Influence of systemic corticotherapy on the triggering of pityriasis versicolor

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Summary

Pityriasis versicolor is a frequent mycosis and the use of systemic corticotherapy is one of its predisposing factors. This is an observational, cross-sectional, analytical and comparative study, conducted from January 2012 to January 2013 in the following outpatient clinics: Dermatology Service, Cassiano Antonio Moraes Hospital (HUCAM), Vitória, ES, Brazil; Nephrology Service, HUCAM; and Leprosy Department, Maruípe Health Unit, Vitória, ES, Brazil. Patients, undergoing long-term systemic corticotherapy (or not), were assessed with respect to the presence of pityriasis versicolor. If there was mycosis, a direct mycological examination would be carried out. The SPSS 17.0 software was used for the statistical analysis. From the total of 100 patients, nine had pityriasis versicolor, being eight from the corticotherapy group and one from the group with no use of corticosteroids. Regarding the patients with mycosis, the prevalent age ranged from 20 to 39 years, with six patients; six were women; seven mixed race; eight were undergoing long-term systemic corticotherapy; seven were taking low-dose systemic corticosteroids; four had leucocytosis; five had normal total cholesterol and triglycerides; and four had normal glycaemia. There was increased frequency of pityriasis versicolor in the group undergoing systemic corticotherapy with statistical significance, corroborating the only study on the topic (1962).

Key words: Pityriasis versicolor, tinea versicolor, Malassezia, corticosteroids, oral administration, risk factors.

Pityriasis versicolor

Pityriasis versicolor is a frequent superficial mycosis, determined by Malassezia yeast, found in normal skin biota of 90% of adults. From the world occurrence, it is most common in tropical regions, due to the hot and humid climate, without a distinction of sex or race.1,2 The presence of lipids in the skin favours Malassezia during postpuberty due to the apex of sebaceous glands development stimulated by sex hormones from this time of life.1,2 In areas rich of sebaceous glands, Malassezia occurs in the yeast phase (saprophytic form) and, under stimulation of trigger factors, it becomes a mycelium (opportunistic phase), causing mycosis.2,9

The triggering of mycosis is due to a set of factors: use of skin moisturisers; high humidity and temperature of the climate; hyperhidrosis; use of systemic corticosteroids; and genetic predisposition, among others.8–11 Systemic corticosteroids would increase the frequency of mycosis by changing the lipid composition of the cutaneous surface or by immunocompromising the individual.12–14 Clinically, the lesions are limited spots, initially rounded, confluent, of varied colours, with
furfuraceous scales, observed by stretching the skin distally (Zilié’s sign), and they predominate in the upper portion of the trunk and proximal areas of the upper limbs. Most cases are asymptomatic.\(^1\) The diagnosis is clinical and obtained through direct mycological examination.\(^2\) For the localised forms, the treatment is topical with antifungal imidazole derivatives. In diffuse forms, 2.5% selenium sulphide in shampoo, 25% sodium hyposulphite, or imidazole derivatives orally administered can be used.\(^{15}\)

**Glucocorticoids**

Glucocorticoids are effective in the management of inflammatory and autoimmune diseases, including dermatologic diseases, due to their anti-inflammatory and immunosuppressive effects. However, their use can trigger complications.\(^{16}\)–\(^{18}\) There are several corticosteroids actions: regulation of carbohydrates, lipids and proteins metabolism; preservation of the normal function of the cardiovascular, immunological and endocrine systems, etc.\(^{16}\)–\(^{19}\)

Glucocorticoids promote hyperglycaemia because they increase hepatic gluconeogenesis and peripheral resistance to insulin. They also alter the lipid metabolism, increasing the lipoproteins of low and high densities and, more commonly, the triglycerides.\(^{16}\)–\(^{18}\) Treatments undergone for more than 30 days are considered long term, forcing gradual discontinuation of the drug.\(^{20}\)

The use of oral corticosteroids in high doses and for long periods can lead to complications.\(^{18}\) The risk of infections, including fungal, is caused by the inhibition of the inflammatory response and the immunosuppressive effects of these drugs.\(^{18}\)–\(^{20}\)–\(^{21}\) In 1962, Boardman et al.\(^{[22]}\) observed the occurrence of pityriasis versicolor in patients taking the medication.

Therefore, this study was conducted to assess whether long-term use of systemic corticosteroids predisposes to increased frequency of pityriasis versicolor and to search how this influence occurs, whether by mechanism of immunosuppression or by change in glucose and lipid metabolism, through white blood cell (WBC) count, lipidogram and glucose levels analyses among patients using systemic corticotherapy or not.

**Materials and method**

This is an observational, cross-sectional, analytical and comparative study, conducted from January 2012 to January 2013 in the following outpatient clinics: Dermatology Service, Cassiano Antonio Moraes Hospital (HUCAM), Vitória, ES, Brazil; Nephrology Service, HUCAM; and Leprosy Department of Maruípe Health Unit, Vitória, ES, Brazil.

