

Oral fluconazole in scalp seborrheic dermatitis in Albania

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Abstract

Aim: Seborrheic dermatitis is a chronic and relapsing disease. The implication of *Malassezia* yeasts in the pathogenesis of seborrheic dermatitis provides the rational basis for the therapeutic use of systemic antifungal agents, including fluconazole. Our aim was to evaluate the efficacy of fluconazole in the treatment of scalp lesions in adult patients with seborrheic dermatitis in Albania.

Methods: This pseudo-experimental study involved 49 patients with seborrheic dermatitis affecting the scalp. The treatment was initiated after a wash-out period of one month for topical treatments and six months for oral antifungals. Fluconazole 150 mg/day was administered twice weekly for two weeks in all patients. Erythema, scaling and itching were assessed using a 0–3 point scale. An overall clinical assessment (OCA) score was calculated as the sum of each separate sign or symptom’s score. Based on clinical findings observed at week 0 (pretreatment visit), patients were categorized as having mild ($OCA \leq 3$), moderate ($OCA > 3$ to ≤ 6), or severe ($OCA > 6$ to ≤ 9) form. Further evaluations were done at weeks 1, 2 and 6.

Results: At the end of the treatment (week 2) a significant improvement versus baseline was reported in all three clinical parameters: erythema, scaling, and itching, in all OCA groups. No further significant improvement (week 6) was observed after the cessation of therapy, although the improvement was maintained up to the end of the study. No adverse events or blood test abnormalities were reported during the study.

Conclusions: Oral fluconazole was safe and beneficial, especially in patients with moderate or severe forms of scalp seborrheic dermatitis.

Keywords: Albania, fluconazole, scalp, seborrheic dermatitis.

Introduction

Seborrheic dermatitis (SD) is a common inflammation of the skin, involving most often the face, scalp and the chest (1).

The etiology of seborrheic dermatitis is not entirely clear, but *Malassezia* yeast (formerly called - *Pityrosporum*) seems to play an important role since SD responds well to treatment with antifungal medication. Overgrowth of the *Malassezia* yeast in the oily skin environment, failure of the immune system to regulate the fungus, and the skin's inflammatory reaction to the yeast overgrowth appear to be the clue factors for seborrheic dermatitis to develop. It has been described that this fungus is responsible for the production of a lipase (2,3) that uses lipids from the human skin surface to produce unsaturated and saturated fatty acids that, in the outer layer of the skin of susceptible individuals, induce an inflammatory response (4,5). Recently, oral systemic antifungals, such as ketoconazole, terbinafine, itraconazole, pramiconazole and fluconazole, have been introduced in the therapy of SD (6). Fluconazole is a broad spectrum fungistatic triazole, distinguished for its excellent bioavailability after oral administration and modest effect on hepatic microsomal enzymes, rendering drug interactions less common. Although clinical evidence favors its use (7,8,9), there are still some controversies (10) on the efficacy of oral fluconazole in the treatment of seborrheic dermatitis.

The aim of this study was to assess the efficacy of oral fluconazole on scalp lesions of patients with seborrheic dermatitis in relation to clinical severity of this disorder.

Methods

This pseudo-experimental (pretest-posttest) study was carried out from November 2012 to February 2014 at the Department of Dermato-Venerology at the Regional Hospital of Durres, Albania. The study was approved by the National Ethics Committee of Albania and a written informed consent form was obtained from all patients.

Study population

The inclusion criteria consisted of male and female patients of any age showing up at the Durres regional hospital and experiencing seborrheic dermatitis localized in the scalp and/or other body locations, regardless of the results obtained from prior therapies. In addition, eligible participants should have been willing to give their informed consent in order to take part in the study. Exclusion criteria consisted of impaired renal and liver function, pregnancy, lactation, and hypersensitivity to fluconazole or other azole drugs. Also, patients treated with other oral antifungals during the last six months were also excluded from the study. After applying the inclusion and exclusion criteria, fifty adult patients agreed to participate in the study. However, one patient withdrew for reasons not related to the study, or study intervention.

Treatment

A two week wash-out period was allowed before study treatment was initiated, during which all topical treatments were stopped, but moisturizing agents were locally applied. Fluconazole 150 mg/day was administered twice weekly for two weeks in all participating patients.

Assessment of lesions

On the initial evaluation and thereafter at each visit, the patients were thoroughly examined and clinical findings were graded numerically for erythema, scaling and itching using a four-point score ranging from 0 to 3 (0: absent; 1: mild; 2: moderate and 3: severe) for each location. The clinical assessment was carried out by the same doctor under standard lighting conditions. The area of involvement was not considered. An overall clinical assessment score (OCA), consisting of the sum of scores for each sign or symptom (erythema, scaling, itching) was calculated. Only data on scalp lesions are analyzed and further discussed in this study. The severity of the disorder was categorized as mild (OCA score ≤ 3), moderate (OCA score >3 to ≤ 6), or severe (OCA score >6 to ≤ 9) based on clinical findings

observed at week 0 (pretreatment visit).

