

New aspects in the clinical course of pityriasis versicolor^{*}

Novos aspectos na evolução clínica da pitiríase versicolor

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Abstract: BACKGROUND: Pityriasis versicolor is an infectious disease caused by several *Malassezia* species which has a tendency to become relapsing or chronic.

OBJECTIVES: This study was conducted in an attempt to investigate the clinical course of pityriasis versicolor with regard to the number of relapses after a 12-month therapy and correlate this number with isolates of *Malassezia* species.

MATERIAL AND METHODS: 102 patients with clinical and laboratory diagnosis of pityriasis versicolor were monitored for 12 months to investigate the number of relapsing episodes of the disease.

RESULTS: After appropriate treatment, pityriasis versicolor presented three types of clinical course: pityriasis versicolor without relapsing episodes (32.35%), relapsing pityriasis versicolor with one to four relapsing episodes (52.94%) due to associated predisposing factors, and chronic pityriasis versicolor with more than four relapsing episodes (14.70%) with no relation to predisposing factors.

CONCLUSIONS: The clinical course of pityriasis versicolor varied according to the number of relapsing episodes of the disease analyzed over a period of 12 months and can be classified as follows: pityriasis versicolor with clinical and mycological clearing, relapsing pityriasis versicolor and chronic pityriasis versicolor.

Keywords: Ketoconazole; *Malassezia*; Mycoses; Therapeutics; Tinea versicolor

Resumo: FUNDAMENTO: A pitiríase versicolor é uma doença infecciosa causada por várias espécies de *Malassezia* com uma tendência a se tornar recidivante ou crônica.

OBJETIVOS. Este trabalho foi conduzido na tentativa de conhecer a evolução clínica da pitiríase versicolor em relação ao número de recidivas após um tratamento adequado no período de 12 meses e correlacionar o número de recidivas com as espécies de *Malassezia* isoladas.

MATERIAL E MÉTODOS. Cento e dois pacientes com diagnóstico clínico e laboratorial de pitiríase versicolor foram acompanhados por um período de 12 meses para observarmos o número de recidivas da doença.

RESULTADOS. A pitiríase versicolor, após um tratamento adequado, apresentou três tipos de evolução clínica num período de 12 meses: pitiríase versicolor sem nenhum episódio de recidiva (32,35%); pitiríase versicolor recidivante, com um a quatro episódios de recidiva (52,94%) devidos a fatores de predisposição relacionados; e pitiríase versicolor crônica, com mais de quatro episódios de recidiva (14,70%) sem nenhuma relação com fatores de predisposição.

CONCLUSÕES. A pitiríase versicolor apresentou uma evolução clínica de acordo com o número de episódios de recidiva da doença analisados durante um período de 12 meses que pode ser considerada da seguinte maneira: pitiríase versicolor com cura clínica e micológica, pitiríase versicolor recidivante e pitiríase versicolor crônica.

Palavras-chave: Ketoconazol; *Malassezia*; Micoses; Terapêutica; Tinha versicolor

Received on 18.04.2010.

Approved by the Advisory Board and accepted for publication on 25.11.10.

^{*} Work conducted at the Dermatology Clinic, Irmandade Santa Casa de Misericórdia de Sao Paulo - Sao Paulo (SP), Brazil.

Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

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INTRODUCTION

In 1874, Malassez determined that pityriasis versicolor was caused by yeasts. The *Malassezia* genus was created by Baillon in 1889 and *Malassezia furfur* was the name given to the etiological agent of pityriasis versicolor. *Malassezia furfur*, an anthropophilic lipodependent yeast, may be oval or cylindrical. Since the 1980s, several species of *Malassezia* have been described in the medical literature for a better understanding of the pathogenicity of the yeast in pityriasis versicolor.¹

Pityriasis versicolor evolves in outbreaks, with improvement and aggravation of the symptoms, becoming relapsing or chronic. Due to the presence of several predisposing factors, relapse is a major problem. For this reason, orientation about the predisposing factors to the disease and about a prophylactic treatment regimen is mandatory.²

