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Effectiveness of silk fabric underwear as an adjuvant tool in the management of vulvar lichen simplex chronicus: results of a double-blind randomized controlled trial

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Abstract

Objective: Avoiding potentially irritating contact is a key point in vulvar lichen simplex chronicus (VLSC) management. This study aims to assess the use of nonirritating silk fabric underwear (Dermasilk) as an adjuvant tool in the treatment of VLSC.

Methods: Twenty women with VLSC were enrolled in a 1-week open-label active treatment phase with topical 0.1% mometasone furoate (MMF) ointment. Participants then entered a 4-week double-blind maintenance phase (MP) in which they were randomized to wear either silk fabric or cotton briefs. During MP, participants were allowed to use MMF on an "as-needed" basis. The main efficacy endpoints were to assess and compare the two intervention groups on the following: (1) number of participants who needed to apply MMF throughout MP; (2) mean number of MMF applications; (3) mean symptom-free interval before MMF reapplication; and (4) changes in the severity of symptoms and signs.

Results: During MP, four women in the silk fabric briefs group applied MMF compared with six women in the cotton briefs group (relative risk, 0.66). The mean number of MMF applications was lower in the silk fabric briefs group than in the cotton briefs group ($P = 0.074$). VLSC symptom-free interval was 22.5 days in the silk fabric briefs group and 7.2 days in the cotton briefs group ($P = 0.0003$). At the end of MP, symptom improvement determined after corticosteroid use increased in the silk fabric briefs group but worsened in the cotton briefs group.

Conclusions: Silk fabric underwear may be a useful tool for the management of VLSC by diminishing external sources of irritation and may reduce use of corticosteroids.

Key Words: Vulvar lichen simplex chronicus – Silk fabric briefs – Cotton briefs – Maintenance – Corticosteroid treatment.

Vulvar lichen simplex chronicus (VLSC) is a benign chronic, exceedingly itchy and distressing disorder characterized by lichenification with varying degrees of overlying excoriations caused by scratching and rubbing.[1-3] It is a relatively common inflammatory dermatosis that develops predominantly in middle to late adult life but may also occur in children. Its incidence and prevalence are not established.[1-3] VLSC can occur de novo in healthy vulvar tissue (primary or idiopathic VLSC) or as a consequence of preexisting underlying itching dermatitis such as psoriasis, lichen sclerosus, and contact dermatitis (secondary VLSC). Both types of VLSC are an expression of the same basic process in which the itch-scratch cycle preponderates in perpetuating the disease. The pathophysiology of primary VLSC is not clear, but atopy is thought to be the primary predisposing factor, as an atopic background is estimated to be found in up to 75% of affected women.[2] Therapy of VLSC is challenging. A large number of topical and systemic treatments have been used, often with unsatisfactory results and unavoidable recurrence.[2-6]

Itching can be elicited by various exogenous irritants such as microbial, chemical, and physical stimuli. It can be hypothesized that the use of underwear made of nonirritating fabric, even with antibacterial properties, could be helpful in the management of VLSC.

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METHODS

Study design and objectives

The present study was conducted between March 2013 and March 2014 at the Vulva Unit of the Dermatology Section of the University of Ferrara (Ferrara, Italy). The study was set up as a single-center, randomized, double-blind, parallel-group, comparative trial.

The main aims of the study were as follows: (1) to assess the efficacy of fine-knitted silk fabric underwear (made of 100% pure sericin-free fibroin) versus cotton underwear in maintaining

improvement in VLSC symptoms and signs obtained with a previous topical corticosteroid treatment; (2) to assess the prognostic significance of demographic and clinical features as potential risk factors for VLSC recurrence; and (3) to assess participant satisfaction with the study briefs.

This was a spontaneous trial with no funding from external sources. Alpretec (San Donà di Piave, Venice, Italy), producer of silk fabric briefs, provided the materials necessary for the study and did not have any role in study design, execution, data analysis and interpretation, and writing of the manuscript.

Study participants

Twenty consecutive adult women with a clinical and, when available, histological diagnosis of VLSC were enrolled in the study. Women were excluded from the study in the presence of the following: systemic or topical VLSC treatment in the 4 weeks before enrollment; active infectious diseases or other dermatoses or carcinoma of the vulva; clinical or histological features showing possible resemblance with other diseases, such as lichen planus, lichen sclerosus, or plasma cell vulvitis; and lack of agreement between clinical and histological features. Throughout the prospective participant screening, four women were not enrolled as they failed to meet the eligibility criteria.

