TREATMENT AND PROPHYLAXIS OF PITYRIASIS VERSICOLOR WITH ORAL FLUCONAZOLE

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Treatment with oral antifungals is usually preferred when pityriasis versicolor (PV) affects large body surface areas, especially in chronic or recurrent cases. In this study, we evaluated the effectiveness of fluconazole in the treatment and prophylaxis of patients with chronic or recurrent, mostly extensive, PV. Treatment regimen consisted of fluconazole 100mg once daily for 10 consecutive days; 3-4 weeks after the end of treatment, patients were evaluated for clinical and mycological response (visit T1). Patients with mycological eradication received fluconazole 200mg/day (100mg twice a day) for two consecutive days per month for 5 months. Clinical and mycological evaluations were performed after 2 months (T2) and 5 months (T3) from visit T1. Mycological efficacy was assessed using microscopic examination and represented the primary efficacy parameter; therefore, positive microscopy at any visit was reason for withdrawal from the study. At visit T1 60 subjects were evaluated; most patients (94%) were clinically cured or improved. Similar clinical response rates were observed at visits T2 and T3. The proportion of patients with eradication of *Malassezia* was 92% at T1 visit, 88% at T2 visit, and 91% at T3 visit. No relevant adverse events occurred.

The results of this open preliminary study suggest that an oral treatment with fluconazole 100mg/day for 10 days is effective in PV. A maintenance monthly treatment with fluconazole 200mg/day for two consecutive days can be very useful to prevent recurrence of PV.

Pityriasis versicolor (PV) is a superficial fungal skin infection which commonly occurs in adulthood, especially in young age. It is characterized by multiple hyper- or hypopigmented, occasionally erythematous, macules with fine scaling. The lesions gradually tend to coalesce and are often asymptomatic; at the most, mild subjective symptoms can be reported. The eruption usually affects the trunk, the neck and the prossimal aspect of arms. The causal agent of PV is the lypophilic yeast *Malassezia*, a normal commensal of the human cutaneous flora which acquires a pathogenic potential through the conversion from the yeast to the mycelial form. The colonization by *Malassezia* spp. and the susceptibility to develop PV can be influenced by numerous predisposing conditions, which are only partially known and include sebum disposition, hyperhidrosis, wet and hot climates, use of drugs (oral contraceptives, systemic corticosteroids, immunosuppressants), and genetic factors (1-3). A direct consequence of these etiopathogenic aspects is that general characteristics of PV are the chronic course and the high rate of recurrences. There is a great variety of options for the therapeutic management of PV. In chronic or recurrent cases with diffuse eruption, especially if refractory to topical approaches, oral treatments can be considered. In this study, we evaluated the therapeutic and prophylactic activity of fluconazole in PV.

Key words: pityriasis versicolor, fluconazole, treatment, prophylaxis

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MATERIALS AND METHODS

Sixty-five subjects (36 males and 29 females; 18 to 61 years old, mean age: 30.5) with active PV entered the study. In all cases, PV had a chronic (with >6 month-duration) or recurrent (>3 episodes/year) course in the previous year. The eruption was diffuse and distributed as follows: back in 19 cases; upper trunk in 16; back and upper arms in 9; back, chest and abdomen in 8; chest, neck and upper arms in 7; back and neck in 6. Clinical diagnosis of PV was confirmed by light microscopic examination with Parker Quink ink/10% potassium hydroxide of specimens obtained with gentle scraping on scaling active borders of lesions.

Prior to the enrolment, any kind of treatment apt to influence PV was discontinued for at least 2 weeks and 2 months in case of topical agents or systemic drugs, respectively; the use of these treatments, including active shampoos and cleansings, was prohibited during the observational period.

The following conditions were excluded in each patient: hypersensitivity to fluconazole or excipients contained in fluconazole capsules; significant liver abnormalities; immunodepression; concomitant disorders which were currently treated with drugs metabolized by the cytochrome P450 system or were likely to require prohibited drugs, including immunosuppressants and corticosteroids; pregnancy, breast-feeding or planning to become pregnant. Female patients were not taking oral contraceptives; anyway, they were instructed to use alternative contraceptive measures to avoid pregnancy.

After the baseline visit T0, patients received fluconazole 100mg once daily for 10 consecutive days and were evaluated for clinical and mycological response at 3-4 weeks following the end of treatment (Visit T1). Patients with mycological eradication were assigned to a maintenance treatment with fluconazole 200mg/day (100mg twice a day) for two consecutive days per month. Clinical and mycological evaluations were performed after 2 months (T2) and 5 months (T3) from visit T1.