Pityriasis versicolor is considered to relapse when it presents a high recurrence rate after antifungal treatment. In 1994 Faergemann noted a relapsing rate of 60% after one year and of 80% after two years of treatment.³ Relapse probably occurs due to the presence of yeasts in the sebaceous follicles and due to several predisposing factors that allow the multiplication and filamentation (pseudohyphal formation) of yeasts. In 2002, Gupta *et al.* cited that whereas pityriasis versicolor is easily treated, endogenous factors of the host and uncontrollable environmental factors play a significant role in the development of the disease in relation to relapse, especially in predisposed individuals.⁴

The objective of this study was to investigate the clinical course of pityriasis versicolor in relation to the number of relapses in a period of 12 months after appropriate treatment, and to correlate the number of relapsing episodes with isolates of *Malassezia* species.

MATERIAL AND METHODS

The study protocol and its informed consent were approved by the Ethics and Research Committee of Santa Casa de Misericórdia de São Paulo. This prospective study was conducted from January 2003 to August 2006. Patients with clinical diagnosis of pityriasis versicolor were selected from January 2003 to December 2004. There was a total of 102 patients; of these, 90 were from the dermatology outpatient clinic of Santa Casa de São Paulo and 12 patients were referred from public health units by other dermatologists. The diagnosis of pityriasis versicolor was confirmed by mycological and clinical examination.⁵ The isolation and identification of *Malassezia* species were in agreement with the biochemical and molecular biology techniques employed in the literature.^{6,7} The investigation of the number of relapsing episodes of pityria-

sis versicolor of the 102 patients was conducted by the same dermatologist and concluded in a period of 12 months. Cases were monitored for a period of 20 months.

The distribution of lesions of pityriasis versicolor by regions of the body was classified into three groups: 1) - Mild: involvement of only one region of the body (neck, anterior and posterior thorax); 2) - Moderate: involvement of more than one region of the body and less than or equal to three regions of the body (anterior thorax + posterior thorax + abdominal region; anterior thorax + posterior thorax + dorsal region; anterior thorax + upper limbs; anterior thorax + posterior thorax + neck; forearms, abdominal region, dorsal region); 3) - Disseminated: involvement of more than three regions of the body (neck + trunk + upper limbs + lower limbs + armpits + groin region).

Treatment of patients with pityriasis versicolor. The treatment was chosen according to the clinical classification of the disease in relation to extent of body surface involvement: a) Single - only topical treatment with ketoconazole shampoo for six weeks; b) Moderate and generalized - oral ketoconazole 200mg/day/20 days associated with topical treatment with ketoconazole shampoo/daily for six weeks.

Prophylactic treatment of patients with relapsing pityriasis versicolor

We used oral ketoconazole 200mg /3 consecutive days per month for six months, associated with ketoconazole shampoo 3x-week for several months.

Cure criteria after treatment of pityriasis versicolor - Cure criteria were defined as follows: a) Clinical criteria - no active lesions (negative Zireli's sign and no peeling); b) Mycological criteria - negative mycological examination of at least five lesions.

Statistical tests - The following statistical tests were employed to verify the associations between variables with relapse and without relapse: chi square test, likelihood-ratio test, Fisher's exact test. Values of $p < 0.05$ were considered statistically significant.

RESULTS

The distribution of pityriasis versicolor by sex was 64.70% male and 35.29% female.

The distribution of pityriasis versicolor by age is shown in Table 1. The most affected age group was 21-30 years (38.23%). 22.54% of the cases affected patients from 31 to 40 years old, 23.55% from 11 to 20 years old, 7.84% from 41 to 50 years old, 3.92% from 61 to 70 years old and 1.96% from 51 to 60 years old. At the extremes, from zero to 10 years old and older than 70, there was one case in each age group, which accounts for a frequency of 0.98%.

TABLE 1: Pityriasis versicolor by age in the patients studied

Number of Cases	Total			
	Male	Female	N	%
Age				
0 to 10 years	0	1	1	0.98
11 to 20 years	16	8	24	23.52
21 to 30 years	24	15	39	38.23
31 to 40 years	17	6	23	22.54
41 to 50 years	5	3	8	7.84
51 to 60 years	1	1	2	1.96
61 to 70 years	3	1	4	3.92
> 70 years	0	1	1	0.98
Total	66	36	102	100.00

The duration of the disease in patients with pityriasis versicolor is shown in table 2. The frequency of duration of the disease from zero to two years was 58.82%; two to five years, 29.41%; five to 10 years, 6.86%; 10 to 15 years, 2.94%, and 15 to 20 years, 1.96%.