Patients with certain underlying disease undergoing long-term corticotherapy or not were selected and they composed two groups: patients using systemic corticosteroids (oral prednisone) for more than 30 days and patients who were not using this therapy. In case they agreed, a dermatological exam of the integument would be performed to verify the existence of pityriasis versicolor and subsequently a standard record would be filled out with identification data and latest results of laboratory exams (WBC count, lipidogram and blood glucose).

In patients with mycosis, scales were collected from the spots with a sterile scalpel blade to confirm the diagnosis through the direct mycological examination. This procedure consisted of applying a drop of 20% potassium hydroxide to the material collected on a glass slide to observe it under an optical microscope. The examination result was positive, observing thick and sinuous pseudofilaments and rounded blastospores, arranged as a bunch of grapes.

In the occurrence of mycosis, the following data of lesions were recorded: colour; location; symptoms; previous history of the disease; family history; and use of skin moisturisers. Based on the research conducted by Framil et al.\(^{[23]}\), the location of lesions was categorised as follows: mild (affecting only one region of the body), moderate (affecting more than one to three regions of the body) and disseminated (more than three regions of the body affected).

The variable ‘corticosteroid dose’ was categorised on the basis of the study conducted by Zonana-Nacach et al.\(^{[24]}\), who assessed the effects of corticotherapy in patients with systemic lupus erythematosus, whose oral doses administered were divided into two categories: high doses (above or equal to 60 mg day\(^{-1}\)) and low doses (less than 60 mg day\(^{-1}\)).

All the patients with mycosis under study had been treated appropriately. Exclusion criteria were as follows: (a) use of glucocorticoids for less than 30 days; (b) use of other immunosuppressive drug; (c) patients with HIV infection; and (d) patients under 18 years of age.

The **spss** version 17.0 software (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis, performing the chi-square test to calculate odds ratio (OR) and 95% confidence interval (95% CI), taking the significance level of \(P \leq 0.05\) as a basis for qualitative variables. The absolute and relative frequencies of the following variables were determined: demographic
(age, sex, occupation and race); clinical (colour of the lesions, location, presence/absence of symptoms, prior personal history of mycosis, family history and use of skin moisturisers), with respect to patients with pityriasis versicolor, using systemic corticotherapy or not and their doses and laboratory exams (WBC count, lipidogram and blood glucose).

The study was approved by the Ethics Committee of the Health Sciences Center, Federal University of Espírito Santo, keeping the privacy of patients who consented in writing to participate in the research.

Results

In the study period, 100 patients with nephrological, rheumatological and dermatological diseases of various aetiologies were cared for. From this group, 50 patients were undergoing long-term systemic corticotherapy and 50 were not. The median age was 40 years, the average was 40 years and 9 months (standard deviation: 13 years and 7 months), the minimum age was 18 years and the maximum 74 years.

Pityriasis versicolor occurred in nine cases out of a total of 100 patients, confirmed by direct mycological examination. Eight patients belonged to the corticotherapy group and one to the group with no treatment, representing a statistically significant difference (OR = 9.33; 95% CI: 1.12–77.7; P = 0.031).

With respect to colour, the analysis of the characteristics of pityriasis versicolor lesions showed predominance of hypochromic spots in eight cases (88.9%) and one (11.1%) with light-brown lesions. Regarding the topography, there were two cases (22.2%) characterised as mild, four moderate cases (44.4%) and three disseminated (33.3%). Four patients (44.4%) had symptoms (itching) and two (22.2%) confirmed prior personal history of mycosis. Four patients (44.4%) have had positive family history for the disease and three (33.3%) commonly applied moisturisers.

The group of patients with pityriasis versicolor was compared with the group without the mycosis with respect to the demographic variables, as shown in Table 1. Table 2 shows the absolute and relative frequencies of demographic characteristics between the groups with and without pityriasis versicolor.

With respect to WBC count and corticotherapy, the group taking oral corticosteroid had the following results: 27 (60%) patients had values between 4000 and 10 000 leucocytes (normal); two (4.4%) had values less than 4000 leucocytes (leucopenia); and 16 (35.6%) had values greater than 10 000 leucocytes (leucocytosis). In the group of patients who were not undergoing corticotherapy, the results were: 34 (77.3%) patients had values between 4000 and 10 000 leucocytes; one (2.3%) had smaller value than 4000 leucocytes; and nine (20.5%) had values greater than 10 000 leucocytes (Fig. 1).