Study procedures and assessment

At inclusion, all enrolled women were randomized (according to a computer-generated simple randomization schedule) to receive a sealed anonymous envelope containing either three pairs of briefs made of silk fabric (Alpretec)—a fine-knitted silk fabric made of 100% pure sericin-free fibroin impregnated with nonmigrating antimicrobial protection (AEM5772/5)—or three pairs of white jersey 100% cotton briefs. The randomization schedule was prepared before enrollment to ensure allocation concealment. Participants were not aware of their group assignment. The content of the envelope was revealed by the producer of the briefs only at the end of the study.

Subjective evaluation of itching, burning, and stinging was obtained by interview at inclusion, using a visual analogue scale (VAS; 0, *absence of symptom*; 10, *highest intensity of symptom*). A global subjective score (GSS) was obtained by summing each symptom parameter (highest score, 30) to ease statistical analyses as previously described.[7,8]

The following six objective parameters were used to evaluate the clinical features and severity of the disease at baseline: (1) erythema, (2) lichenification, (3) hyperpigmentation, (4) itching-related excoriations, (5) purpuric lesions, and (6) scaling. Objective assessment of each sign was performed by investigators using a four-point scale (0, *absent*; 1, *mild*; 2, *moderate*; 3, *severe*). A global objective score (GOS) was obtained by summing each clinical parameter (highest score, 18). Baseline balance of demographic and clinical features among the two study groups was assessed by one-way analysis of variance.

All enrolled women entered a 1-week open-label active treatment phase (ATP) in which participants applied topical 0.1% mometasone furoate (MMF) ointment once daily on the affected vulvar surface. During ATP, women were instructed to wear their own briefs and not the study briefs. At the end of ATP, all participants, regardless of VLSC improvement, discontinued MMF application and entered a 4-week maintenance phase (MP), in which they always wore the study briefs randomly assigned. At the beginning of MP, participants were asked by telephone interview to rate their itching, burning, and stinging intensity using the VAS (0-10). During MP, participants were allowed to use topical MMF once daily at the first symptoms of disease exacerbation on an "as-needed" basis, until symptoms healed. Participants were required to record the date and time of corticosteroid application throughout the 4-week MP. During the entire study duration, no additional local or systemic corticosteroids, immunosuppressive treatments, or cosmetic products expected to relieve VLSC were allowed. No other briefs, apart from the study briefs, were allowed either.

Objective and subjective participant assessment was performed by the same investigators (A.V. and M.C.) blinded to intervention assignment at baseline and at the 4-week control visit.

The primary efficacy endpoint was to assess the following: (1) number of participants in each group who needed to apply MMF during MP; (2) mean number of MMF applications throughout MP in each intervention group; and (3) mean VLSC symptom-free interval before MMF reapplication. These parameters were compared between the study groups. The secondary efficacy endpoint was comparison of changes in the severity of symptoms and signs from baseline to the end of the study between the two treatment groups. Within each group, we assessed changes in VLSC-related symptoms, considered as VAS scores for itching, burning, stinging, and GSS, after both ATP and 4-week MP. Changes in VLSC-related signs, meant as mean GOS, were assessed after MP compared with baseline.

The following demographic and clinical features of enrolled women were statistically elaborated to identify factors potentially predisposing to VLSC relapse during MP: age at inclusion, duration of the disease before study entry, atopy, and clinical features of VLSC (such as severity of signs and symptoms) at baseline.

To assess participant satisfaction with the study underwear, we invited each woman to answer the following questions (yes/no) at study completion: (1) Was the study underwear convenient and comfortable? (2) Did you like the underwear fabric? (3) Overall, did you find the study underwear better than what you usually use? (4) Would you continue wearing it in the future?

Adverse events and causal relationship with the study underwear were assessed.

Statistical analyses

Efficacy analysis was based on the intent-to-treat population (defined as all women enrolled in the study).