The frequency of relapsing episodes of pityriasis versicolor in the period of 12 months is shown in Table 3. The frequency of patients with one to four relapses of the disease per year was 52.94%; the frequency of patients with no relapses was 32.35%; those with more than four relapses per year accounted for 14.70%.

Isolates of *Malassezia* were *Malassezia sympodialis* (16.66%), *Malassezia furfur* (12.50%), *Malassezia globosa* (11.45%) and *Malassezia slooffiae* (2.10%).⁸

Table 4 shows the relationship between

Table 2: Pityriasis versicolor by duration of the disease in the patients studied

Duration of the disease	N	%
0 to 2 years	60	58.82
> 2 to 5 years	30	29.41
> 5 to 10 years	7	6.86
> 10 to 15 years	3	2.94
> 15 to 20 years	2	1.96
Total	102	100

Malassezia species and the number of relapses in 12 months. 14.63% of the cases caused by *Malassezia sympodialis* had no relapses, 12.20% had 1 to 4 relapses and 12.20% had more than 4x relapses. 2.44% of the cases caused by *Malassezia furfur* had no relapses and 26.83% had 1 to 4x relapses. 14.83% of the cases caused by *Malassezia globosa* had no relapses, 9.75% had 1 to 4x relapses and 2.44% had \geq 4x relapses. 2.44% of the cases caused by *Malassezia slooffiae* had no relapses and 2.44% had 1 to 4x relapses.

DISCUSSION

The 102 patients with clinical and laboratory diagnosis of pityriasis versicolor were protocolled for assessment of data such as sex, age, *Malassezia* species, duration of the disease and number of relapses observed in the period of 12 months and follow-up of 20 months.

There was a slight predilection for men in our sample. It is very difficult to relate the influence of sex on the incidence of pityriasis versicolor, since patients treated in our service are mostly women.

Yeasts of the *Malassezia* genus usually start colonization at puberty. Through androgen stimulation, sebaceous glands reach their peak at this stage, and this would explain the higher incidence of pityriasis versicolor in adolescence and adulthood. This incidence significantly drops at age extremes.^{9,10,11} In our study, age ranged from 7 to 76 years. The age groups of 21 to 30 years (38.23%), 31 to 40 years (22.54%) and 11 to 20 years (23.52%) prevailed, and

TABLE 3: Pityriasis versicolor in relation to the 41 *Malassezia* isolates and the number of relapsing episodes in the patients studied

Number of relapsing episodes	Zero relapses		1 to 4 x relapses		> 4x relapses		Total	
	N	%	N	%	N	%	N	%
<i>M. sympodialis</i>	6	14,63	5	12,20	5	12,20	16	39,03
<i>M. furfur</i>	1	2,44	11	26,83	0	0	12	29,26
<i>M. globosa</i>	6	14,63	4	9,75	1	2,44	11	26,82
<i>M. slooffiae</i>	1	2,44	1	2,44	0	0	2	4,87
Total	14	34,14	21	51,21	6	14,64	41	100

TABLE 4: Pityriasis versicolor by the number of relapsing episodes in the 102 patients studied

Number of relapsing episodes in 2 years	Nº of cases	%
Zero	33	32,35
1 – 4X	54	52,94
> 4X	15	14,70
Total	102	100

these results are in agreement with those of most works described.

The duration of the disease in our sample ranged from 3 months to 20 years, and this is in agreement with most studies already published. In 1997, Furtado *et al.* cited an evolution course that varied from 2 days to 15 years. In 2003 Aljabre studied 110 cases of intertriginous pityriasis versicolor with duration of 2 to 20 years. Crespo-Erchiga *et al.*, 2006, cited cases ranging from 15 days to 30 years in length.^{1,12,13}

After clinical and laboratory diagnosis of pityriasis versicolor, appropriate treatment should be initiated and the evolution of pityriasis versicolor should be monitored for at least 12 months to investigate the number of relapsing episodes during this period. A first group of individuals with pityriasis versicolor of single, partial or generalized involvement of the body was treated according to the standard treatment adopted and had no relapses. The frequency found in this group of patients was 32.35%. Patients who received adequate treatment and had no relapsing episodes within 12 months were classified as having pityriasis versicolor with clinical and mycological clearing.

