



Original Research

Hydrocortisone 1% cream and sertaconazole 2% cream to treat facial seborrheic dermatitis: A double-blind, randomized clinical trial^{☆,☆☆}K. Balighi^a, S.Z. Ghodsi^a, M. Daneshpazhooh^a, S. Ghale-Baghi^b, M. Nasimi^a, A. Azizpour^{a,*}^a Department of Dermatology, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran^b Research Center and Department of Head and Neck Surgery, Hazrat-e-Rasool Akram Hospital, Iran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Background: Seborrheic dermatitis (SD) is a chronic dermatitis with periods of remission and relapse that requires long-term treatment.**Objective:** We compared the efficacy and safety of treatment with sertaconazole with standard corticosteroid medications in adults with facial SD.**Methods:** In this double-blind, randomized controlled trial, 60 patients with a diagnosis of SD were enrolled. Patients were instructed to apply either sertaconazole 2% cream (30 patients) or hydrocortisone 1% cream (30 patients) twice daily to the affected area of the face. The severity of facial SD was assessed at 0, 2, and 4 weeks of treatment. Secondary efficacy measures included patient assessment of seborrhea, adverse events, and improvement percentage (IP).**Results:** SD lesions cleared significantly ($p < .05$) and similarly in both treatment groups ($p > .05$). Both treatments resulted in significant improvement of SD lesions and the rate of adverse events was similar in both groups. The IP was higher for treatment with hydrocortisone in Week 2 and similar in both groups at the end of the study.**Limitations:** Limitations include the small number of patients who were recruited for this study and the lack of evaluation of time to relapse.**Conclusion:** Treatment with topical sertaconazole may be regarded as a substitute for topical corticosteroid medications due to the fewer adverse events and similar efficacy.© 2016 The Authors. Published by Elsevier Inc. on behalf of Women's Dermatologic Society. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Seborrheic dermatitis (SD) is a common, chronic, and relapsing dermatitis that is primarily patterned on sebum-rich parts of the scalp, face, trunk, and intertriginous areas. Treatment for SD depends on many factors including location on the body (Schmidt, 2011). Topical agents that reduce inflammation and scale production have been shown to be effective in the management of SD. Agents that were used in the treatment of SD are either symptomatic (e.g., keratolytic treatments) or etiologic therapies (e.g., antifungal and corticosteroid treatments).

Malassezia infection is an important pathogenic factor in SD. The density of this pathogen on the skin positively correlates with the severity of SD (Dessinioti and Katsambas, 2013; Gupta and Bluhm, 2004; Schwartz et al., 2006). Topical antifungal treatments reduce malassezia proliferation and the resulting inflammation, leading to the improvement of SD. Corticosteroid treatments are generally used to reduce inflammation. Hydrocortisone is a mild topical corticosteroid that is used to reduce swelling, redness, and itching in various inflammatory skin disorders including SD (Papp et al., 2012; Rovelli et al., 2011). A new imidazole antifungal agent that is used in the treatment of SD is sertaconazole, which inhibits the synthesis of ergosterol in the cell wall of fungi (Weinberg and Koestenblatt, 2011).

The aim of this study was to compare the efficacy and side effects of sertaconazole 2% cream with those of hydrocortisone 1% cream in the treatment of SD.

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Methods and materials

Patient selection

The present study was a single-center, double-blind, randomized, and controlled study. Patients aged 18 years or older with SD on the face were screened for the study. The minimum number of patients was 30, which was calculated with the hypothesis of 80% improvement in the hydrocortisone treatment group and 50% in sertoconazole treatment group. Confidence interval was 95%, and the power of the study was 80%.

Patients who had a history of significant medical conditions that were not well controlled, had any known or suspected hypersensitivity to any constituent of the study medications, were under treatment for facial acne, had untreated or uncontrolled infection involving the face, were under treatment with SD-developing drugs, were receiving systemic corticosteroid therapies, or were pregnant or breastfeeding were excluded from the study. Topical emollients were the only topical agents that were allowed within 2 weeks before and during the study period.

Study protocol

This double-blind, randomized trial was approved by the ethics committee of the Tehran University of Medical Sciences and conducted between May 2014 and May 2015. Patients randomly (block randomization) received treatment with either topical hydrocortisone 1% or topical sertoconazole 2%. The creams were filled in identical cream boxes and marked as A and B, respectively. The treatment was blinded to the patient and the primary physician. Patients were instructed to apply a thin layer of cream on the affected areas of the face twice daily. They were also asked to provide demographic information and indicate the location of skin involvement, severity of disease, presence of dandruff, and total score for the disease (range, 0 = no seborrhea to 10 = worst seborrhea imaginable).

