

## Original papers

## Treatment of seborrheic dermatitis: The efficiency of sertaconazole 2% cream vs. tacrolimus 0.03% cream

Mohamad Goldust<sup>1</sup>, Elham Rezaee<sup>2</sup>, Ramin Raghifar<sup>1</sup>, Sevil Hemayat<sup>3</sup>

<sup>1</sup> Student Research Committee, Tabriz University of Medical Sciences, Iran

<sup>2</sup> Department of Medicinal Chemistry, Shahid Beheshti University of Medical Sciences, Teheran, Iran

<sup>3</sup> Teheran Azad University of Medical Sciences, Teheran, Iran

Corresponding author: Mohamad Goldust; e-mail: Drmgoldust@yahoo.com

**ABSTRACT.** The treatment of seborrheic dermatitis (SD) includes topical antifungal agents to eradicate *Malassezia* spp. corticosteroids to treat the inflammatory component of the disease, and keratolytics to remove scale and crust. The aim of this study was to compare the efficiency of sertaconazole 2% cream and tacrolimus 0.03% cream in the treatment of seborrheic dermatitis. In this clinical trial study, sixty patients suffering from SD were studied. Thirty patients received local sertaconazole 2% cream with a recommendation to use the cream twice a day for 4 weeks. In the control group, thirty patients received tacrolimus 0.03% cream twice a day for four weeks. At the time of referral, and 2 and 4 weeks after first visit, the patients were examined by a dermatologist to check the improvement of clinical symptoms. The mean ages of the sertaconazole and tacrolimus groups were  $30.98 \pm 12.24$  and  $34.67 \pm 10.82$ , respectively. The highest level of satisfaction (90%) was observed 28 days after sertaconazole use. Only 83.3% satisfaction was noted in the tacrolimus group. The relationship between patient satisfaction and sertaconazole 2% cream receive in 28th day was significant ( $P=0.006$ ). Sertaconazole 2% cream may be an excellent alternative therapeutic modality for treating seborrheic dermatitis.

**Key words:** seborrheic dermatitis, *Malassezia* spp., Sertaconazole 2% cream, Tacrolimus 0.03% cream

### Introduction

Seborrheic dermatitis is a common condition that makes the skin look greasy, scaly and flaky. It usually affects the scalp [1–3]. In adolescents and adults, seborrheic dermatitis is commonly called „dandruff” [4–6]. Seborrheic dermatitis can also affect the skin on other parts of the body, such as the face and chest, and the creases of the arms, legs and groin [7–9]. The cause or causes of seborrheic dermatitis are incompletely understood [10–12]. Despite its name, seborrheic dermatitis is not regularly associated with excessive secretion of sebum nor are the sebaceous glands primarily involved [13–15]. However, functioning sebaceous glands may be a permissive factor because seborrheic dermatitis occurs most often during periods of active sebum production and in areas of the skin where sebum is produced [16–17]. There is no clear genetic predisposition. The histological

pattern of the disease reveals a spongiform pattern; older lesions exhibit parakeratotic and orthokeratotic follicular plugging and an irregular rete ridge pattern [18]. Edema and subsequent intermittent infiltration with granulocytes erupting from dermal papillae have been described during periods of disease exacerbation [19]. The number of yeasts decreases with antimycotic treatment, resulting in clinical improvement, and increases in periods of exacerbation [20].

Treatment options include application of selenium sulfide, pyrithione, terbinafine solution, topical sodium sulfacetamide and topical corticosteroids [21–23]. Topical tacrolimus is FDA-approved in the United States for treatment of atopic dermatitis and has also been shown to be effective in the treatment of other inflammatory dermatoses including seborrheic dermatitis [24]. Effective reduction in signs and symptoms coupled with favorable safety with chronic administration

supports their consideration as viable treatment options for managing seborrheic dermatitis [25]. Sertaconazole is an imidazole-type antifungal agent that has shown considerable in vitro activity against pathogenic fungi [26]. Various studies carried out in animal models, clinical and toxicologic trials have confirmed the value of sertaconazole in the topical treatment of superficial mycoses in dermatology and gynecology [27]. Considering the high prevalence of seborrheic dermatitis, the lack any effective treatment without side effects and the ambiguous results yielded by current studies concerning the effects of sertaconazole, the aim of the present study is to compare the efficiency of sertaconazole 2% cream vs. tacrolimus 0.03% cream in the treatment of seborrheic dermatitis.

