Clinical outcomes and adherence to topical corticosteroid therapy in women with vulvar lichen sclerosus: A retrospective cohort study

Jaden R. Kohn, MD, MPH,[a,b] Trissa M. Connors, MD, MPH,[a,c] Warren Chan, BS, MS,[a] Cynthia S. Liang, BS,[a] Harry Dao, Jr, MD,[c,d] and Anuja Vyas, MD[e,f]
Houston, Texas; Baltimore, Maryland; and Loma Linda, California

Background: Vulvar lichen sclerosus is a progressive dermatitis with significant itching, pain, and sexual dysfunction.

Objective: To investigate topical steroid use and clinical improvement across multiple specialties.

Methods: Retrospective cohort study at dermatology, gynecology, and vulvovaginal specialty clinics from 2012 to 2017. Descriptive statistics and panel logistic regression were performed.

Results: A total of 333 women attended 1525 visits (median 6/patient; range, 1-24 visits). Patients used steroids exactly as prescribed at 66% of visits, less than prescribed at 26%, and not at all at 8%. Versus no use, exact use improved symptoms (odds ratio [OR], 4.6; 95% confidence interval [CI], 2.2-9.6) and physical examination findings (OR, 6.9; 95% CI, 2.7-17.6) more than infrequent steroid use (symptoms: OR, 2.5; 95% CI, 1.2-5.4; physical examination findings: OR, 4.2; 95% CI, 1.6-11.0). Sexual activity status was noted in 93% of vulvovaginal, 29% of gynecology, and 0% of dermatology visits. At intake, 42% of women were sexually inactive because of pain; of these, 37% became sexually active after steroid treatment. Steroid adherence was not associated with change in sexual activity.

Conclusions: Women with vulvar lichen sclerosus improve more when topical steroids are used exactly as prescribed, although some improvement occurs with imperfect use. Sexual activity documentation is inconsistent, limiting quality of life follow-up. (J Am Acad Dermatol 2020;83:1104-9.)

Key words: female genitalia; lichen sclerosus et atrophicus; retrospective cohort; sexual function; topical corticosteroid; vulva; vulvar lichen sclerosus.

Genital lichen sclerosus in women is a chronic, progressive dermatitis associated with inflammation and vulvar epithelial thinning, which are often accompanied by intense pruritus and pain.[1] As many as 1 in 30 postmenopausal women may be affected.[2] Vulvar lichen sclerosus (VLS) is characterized by irregular, hypopigmented patches of wrinkled, atrophic skin on the vulva, perineum, and perianal area. The skin of these areas is easily traumatized. Ongoing inflammation results in scarring and loss of vulvar architecture, including atrophy and fusion of the labia minora, narrowing and stenosis of the vaginal introitus, and phimosis of the clitoral hood. This inflammation can

From the Baylor College of Medicine, Houston[a]; Department of Gynecology and Obstetrics, Johns Hopkins Hospital, Baltimore[b]; Department of Dermatology, Baylor College of Medicine, Houston[c]; Department of Dermatology, Loma Linda University[d]; Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston[e]; and Houston Methodist Obstetrics and Gynecology Associates.[f]
Drs Kohn and Connors are cofirst authors.
Funding sources: None.
Conflicts of interest: None disclosed.
IRB approval status: The Baylor College of Medicine Institutional Review Board approved this study. (Protocol Number: H40206. Status: Approved.)
Accepted for publication May 1, 2020.
Reprints not available from the authors.
Correspondence to: Jaden R. Kohn, MD, MPH, 600 N Wolfe St, Baltimore, MD 21287. E-mail: jrskohn@gmail.com.
Published online May 6, 2020.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2020.05.006

result in ulceration, fissures, and/or ecchymoses, and distortion of normal vulvar architecture can lead to significant urinary and sexual dysfunction (dyspareunia, anorgasmia, diminished sensation).[3] Compared with healthy women, women with biopsy-proven vulvar lichen sclerosus are more likely to have sexual activity less than once per week and to have sexual activity that is never or rarely satisfying to them.[4] Another study showed that sexual function was the most impaired factor when various measures of quality of life were assessed in patients with lichen sclerosus.[5]

