

## Original papers

## A double blind study of the effectiveness of sertaconazole 2% cream vs. metronidazole 1% gel in the treatment of seborrheic dermatitis

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**ABSTRACT.** Seborrheic dermatitis (SD) is generally treated with topical steroids, antifungals, or both. The aim of this study was to compare the efficacy of sertaconazole 2% cream vs. metronidazole 1% gel in the treatment of seborrheic dermatitis. A group of 156 patients suffering from SD were studied. The patients were randomly divided into two groups. The first group received local sertaconazole 2% cream and they were recommended to use the cream twice a day for 4 weeks. In the control group, thirty patients received metronidazole 1% gel twice a day for four weeks. At the point of referral, and also 2 and 4 weeks after the first visit, the patients were examined by a dermatologist to identify improvement of clinical symptoms. A higher level of satisfaction was observed after 28 days in the sertaconazole group (87.1%) than the metronidazole group (56.4%). Considering its efficacy, safety, and acceptability profiles, sertaconazole 2% cream is a worthwhile alternative to existing antifungal therapies for the treatment of seborrheic dermatitis.

**Key words:** seborrheic dermatitis (SD), *Malassezia*, sertaconazole 2% cream, metronidazole 1% gel

### Introduction

Seborrheic dermatitis is an inflammatory skin condition that most often affects the scalp, face and neck, but also less frequently, the chest, armpits and genital area. It can occur at any age [1–3]. When it's mild and only affects the scalp, it's simply referred to as „dandruff” [4–6]. In the acute phase, the scales cover a slightly moist surface. Infrequently, marginated lesions occur on the male external genitalia. Itching is moderate and usually limited to the scalp and the external auditory meatus [7–9]. The disorder may be socially embarrassing, especially because of the scaling scalp, which may cause particular uneasiness because of a perceived association with psoriasis [10–12]. The role of the commensal yeast, *Malassezia*, in the pathogenesis of seborrheic dermatitis is based on multiple studies [13–15]. A variety of species of *Malassezia* have been identified based on advances in evaluating ultrastructural, morphologic, biologic and molecular

properties among this unique collection of yeast forms [16–18].

While seborrheic dermatitis cannot be cured, in most cases, it responds quickly to proper treatment. Treatment often involves topical corticosteroids or antifungal products, often with concomitant use of shampoos containing ketoconazole, selenium sulfide, or zinc pyrithione [19–20]. Clinical trials have also demonstrated varying success with topical lithium succinate, vitamin D3 derivatives, and most recently, topical immunomodulators such as tacrolimus and pimecrolimus [21]. There are a few reports of the use of metronidazole gel in seborrheic dermatitis [22]. Koca et al. [23] used 0.75% metronidazole gel for treatment of mild to moderate facial seborrheic dermatitis. They concluded that there was no significant difference between 0.75% metronidazole gel and placebo with regard to the mean severity score of the seborrheic dermatitis after treatment. High doses and/or long-term treatment with metronidazole is associated with the

Table 1. Baseline demographics

Variable	Sertaconazole N (%)	Metronidazole N (%)	P
<b>Gender</b>			
Men	36 (47.3)	34 (43.5)	
Women	42 (52.7)	44 (56.5)	
<b>Age</b>	30.18 ± 12.64	34.14 ± 10.68	0.24
<b>Kind of lesion</b>			0.32
Localized	43 (55.1)	45 (57.6)	
Generalized	35 (44.9)	33 (52.4)	

development of leukopenia, neutropenia, increased risk of peripheral neuropathy and/or CNS toxicity. Metronidazole is also listed by the US National Toxicology Program (NTP) as being reasonably anticipated to be a human carcinogen.