Binary data were analyzed with χ^2 test or Fisher's exact test according to conditions. Quantitative data were analyzed with *t* test (normality and homoscedasticity) or, alternatively, with Mann-Whitney *U* test. Normality of groups was assessed by

TABLE 1. *Demographic and clinical data of all enrolled participants and of the two study groups*

	Participants	
	Silk fabric briefs group (n = 10)	Cotton briefs group (n = 10)
Age at VLSC diagnosis, mean (SD) [range], y	41.0 (13.1) [18-60]	49.7 (13.1) [32-68]
Age at VLSC onset, mean (SD) [range], y	37.7 (13.7) [14-57]	43.2 (13.4) [26-59]
Delay in diagnosis of VLSC, mean (SD) [range], mo	18.8 (13.6) [0-48]	20.9 (16.4) [1-60]
Duration of VLSC, mean (SD) [range], y	3.3 (3.1) [1-12]	6.5 (2.9) [2-11]
History of atopy, n (%)	1 (10.0)	4 (40.0)
Histology, n (%)	3 (30.0)	1 (10.0)
History of intolerance to cosmetics or topical drugs, n (%)	2 (20.0)	1 (10.0)
Participants who had previously changed kind of underwear	9 (90.0)	8 (80.0)
Participants who had used previous therapy, n (%)	9 (90.0)	8 (80.0)
Previous therapy, n (%)		
Corticosteroids	7 (70.0)	5 (50.0)
Antimycotics	2 (20.0)	2 (20.0)
Antibiotics	2 (20.0)	3 (30.0)
Emollients	8 (80.0)	10 (100.0)
Unprecise	3 (30.0)	1 (10.0)

VLSC, vulvar lichen simplex chronicus.

Kolmogorov-Smirnov test; homoscedasticity of groups was assessed by Levene's test and Brown-Forsythe test.

$P < 0.05$ was considered statistically significant.

RESULTS

Participant characteristics

Table 1 presents the demographic and clinical data of women with VLSC (N = 20) who entered the ATP study. None of the enrolled women were used to wearing silk underwear.

At the end of ATP, all 20 participants entered MP and were included in the intent-to-treat population, randomized to wear either silk fabric briefs (Dermasilk) (10 women) or cotton briefs (10 women). Demographic and disease features were well balanced between the two MP groups (for each parameter, significance was assessed by one-way analysis of variance). No participant dropped out of the study, and none reported to have missed wearing the study underwear.

Efficacy evaluations

During MP, four and six participants in the silk fabric briefs group and cotton briefs group, respectively, reapplied MMF at least once (Table 2). The rate of women who needed to reapply the topical corticosteroid (relapsing participants) was not significantly different between the study groups ($P = 0.65$; Fisher's exact test). The relative risk for corticosteroid reapplication was 0.66 (95% CI, 0.26-1.66) in silk fabric briefs participants compared with cotton briefs participants. The mean number of MMF applications during MP was 1 (range, 0-7) in the silk fabric briefs group and 3.8 (range, 0-18) in the cotton briefs group. This result indicated that using silk fabric briefs reduced the mean number of monthly corticosteroid applications in an almost significant way ($P = 0.074$; t test). The mean VLSC symptom-free interval before MMF reapplication was 22.5 days (range, 20-25) in the silk fabric briefs group and 7.2 days (range, 1-11) in the cotton briefs group. The between-group difference in symptom-free interval was statistically significant ($P = 0.0003$; t test) for the silk fabric briefs group.

Symptom severity obtained by telephone call at the end of ATP is presented in Table 3. Mean values for itching, burning, and stinging decreased significantly in both silk fabric briefs and cotton briefs participants after 1-week MMF treatment compared with baseline (Table 3, Fig.). Overall, mean GSS decreased significantly both in silk fabric briefs participants and in cotton briefs participants. At the end of the 4-week MP, the improvement in mean values for itching, burning, stinging, and GSS obtained after corticosteroid treatment was maintained and even increased in silk fabric briefs participants (Table 3, Fig.). On the other hand, among cotton briefs participants, mean symptom values worsened compared with the end of ATP; for GSS, worsening was statistically significant (Table 3). Mean GOS decreased among both silk fabric briefs participants ($P = 0.006$; t test), in which objective improvement was significant, and cotton briefs participants ($P = 0.081$; Mann-Whitney U test) compared with baseline. Comparing the efficacy of the study underwear in maintaining the symptom and objective improvement achieved after corticosteroid treatment, we found silk fabric briefs to be more efficacious than cotton briefs in controlling itching ($P = 0.013$; t test), burning ($P = 0.174$; Mann-Whitney U test), stinging ($P = 0.081$; Mann-Whitney U test), GSS ($P = 0.030$; t test), and GOS ($P = 0.294$; t test).