The first-line therapy for lichen sclerosus is application of topical corticosteroids, which can relieve pruritus. Topical corticosteroids are categorized into 7 potency classes (super high potency, class 1; high potency, classes 2 and 3; moderate potency, classes 4 and 5; and low potency, classes 6 and 7).[6] Potency is determined by measuring the cutaneous vasoconstriction caused by the steroid. Topical steroids can be delivered through a vehicle such as a solution, lotion, cream, or ointment.[6] Ointments provide the strongest absorption and are the vehicle that is best tolerated on the modified mucous membranes of the vulva.[6] Although the recommendation for other genital dermatoses is to use low-potency topical corticosteroids for a limited period of time, the standard recommendation for vulvar lichen sclerosus is to use an ultra-high- or high-potency steroid ointment on multiple days per week to achieve remission, followed by maintenance therapy.[7] Long-term maintenance therapy with topical steroids is important for suppression of ongoing inflammation—which prevents the progression of skin changes, reduces the risk of scarring and architectural distortion, and decreases the risk of developing vulvar squamous cell carcinoma.[8] However, the application of topical creams and ointments on a daily therapeutic or weekly maintenance regimen can be difficult to sustain. One study showed that approximately 30% of patients were only partially compliant with the recommended long-term maintenance therapy.[9]

Our objective was to investigate the relationship between patient compliance with topical steroids and patients' perceived symptoms, progression of physical examination changes, and sexual function.

CAPSULE SUMMARY

- Women with vulvar lichen sclerosus who use corticosteroids as prescribed experience greater improvement in symptoms and physical examination findings compared to infrequent or no steroid use. Documentation of sexual activity status is inconsistent, limiting assessment of quality of life.
- Providers should routinely counsel patients about therapy adherence and assess quality of life, including sexual activity.

METHODS

We performed a retrospective cohort study of adult women diagnosed with VLS who presented for care between January 1, 2010, and May 31, 2017, at 1 of 3 clinics at a tertiary academic institution. These clinics included a general dermatology clinic, a general gynecology clinic, and a vulvovaginal specialty care clinic. Our institutional review board granted approval for this study before review of electronic medical records for data acquisition.

Patient identifiers were obtained from clinical rosters and from electronic queries of the medical record database; we identified women 18 years or older at the time of encounter with a diagnosis of International Classification of Diseases (ICD), Ninth Revision—Clinical Modifi-cation (CM) 701.0 (circumscribed scleroderma, includes lichen sclerosus); ICD, Tenth Revision—CM L90.0 (lichen sclerosus et atrophicus), or ICD, Tenth Revision—CM N90.4 (leukoplakia of vulva). Identified records were screened to verify whether physician documentation included a diagnosis of vulvar lichen sclerosus within the assessment and plan. If a patient fulfilled the eligibility criteria, we extracted data regarding demographics, medical history, and clinical visits.

Demographic and medical history extracted included age; race/ethnicity; body mass index at first encounter; gravidity and parity; menopausal status; medical comorbidities; and sexual activity status. Information from clinical visits included patient-reported use of previously prescribed medications, reported symptoms, physical examination findings, visit diagnosis, medications prescribed, and whether a photograph or a biopsy was taken at that visit. For all patients prescribed a topical steroid during their initial or follow-up visit, at their next clinical visit, we categorized patient-reported adherence to the steroid regimen documented by the clinician as "used exactly as prescribed, including amount and frequency of application," "used less than prescribed, either in amount or frequency of application," or "did not use at all."

Abbreviations used:

CI: confidence interval
CM: Clinical Modification
ICD: International Classification of Diseases
OR: odds ratio
VLS: vulvar lichen sclerosus

Data analysis was performed using STATA 14.2 for Mac (StataCorp, College Station, TX). Descriptive statistics for panel data were used to describe patient characteristics and to summarize clinical management patterns and patient outcomes. We compared demographics, management activities, and outcomes using parametric and nonparametric tests as appropriate for variable distribution. We used panel logistic regression to explore the odds of improvement in patient symptoms, physical examination findings, and sexual function associated with medication regimens and patient-reported compliance with medication regimen, while adjusting for patient characteristics.

RESULTS

Patient characteristics

Over 65 months, 333 women attended 1525 visits—of these, 998 visits (65%) occurred in vulvovaginal gynecology specialty clinics, 402 visits (26%) occurred in general gynecology clinics, and 125 visits (8%) occurred in dermatology clinics. There was a median of 6 visits per patient, but this ranged from 1 to 24 visits. For the dermatology and vulvovaginal specialty clinics, the median number of visits per patient was 7 (interquartile range, 4-8 for vulvovaginal and 3-18 for dermatology), whereas for patients in the general gynecology clinic, the median number of visits per patient was only 3 (interquartile range, 2-6).

