

ORIGINAL ARTICLE

Comparison of sertaconazole 2% cream versus hydrocortisone 1% ointment in the treatment of atopic dermatitis

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Introduction: Atopic dermatitis (AD) is a common chronic inflammatory skin disease. Topical corticosteroids as the mainstay of treatment have many side effects, both cutaneous and systemic. Sertaconazole is an antifungal cream with anti-inflammatory, antipruritic and antistaphylococcal activity. In this study, the authors compare the effect of hydrocortisone ointment and sertaconazole cream in the treatment of AD. **Materials and methods:** This study was a double-blind bilateral comparison study. Forty-five patients applied sertaconazole 2% cream twice daily on one side of the body and hydrocortisone 1% ointment twice daily on the opposite side for 1 month. The authors used a modified SCORAD score to assess the severity of the disease before and after therapy. **Results:** There was no significant difference between the two drugs in decreasing erythema, swelling, crust, scratch marks, lichenification, xerosis and pruritus ($p = 1, 1, 0.82, 0.625, 0.761, 0.125, 0.54$, respectively). Sertaconazole was significantly better in decreasing the total score ($p = 0.023$). In terms of patients' overall idea about the drugs, sertaconazole was significantly superior to hydrocortisone ($p = 0.023$). **Conclusion:** The study showed that sertaconazole was significantly better in decreasing the total score of the disease and patients' ideas. There was no significant difference between the two drugs regarding each sign by itself. Sertaconazole could be a safe and efficient treatment in AD.

Key words: sertaconazole, hydrocortisone, atopic dermatitis, modified SCORAD score

Introduction

Atopic dermatitis (AD) is a common chronic inflammatory skin disease that can affect all age groups worldwide. Due to its chronic relapsing nature, it causes a great social and economic burden. According to literature prevalence of AD is increasing (1,2).

It can present as infantile, childhood and adulthood form. Pruritus is a major symptom of this disease and results in scratching that can aggravate the inflammation and so the severity of the disease (3).

Microorganisms, especially *Staphylococcus aureus* colonizes more than 90% of AD lesions. Microbial components can act as foreign antigens and exacerbate dermatitis.

Staphylococcus super antigens and fungi such as *Malassezia* specifically have a causative role in pathogenesis of AD, in

addition to be a secondary complication (4,5). It is proven that atopic patients may benefit from a course of azoles. In 2009, Darabi et al. did a great job in reviewing the role of *Malassezia* in head and neck AD and mentioned previous studies regarding the benefits of antifungals in treatment of AD (6).

Basic therapy for AD includes avoidance of environmental factors, supportive care such as emollients and topical and occasionally systemic anti-inflammatory drugs (7). Topical corticosteroids are usually the mainstay of treatment. Antimicrobials are also important. Antistaphylococcal therapy improves superimposed infection and has also benefits in non-infected AD lesions (8).

Sertaconazole is an imidazole antifungal agent with a wide range of antimicrobial activity including dermatophytes, yeasts and also Gram-positive bacteria (9). It also has an antipruritic activity. Kaur et al. showed that sertaconazole may mediate its antipruritic activity by inducing PGD2 by activation of the P38-MAPK pathway. PGD2 is known to have antipruritic activity by suppressing histamine release (10). Sertaconazole has also anti-inflammatory activity. It suppresses the release of cytokines from keratinocytes and mononuclear cells. Activation of p38-COX-2-PGE2 pathway may be responsible for this anti-inflammatory effect (11). Sertaconazole can be used in a single daily dose with comparable results with twice-daily administration (12). This can be very important in patient adherence to treatment in a chronic disease, such as AD.

Sertaconazole can be a good therapeutic choice in AD due to its anti-inflammatory, antipruritic, antistaphylococcal activity and also lower frequency of therapy.

The aim of this study was to compare the effect of hydrocortisone ointment and sertaconazole cream in the treatment of AD.

Materials and methods

This study was a double-blind bilateral comparison study conducted at dermatology teaching clinic, Shiraz University of Medical Sciences, Shiraz, Iran. A total of 45 consecutive patients with mild to moderate AD diagnosed according to Hanifin criteria were enrolled in the study. Patients who had history of use of any topical medications or systemic anti-inflammatory drugs such as steroids, cyclosporine, cellcept, azathioprine, hydroxychloroquine or biologic agents during the last 2 weeks were excluded from the study. History of phototherapy during the last 2 weeks was another exclusion criterion. Pregnant and

Table I. The scoring system used in the study.

		None	Mild	Moderate	Severe
Objective measures of intensity	Redness	0	1	2	3
	Swelling	0	1	2	3
	Oozing/Crusting	0	1	2	3
	Scratch marks	0	1	2	3
	Lichenification	0	1	2	3
Pruritus	Xerosis	0	1	2	3
	0–10				
Patients' general idea about the drug	0–10				

Modified SCORAD.
SCORAD = SCORing Atopic Dermatitis.

lactating women and those patients without symmetric lesions were also omitted.

All patients entering the study signed the informed consent form. Patients were asked to apply sertaconazole (Dermofix) cream 2% (Ferrer Co., Spain) twice daily on one chosen target eczematous area located on one side of the body and apply hydrocortisone 1% ointment (Aburaihan Co., Tehran, Iran) twice daily on a symmetrical target eczematous area on the opposite side of the body. The two drugs were given to the patients in identical 20 g containers. Duration of treatment was 4 weeks. A randomized list was used to determine which side the patient applied each medication.

Patients were required to discontinue any other topical or systemic preparations during the study.

A questionnaire was administered for each patient to obtain demographic information, duration of the disease, history of asthma, allergic rhinitis, food allergy, family history and severity scores before and after treatment. In addition, patients' overall ideas about the usefulness of the two drugs, using a range of score (0 = least efficacy to 10 = best efficacy) were also recorded after the completion of the study.