TABLE 2. *Primary efficacy endpoint: reapplication of MMF ointment during MP within the two study groups*

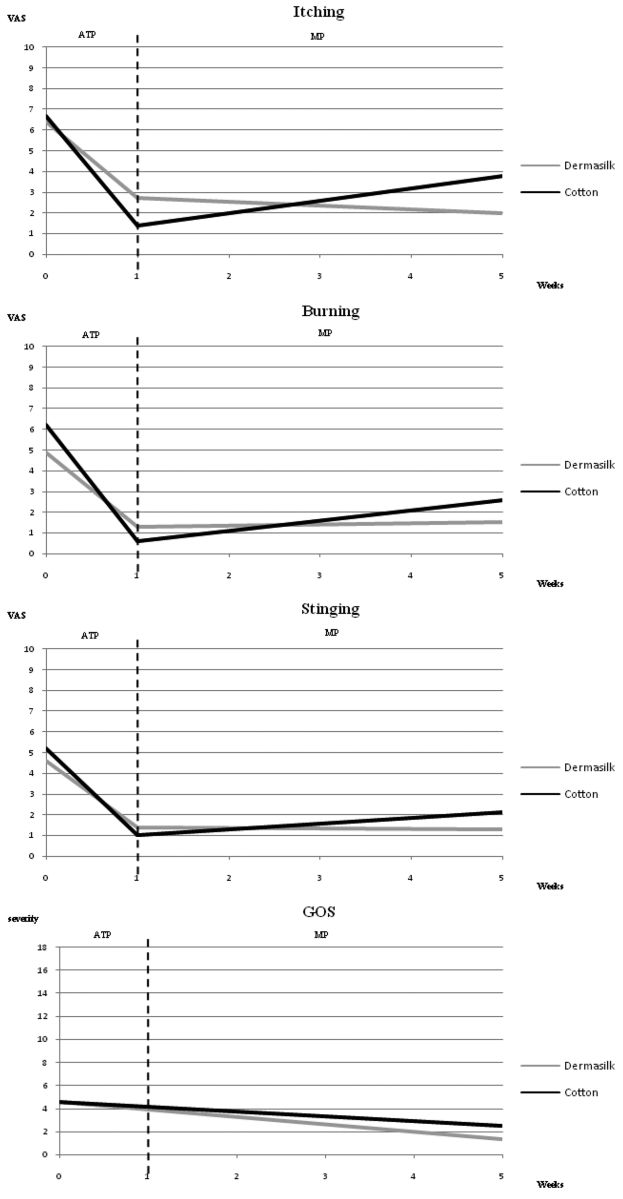
	Participants		
	Silk fabric briefs group (n = 10)	Cotton briefs group (n = 10)	*P*
Participants who reapplied MMF, n (%)	4 (40)	6 (60)	0.65
Number of MMF applications, mean [range]	1 [0-7]	3.8 [0-18]	0.074
Symptom-free interval among relapsing participants, mean [range], d	22.5 [20-25]	7.2 [1-11]	0.0003

MMF, 0.1% mometasone furoate; MP, maintenance phase.

TABLE 3. *Subjective and objective scores for the two study groups*

	Comparison of groups									
	Baseline		After 1-wk therapy (at end of ATP)				After 4-wk therapy (at end of MP)			
	Silk fabric briefs group (n = 10)	Cotton briefs group (n = 10)	Silk fabric briefs group (n = 10)	*P*	Cotton briefs group (n = 10)	*P*	Silk fabric briefs group (n = 10)	*P*	Cotton briefs group (n = 10)	*P*
Symptoms[a]										
Itching	9 [90] **6.400** (2.0)	10 [100] **6.700** (3.020)	8 [80] **2.7** (2.002)	**0.006**	5 [50] **1.400** (1.712)	**0.017**	5 [50] **2.00** (2.708)	0.259	8 [80] **3.800** (3.155)	0.063
Burning	7 [70] **4.900** (2.162)	9 [90] **6.200** (2.828)	3 [30] **1.300** (2.162)	**0.041**	4 [40] **0.600** (0.843)	**0.013**	3 [30] **1.500** (2.592)	0.968	7 [70] **2.600** (2.951)	0.089
Stinging	7 [70] **4.600** (1.646)	8 [80] **5.20** (3.047)	5 [50] **1.400** (1.646)	**0.012**	3 [30] **1.000** (1.699)	**0.007**	3 [30] **1.300** (2.584)	0.522	6 [60] **2.100** (2.183)	0.226
GSS	**16.200** (5.274)	**17.70** (6.183)	**5.400** (5.274)	**0.004**	**3.000** (3.711)	**0.0003**	4.800 (7.743)	0.421	8.500 (6.363)	**0.0148**
Signs[b]										
Erythema	8 [80] **1.200** (0.7888)	7 [70] **1.100** (0.994)	–		–		2 [20] **0.200** (0.421)		3 [30] **0.500** (0.971)	
Desquamation	4 [40] **0.500** (0.707)	5 [50] **0.500** (0.527)	–		–		0 [0] **0** (0)		2 [20] **0.200** (0.421)	
Hyperpigmentation	5 [50] **0.800** (1.032)	5 [50] **0.700** (0.948)	–		–		5 [50] **0.600** (0.707)		4 [40] **0.600** (0.966)	
Lichenification	8 [80] **1.500** (1.414)	9 [90] **1.500** (0.971)	–		–		5 [50] **0.500** (0.707)		7 [70] **0.900** (0.875)	
Itching-related excoriations	3 [30] **0.500** (0.707)	2 [20] **0.400** (0.966)	–		–		0 [0] **0** (0)		1 [10] **0.300** (0.948)	
Ecchymosis	1 [10] **0.100** (0)	2 [20] **0.400** (0.966)	–		–		0 [0] **0** (0)		0 [0] **0** (0)	
GOS	**4.600** (3.565)	**4.600** (3.921)	–		–		**1.300** (1.337)	**0.006**	**2.500** (2.990)	0.081