Relapses were not observed during the 20-month follow-up.

A second group of patients with pityriasis versicolor of single, partial or generalized involvement of the body was treated properly and had one to four relapsing episodes of the disease, at a frequency of 52.94%. The relapsing episode was clinically confirmed by a positive Zireli's sign and positive microscopic examination. In these cases prophylactic treatment with ketoconazole 200mg/day/3days/month/6 months, associated with topical treatment with ketoconazole shampoo 3x week, with control of clinical lesions, was mandatory. During the 20 month-follow up, relapse of skin lesions was referred during periods of excessive sweating caused by physical exercise or after patients spent some time at the beach, pool or farms. Patients also associated relapses with higher temperatures (summer) or use of oily products in the body (moisturizers, sunscreens).¹²⁻¹⁵ Patients with pityriasis versicolor with one to four relapsing episodes in 12 months were classified as having relapsing pityriasis versicolor. In the medical literature it is cited as recurrent, recalcitrant or relapsing pityriasis versicolor. In a study to identify *Malassezia* species as the etiologic agents of pityriasis versicolor, the authors found the description of several relapsing episodes. A group of patients had only one relapsing episode, another group had two to five episodes and another more than five episodes, but there is no reference to follow-up after treatment. The authors concluded that there is no correlation between *Malassezia* species, the clinical presentation of the disease and relapsing episodes.^A

A third group of patients with pityriasis versicolor had more than four relapsing episodes within 12 months. The frequency found in this group was

14.70%. Individuals with pityriasis versicolor of partial or generalized involvement of the body underwent treatment with ketoconazole 200 mg/day/20 days associated with topical treatment with ketoconazole shampoo. Clinical lesions reappeared within varying periods of time for each patient. Some had a relapsing episode in about seven days, others in about 30 or 60 days, and a couple of the individuals in this group of patients (n=2) showed no clinical improvement. All the cases were confirmed by a positive Zireli's sign, positive direct microscopic examination and presence of rare fungal structures. Prophylactic treatment with ketoconazole 200mg/day/3days/month/6 months, associated with topical treatment with ketoconazole shampoo 3x week, was adopted. Despite prophylactic medication, there was no clinical improvement, once again confirmed by a positive Zireli's sign and positive direct microscopic examination. Patients did not refer any triggering factor of pityriasis versicolor and had no familial cases of the disease.¹⁶⁻²⁰ The group of patients with more than four relapsing episodes within 12 months received adequate treatment, but chronically evolved with constant bouts of relapse despite prophylaxis, with no significant clinical and mycological improvement. They were classified as having chro-

nic pityriasis versicolor. In our study we did not observe any correlation between *Malassezia* species and number of relapsing episodes observed during a period of 12 months. The medical literature does not cite this type of chronic course of pityriasis versicolor, in which we observe the relapse of lesions without associated predisposing factors with little or no response to proper systemic, prophylactic and topical treatment.

CONCLUSION

Despite the fact that pityriasis versicolor is a tropical disease that is very common in our country, a follow-up of at least 12 months is needed to investigate the number of relapsing episodes and to classify pityriasis versicolor into three types regarding its clinical course: pityriasis versicolor with mycological and clinical clearing, relapsing pityriasis versicolor, which is closely related to predisposing factors, and chronic pityriasis versicolor, with no clinical and mycological improvement despite adequate treatment.

Further studies are needed for us to observe the virulence factors related to *Malassezia* or host immunity that allow chronic pityriasis versicolor to evolve unresponsive to appropriate antifungal therapy. □

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How to cite this article/Como citar este artigo: Framil VMS, Melhem MSC, Szeszs MW, Zaitz C. Novos aspectos na evolução clínica da pitiríase versicolor. *An Bras Dermatol.* 2011;86(6):1135-40.