The characteristics of patients are shown in Table I. At presentation, the median age was 62.7 years but ranged from 23 years to 90 years. Most patients were non-Hispanic white and, of the 250 for whom menopausal status was available, 78% were postmenopausal. Of 235 patients for whom obstetric history was documented, approximately one fifth had never been pregnant or given birth. There were high rates of comorbid atopy (allergies, asthma, or eczema), hypothyroidism, depression, anxiety, autoimmune conditions, and herpes simplex virus. The most common presenting symptom at the initial visit for care was vulvar itching (33%, n = 107); vulvar pain, burning, or discomfort (23%, n = 76); or architectural changes or a lesion (7%, n = 23). The primary presenting symptom was not documented for 37%.

Clinical management

There were significant differences between specialties in the treatment of patients. Topical steroids

Table I. Patient characteristics

Characteristics	Combined N = 333	Dermatology n = 32	Vulvovaginal gynecology n = 163	Gynecology n = 138	*P* value
Demographics					
Age at first visit, y, median (IQR)	62.7 (54.2-70.2)	67.9 (59.6-71.7)	59.6 (52.8-68.4)	64.6 (57.5-71.2)	.08
BMI, kg/m^2 median (IQR)	27.0 (22.6-32.2)	26.8 (25.4-29.4)	27.5 (23.2-32.4)	25.3 (22.2-32.5)	.11
Race, n (%)					.57
Non-Hispanic white	249 (82)	24 (77)	125 (80)	100 (85)	
Hispanic	19 (6)	3 (10)	11 (7)	5 (4)	
Non-Hispanic black	6 (2)	0 (0)	2 (1)	4 (3)	
Asian	2 (1)	0 (0)	2 (1)	0 (0)	
Not available	28 (9)	4 (13)	15 (10)	9 (8)	
Gynecologic characteristics, n (%)					
Nulligravidity	37 (16)	0 (0)	26 (18)	11 (13)	.45
Nulliparous	52 (22)	0 (0)	32 (22)	20 (23)	.63
Postmenopausal	196 (78)	7 (22)	119 (78)	70 (77)	.36
Autoimmune and dermatologic comorbidities, n (%)					
Atopy	132 (42)	12 (63)	85 (53)	35 (26)	.00
Hypothyroidism	98 (31)	7 (37)	52 (33)	39 (28)	.64
Autoimmune conditions	54 (17)	10 (53)	28 (18)	16 (12)	<.01
Depression and/or anxiety	98 (31)	7 (37)	65 (41)	26 (19)	<.01
HSV	36 (11)	0 (0)	21 (13)	15 (11)	.23

BMI, Body mass index; *HSV,* herpes simplex virus; *IQR,* interquartile range.

were prescribed at 1325 visits. Ultra-high-potency steroids were most commonly used (75% of visits), whereas high-, moderate-, and low-potency steroids were prescribed at significantly fewer visits (14%, 3%, and 8% of visits, respectively). General gynecologists were more likely to prescribe moderate-potency steroids ($P = .0001$). Vulvovaginal specialists were more likely than dermatologists or general gynecologists to prescribe high- or low-potency steroids ($P < .0001$ for both).

Clinicians inquired about and documented patients' sexual activity inconsistently. Overall, sexual activity was documented at 1043 visits (68% of all visits across specialties); 93% of vulvovaginal specialist visits documented sexual activity status. Of general gynecology visits, only 29% documented sexual activity. No dermatology visits for vulvar lichen sclerosus noted whether a patient was sexually active.

Clinical impact of treatment adherence

At 1139 follow-up visits, the patient's reported use of a prescribed topical steroid was documented at only 69%—of those, patients reported using steroids exactly as prescribed at 66%, using steroids less than prescribed at 26%, and not using steroids at all at 8% of visits. In these 1139 follow-up visits, 35% documented that the patient had reported improved symptoms, 14% had worsened symptoms, and 45% had no change in their symptoms (of whom 33% were symptom free and 12% had bothersome symptoms). Regarding physical examination findings, 14% experienced net worsening, 42% experienced no change, and 43% experienced net improvement.