Data are presented as n [%] and mean (SD); boldface is mean value.
ATP, active treatment phase; MP, maintenance phase; GSS, global subjective score (0-30); GOS, global objective score (0-18).
[a]Calculated as visual analogue scale (0-10).
[b]Calculated from 0 to 3.



ATP, Active Treatment Phase; MP, Maintenance Phase; VAS from 0 to 10; GOS, Global Objective Score (0-18)

FIG. Mean symptom and global objective score (GOS; 0-18) severity at the beginning and end of the study. VAS, visual analogue scale (0-10); ATP, active treatment phase; MP, maintenance phase.

Demographic and clinical predicting factors for VLSC relapse

Neither age at inclusion ($P = 0.13$; t test), duration of the disease before study entry ($P = 0.88$; Mann-Whitney U test), nor atopy ($P = 0.60$; Fisher's exact test) was found to significantly relate to VLSC relapse in our study participants.

Among the subjective parameters evaluated at baseline, burning severity was found to be related to the risk of disease relapse ($P = 0.053$); neither itching ($P = 0.27$) nor stinging ($P = 0.44$) was associated with VLSC relapse and retreatment, according to t test. Severity of objective clinical signs was evaluated as GOS at baseline. GOS was not significantly different between participants who experienced a relapse and participants who did not relapse ($P = 0.45$; t test).

Participant satisfaction

Table 4 presents the answers of the 20 participants who completed the study protocol and underwent the interview on satisfaction. The rate of women who preferred the study underwear to what they usually wore was significantly higher in silk fabric briefs participants than in cotton briefs participants ($P = 0.010$; Fisher's exact test).

Safety evaluation

During the entire study, no adverse effects related to the use of silk fabric or cotton briefs, including contact dermatitis, were noticed, and none of the participants complained of local adverse events.

DISCUSSION

Owing to the chronic and relapsing nature of VLSC, an effective therapeutic strategy requires a multifaceted approach that involves control of skin inflammation, improvement of skin barrier, and identification and elimination of triggering factors. In particular, relapse and persistence of symptoms may be triggered by direct contact with tight underwear or irritant fabric (namely, harsh textile fibers) or by use of nonbreathable fabric underwear (ie, nylon, viscose, etc) supporting a warm environment, sweat retention, and excess moisture.[1-3] Avoidance of irritant or synthetic underwear is usually recommended, and use of cotton briefs is often suggested. However, previous studies of children affected by atopic dermatitis suggested that cotton may present roughness that is capable of irritating skin that is already impaired.[9,10] In contrast, silk has perfectly smooth, regular, and rounded fibers. For this reason, silk produces very little friction against skin and is not irritating.[10,11] Furthermore, in the case of irritated skin, recovery has been shown to be significantly faster when in contact with soft fabrics.[10,11] Based on this, silk underwear could be more advisable than cotton underwear in reducing mechanical irritation and in preventing VLSC-related symptom exacerbation.

