Overnight 5% Lidocaine Ointment for Treatment of Vulvar Vestibulitis

Denniz A. Zolnoun, MD, MPH, Katherine E. Hartmann, MD, PhD, and John F. Steege, MD

OBJECTIVE: To assess the effectiveness of nightly application of 5% lidocaine ointment for treatment of vulvar vestibulitis.

METHODS: Over 17 months, we assessed women presenting to our pain clinic for evaluation of introital pain; 61 women met the criteria for vulvar vestibulitis and participated in a treatment trial. We measured daily pain and intercourse-related pain using a 100-mm visual analog scale. We compared ability to have intercourse and pain ratings before and after treatment, and investigated whether prior treatment or gynecologic comorbidities predicted response to treatment.

RESULTS: After a mean of 7 weeks of nightly treatment, 76% of women reported ability to have intercourse, compared with 36% before treatment ($P = .002$). Intercourse-related pain score was 39.11 (95% confidence interval [CI] 30.39, 47.83) points lower after treatment ($P < .001$), with a decrease of 10.37 (95% CI 3.53, 17.21) points in daily pain score ($P = .004$). We found no association between response to prior episodic use of lidocaine and response to nightly therapy with lidocaine ointment. Few patient characteristics predicted response to treatment; however, women with interstitial cystitis and other vulvar conditions were least likely to benefit.

CONCLUSION: Long-term, nightly application of 5% lidocaine ointment shows promise as a treatment for management of vulvar vestibulitis; a randomized, double-blind, clinical trial is warranted. (Obstet Gynecol 2003;102: 84–7. © 2003 by The American College of Obstetricians and Gynecologists.)

Since its description by Skene more than a century ago, vulvar vestibulitis has been an elusive disorder with poorly understood etiology, pathophysiology, and treatment.[1] In 1987, Friedrich proposed the first clinical diagnostic criteria for vulvar vestibulitis: severe pain on vestibular touch and entry dyspareunia, tenderness to pressure localized within the vestibule, and physical findings limited to erythema of various degrees.[2,3] The pain may be present only during attempted coitus and/or during other daily activities. The population prevalence of vulvar vestibulitis is unknown; a single study of 210 consecutively evaluated gynecology patients in a community setting reported that 15% of women met criteria for vulvar vestibulitis.[4]

Though vulvar vestibulitis is likely common, the optimal therapy is unknown. Treatments studied have included long-term fluconazole and topical cromolyn, interferon alpha-2b injection, cognitive behavioral therapy, vestibuloplasty, and laser treatment. Of these, the most promising to date have been cognitive behavioral therapy, with 20–38% reduction in pain scores,[5] and vestibuloplasty, with 60–89% of patients reporting satisfaction with pain reduction and/or sexual function after surgery.[5–7]

We have been intrigued with the degree to which vulvar vestibulitis shares characteristics of other neuroinflammatory conditions such as postherpetic neuralgia. In such pain syndromes, initial nerve injury provokes sensitization of nociceptors and perpetuates release of neuropeptides that maintain an inflammatory process.[8,9] As in postherpetic neuralgia, women with vulvar vestibulitis demonstrate allodynia (perception of pain from nonpainful stimuli) and respond variably to treatment.[8–11] Long-term use of lidocaine skin patches has led to improvement of pain in patients with postherpetic neuralgia. By analogy, we sought to investigate extended use of topical anesthetic treatment of vulvar vestibulitis. The objective of our study was to describe the response of women with vulvar vestibulitis to treatment with nightly application of 5% lidocaine ointment.

MATERIALS AND METHODS

Between November 1999 and March 2001, we evaluated all women referred to the University of North Carolina Pelvic Pain Clinic for management of vulvar pain for eligibility for enrollment. This study was approved by the Institutional Review Board of the University of

From the Department of Obstetrics and Gynecology, University of North Carolina School of Medicine, Chapel Hill, North Carolina.

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North Carolina School of Medicine. All patients referred for evaluation of vulvar pain had a standardized history and physical examination. After completion of the history, they were asked to rate their discomfort level during daily activity and attempted intercourse using a pencil and paper 100-mm visual analog scale.

We performed comprehensive physical examinations for all women using a standardized form to record findings. We used a cotton-tipped applicator to touch the labia majora, labia minora, and the vestibule, and recorded the presence or absence of allodynia, sensory loss, and any visible inflammatory changes. We diagnosed vulvar vestibulitis using Friedrich criteria.[3] All women with the diagnosis of vulvar vestibulitis and mixed diagnoses were offered enrollment in the study.

Upon establishing the diagnosis, we instructed the study participants on the proper application of the ointment. Using a mirror, we reviewed the anatomy of the involved area with the patients. Patients were instructed to apply a copious amount of 5% lidocaine ointment to the affected area at bedtime and were asked to place a cotton ball generously coated with the 5% lidocaine ointment in the vestibule to assure continuing overnight application. We instructed patients to use the treatment nightly, for 8 or more hours.