The odds of improvement in symptoms and physical examination findings according to adherence to the topical steroid regimen are shown in Fig 1. Compared to no use of topical steroids, use

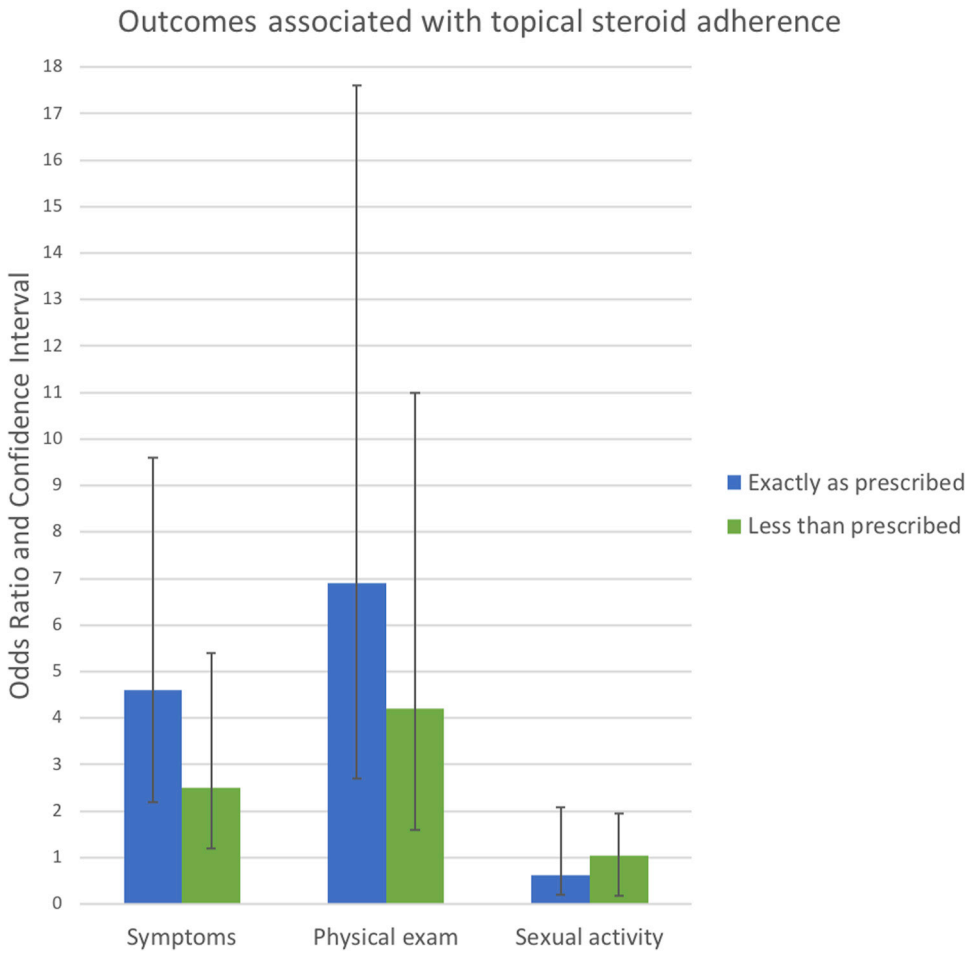

Fig 1. The odds of improvement in symptoms, physical examination findings, and sexual activity associated with perfect and imperfect compliance with topical corticosteroids compared to no steroid use.

exactly as prescribed strongly predicted improvement in both symptoms (odds ratio [OR], 4.6; 95% confidence interval [CI], 2.2-9.6) and physical examination findings (OR, 6.9; 95% CI, 2.7-17.6). Using steroids less than prescribed improved symptoms (OR, 2.5; 95% CI, 1.2-5.4) and physical examination findings (OR, 4.2; 95% CI, 1.6-11.0) to a lesser extent. Compared to moderate- and low-potency steroids, improvement was more likely with super-high- or high-potency steroid for both symptoms (OR, 2.2; 95% CI, 1.3-3.8) and physical examination findings (OR, 1.7; 95% CI, 1.0-2.9). Specifically examining steroid classes, the use of class 1 steroids was associated with increased likelihood of improvement in physical examination findings compared to class 2 or 3 steroids (OR, 1.9; 95% CI, 1.2-2.9); there was no difference between class 1 steroids and class 4 through 7 steroids, likely because of the limited use of moderate- and low-potency steroids.

When sexual activity was documented at the first visit, 71 patients were sexually active, and 133 patients were not sexually active. Of those who were not sexually active, 65% were not sexually active because of pain, and 22% reported that they did not have a partner. Of those who were sexually active at their initial visit, nearly 60% experienced pain with sex. Only 17 patients who were sexually active at their first visit did not experience any pain. During follow-up, 37% of women who initially avoided sex because of pain reported that they had become sexually active (n = 32/86). Adherence to the prescribed steroid regimen was not associated with improvement in sexual activity (Fig 1). Similarly, there was no association with steroid class and improvement in sexual activity.