At each visit, signs and symptoms of PV (erythema, scaling, itch/burning, hyperpigmentation, hypopigmentation) were graded on a 4-point scale (0= absent; 1= mild; 2= moderate; 3= severe). Wilcoxon's test was used for the statistical analysis of the differences from baseline and significance was defined as $p<0.05$. Clinical response was rated in comparison with baseline conditions as: cure (complete disappearance of clinical signs and symptoms), improvement (partial disappearance or reduction in the severity of signs and symptoms), or failure (worsening or no change of lesions).

Mycological efficacy was assessed using microscopic examination; the examination was not performed only when lesions (including dyschromic changes) were completely absent. The response was categorized as persistence (positive microscopy) and eradication (disappearance of *Malassezia*); in turn, eradication was considered presumable when lesions were completely absent. Mycological response represented the primary efficacy parameter; therefore, a positive microscopy at any time of the post-baseline period indicated ineffectiveness of treatment and caused withdrawal from the study.

RESULTS

At visit T1, 60 patients were evaluated; in fact, 3 patients were lost to follow-up and 2 patients were excluded from the analysis because of the use of prohibited products. After the first phase of treatment with fluconazole, most patients obtained clinical benefits (Tab. I) in terms of cure (32%) or improvement (62%). In cured patients *Malassezia* was assumed as eradicated due to the absence of lesions accessible to the microscopic examination. In the remaining patients, microscopy was negative in all cases but 5 (8%), who were withdrawn from the study.

Thus, 55 patients with negative microscopy were eligible for the maintenance treatment with fluconazole. During this 5-month period, a total of 5 patients dropped-out of the study due to administrative reasons. Treatment failed to maintain satisfactory clinical results in 6% of patients evaluated at visit T2 and in 7% at visit T3 (Tab. I). Eradication of *Malassezia*, either presumable or proven by microscopy, was observed in 88% of cases (46/52) at visit T2 and in 91% (40/44) at visit T3.

The overall change in the severity of signs and symptoms from baseline (Tab. I) was statistically significant at each assessment ($p<0.05$). In patients with clinical improvement the most persistent sign throughout the study period was hypopigmentation. This was also due to the fact that several patients were recruited during summer months and were tanned at the baseline.

Tab. I. *Summary of clinical results.*

Clinical response N. (%)		Visit T1 (patients: 60)	Visit T2 (patients: 52)	Visit T3 (patients: 44)
Cure + improvement		56 (94%)	49 (94%)	41 (93%)
Failure		4 (6%)	3 (6%)	3 (7%)
		Mean total score		
Sign/symptom	Visit T0 (patients: 65)	Visit T1* (patients: 60)	Visit T2* (patients: 52)	Visit T3 * (patients: 44)
Erythema	0.8	0.15	0.05	0.03
Scaling	1.6	0.3	0.1	0.1
Itch/Burning	0.4	0.1	0	0
Hyperpigmentation	1.25	0.4	0.1	0.1
Hypopigmentation	1.5	0.9	0.4	0.2

* *Differences* versus *baseline for each item: $p<0.05$.*

No clinical adverse reactions were observed either in the 10-day treatment phase with fluconazole 100mg/day or during the maintenance monthly courses.

DISCUSSION

PV is frequently treated with specific or non-specific antifungal topical agents; however, in common practice, a short-term treatment with systemic drugs is preferred when PV affects large areas of the skin or had a chronic or recurrent course. The patient's preference and compliance are also very high with oral treatments (1-3).

The results of this open preliminary study suggest that an oral treatment with fluconazole 100mg/day for 10 days is effective and well tolerated in patients with PV. A maintenance monthly treatment with fluconazole 200mg/day for two consecutive days prevented the recurrence of PV in the majority of patients. The proportion of patients with eradication of *Malassezia* was 92% at visit T1, 88% at visit T2, and 91% at visit T3.

Fluconazole is a triazole antifungal agent which, after oral administration, rapidly penetrated in the skin where high levels are accumulated, especially into the stratum corneum. The elimination from the skin seems to be slow (4-5).

Several open studies (6-8) have demonstrated the value of fluconazole, used at different dosages and with variable regimens, in the treatment of PV as confirmed by comparative studies (9-12). To our knowledge, this is the first experience evaluating the prophylactic role of fluconazole in PV. The results obtained in our open study are almost comparable to those achieved after a 6-month prophylactic treatment with itraconazole in a large randomized, double-blind placebo-controlled study (13).

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