We obtained repeat visual analog scale scores for pain with daily activity and pain with intercourse at the follow-up visit scheduled 6–8 weeks after initiation of treatment. Patients were also asked about ability to have intercourse at both the initial and the follow-up visit. Patients were defined as able to have intercourse if they reported any intercourse during a given month, regardless of frequency or degree of discomfort. Those who were celibate because of severity of symptoms were defined as unable to have intercourse. Regardless of the patients' compliance with treatment, or subsequent additional diagnoses, the data for all the patients who met criteria, were offered treatment, and kept their clinical follow-up appointment visit were analyzed.

We used chart review, telephone interview, and direct interview to obtain and confirm additional demographic information. Long-term response to treatment was assessed by sending a follow-up questionnaire and visual analog scale rating a minimum of 6 months after the initiation of treatment.

The primary outcome was a change in daily and intercourse-related visual analog scale scores with treatment. Because sexual dysfunction is the primary concern for patients, we also assessed patients' self-reported ability to have intercourse, and examined the dichotomous outcome of achieving a 50% reduction in intercourse-related pain after treatment. We performed univariate descriptive tabulations and bivariate analyses. Paired *t* tests were used to assess changes in continuous outcomes; Pearson χ^2 and exact tests were used for categoric data.

Table 1. Characteristics of Eligible Subjects

Patient characteristics	Values	*n**
Mean ± SD (y)	30 ± 6	61
Race		61
White	94%	
Black	2%	
Other	3%	
Duration of symptoms (mo)†	31 (5–216)	60
Diagnosis		61
VS	47 (77%)	
VS + vulvodynia	1 (2%)	
VS + others	13 (21%)	
Nulliparous	75%	59
Symptom associated with child birth	14%	58
NSVD 10%		
Cesarean delivery 4%		
Endometriosis	14%	57
Interstitial cystitis	10%	57
No history of STI	88%	57
No. of sexual partners		46
1	23 (49%)	
2–5	18 (38%)	
>5	6 (14%)	
No. of physicians seen	3 ± 2	47
Used 2% lidocaine episodically	21 (39%)	54
Used Elavil	22 (41%)	53
Used topical estrogen cream	40 (70%)	57
Used herbal remedies	12 (20%)	57
TCA application	10 (18%)	56
Topical steroids	32 (56%)	57
Metronidazole gel	26 (46%)	56
Antifungal cream	34 (59%)	57
Surgical procedure for treatment‡	6 (10%)	60

SD = standard deviation; VS = vulvar vestibulitis; NSVD = normal spontaneous vaginal delivery; STI = sexually transmitted infection; TCA = trichloracetic acid.

* Varies based on availability of data (chart review, telephone calls, questionnaires).

† Values are given as medians and ranges.

‡ Laser ablation, revision of episiotomy, vestibuloplasty, etc.

RESULTS

A total of 71 patients were offered treatment. Of these patients, two declined treatment and eight patients had no clinical follow-up data available. This report is based on the remaining 61 patients. The average patient age was 30 ± 6 years, most were white, and the majority had been evaluated by at least one physician for their symptoms (Table 1). Before their initial visit to our clinic, the participants had seen a mean of three different physicians over an average interval of 32 months (range 5–216) since the onset of symptoms. Our primary diagnosis was vulvar vestibulitis in 47 women (77%). Thirteen women (23%) had other concomitant diagnoses

Table 2. Outcomes of Treatment With Nightly 5% Lidocaine Ointment

Outcome	Before treatment	After treatment	*P* or mean difference (95% CI)
Ability to have intercourse (%)	36	76	.002
Daily VAS score	27.36	16.98	10.37 (3.53, 17.21)*
Intercourse-related VAS score	76.15	37.04	39.11 (30.39, 47.83)†

CI = confidence interval; VAS = visual analog scale for pain where 0 = none and 100 = most severe.
* $P = .004$.
† $P = .001$.

(four had vaginismus; three, culture-proven chronic recurrent yeast infection; one, recurrent herpes; one, lichen sclerosis; one, proctalgia fugax; one, obsessive-compulsive disorder involving genital cleansing; and one, postepisiotomy perineoplasty pain).

Most women had tried other treatments, including topical medications (lidocaine 2% used episodically, estrogen cream, metronidazole gel, antifungal cream, corticosteroid cream, and trichloroacetic acid), amitriptyline, oral herbal remedies, and operations (laser ablation, revision of episiotomy, and vestibuloplasty).