DISCUSSION

Women with vulvar lichen sclerosus are more likely to improve clinically in both their reported symptoms and physical examination findings when topical steroids are used exactly as prescribed. However, some degree of improvement may occur when topical corticosteroids are used less than prescribed in either frequency or amount. One prospective cohort study showed similar findings—30% of their patients used topical corticosteroids less than prescribed, and this group had a lower rate of symptom suppression (58% vs 93%), a higher rate of adhesions and scarring (40% vs 3%), and more frequent squamous cell carcinoma or vulvar intraepithelial neoplasia (5% vs 0%).[9] We anticipate that our study can aid clinicians when counseling patients—to reinforce with patients that strict adherence to therapy is associated with significantly higher odds of improvement in symptoms and physical examination findings and that imperfect use of corticosteroids may not lead to a similar improvement.

Sexual activity is negatively affected in a very significant way for many women with vulvar lichen sclerosus.[4,5] However, we show that sexual activity is documented inconsistently between specialties—93% of vulvovaginal subspecialists, 29% of gynecologists, and 0% of dermatologists. Lack of clinician inquiry into or documentation of this important quality of life outcome limits the ability to determine whether the current therapeutic regimen is adequately meeting the patient's needs. Focusing on patient's sexual well-being by regularly inquiring about and documenting sexual function can help improve the clinical care provided to these women. Validated questionnaires assessing sexual function such as the Female Sexual Function Index and Female Sexual Distress Scale[5,10] could be incorporated into regular clinical care to objectively assess improvements in women's sexual function related to vulvar lichen sclerosus.

Our study has multiple strengths, including the large sample size and the longitudinal study design over more than 5 years for this cohort study. Additionally, our study includes patient outcomes across different specialty practices. Limitations include the retrospective study design and the fact that our data collection was restricted to information documented in the patient's chart. Differing documentation practices between specialties may make it appear that there are interspecialty differences that may not actually exist within the population of interest.

CONCLUSION

This longitudinal retrospective cohort study showed that patients using topical corticosteroids exactly as prescribed are significantly more likely to have improvements in both symptoms and physical examination findings. Ultra-high- and high-potency steroids were much more likely to result in symptomatic and physical examination finding improvement. Compliance with the corticosteroid regimen was not statistically associated with changes in sexual activity, although our study may have been underpowered to detect this, given the lack of routine documentation by all specialists. However, as a result of care for VLS, many women can experience improvement in sexual function.

REFERENCES

1. Funaro D. Lichen sclerosus: a review and practical approach. *Dermatol Ther*. 2004;17(1):28-37.
2. Leibovitz A, Kaplun V, Saposhnicov N. Vulvovaginal examinations in elderly nursing home women residents. *Arch Gerontol Geriatr*. 2000;31(1):1-4.

3. Neill SM, Lewis FM, Tatnall FM, Cox NH, British Association of Dermatologists. British Association of Dermatologists' guidelines for the management of lichen sclerosus 2010. *Br J Dermatol*. 2010;163(4):672-682.
4. Haefner H, Aldrich N, Dalton V, et al. The impact of vulvar lichen sclerosus on sexual dysfunction. *J Womens Health (Larchmt)*. 2014;23(9):765-770.
5. Van de Nieuwenhof HP, Meeuwis KA, Nieboer TE, Vergeer MC, Massuger LF, De Hullu JA. The effect of vulvar lichen sclerosus on quality of life and sexual functioning. *J Psychosom Obstet Gynaecol*. 2010;31:279-284.
6. Gabros S, Zito PM. Topical corticosteroids. StatPearls. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532940/. Accessed November 29, 2019.
7. Chi CC, Kirtschig G, Baldo M, Brackenbury F, Lewis F, Wojnarowska F. Topical interventions for genital lichen sclerosus. *Cochrane Database Syst Rev*. 2011;2011(12):CD008240.
8. Kirtschig G, Becker K, Günthert A, et al. Evidence-based (S3) guideline on (anogenital) lichen sclerosus. *J Eur Acad Dermatol Venereol*. 2015;29(10):43.
9. Lee A, Bradford J, Fischer G. Long-term management of adult vulvar lichen sclerosus: a prospective cohort study of 507 women. *JAMA Dermatol*. 2015;151(10):1061-1067.
10. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Martial Ther*. 2000;26:191-208.