A Single-Center, Double-Blind, Randomized Trial of the Atrophogenic Effects of Fluocinonide Cream 0.1% Versus Clobetasol Propionate Cream 0.05% in Participants With Corticosteroid-Responsive Dermatoses

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To compare the atrophogenic effects of fluocinonide cream 0.1% versus clobetasol propionate cream 0.05%, 20 participants with corticosteroid-responsive dermatoses were randomly assigned to receive fluocinonide cream 0.1% on one arm and clobetasol propionate cream 0.05% on the other arm. Study medications were applied to disease-free target areas on the inner arms twice daily for 2 weeks. The epidermal thickness of pretreatment and posttreatment punch biopsy specimens was measured. Skin examinations were performed evaluating clinical signs of atrophy. No significant reduction in epidermal thickness was observed in the fluocinonide-treated sites (mean, −0.0318 mm; standard deviation, 0.0239; P=*.1991). A significant reduction in epidermal thickness was seen in the clobetasol-treated sites (mean, −0.1825 mm; standard deviation, 0.0239;* P<*.0001). This reduction was significantly greater than results from sites treated with fluocinonide cream 0.1% (difference, −0.1507; standard deviation, 0.0131;* P<*.0001).*

*Although topical corticosteroids often are the first-line treatment for patients with various dermatoses, a side effect of continuous use is cutaneous atrophy. Our study demonstrated that clobetasol propionate cream 0.05% caused a significantly greater reduction in epidermal thickness compared with fluocinonide cream 0.1% when used twice daily for 2 weeks (*P<*.0001). However, neither drug caused significant clinical signs of atrophy.*

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Topical corticosteroids are potent anti-inflammatory, antipruritic, vasoconstrictive agents that help relieve the discomfort of a wide range of dermatologic conditions.[1] Because of their broad therapeutic effects, topical corticosteroids

often are used to treat inflammatory skin conditions, including atopic dermatitis, plaque psoriasis, and contact dermatitis. Widely prescribed, topical corticosteroids often are the first line of treatment recommended by physicians.

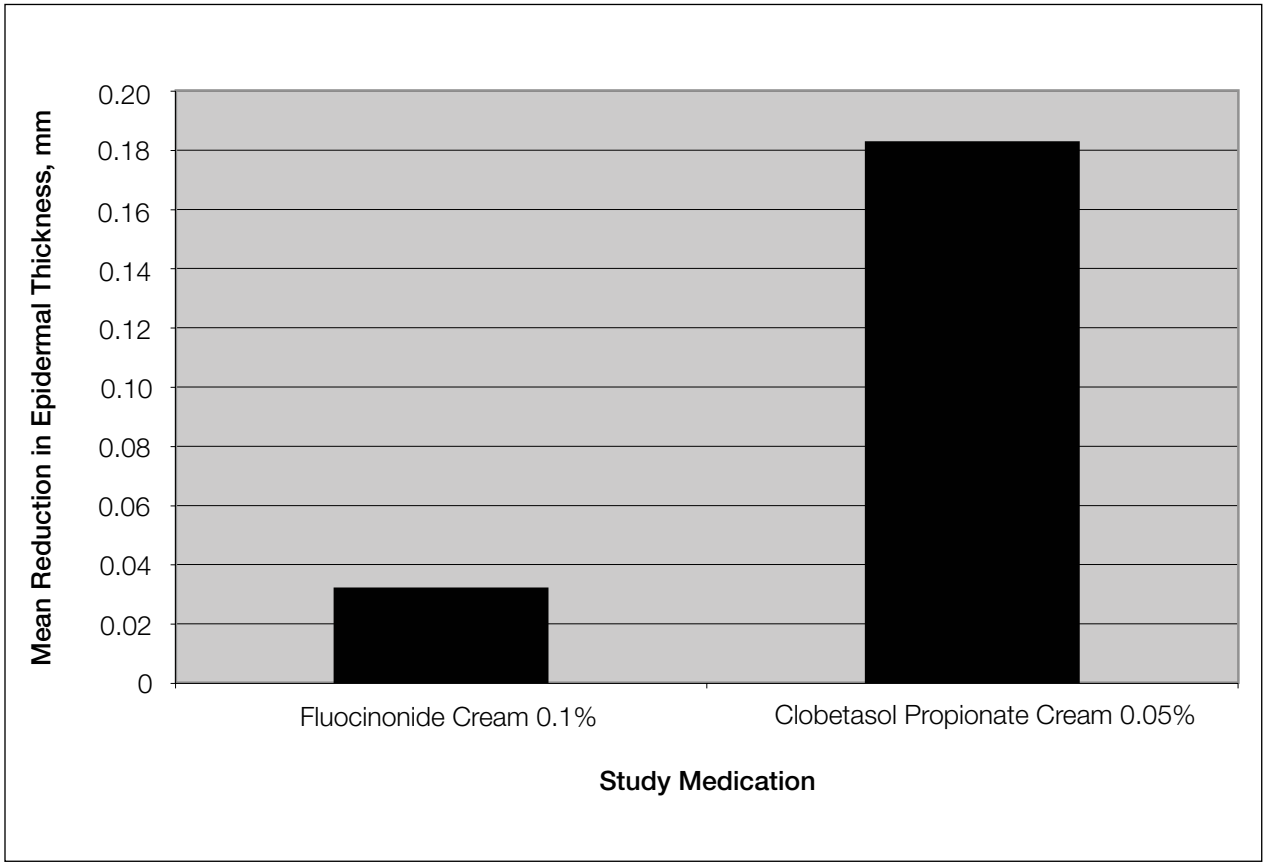
A common side effect of continuous topical corticosteroid use is cutaneous atrophy manifesting as skin thinness, shininess, striae, telangectasia, purpura and/or ecchymosis, loss of elasticity, and loss of normal skin markings.

