ORIGINAL ARTICLE

A double-blind, randomized prospective study evaluating topical clobetasol propionate 0.05% versus topical tacrolimus 0.1% in patients with vulvar lichen sclerosus

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Background: Vulvar lichen sclerosus is a chronic condition usually responsive to topical corticosteroids.

Objective: We sought to evaluate the efficacy (reduction of signs and symptoms) and safety of clobetasol propionate 0.05% and tacrolimus 0.1% in the treatment of vulvar lichen sclerosus.

Method: This double-blind, randomized study comparing 2 treatments over a 3-month period, enrolled 58 female patients with newly diagnosed vulvar lichen sclerosus or untreated vulvar lichen sclerosus for at least 1 month.

Results: In all, 55 patients were included in the statistical analysis. A total of 28 patients were assigned to the tacrolimus group and 27 patients to the clobetasol group. Both groups showed a significant difference in the decrease of symptoms and signs of lichen sclerosus. At the end of the study, 28 participants (19 tacrolimus and 9 clobetasol) still had some clinical signs of lichen sclerosus (χ^2 = 6.56, P = .015). However, a significantly higher number of patients in the clobetasol group (n = 15) had absence of signs and symptoms of lichen sclerosus (χ^2 = 10.35, P = .002; χ^2 = 10.35, P = .002). No adverse events were reported.

Limitations: Short length of trial and recruitment through our vulvar disease referral center are limitations.

Conclusion: This study showed that topical clobetasol propionate was significantly more effective in treating vulvar lichen sclerosus than topical tacrolimus. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2014.02.019.)

Key words: anogenital; carcinoma; clobetasol propionate; lichen sclerosus; tacrolimus; topical calcineurin inhibitor; vulva.

BACKGROUND

Over the last decade, several studies on the use of topical immunomodulators in patients with lichen sclerosus have shown promising results.[1-14] We conducted this prospective, double-blind

Abbreviations used:

VAS: visual analog scale
VAS-BP: visual analog scale burning/pain
VAS-PR: visual analog scale pruritus

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randomized study to evaluate the efficacy of tacrolimus 0.1% ointment and clobetasol propionate 0.05% ointment.

Study goals

Our research group evaluated the efficacy of tacrolimus 0.1% ointment and topical clobetasol propionate 0.05% (Dermovate, Taro Pharma, Brampton, Ontario, Canada) in the treatment of vulvar lichen sclerosus. The primary goal of this study was to evaluate the efficacy of both treatments in reducing signs and symptoms of lichen sclerosus as clinically assessed by the study investigators and as subjectively reported by participants. A secondary goal was to assess reported side effects upon application of the studied ointments.

CAPSULE SUMMARY

- Topical corticosteroids are the first-line treatment for vulvar lichen sclerosus.
- This study showed that topical clobetasol propionate was significantly more effective in treating signs and symptoms of vulvar lichen sclerosus than topical tacrolimus.
- The long-term safety of either preparation in treating vulvar lichen sclerosus remains unknown.

METHODS

Study group

A total of 58 female participants were enrolled in the study at Ste-Justine Hospital, Montreal, Quebec, Canada, through our vulvar disease clinic from September 2006 to July 2009. Participants were eligible for inclusion if they were aged 2 years or older with newly diagnosed vulvar lichen sclerosus or untreated lichen sclerosus for at least 1 month. The adult participants were referred to our clinic with vulvar lichen sclerosus that was biopsy proven or suspected clinically and then underwent biopsy to confirm diagnosis. All biopsy specimens were read by a dermatopathologist. In children, clinical diagnosis of vulvar lichen sclerosus was deemed sufficient if biopsy proved to be impossible.

Exclusion criteria were: absence of lichen sclerosus after biopsy, known hypersensitivity to the studied products or their vehicle, a history of vulvar intraepithelial neoplasia or anogenital epidermoid carcinoma, presence of condyloma, hyperkeratotic lichen sclerosus, physical limitation preventing application of the study ointment, children in diapers, and finally the use of topical corticosteroids or a calcineurin inhibitor the month before the study.

The study was approved by Sainte-Justine Hospital's Research Ethics Board. A consent form was signed by adult participants or by parents/legal tutors of participating children.

Study design

This was a double–blind randomized study comparing 2 treatment groups. One group received tacrolimus 0.1% ointment and the other, clobetasol propionate 0.05% ointment. Both participants and investigators were blinded to the administered treatment. The hospital's pharmacy department prepared the ointment tubes and insured double-blindness and randomization. Block randomization was used (blocks of 4) to control for the numbers of participants allocated to each group during the enrollment phase of the study. Both groups were instructed on how to apply their ointment on the vulva, nightly, during a 3-month period. If lesions resolved before the end of the 3-month period, participants were still followed up until the end of the study and used their treatment as maintenance therapy, ie, twice weekly application of their ointment.

Participants were seen 4 times during the study. There was an initial visit (visit 1) and 3 follow-up visits, 1 every month (visits 2, 3, and 4).

On visit 1, participants or parents/tutors of participants completed a standardized questionnaire on lichen sclerosus symptoms and treatment history. A review of their medical and surgical history was done. They underwent a complete cutaneous examination by the study dermatologist. Digital photographs of the anogenital area were taken on visit 1 and on visit 4, to assess clinical response to treatment. They underwent blood work including complete blood cell count, fasting glucose, vitamin B12, and an evaluation of thyroid function for screening of known associated autoimmune diseases.

The primary efficacy variable was clinical improvement of lichen sclerosus as determined by the study investigator after the participants' vulvar examination on visits 2, 3, and 4. The study investigator, who was blind to the treatment, assessed clinical signs (white papules and/or patches, atrophy, erosion and ulcerated lesions, erythematous patches, lichenification) in 5 specific regions of the anogenital area: perianal, perineal, labia majora, labia minora, and the clitoris. The main measure for the clinical evaluation was a score of 0 to 3 (no clinical sign, and mild, moderate, or severe clinical signs) given to each participant by the study