The silk fabric underwear used in the present study is made of high-technology fabric that combines the properties of knitted pure silk fibroin (medical-grade sericin-free silk), such as softness, high breathability, and hygroscopic and heat-regulating

TABLE 4. *Patient satisfaction with study underwear*

	Study briefs			
Participants	Convenient/comfortable	Pleasant fabric	Better than usual underwear	Intends to use it in the future
Silk fabric briefs group (n = 10)	9 (90)	10 (100)	6 (60)	9 (90)
Cotton briefs group (n = 10)	8 (80)	10 (100)	0 (0)	5 (50)
P	1	1	0.010	0.140

Data are presented as n (%).

properties, with an antimicrobial agent.[10,12,13] Removal of sericin minimizes the possibility of any contact allergic reaction, and the fabric has extremely low frictional properties because of its long, smooth, cylindrical filaments. The protein structure of fibroin is similar to the stratum corneum of human skin; thus, silk fabric is able to absorb a high percentage of moisture without becoming damp while maintaining a stable heat-humidity balance next to skin and constant skin temperature. The antimicrobial substance that protects silk fabric has no contraindications or undesired effects because it is fixed permanently onto the fiber by covalent bonding and is not released from the fabric. Moreover, it does not alter the composition of normal bacterial flora.[12,13] Silk fabric has been shown to restore skin barrier function (altered by inflammation, irritation, and infections) in several skin disorders such as atopic dermatitis, vulvar lichen sclerosus, and recurrent vulvovaginal candidosis.[10,12-15]

With regard to the efficacy parameters assessed in the present study, after a 4-week MP, daily use of silk fabric briefs has been shown to be effective in controlling the disease and in delaying VLSC exacerbation. In fact, silk fabric briefs were shown to efficiently protect from symptom relapse, as the number of participants requiring corticosteroid retreatment during MP was lower in the silk fabric briefs group than in the cotton briefs group (relative risk, 0.66). Similarly, the mean number of monthly applications of corticosteroid was found to be lower among women wearing silk fabric briefs than among women using cotton underwear, with a difference close to statistical significance. Moreover, considering the effect of sericin-free silk underwear on VLSC symptom-free interval, our results showed that "time before needing corticosteroid reuse" was much significantly longer in silk fabric briefs participants in comparison with cotton briefs participants. Consistent with these findings, silk fabric underwear may be considered a corticosteroid-sparing tool, providing relief of symptoms more effectively than normal cotton underwear.

During MP, participants assigned to the cotton briefs group used topical corticosteroid more often than participants in the silk fabric briefs group; nonetheless, a more effective maintenance of the symptom improvement achieved after ATP was recorded in silk fabric briefs participants (Fig.). Silk fabric was found to be more effective than cotton in controlling disease course and in maintaining symptom alleviation, with even significant differences for itching and GSS. In our participants, objective assessment of VLSC was not performed after ATP. At MP completion, the degree of GOS improvement from baseline was greater in silk fabric briefs participants than in cotton briefs participants. In the former, GOS improvement was statistically significant compared with baseline, whereas cotton briefs participants showed no significant improvement.

Regarding participant satisfaction with underwear use, almost all of the women found the study briefs comfortable, and all enrolled participants, regardless of group assignment, judged the underwear fabric as pleasant. Most participants who wore silk fabric briefs judged them to be preferable to their usual underwear, whereas no participants among those assigned to cotton underwear stated this. Consistent with this, sericin-free silk underwear seems to be more suitable than normal cotton briefs for women with VLSC. In fact, nine participants in the silk fabric briefs group declared their intention to use the study briefs in the future, against only five participants in the cotton briefs group.

Silk allergy among consumers has only rarely been described[16,17] because the final textile products in silk are mostly nonallergenic.[18] In our study, no adverse or allergic reactions were observed; to the best of our knowledge, no reactions to silk fabric have been reported in the literature.

The results reported herein should be viewed in the light of the limitations of the study, such as the relatively small number of enrolled participants in each intervention group. Furthermore, univocal and validated methods for assessing VLSC severity are not available. Randomization led us to include more atopic women in the cotton briefs group than in the silk fabric briefs group, and we cannot exclude that this could have impacted the results. Although participants were blinded to their group allocation, complete cover-up of the fabric of their assigned study underwear could not be guaranteed. Because participants were not aware of the exact composition of their briefs compared with those used in the other arm of the study, potential bias was minimized.

CONCLUSIONS

The results of the present study provide evidence that silk fabric underwear may be a useful tool for VLSC management by diminishing external sources of irritation and by synergizing with the anti-inflammatory action of topical corticosteroids. Symptom relief is expected to reduce the use of corticosteroids while improving women's quality of life.

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