Patient evaluation

Patients were assessed at the beginning of the study and at 2- and 4-week timepoints by the primary investigator. The face was classified into four regions: eyebrows, nose, nasolabial fold, and ears. The scoring index (SI) that is recommended by Koca et al. (2003) was used. Each region was clinically evaluated for erythema, scale, pruritus, and papules and given a score from 0 to 3 (0 = clear, 1 = mild, 2 = moderate, and 3 = severe). On the basis of the SI, the sum of these scores was categorized in three groups: mild (score 0–4), moderate (5–8), and severe (9–12).

At each visit, changes in the severity of SD were assessed. A decrease in severity score could lead to a complete remission in some patients; therefore, to differentiate complete remission from the same amount of decrease without clearing of all lesions, we defined a variable called improvement percentage (IP). IP is calculated by dividing the decrease in SD score by the initial SD score. Patients were asked about the tolerability of the medication and possible medication-related adverse effects including pruritus and irritation. Patients who showed any intolerable side effects were excluded from the study. In addition, a visual analogue scale (VAS) with a 10-point scale was used to determine patients' degree of satisfaction.

Statistical analysis

Statistical analysis was performed on a 'per protocol' population that did not drop out of the study. SPSS Statistics Version 19.0 (SPSS Inc, Chicago, IL, USA) was used to conduct the statistical analysis and *p*-values less than 0.05 were considered significant. Independent

t tests were used to compare the efficacy of the treatment groups. Paired *t* tests were applied to evaluate the efficacy of each treatment at 2- and 4-week timepoints after treatment initiation.

Results

A total of 64 patients were initially included in the study, 60 of whom were randomized to the study treatment. Four patients declined to take part in the research. Thirty patients were randomized to the hydrocortisone 1% cream treatment group and the remaining 30 patients to the sertoconazole 2% cream treatment group. All patients in both groups completed the 4-week study. Table 1 shows a summary of the baseline demographics of the two treatment groups, which were similar. Most participants were male (56.65%) and the male/female ratio was similar in both treatment groups.

The mean age of all patients was 33.47 years, with a range of 19 to 80 years. The mean decrease in seborrhea score at the end of Week 2 was 3.80 (79.91%) in the hydrocortisone group and 2.73 (67.49%) in the sertoconazole group ($p > .05$). At Week 4 of the study, the decrease in seborrhea score was 4.00 (95.78%) in the hydrocortisone group and 4.53 (96.50%) in the sertoconazole group ($p > .05$). In both groups, the decrease in seborrhea score compared with the baseline score was statistically significant (both $p < .05$; Fig. 1). The decrease in the seborrhea index was similar in both groups ($p > .05$); however, the IP showed better results in the hydrocortisone treatment group at Week 2 ($p < .05$) and similar results after 4 weeks of treatment ($p > .05$).

Both treatments were well tolerated by the patients. Two patients complained of hypopigmentation after hydrocortisone treatment and two patients complained of xerosis with sertoconazole treatment. No significant relation was found between the age or sex of the patients and the clinical response; however, a negative correlation was observed between the severity of SD (seborrhea score) and the amount of improvement ($p < .05$). At the end of the study period, 60% of each group was completely clear (seborrhea score = 0).

Discussion

Various treatment options that can effectively treat SD are currently available. These treatments focus mainly on controlling acute

Table 1

	Hydrocortisone 1% (n = 30)	Sertoconazole 2% (n = 30)
Mean age (year)	32.27	34.67
Male, (%)	53.3	60
Female, (%)	46.7	40
Present in baseline (%)		
Erythema	93.3	90
Scale	86.7	93.3
Pruritus	76.7	83.3
Papule	40	30
Scalp dandruff	93.3	86.7
Patient assessment score	4.87	4.20
Based on scoring system by Koca et al. (2003)		
Nose	3.03/3.33 (77)	2.73/2.94 (65)
Nasolabial	2.97/3.23 (80)	3.60/3.00 (61)
Ear	2.07/3.69 (77)	2.37/3.36 (66)
Eyebrow	3.40/3.95 (77)	3.40/2.86 (59)
Total	11.47/8.93 (80)	12.10/7.53 (67)
Improvement after 4 weeks, score (%)		
Nose	4.05 (96)	4.33 (95)
Nasolabial	3.82 (94)	4.55 (93)
Ear	4.69 (98)	4.79 (94)
Eyebrow	4.75 (93)	4.57 (94)
Total	10.90 (97)	11.37 (96)