Assessment of efficacy

Clinical efficacy was determined by percentage reduction in OAC score measured at each visit against baseline. The result of the treatment was considered excellent if OCA score was reduced by 100% (complete disappearance of signs and symptoms), very good if OCA score reduction was $\geq 75\%$, good if the reduction ranged between 50-75%, moderate to poor if $< 50\%$ and no change if OCA score remained unchanged. The patients were evaluated after 1, 2 and 6 weeks.

Assessment of safety

The patients were asked for the occurrence of any adverse events at each visit. The patients were asked to report immediately to the investigator any troublesome and persistent (more than few days) adverse event, appearing at any time during the study. Blood samples were taken for routine hematologic and biochemical analyses at the

beginning of the study, at the end of the treatment and at the completion of the study.

Statistical analysis

Proportions were compared using the chi square or Fisher's exact tests. Shapiro-Wilk test was used to determine normality of data because we had a small group of study participants ($N < 50$). Continuous variables were reported as arithmetic mean \pm standard deviation.

One-way ANOVA was used to check for statistically significant differences of mean values between the study groups. In all cases, differences were considered statistically significant if $P \leq 0.05$. The statistical software SPSS 16 was used for data analysis.

Results

Based on the OCA score at the baseline, the prevalence of mild, moderate and severe disorder was 32.7%, 51% and 16.3%, respectively (Table 1).

Table 1. OCA score before treatment, at the end of the treatment, and at the end of the study

Stage of the Study	Severity of Seborrheic Dermatitis		
	Mild form (n=16)	Moderate form (n=25)	Severe form (n=8)
Before the treatment	2.13 \pm 0.9*	4.72 \pm 0.8	8.25 \pm 0.9
At the end of the treatment (week 2)	1.13 \pm 1.3	2.28 \pm 1.5	2.75 \pm 2.1
At the end of the study (week 6)	1.38 \pm 1.3	2.24 \pm 1.7	2.13 \pm 2.4

* OCA score (mean \pm SD).

Figure 1 shows the scores for erythema, desquamation, pruritus and OCA score obtained during the study. A significant change in the mean score was observed between week 0 (before the treatment) and week 2 (end of the treatment) for all the three

forms of the SD ($P < 0.05$), whereas there were no significant changes in the respective mean scores between week 2 (end of the treatment) and week 6 (end of the study).

Figure 1. Erythema, desquamation, pruritus and OCA scores before treatment, at the end of the treatment, and at the end of the study