Sertaconazole is a new antifungal agent used to treat tinea pedis (athlete's foot; fungal infection of the skin on the feet and between the toes). Sertaconazole is in a class of medications called imidazoles. It works by slowing the growth of fungi that cause infection [24], and is usually applied to the skin as a cream, twice a day for 4 weeks [25]. Considering the high prevalence of seborrheic dermatitis, and the lack of treatment known to be without side effects, and contradictory of current studies on effects of sertaconazole, the present study is aimed at comparing the efficiency of sertaconazole 2% cream with that of metronidazole 1% gel in the treatment of seborrheic dermatitis.

## Materials and Methods

In this clinical trial study, 156 patients aged 8 to 64 years (mean 34±14.84), referred to Tabriz special clinic from March 2010 to March 2013 with a diagnosis of seborrheic dermatitis, were studied. The study was approved by local ethics committee and written consent was obtained from all the patients. The exclusion criteria included the use of SD-developing drugs, including methyl dopa, chlorpromazine and cimetidine, or the use of local or systemic anti-acne drugs, within one month of the time of referral, and the presence of systemic diseases.

Each patient was subjected to a complete clinical examination by a dermatologist. A description of the lesions were separately registered for every patient: whether they were generalized (involvement of

more than one area) or localized (involvement of one area), also, the descriptive position of the lesions and the number of inflammatory lesions was noted, as well as the presence of erythema, desquamation, itching or irritation.

To determine SD severity, the Scoring Index (SI) ranking system recommended by Koca et al. [23] 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 amounts was regarded as the SD rank and classified into the following three categories: 0–4 (mild), 5–8 (moderate) or 9–12 (severe). Accordingly, every patient was awarded a special SI before treatment.

The patients who satisfied the above criteria were divided into two groups randomly. The first group received sertaconazole 2% cream (group A), and the other group received metronidazole 1% gel (group B) in a double-blind manner. The choice of cream was unknown to both the patients and the research team. The treatment consisted of two applications of the product twice a day for four weeks. At the point of referral, and also 2 and 4 weeks after the first visit, the patients were examined by a dermatologist to check for any improvement of clinical symptoms or side effects of the drug. The clinical findings were recorded and again awarded a post-treatment SI value. The final recovery rate was calculated based on the difference between the pre-treatment and post-treatment ranks. Additionally, patient satisfaction from the drug was also evaluated at the end of treatment as either no-change (0), mild (1), moderate (2) or good (3).

**Statistical analysis.** All statistical analysis was performed with SPSS 16 software. The coupled T-test and non-parametric test (Wilcoxon) were used to compare pre-treatment and post-treatment results,

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

Days	First day		14 <sup>th</sup> day		28 <sup>th</sup> day	
	Metronidazole	Sertaconazole	Metronidazole	Sertaconazole	Metronidazole	Sertaconazole
SI	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Mild	4(5.1)	5(6.4)	35(44.8)	44(56.4)	45(57.7)	65(83.3)
Moderate	60(76.9)	58(74.3)	33(42.3)	29 (37.1)	32 (41.1)	11(14.1)
Severe	14(18)	15(19.3)	10(12.9)	5 (6.5)	1 (1.2)	2(2.6)
Total	78(100)	78(100)	78(100)	78(100)	78(100)	78(100)

and the variance analysis test, for repeated measurements, was used for data analysis. Kappa agreed coefficients and the Chi-square test were used to determine satisfaction rate. A P-value of <0.05 was considered significant.

## Results

In this research, 156 patients suffering from SD were studied. The population comprised 55.2% women and 44.8% men. The youngest and oldest patients were respectively 8 and 64 years old with a mean age of  $32.34 \pm 12.56$ . The mean ages of the sertaconazole and metronidazole groups were  $30.56 \pm 12.98$  and  $34.66 \pm 10.12$ , respectively, and localized and generalized lesions were found in 56.4% and 43.7% of the patients, respectively (Table 1). The lesions were observed on the head in 56% of the patients, the face in 2%, the head and face in 36%, on the head, face and body in 4% and on the head and body area in 2%.