The lipidograms were analysed with respect to the use/non-use of oral corticosteroid and, considering normal values up to 200 mg dl⁻¹ and increased values above this level. The analyses revealed the

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The following results: the group undergoing corticotherapy had 22 (52.4%) patients with total cholesterol less than 200 mg dl\(^{-1}\) and 20 (47.6%) with total cholesterol greater than this value. The group that was not using corticosteroids had: 26 (65%) patients with normal values of total cholesterol and 14 (35%) with increased total cholesterol, without statistical significance (OR = 0.592; 95% CI: 0.244–1.440; \(P = 0.270\)). The distribution is shown in Fig. 2.

Still, with regard to the lipidograms, the results obtained for triglycerides – considering normal values up to 150 mg dl\(^{-1}\) and increased values above this level – were: 16 (43.2%) patients with normal values of triglycerides; and 21 (56.8%) with increased values in the group taking systemic corticosteroid; and 25 (62.5%) patients within the normal range of triglycerides; and 15 (37.5%) with increased levels in the group that was not using corticosteroids, without statistical significance (OR = 0.457; 95% CI: 0.184–1.139; \(P = 0.112\)). The distribution of the variable is shown in Fig. 3.

Regarding the glucose metabolism, values up to 100 mg dl\(^{-1}\) were considered normal fasting blood glucose and values above this level were considered increased (glucose intolerance). Thus, it was observed that from the individuals taking systemic corticosteroid, 32 (82.1%) had normal fasting blood glucose and seven (17.9%) had it increased. In the group with no treatment, 31 (73.8%) patients were within the range considered normal and 11 (26.2%) within the altered range, without statistical significance (OR = 1.622; 95% CI: 0.557–4.723; \(P = 0.431\)).

**Discussion**

Even though the relationship between systemic corticosteroids and fungal infections have been studied in the past, only a systematic and controlled research...
was intended to assess the effects of corticotherapy on pityriasis versicolor.

In this study, 16% cases of pityriasis versicolor were found in patients undergoing long-term systemic corticotherapy, compared to the group that was not using corticosteroid (2%), with statistical significance ($P = 0.031$), corroborating the data obtained by Boardman et al. (1962), who found 10 (9.4%) individuals with pityriasis versicolor among 106 patients undergoing corticotherapy and no case in the group of 82 patients that were not undergoing the therapy. Experimentally, another study conducted by Burke et al. (1961) assessed the relationship between tinea versicolor and corticosteroids. Scales of mycoses or cultures of *Pityrosporum orbiculare* were inoculated in 21 individuals, six of which had endogenous or exogenous hypercortisolism. These six patients developed, at least, microscopic evidence of the presence of *Malassezia furfur*, whereas only one patient from the other 15 without hypercortisolism developed mycosis.

With respect to the colour of the fungal lesions, there was a predominance of hypochromic spots, corroborating the results obtained by Chetty et al. (1962), Morais et al. (1966), Ghosh et al. (1967) and Santana et al. (1968).

Most patients had more than one topography affected by mycosis, with a prevalence of moderate forms, followed by the disseminated form. This result is similar to that found by Framil et al. (1963), whereas Morais et al. (1966) found predominance of the disseminated form. The three studies reinforce the data in the literature, which state that confluence of lesions until they reach large areas of skin is common.

The results for the variable ‘symptoms’ were balanced, resembling the results obtained by Morais et al. (1966), Ghosh et al. (1967) and Rao et al. (1968). However, the results of this study are in contrast with those in the literature, which describes the disease as asymptomatic or oligosymptomatic, in most cases.

The previous personal history of pityriasis versicolor was negative in 77.8% of the cases; however, Morais et al. (1966), Ghosh et al. (1967) and Santana et al. (1968) found balanced results, with 52.6%, 48.1% and 55.2% respectively. The result of this study differed from that of the literature, which mentions the recurrences of mycoses as common, contributing to its recidivating characteristic and occurring in 60% patients in the first year after treatment and 80% in the second year.

The family history was positive in almost half the cases. This result is comparable to that obtained by Rao et al. (1968) (38.3%), Hafez et al. (1970) (39%) and Terragni et al. (1971) (43.8%) and in disagreement with Chetty et al. (1963) (21%), Burke et al. (1964) (17%), Ghosh et al. (1967) (25.5%), Faergmann et al. (1969) (18.8%) and He et al. (1971) (21.2%).

Hafez et al. (1970) and He et al. (1971) studied the influence of genetics on mycoses and they found a likely multifactorial inheritance pattern for pityriasis versicolor, following a polygenic additive model. The factors precipitated the disease in genetically predisposed individuals.

Regarding the use of skin moisturisers, the results (relative frequencies) were similar to those found by Morais et al. (1966). Roed-Petersen et al. (1972) argued that the use of lotions in the integument would favour *Malassezia* and pityriasis versicolor, by making the skin more oily and due to the fact that long-chain fatty acids favour fungal proliferation by serving as substrates.