The authors used a modified SCORAD (SCORing Atopic Dermatitis) (Table I) score to assess the severity of the disease before and after therapy as follows:

1. Objective measures of intensity including six symptoms: redness, swelling, oozing/crusting, scratch marks, lichenification and xerosis. Each of these signs were scored as none (0), mild (1), moderate (2), severe (3) with a maximum score of 18.
2. Pruritus as a subjective symptom. It was scored as 0 meaning no itch and 10 meaning worst imaginable

Table II. Percentage of patients with decrease in each item in the two groups.

	Percentage of patients with decrease in the item in the sertaconazole group	Percentage of patients with decrease in the item in the hydrocortisone group	<i>p</i> -value
Erythema	85%	85%	1
Swelling	67.5%	67.5%	1
Crust	32.5%	30%	0.82
Scratch marks	67.5%	62.5%	0.625
Lichenification	37.5%	32.5%	0.761
Xerosis	80%	70%	0.125
Pruritus	43%	43%	0.39
Total score	92.5%	92.5%	0.023

Table III. Percentage (and number) of patients in each classified response group.

	Hydrocortisone group	Sertaconazole group
Excellent response	22.5% (9)	32.5% (13)
Good response	35% (14)	30% (12)
Fair response	27.5% (11)	22.5% (9)
Poor response	15% (6)	15% (6)

itch. Patients over 6 years of age who could describe pruritus were only included. The scores on each side of the body were calculated before and after the treatment. A classification was arranged so that a decrease in the total score of more than 75% was assigned as excellent response, between 50% and 75% as good response, between 25% and 50% as fair response and less than 25% as poor response.

This study was approved by Medical Ethics Committee, Shiraz University of Medical Sciences.

Statistical analysis was performed with the SPSS 19.0 statistical package (SPSS Inc., Chicago, IL, USA), using paired *t*-test, McNemar test and descriptive methods. The criterion for statistical significance was at $\alpha = 0.05$.

Results

A total of 40 patients completed the study. Three patients didn't come for follow-up visit. One patient had irritation with both drugs and another one had irritation with sertaconazole and were omitted from the study. The patients were between 6 months and 32 years of age. Sixteen (40%) were under 2 years, 18 (45%) were 2–12 years old and 6 (15%) were more than 12 years. Twenty-three (57.5%) patients were male and 17 (42.5%) were female. Nineteen (47.5%) patients had history of AD or allergic rhinitis in their families.

Both drugs improved erythema, swelling, crust, scratch marks, lichenification, xerosis and pruritus but with no significant difference between the two groups ($p > 0.05$) (Table II). In the hydrocortisone group, 23 patients (57.5%) completed with a successful treatment (excellent and good) results versus 25 (62.5%) patients in the sertaconazole group (Table III). Sertaconazole was significantly better in decreasing the total score (p value = 0.023).

Sertaconazole was also significantly superior to hydrocortisone in terms of patients' overall idea about the drugs ($p = 0.023$).

Conclusion and discussion

AD is a common chronic skin problem. Both genetics and environment play a role in its pathogenesis. Lifestyle change and prohibition from environmental exacerbating factors is critical in disease control. To date, steroids are the mainstay of therapy, with immunosuppressants, phototherapy, antibacterials and antifungals as next lines of treatment (1,6–8).

Topical steroids have many short- and long-term side effects, both cutaneous and systemic. Due to these side effects, long-term use of steroids in chronic skin conditions such as AD should be limited. In AD, steroid is most useful in short-term courses during exacerbations. Development of other topical or systemic anti-inflammatory drugs that lack side effects of steroids would be of great importance in therapeutic armamentarium of AD.

There are literature regarding the benefits of antifungals in the treatment of AD, one of the best is a review done by Darabi et al. They suggested that atopic patients will benefit

from a 1- to 2-month course of itraconazole or ketoconazole followed by maintenance treatment with twice-weekly itraconazole or ketoconazole. Topical ciclopirox olamine cream was also useful (6).

In 2008, Wong et al. did a half-side comparison study with 1% hydrocortisone cream plus miconazole cream on one side and 1% hydrocortisone cream on the other side. They found that the addition of antifungal ointment did not add extra benefit to the topical corticosteroid treatment (13).

Sertaconazole is a new azole antifungal drug with some practical benefits. It has a wide range of antimicrobial activity including dermatophytes, yeasts and also Gram-positive bacteria (9). It is also antipruritic probably via inducing PGD₂ and therefore suppressing histamine release (10). Moreover, it has also anti-inflammatory activity and suppresses release of cytokines from keratinocytes and mononuclear cells (11). Sertaconazole is considered as an alternative to topical steroid therapy in seborrheic dermatitis (14).

In addition, it can be used once daily with comparable results with twice-daily administration (12). This can be very important in patient adherence to treatment in a chronic disease, such as AD. As per the authors' knowledge, this study was the first study to evaluate the efficacy of sertaconazole in the treatment of AD, compared with steroid. This study showed that sertaconazole was significantly better than hydrocortisone in decreasing the total score of the disease. Sertaconazole was also significantly better than hydrocortisone in terms of patients' general idea about the drugs. There was no significant difference between the two drugs regarding each sign by itself. This could be more investigated in future studies, with larger sample sizes or wider range scoring systems, so that minor differences will be magnified that way. Also, there was no significant difference between the two drugs regarding pruritus, however patients over 6 years of age who could describe pruritus were only included. This may be due to the fact that it may be sometimes quite difficult to exactly attribute the pruritus sensation to one side of the body or the other. Future studies on larger study populations or extended follow-up time are needed to evaluate the benefits of sertaconazole in the treatment of AD.

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