While the most common SI of patients assigned metronidazole 1% gel was moderate (76.9% of patients) at the pre-treatment stage, the most common SI was found to be mild (57.7%) at the post-treatment stage. Similarly, in the sertaconazole

2% group, the most common pre-treatment SI class was observed to be moderate (in 74.3% of cases), compared with mild at the post-treatment stage (80.3%) (Table 2). Although a statistically significant relationship was found between the SI values of the 28<sup>th</sup> day and sertaconazole 2% cream administration ( $P=0.009$ ), this relationship was not found in the metronidazole 1% gel group ( $P=0.32$ ).

The frequency distribution of the patient satisfaction values after consumption of sertaconazole 2% cream and metronidazole 1% gel at 14 and 28 days of treatment is given in Table 3. The highest level of satisfaction (87.1%) was observed 28 days after sertaconazole 2% cream consumption. Twenty-eight days after metronidazole 1% gel consumption, the satisfaction level was about 56.4%. According to the chi-square test, no significant difference was observed between the sertaconazole 2% cream and metronidazole 1% gel groups with regard to patient satisfaction at day 14. The relationship between patient satisfaction and sertaconazole 2% cream on day 28 was ( $P=0.006$ ). It should be mentioned that no relapse of the disease was observed in either group one month after the end of treatment.

Table 3. Frequency distribution of patient satisfaction after the 14th and 28th days of treatment

Level of satisfaction	Satisfaction with Sertaconazole		Satisfaction with Metronidazole	
	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day
None	2(3.6)	2(3.6)	4(5.1)	2(3.6)
Mild	10(12.8)	2(3.6)	12(15.4)	2(3.6)
Moderate	16 (20.5)	6(7.7)	26(33.3)	30(38.5)
Good	50(64.1)	68 (87.1)	36(46.2)	44(56.4)
Total	78(100)	78(100)	78(100)	78(100)

## Discussion

Seborrheic dermatitis is a chronic scaling condition of the skin that usually involves the scalp and face, and sometimes the ears and chest. It often causes itching and flaking [26]. Although there is no cure for seborrheic dermatitis, it can be controlled. Hygiene issues play a key role in controlling seborrheic dermatitis: frequent cleansing with soap removes oils from the affected areas and improves seborrhea. Patients should be counseled that good hygiene must be a lifelong commitment [27]. The therapeutic response and safety found with sertaconazole 2% cream in the present study both confirms and extends the findings of previous studies, and demonstrates that its therapeutic effect is comparable to that of topical metronidazole 1% gel.

There are a few reports of the use of metronidazole gel in seborrheic dermatitis. Parsad et al. [28] evaluated the efficacy of 1% metronidazole gel in a double-blind, placebo-controlled study and showed that 66% of patients demonstrated marked improvement to complete clearance of their lesions in the metronidazole group versus 12% in the placebo group. They concluded that 1% metronidazole gel was effective in treatment of seborrheic dermatitis. Siadat et al. [29] report that 1% metronidazole gel is effective for seborrheic dermatitis of the face.

Sertaconazole is the most recently introduced topical antifungal agent in the United States; it was approved by the US Food and Drug Administration in 2003 for the treatment of tinea pedis [30]. It has since been used around the world for the treatment of a number of cutaneous fungal infections and vulvovaginal candidiasis [31]. The two treatments were found to have very similar effects.

Sertaconazole is a new topical drug for the treatment of dermatitis and few studies have been published comparing its efficacy and safety in the treatment of seborrheic dermatitis. A study by Elewski et al. [32] demonstrates the efficacy of sertaconazole 2% cream in the treatment of seborrheic dermatitis, with a low incidence of side effects in both groups. Similarly, sertaconazole was not found to be associated with any serious adverse events in our study. In summary, these results suggest that sertaconazole 2% cream is a well-tolerated and effective treatment for seborrheic dermatitis.

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Received 10 June 2013

Accepted 5 September 2013