In this phase 4, single-center, double-blind, randomized trial, the atrophogenic effects of fluocinonide cream 0.1% versus clobetasol propionate cream 0.05% applied twice daily for 2 weeks in participants with corticosteroid-responsive dermatoses were compared.

Methods

This double-blind randomized trial evaluated and compared the atrophogenic effects of fluocinonide cream 0.1% and clobetasol propionate cream 0.05% in 20 adults with corticosteroid-responsive dermatoses. All participants provided written informed consent. Prior to study initiation, institutional review board approval was obtained. Participants were 18 years or older with corticosteroid-responsive dermatoses on both arms with disease-free sites suitable for target areas. Participants were excluded if they were lactating or pregnant, had hypersensitivity to the study medications, or had used corticosteroids or any investigational drug within 4 weeks of day 0 (baseline).

Participants, investigators, and all study staff except pharmacists were blinded to treatment assignments. Randomization was performed via a computer-generated 1:1 randomization schedule with participant numbers and study medications sequentially allocated as participants enrolled in the study. Participants randomly were assigned to receive either fluocinonide cream 0.1% on the left arm and clobetasol propionate cream 0.05% on the right arm, or fluocinonide cream 0.1% on the right arm and clobetasol propionate cream 0.05% on the left arm. Tubes of medication were supplied with blinded labeling; they were prelabeled as left or right. Participants were instructed to apply medicine from the tube labeled left on their left arms and medicine from the tube labeled right on their right arms. Study medication (0.5 fingertip unit)[2] was applied in a thin layer to disease-free target areas



A comparison of the atrophogenic effects of fluocinonide cream 0.1% versus clobetasol propionate cream 0.05% based on the results of a 2-week study in 20 participants.

approximately 5×5 cm on the inner arms twice daily for 2 weeks.

At the baseline visit, a pretreatment punch biopsy specimen was taken from a healthy area of skin on the left and right inner arms of each participant. On treatment completion, a posttreatment punch biopsy specimen was taken from the treated target areas on both arms of each participant at day 14. Epidermal thickness of the pretreatment and posttreatment specimens was measured. For each biopsy specimen, the epidermal thickness was measured between rete ridges at 5 separate locations and was averaged.

Skin examinations of target areas were performed at each visit (baseline/day 0, and days 7 and 14) evaluating clinical signs of atrophy. A follow-up visit occurred at day 21; skin examinations were performed and sutures were removed. Skin thinness, shininess, striae, telangiectasia, purpura and/or ecchymosis, loss of elasticity, and loss of normal skin markings were assessed on a scale of 0 to 3 (0=none, 1=mild, 2=moderate, 3=severe). Dermoscopy was used for the evaluation of telangiectasia. The investigator global assessment of cutaneous atrophy was based on a scale of 0 to 3 (0=no signs or symptoms of cutaneous atrophy; 1=mild signs or symptoms of cutaneous atrophy; 2=moderate signs or symptoms of cutaneous atrophy; 3=severe signs or symptoms of cutaneous atrophy). Statistical evaluations were performed.

Results

Epidermal Thickness—No significant reduction in epidermal thickness was observed in the fluocinonide-treated sites (mean, −0.0318 mm; standard deviation, 0.0239; $P=.1991$). A significant reduction in epidermal thickness was seen in the clobetasol-treated sites (mean, −0.1825 mm; standard deviation, 0.0239; $P<.0001$). This reduction was significantly greater than results from sites treated with fluocinonide cream 0.1% (difference, −0.1507; standard deviation, 0.0131; $P<.0001$). Results are summarized in the Figure.

Investigator-Performed Skin Examinations for Signs of Cutaneous Atrophy—Telangiectasia was the only condition that changed with treatment. Only 4 of 20 participants experienced a change in telangiectasia (worsening in all cases) at some point during follow-up. One participant experienced worsening of telangiectasia on the fluocinonide-treated side and not on the clobetasol-treated side. Three participants experienced worsening of telangiectasia on the clobetasol-treated side and not on the fluocinonide-treated side. Of note, 16 of 20 participants did not experience clinical signs of cutaneous atrophy when exposed to either drug. The McNemar test was used to determine an association between treatment and worsening of telangiectasia; no significant difference between fluocinonide cream 0.1% and clobetasol propionate cream 0.05% with respect to the development of telangiectasia was found ($P=.6171$).

Participant Self-assessment—None of the participants assessed their skin as changing over the course of treatment.

Investigator Global Assessment of Cutaneous Atrophy—Only 1 participant had an investigator global assessment change over the course of treatment. The score was 1 (mild signs or symptoms of cutaneous atrophy) at baseline and 0 (no signs or symptoms of cutaneous atrophy) at days 14 and 21.

Comment

Because of their potent anti-inflammatory effects, topical corticosteroids often are the first-line treatment for patients with various dermatoses. Although topical corticosteroids yield broad therapeutic effects, duration of treatment often is limited by the occurrence of both cutaneous and systemic side effects. In addition to causing the development of striae, telangiectasia, purpura, hypothalamic-pituitary-adrenal axis suppression, rosacea dermatitis, and acneform eruptions, long-term topical corticosteroid use also may result in cutaneous atrophy. The purpose of this study was to compare the atrophogenic potential of 2 topical corticosteroids. Our study demonstrated that clobetasol propionate cream 0.05% caused a significantly greater reduction in epidermal thickness compared with fluocinonide cream 0.1% when used twice daily for 2 weeks ($P<.0001$). However, neither drug caused significant clinical signs of atrophy.

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