Mycosis predominated within the range from 20 to 39 years of age, corroborating with data found by Burke et al. (1964), Rao et al. (1968), He et al. (1970) and Framil et al. (1971). In other studies, such as those conducted by Chetty et al. (1962), Morais et al. (1966) Ghosh et al. (1967) and Arenas et al. (1971) the first decade was the predominant group. The results reinforce the literature that describe tinea versicolor as more frequent in adolescents and young adults.

Females were predominant in the group with pityriasis versicolor, as observed by Santana et al. (1968), Faergmann et al. (1969), Furtado et al. (1971) and Belém et al.
[41] and Miranda et al. [42]. This result disagrees with those found by Chetty et al. [12], Burke et al. [25], Morais et al. [26], Ghosh et al. [27], Rao et al. [30], He et al. [36] Framil et al. [38] and Kyriakos et al. [43], in which males were prevalent.

Kyriakos et al. [43] attributed the predominance of male cases to excessive sweating due to increased exposure of men to physical efforts, whereas He et al. [35] suggested that there was greater activity of the sebaceous glands in men due to increased production of sex hormones. There was a predominance of females in other studies and He et al. [35] attributed the fact to women’s aesthetics concern.

Mycosis prevailed in mixed race patients, corroborating data found by Morais et al. [26] and differing from Burke et al. [25] and Belém et al. [41], who found predominance of white patients. These divergent results may be explained by the epidemiological differences between populations of each sample. Chetty et al. [12] observed high incidence of tinea versicolor in Madras (India), a region with tropical climate, and proposed that this fact was a result of the largest number of sebaceous glands of black inhabitants of tropical areas.

The region of the study has hot and humid climate and racial variation, with significant share of browns and blacks. The tropical climate favours for hyperhidrosis, which in turn contributes to the outbreak of tinea versicolor. This relationship, however, is difficult to measure and still, some authors reported no racial differences in sweating.44,45

To assess how the influence of corticotherapy on the triggering of pityriasis versicolor occurs, the variables WBC count, lipidogram and blood glucose were analysed in relation to the use or non-use of systemic corticosteroid and the absolute and relative frequencies of these variables among patients with and without mycosis were described.

Systemic corticotherapy caused little leucopenia, keeping a normal number of leucocytes in most cases. Regarding the group without corticotherapy, the treatment led to more cases of leucocytosis. These data also corresponded to the results of WBC count in patients with pityriasis versicolor. Therefore, the mechanism of immunosuppression caused by the drug was not due to leucopenia.16,18

Indeed, corticotherapy causes leucocytosis, mainly at the expense of neutrophilia. Thus, the results obtained allow concluding that the mechanism by which the corticosteroids increase the frequency of pityriasis versicolor might even be due to an immunosuppressant effect, in this case qualitative, but not measurable in the study. The hypothesis that immunosuppression is due to the overall decrease of leucocytes (quantitative) has been discarded.16,18

The distribution of the variable ‘dose’ between the groups with and without pityriasis versicolor showed predominance of lower doses in the group with mycosis, suggesting that high doses (immunosuppressive) were not required to cause fungal infection and that, therefore, it may not be caused by immunosuppression.

The effect of systemic corticosteroid on the lipidogram showed a greater number of cases in which there was hypercholesterolaemia and hypertriglyceridaemia when compared to the group without corticotherapy. These results corroborate with the literature that describes increased LDL cholesterol and triglycerides in patients undergoing corticotherapy. However, in the description of the lipidogram frequencies, most patients with pityriasis versicolor showed normal cholesterol and triglyceridaemia, hindering the hypothesis that while altering the lipid metabolism, glucocorticoids would change the cutaneous lipid composition, thus favouring mycosis.16,18

Burke et al. [25] suggested that a biochemical or functional change on the cutaneous surface would make an individual susceptible to tinea versicolor and this change in the lipid film of the integument would be genetically predetermined and precipitated by other factors, such as the systemic corticotherapy. On the other hand, Boardman et al. [22] studied the composition of the skin of patients with and without pityriasis versicolor and found no significant differences between the groups.

Finally, normal fasting blood glucose was prevalent among patients with mycosis. This result is consistent with those obtained by comparison between levels of fasting blood glucose and use/non-use of corticosteroids, which in turn revealed no significant number of patients with hyperglycaemia in the group taking systemic corticosteroids. This fact reinforces the suggestion by Mandel et al. [46], who stated that increased blood glucose levels would not function as an isolated precipitating factor for the development of mycosis. It also corroborates the findings of García-Ilumbría et al. [47] who did not observe greater susceptibility to pityriasis versicolor in diabetic patients when compared to non-diabetic patients.

It is concluded that long-term systemic corticotherapy increased the frequency of pityriasis versicolor, but the distribution of laboratorial variables among patients with pityriasis versicolor showed predominance of normal WBC count, lipidogram and fasting blood glucose.
Acknowledgments

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Conflict of interest

There is no conflict of interest.

References