## Materials and Methods

This clinical trial study was conducted on 60 patients suffering from SD and referred to the Dermatology outpatient clinic, Tabriz special clinic. This study was approved by the local Ethics Committee. Patients who had consumed SD-developing drugs such as methyl dopa, chlorpromazine or cimetidine, those who had used local or systemic anti-acne drugs either one month before referral to the center or concurrently, and those suffering from systemic diseases were excluded from the study. Before commencing the study and after obtaining their written consent, every patient was completely clinically examined by a dermatologist.

The following characteristics were separately registered for every patient: kind of lesion (generalized, involvement of more than one area or localized, involvement of one area), as well as the descriptive position of the lesions, number of inflammatory lesions, presence of erythema, desquamation, itching, or irritation. To determine SD severity, the Scoring Index (SI) ranking system recommended by Koca et al. was used. According to this system, erythema, desquamation, itching and irritation of each area was ranked from zero to three (nonexistence=0, mild=1, moderate=2, severe=3). The sum of these values was regarded as SD rank: 0–4 (mild), 5–8 (moderate) and 9–12 (severe). Accordingly, every patient was awarded a special SI before treatment.

Thirty patients received local sertaconazole 2% cream and they were advised to use the cream twice a day and for 4 weeks. To create a control group,

thirty patients received tacrolimus 0.03% cream twice a day for four weeks. At the time of referral and also 2 and 4 weeks after the first visit, the patients were examined by a dermatologist to check improvement of clinical symptoms and drug side effects. The clinical findings were registered and another SI was awarded. The recovery rate was then calculated based on the pretreatment and post-treatment ranks.

Additionally, patient satisfaction with the drug was also evaluated. At the end of treatment on a four-point scale: no-change (0), mild (1), moderate (2), and good (3) conditions.

Statistical calculations were performed using SPSS version 16. The Coupled T-test and Wilcoxon non-parametric test were used to compare pretreatment and post-treatment results while a variance analysis test for repeated measurements was used for data analysis. Kappa-agreed coefficients and Chi-square test were used to determine the satisfaction rate. A P-value of <0.05 was considered significant.

## Results

In this study, 60 patients suffering from SD were examined. The statistical population consisted of 63.3% women and 36.7% men. The youngest and oldest patients were respectively 6 and 72 years old with mean age of  $32.45 \pm 12.78$ . The mean ages of the sertaconazole and tacrolimus groups were  $30.98 \pm 12.24$  and  $34.67 \pm 10.82$ , respectively. As can be seen in Table 1, 58.3% and 41.7% of patients had localized and generalized lesions, respectively. In all, 58% of the lesions were observed in the head, 2% in the face, 35% in the head and face, 3% in the head, face and body and 2% in the head and body area (Table 1).

In the tacrolimus 0.03% group, patients with moderate SI were the most common (70%) at the

Table 1. Baseline demographics

		Sertaconazole N (%)	Tacrolimus N (%)	P
Gender	Men	10 (33.4)	12 (40)	
	Women	20 (66.6)	18 (60)	
Average Age		$30.98 \pm 12.24$	$34.67 \pm 10.82$	<b>0.27</b>
Kind of lesion	Localized	17 (56.6)	18 (60)	<b>0.35</b>
	Generalized	13 (37.3)	12 (40)	

Table 2. Frequency distribution in terms of SI before and after treatment

Days	Beginning day		14 <sup>th</sup> day		28 <sup>th</sup> day	
	Tacrolimus	Sertaconazole	Tacrolimus	Sertaconazole	Tacrolimus	Sertaconazole
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Mild SI	2(6.7)	1(3.4)	16(53.3)	17(56.6)	24(80)	25(83.3)
Moderate SI	21(70)	24(80)	12(40)	11(36.6)	6(20)	5(16.7)
Severe SI	7(23.3)	5(16.6)	2(6.7)	2(6.6)	0(0)	0(0)
Total SI	30(100)	30(100)	30(100)	30(100)	30(100)	30(100)

pretreatment stage, however, patients with mild SI were the most common (80%) at the post-treatment stage. In the sertaconazole 2% group, 80% of patients had moderate SI at the pretreatment stage while patients with slight SI were most common (83.3%) at the post-treatment stage (Table 2). Statistical analysis revealed a significant relationship between SI values of the 28th day in the sertaconazole 2% cream group ( $P=0.006$ ), and this relationship was also significant in the tacrolimus 0.03% group ( $P=0.008$ ). The frequency distribution of patient satisfaction after consumption of sertaconazole 2% cream and tacrolimus 0.03% cream at 14 and 28 days of treatment is shown in Table 3. The highest level of satisfaction (90%) was observed 28 days after sertaconazole 2% cream consumption, while the satisfaction level 28 days after tacrolimus 0.03% cream consumption was about 83.3%.