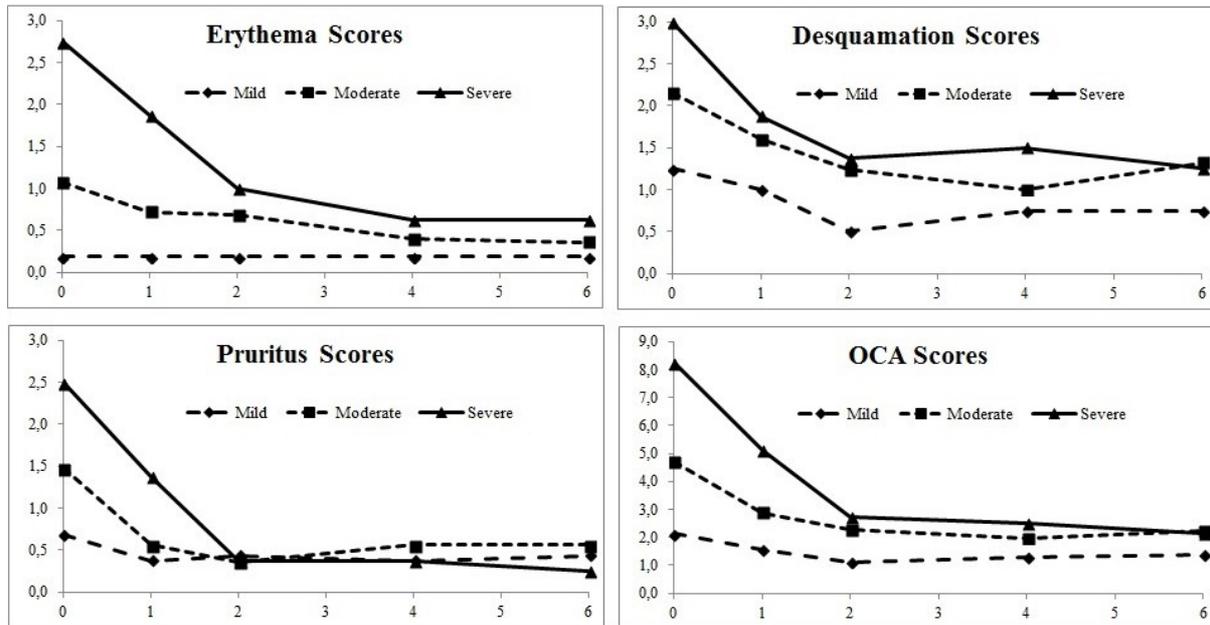


Table 2 presents data about efficacy of treatment by severity group and study stage. The efficacy of treatment was greater for patients belonging to severe SD group as measured by OCA reduction

percentage. For example, OCA score was reduced by 74% for patients with severe SD at baseline compared to 35% reduction for the patients with mild SD at the baseline (Table 2).

Table 2. Percent OCA score changes at week 2 (end of the treatment) and at week 6 (end of the study)

Variable	Severity of Seborrheic Dermatitis		
	Mild	Moderate	Severe
Mean OCA Score at baseline (week 0)	2.13	4.72	8.25
Percent OCA Score change from baseline at week 2*	47%	52%	67%
Percent OCA Score change from baseline at week 6†	35%	53%	74%

* Percent OCA Score change from baseline at week 2 was calculated using the following formula $[(OCAS \text{ week}0 - OCAS \text{ week}2)/OCAS \text{ week}0]*100\%$.

† Percent OCA Score change from baseline at week 2 was calculated using the following formula $[(OCAS \text{ week}0 - OCAS \text{ week}6)/OCAS \text{ week}0]*100\%$.

The efficacy of treatment at week 6 of the study against baseline values by severity of SD is displayed in Table 3. In total, 22.45% of patients showed excellent response, 16.3% showed very good response, 22.5% good, 16.3% moderate to

poor whereas 22.5% showed no change or further deterioration (Table 3). Among the later, at baseline 63.6% had mild form of seborrheic dermatitis, while the others had moderate form of seborrheic dermatitis.

No adverse events were reported.

Table 3. Percent OCA score changes at week 6 (end of the study) against baseline scores

Response to Treatment	Severity of Seborrheic Dermatitis			Total
	Mild	Moderate	Severe	
Excellent	37.5%	12.0%	25.0%	22.5%
Very good	-	20.0%	37.5%	16.3%
Good	6.3%	36.0%	12.5%	22.5%
Moderate to poor	12.5%	16.0%	25.0%	16.3%
No response	43.8%	16.0%	-	22.5%

Discussion

Systemic antifungals have been introduced in clinical practice during the past decade as a useful option in the treatment of seborrheic dermatitis. The efficacy of oral antifungals is thought to be linked to their antifungal and/or anti-inflammatory effects. Pulse or continuous systemic use of itraconazole (11-17) and terbinafine (18-21) has been associated with good clinical response in several studies. Attention has been focused on pulse administration as a possible tool to reduce systemic exposure, without reducing the efficacy.

Oral fluconazole, which is a highly effective drug against a wide spectrum of dermatophytes and yeasts, has also been tried in seborrheic dermatitis. The first published evidence to our knowledge comes from the study of Zisova (7), where the patients were treated with 50 mg/day of fluconazole for two weeks. The therapeutic results in patients treated with oral fluconazole were excellent in about 1/3 of patients, with remaining showing clinical improvement. The test for *Malassezia* spp. after treatment was negative in 3/4 of patients. Results of two recently published studies (8,9) have also demonstrated the efficacy of pulse oral fluconazole therapy in seborrheic dermatitis patients. However, results of these studies are in contrast with those obtained by Cömert et al. in a randomized

Conflicts of interest: None declared.

clinical trial involving sixty-three patients with mild-to-moderate SD that received either oral fluconazole 300 mg in a single dose per week or placebo for 2 weeks (10). The researchers found a statistically significant improvement after treatment with fluconazole but not with placebo compared to baseline, and a non-significant difference between fluconazole group and the placebo group (10).

Our data also showed that the treatment with pulse oral fluconazole 150 mg twice per week for two weeks improves the severity of symptoms and signs of seborrheic dermatitis and can even induce its complete resolution. Furthermore, the clinical improvement is maintained for other four weeks after cessation of the therapy. Our findings are compatible with results of other studies cited above. Interestingly, pulse oral fluconazole seems to be more effective as the severity of the disease increases, which partially may explain the findings of the Cömert's study (10).

Conclusion

Pulse oral fluconazole 150 mg twice per week for two weeks may be a useful alternative therapy, especially in patients with moderate or severe forms of seborrheic dermatitis who need a systemic treatment.

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