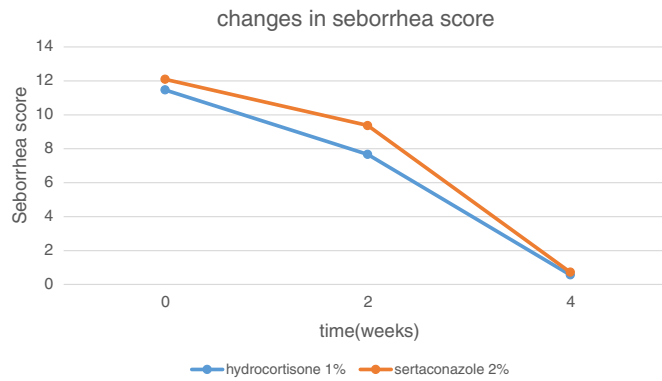


Fig. 1. Within-group decrease in seborrhea score from baseline to study end ($p < .05$ for both treatment groups). There was no significant difference between the treatment groups at any timepoint.

flares and maintaining remission. Because no permanent cure for SD exists, long-term treatment is required in patients (Dessinioti and Katsambas, 2013; Gupta and Bluhm, 2004). Effective therapies that have been reported for SD include anti-inflammatory agents, keratolytic agents, antifungal treatments, and alternative medications (Bikowski, 2009; Koca et al., 2003; Naldi and Rebora, 2009; Schwartz et al., 2006). In this randomized, controlled trial, we compared the efficacy and safety of topical hydrocortisone 1% with topical sertaconazole 2% in the treatment of facial SD.

Our results showed an equal decrease in the SD severity score after 2- and 4-week timepoints of treatment between the both agents ($p > .05$). The efficacy of the two topical agents was also compared with a new variable called IP. On the basis of the IP, hydrocortisone 1% achieved better therapeutic results after 2 weeks of treatment; however, similar results were obtained in both groups at Week 4 of the study. Conclusively, the treatment of SD by topical hydrocortisone 1% can lead to earlier improvement of the condition; however, hydrocortisone 1% and sertaconazole 2% eventually show similar therapeutic responses after 4 weeks of treatment. Patients' global satisfaction with treatment also suggested similar results in both groups (Fig. 2).

Sertaconazole is an antifungal agent of the imidazole class that has antibacterial, anti-inflammatory, and antipruritic potential (Carrillo-Muñoz et al., 2011). Given the chronicity of SD, long-term treatment with topical agents is almost always the need of the hour. Our findings indicate that topical sertaconazole has an effect that is equal to treatment with topical hydrocortisone in clearing of SD lesions. This is an important observation because sertaconazole has fewer medication-related adverse effects with long-term treatment.

Our results are similar to those from previous studies that evaluated the efficacy of topical sertaconazole in patients with SD

(Elewski and Cantrell, 2011; Firooz et al., 2006; Goldust et al., 2013a, 2013b; Papp et al., 2012). In a double-blind, randomized, controlled study, Goldust et al. (2013a) compared the efficacy of twice daily application of topical hydrocortisone 1% with that of topical sertaconazole in 69 consecutive patients in each treatment group. Both groups underwent 4 weeks of treatment. The majority of patients had a moderate SD index in the pretreatment stage and most patients showed a mild SD index in the posttreatment stage ($p > .05$). Patient satisfaction was the highest among those who were treated with sertaconazole after 28 days of treatment ($p < .05$; Goldust et al., 2013a, 2013b). These results are similar to our present findings and confirm the efficacy of topical sertaconazole in the treatment of patients with facial SD.

Conclusions

In conclusion, the results of the current study agree with those of similar trials that researched topical sertaconazole 2% as treatment for patients with SD. The limitations of this work include the small number of patients who were recruited for the study and the lack of evaluation of time to relapse. Despite these limitations, the efficacy of sertaconazole to treat patients with SD and its lower side effects provide enough rationale to assess the use of topical sertaconazole in larger, longer-term, randomized, double-blind trials. Because the chronicity of SD requires long-term treatment to maintain disease control, topical sertaconazole, which has similar effect and lower adverse events compared with topical steroid therapies, may be regarded as an excellent substitute for topical steroids in the treatment of patients with SD if proven to have the same efficacy in long-term trials.

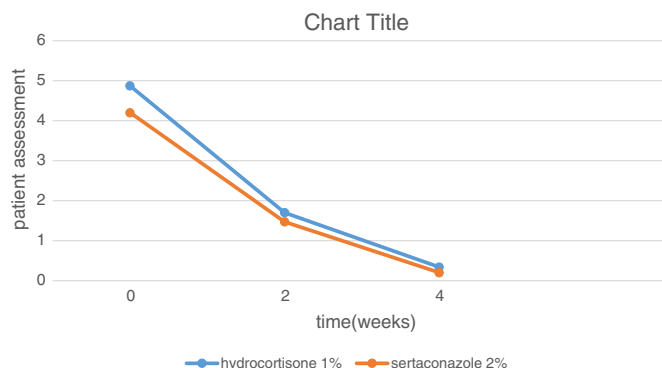


Fig. 2. Within-group decrease in patient satisfaction from baseline to study end ($p < .05$ for both treatment groups). There was no significant difference between the treatment groups at any timepoint.

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