain. As expected, Hurley score (which is a static staging score based on scarring) and fistulas (which tend to be permanent epithelialized tracts) did not change over the course of treatment. It is worth noting that fistula count did not increase over the follow-up period.

Our results demonstrated reductions in HS-PGA score and lesion count similar to those reported by Lee and Fisher.[5] Longer treatment was necessary to demonstrate significant reduction in the patient reported pain in our patients. Chronic pain is an important contributor to HS-related disability,[7] and the prevalence of opioid misuse in patients with HS is almost 3 times that in those without HS.[8] Continuous systemic therapy for HS may reduce the need for analgesics.

Previous studies have reported disease response with spironolactone doses of 100 to 125 mg daily.[3,5] In our cohort, however, lower dosing was found to be similarly effective. Although spironolactone dosing for blood pressure indications start at 25 mg/d, typical off-label dosing for androgen-mediated dermatologic conditions (including hirsutism, acne, and androgenic alopecia) ranges from 100 to 200 mg/d,[9] with treatment success at lower doses also reported.[10,11] Spironolactone and its metabolites, which have longer half-lives than spironolactone does,[12] may have different affinities for androgen receptors that mediate HS disease.[13,14] Because of increased side effects at higher dosing (including amenorrhea and electrolyte abnormalities), lower initial dosing should be considered for patients with HS, who are at higher likelihood of tolerability issues.

Limitations of this study included its retrospective nature, small sample size, and listwise deletion of unmatched data. Additionally, follow-up varied, and the measures of severity used differed by assessing physician, adding possible biases. Lastly, the observation period needed to achieve maximal improvement may be longer than we were able to assess in this review. We anecdotally observe that the peak efficacy occurs over 6 to 12 months. Nevertheless, both our physician- and patient-reported outcomes suggest that spironolactone is a reasonably effective treatment option for women with HS. Many of the patients in this study had previously failed other treatments but achieved disease improvement when taking spironolactone. This finding supports the concept that a hormonally mediated HS phenotype may exist, as it does in

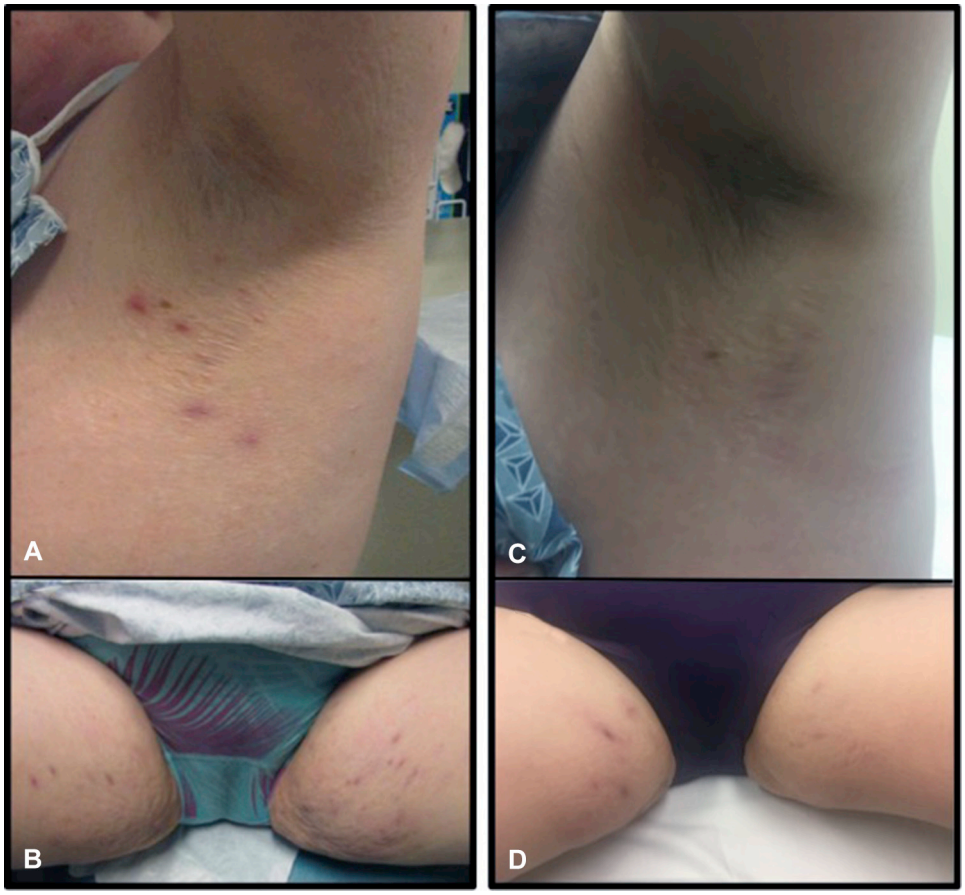

Fig 2. Hidradenitis suppurativa. Patient at baseline with multiple erythematous inflammatory papules in the left axilla (**A**) and bilateral medial aspect of the thighs (**B**) and at 14 months after initiation of spironolactone therapy with clearance of the left axilla (**C**) and postinflammatory erythema bilaterally in the medial aspect of the thighs (**D**).

acne.[15] Further studies should be performed to better characterize patients who are more likely to be responders to antiandrogen therapy and to identify the optimal spironolactone dosing and the effects of treatment over longer durations.

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