The  $\chi^2$  test was used to evaluate the relationship between patient satisfaction at the 14th day for both the sertaconazole 2% cream and tacrolimus 0.03% cream. No significant difference was observed between these two groups.

The relationship between patient satisfaction and sertaconazole 2% cream receive in 28th day was meaningful ( $P=0.006$ ). It should be mentioned that no relapse of the disease was observed one month

after stopping treatment in both groups treated with sertaconazole 2% cream and tacrolimus 0.03% cream.

## Discussion

This study indicates that sertaconazole 2% cream applied twice daily is efficacious in a high proportion of patients and generally well-tolerated for the treatment of seborrheic dermatitis. In our study, while most patients in the tacrolimus 0.03% cream group had moderate SI scores at the pretreatment stage, most had mild SI scores at the post-treatment stage. Our findings support the results of Papp et al. [28] study evaluating the efficacy of tacrolimus ointment for the treatment of seborrheic dermatitis.

Baraza et al. [29] also demonstrated the effectiveness of tacrolimus in the treatment of seborrheic dermatitis. In patients receiving sertaconazole 2% cream, the highest frequency was observed in 80% of cases with moderate SI at pretreatment stage while patients with slight SI had the highest frequency (83.3%) at post-treatment stage. This finding was in accordance with Elewski et al. [30] which confirms the efficacy of sertaconazole in the treatment of seborrheic dermatitis.

Table 3. Patient frequency distribution regarding satisfaction after treatment in the 14<sup>th</sup> and 28<sup>th</sup> days of treatment

Level of satisfaction	Satisfaction with Sertaconazole N (%)		Satisfaction with Tacrolimus N (%)	
	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day
None	2(6.6)	0(0)	2(6.7)	0(0)
Mild	3(10)	1(3.4)	4(13.3)	1(3.4)
Moderate	5(16.6)	2(6.6)	6(20)	4(13.3)
Good	20(66.6)	27(90)	18(60)	25(83.3)
Total	30(100)	30(100)	30(100)	30(100)

In our study, 28 days after tacrolimus 0.03% cream consumption, the satisfaction level was about 83.3% since the highest level of satisfaction (90%) was observed 28 days after sertaconazole 2% cream consumption. The relationship between patient satisfaction and sertaconazole 2% cream receive in 28th day was meaningful since this relationship was not significant in the tacrolimus 0.03% cream group.

It was hoped that the use of the nonsteroidal cream would have the additional benefit of eliminating corticosteroid associated side effects, including skin atrophy, steroid induced acne, and tachyphylaxis, as well as rebound when treatment was stopped. The results of this clinical trial study suggest that sertaconazole 2% cream is effective in treating seborrheic dermatitis. Our results indicate that topical sertaconazole is equally effective at clearing seborrheic dermatitis as tacrolimus 0.03% cream. Although clinical assessment and physician global assessment scores showed similar improvements with either topical sertaconazole or tacrolimus 0.03% cream, the patients' subjective global assessment suggests that dermatitis was less severe at study end in those treated with sertaconazole. Both treatments demonstrated statistically significant reductions in SI score, effective relief of disease signs and symptoms.

Topical sertaconazole therapy is a considerable advance on treatment with tacrolimus. The cure rate was somewhat higher in the sertaconazole group and it can be considered as the nonsteroidal alternative to topical steroid therapy in seborrheic dermatitis. In accordance with previous studies, the similar efficacy of the sertaconazole and tacrolimus cream extends to the safety profiles of these agents [31–32]. The differences between groups were not statistically significant, with overall safety rated as excellent for more than 98% of the individuals in each treatment group.

## Conclusions

Our results demonstrate that seborrheic dermatitis was equally controlled by treatment with topical sertaconazole 2% cream and tacrolimus 0.03% cream. The results reported here suggest that topical sertaconazole may be an effective and cosmetically favorable treatment for seborrheic dermatitis.

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