Nightly topical 5% lidocaine ointment was associated with an improvement in symptoms in the majority of women. After a mean of 7 weeks' treatment, the daily pain rating was 10.37 (95% confidence interval [CI] 3.53, 17.21) points lower than in pretreatment ($P = .004$). The intercourse-related pain score was 39.11 (95% CI 30.39, 47.83) points lower after treatment, $P < .001$ (Table 2). Seventy-six percent of women reported ability to have intercourse after treatment compared with 36% at the initial visit ($P = .002$). We found no association between prior episodic use of lidocaine and response to nightly treatment. Duration of symptoms, presence of endometriosis, and symptom onset associated with childbirth were not related to response to treatment. The presence of interstitial cystitis and other concomitant vulvar disease was significantly associated with failure to benefit from treatment, $P = .001$ and $P = .05$, respectively.

If we define a 50% or greater decline in pain with intercourse as successful treatment, 57% (36 of 61) achieved this level of success. Women with interstitial cystitis were more than two-fold less likely to respond to treatment (relative risk 2.61; 95% CI 1.05, 6.51), as were those with other vulvar diseases (relative risk 2.1; 95% CI 0.95, 4.63). Other factors examined were not associated with response to lidocaine. Forty-nine percent (30 of 61) of women returned the 6-month follow-up questionnaire. Among those with follow-up information, 77% (23 of 30) reported ongoing use of 5% lidocaine ointment (12 patients were using it infrequently, several times a week, weekly or less). Of the remaining seven patients who stopped using 5% lidocaine, 86% (six of seven) reported sustained improvement in their symptoms and ability to have intercourse.

DISCUSSION

Most women treated with topical lidocaine 5% ointment, applied nightly, noted improvement in symptoms. The majority had tried other medications without relief. This treatment is simple, safe, and inexpensive (approximately $10 for a 35-g tube). We patterned our regimen after the initial trial done by Rowbotham and Fields using 5% lidocaine under a dressing for a 12-hour period for treatment of postherpetic neuralgia.[12] Given the anatomic difficulty of covering the vestibular region, we devised an approach using a medication-coated cotton ball. The cotton ball remains in place overnight and is well tolerated. No protective undergarment is required. Some patients experience transient burning after application, lasting about 15 seconds.

This before-and-after study benefits from prospective use of a simple but well-validated pain assessment technique using consistent records and treatment instructions by a small team of physicians. Nonetheless, we realize that placebo response and patient desire to report favorable results to the clinical care team may account for some of the observed benefits. However, given the persistence of this patient population in seeking relief when not improved (averaging three prior physicians) and the severity of initial presentation compared with follow-up examinations, we believe that a placebo or emollient effect is unlikely to have accounted for the full extent of symptom relief observed. We also recognize the comparatively brief time window for evaluation of the duration of treatment effect. Follow-up is often difficult in referral populations[13]; as such, we have limited ability to assess the longer-term efficacy of this treatment given suboptimal return of 6-month questionnaires.

The potential mechanism of action of 5% topical lidocaine in treating this condition is unknown. Histologic studies show a proliferation of C-fibers (which carry pain sensation) and the presence of calcitonin gene-related peptide (commonly seen with nerve irritation) in vulvar vestibulitis patients.[9,11] In addition, patients with vulvar vestibulitis have abnormalities of sensory perception, such as heat and touch.[8] Lidocaine blocks transmission of C-fibers. Continuous exposure to lidocaine inhibits

"irritable nociceptors" and is the purported mechanism by which it provides benefit in treatment of chronic pain.[14] We postulate that lidocaine's slow onset of action and moderate duration makes it a potentially useful treatment for chronic pain disorders such vulvar vestibulitis.

Topical and injected local anesthetics have been found effective in treating post-herpetic neuralgia.[12] Some patients using topical anesthetics attain sustained relief, whereas others many need to continue treatment for many years to maintain pain relief.[15] In this group with severe symptoms, lidocaine has been the only beneficial treatment. In such patients, adverse events and tachyphylaxis to lidocaine patch therapy have not been seen with long-term use.

Our patients with interstitial cystitis tended to have involvement of anterior vestibule, characterized by exquisite allodynia. Furthermore, two of the six women with interstitial cystitis reported numbness (these two had severe cystitis for many years), or limited perception of touch on the labia minora at presentation. These patients were least likely to respond to our treatment regimen. Women with severe allodynia over the anterior vestibule tended to not respond as well to the treatment. Those with prior surgery responded favorably to the treatment as long as the area of allodynia and tenderness was limited to the posterior vestibule. This before-and-after study suggests nightly topical lidocaine therapy improves symptoms in women with refractory vulvar vestibulitis. Although information bias and placebo effect may have accounted for some of the observed benefit, we doubt that these could account for the substantial benefit seen in most patients. Indeed, after therapy, the proportion of patients who could have coitus doubled. Based on this series, we believe that a randomized controlled trial is warranted to test these encouraging preliminary results.

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Address reprint requests to: Denniz Zolnoun, MD, MPH, CB#7570, University of North Carolina, School of Medicine, Chapel Hill, NC 27599-7570; E-mail: denniz_zolnoun@med.unc.edu.

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