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Short Communication

A Comparative Survey of Serum Androgenic Hormones Levels between Male Patients with Dermatophytosis and Normal Subjects

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SUMMARY: Fungal growth can be influenced by human physiological mediators such as androgenic hormones. The aim of this study was to investigate a possible relationship between androgenic hormones and susceptibility to dermatophytosis. To this purpose we measured the levels of testosterone, androstendione, and dehydroepiandrosterone sulfate (DHEA-S) in 60 male patients with dermatophytosis due to *Epidermophyton floccosum* and *Trichophyton rubrum* by enzyme link immunoassay. Serum testosterone concentration was found to be significantly lower in patients with *E. floccosum* than in healthy subjects. No significant differences in androstendione and DHEA-S levels were noted between the patients and the healthy individuals. The results showed that testosterone concentration can be considered a predisposing factor for tinea cruris infection.

Physiological mediators such as hormones play an imperative role in the fungus-host relationship (1). The inhibitory effects of sex hormones against fungal growth have been demonstrated in previous studies (2-4). However, these inhibitory effects depend on hormone structure and dermatophyte species. Among the 11 species of dermatophytes which are considered the major agents of dermatophytosis, *Trichophyton rubrum* rarely causes tinea capitis and *Epidermophyton floccosum* never does so (5,6). These species are also considered the two most common agents involved in tinea cruris worldwide (7-9). It has been shown in vitro that sex hormones have protective effects against dermatophyte growth in a dose-dependent fashion (10,11). Brasch and Flader reported that *T. rubrum* and *E. floccosum* had the highest sensitivity to androgenic hormones in vitro among the examined dermatophytes (12). Conversely, zoophilic species such as *Trichophyton mentagrophytes* and *Microsporum canis* were shown to be less responsive to the inhibitory effects of most tested hormones (12,13).

The discovery of fungal receptors for human hormones in recent decades (14-16) has revealed new aspects of fungal pathogenesis. However it is still unclear why certain dermatophytes tend to cause infection in specific sites of the body. Although it is widely believed that the severity and location of dermatophytic infections depend on host specificity, the mechanism of this process is not fully understood. For this reason, we measured serum level of testosterone, androstendione, and dehydroepiandrosterone sulfate (DHEA-S) in male patients with dermatophytosis and in healthy men in order to determine the effects of sex hormones on dermatophytosis in vivo.

The patients were admitted to the Medical Mycology and Parasitology Department in Tehran University of Medical Sciences, Tehran, Iran. After examination by a dermatologist, patients were sampled by the scraping of lesions. None of the patients had taken antifungal agents at least 2 weeks before sampling. All specimens were examined by KOH 10% and cultured on Sabouraud dextrose agar containing cyclohexamide and chloramphenicol. A blood sample was also taken from each patient with confirmed dermatophytosis caused by *E. floccosum* or *T. rubrum* as well as from healthy controls. Each serum sample was dispersed immediately and then frozen at −20°C in order to keep the serum stable. Concerning hormone variation during 24 h, all blood samples were taken from 8 a.m. to 10 a.m. when the sex hormone level was maximum. We excluded from the study those people whose daily habits are generally nocturnal, since such individuals have a different hormone rhythm.

Serum levels of testosterone, androstendione, and DHEA-S were measured in both groups by means of the enzyme linked immunoassay (ELIZA) method. Commercially available kits from DRG international, Ins. (New York, N.Y., USA) were used. Tests were performed according to the manufacturer's instructions. The serum hormone levels of all groups were compared using Student's *t* test. *P* values <0.05 were considered significant. Statistical analysis was performed by SPSS software.

The patient group consisted of 60 male patients aged between 20 - 40 years old (mean: 27.8 ± 6.1) with confirmed dermatophytosis caused by *E. floccosum* (46 cases) or *T. rubrum* (14 cases). The control group consisted of 30 age-matched male volunteers with no pervious history of dermatophytosis. Table 1 shows the distribution of lesions in the 60

Table 1. Distribution of isolated *E. floccosum* and *T. rubrum* based on the site of infection

Site of lesion	Number of positive cultures		Total	%
	E. floccosum	*T. rubrum*		
Groin	45	3	48	80.0
Foot	1	7	8	13.3
Hand	–	3	3	5.1
Neck	–	1	1	1.6
Total	46	14	60	100.0

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Table 2. Mean serum concentration of androgenic hormones in male patients with dermatophytosis and in healthy individuals

Groups	Serum hormone concentration					
	Testosterone		Dehydroepiandrosterone sulfate		Androstendione	
	Mean (ng/ml)	SD	Mean (μg/ml)	SD	Mean (ng/ml)	SD
E. floccosum	5.51	1.39	2.56	1.23	1.02	1.03
T. rubrum	6.64	1.88	2.77	1.35	0.99	0.64
Control	7.35	1.42	2.97	1.20	1.06	0.75

selected patients who showed positive culture yielding *E. floccosum* or *T. rubrum*.

The serum concentration of the tested hormones is shown in Table 2. The mean concentration of testosterone in patients with *E. floccosum* and *T. rubrum* were 5.51 ng/ml (±1.39) and 6.64 ng/ml (±1.88), respectively. Our results show that testosterone levels were significantly lower in patients with *E. floccosum* than in healthy controls ($P < 0.01$) (Table 2). However, no significance was seen in a comparison between the serum testosterone levels of patients with dermatophytosis caused by *T. rubrum* and those of healthy subjects. As well, no differences in androstendione and DHEA-S levels were noted between the patient group and the healthy controls.

Contrary to most other dermatophyte hosts, humans are differentiated by a high cutaneous concentration of the adrenal androgen dehydroepiandrosterone (DHEA) and its metabolites (17). These hormones, which are present within the pilosebaceous units of human skin, have various inhibitory effects on the growth of dermatophytes in vitro (13). However, this inhibitory effect depends on hormone structure and dermatophyte species. Moreover, the sex hormones are metabolized within human follicular tissue and thereby can influence the colonization of dermatophytes within the hair follicles (18). Receptor-mediated effects and an unspecific interference with fungal sterol metabolism are probable mechanisms of the fungal growth inhibition by steroidal hormones. (2,15,19) However, it had been shown that some fungi could escape from this inhibitory affect by metabolizing these hormones to low potent derivatives (17,20).

Anthropophilic dermatophytes have been shown to be more generally responsive to steroid hormones than are zoophilic species (11,12). This suggests a correlation of steroid susceptibility with adaptation to human skin (13). The high susceptibility of *T. rubrum* and *E. floccosum* to intrafollicular DHEA and its metabolites could be one reason that these two species are unable to cause tinea capitis (12). Equally our results revealed that the testosterone level is significantly lower in patients with dermatophytosis caused by *E. floccosum* in comparison with healthy controls. However, comparison of these two groups showed no statistically significant difference in regard to androstendione and DHEA.

5 alpha (5 α)-reductase, which is present in many mammalian tissues, is a key enzyme in metabolizing androgenic hormones in the skin (21). The physiological importance of this enzyme is derived from its capability for converting testosterone to dehydrotestosterone (DHT), and for converting progesterone and deoxycorticosterone (DOC) to their respective 5-α-reduced derivatives (22). Compared with testosterone, its hydroxylated metabolites such as DHT had showed a lower inhibitory effect on dermatophytes (20). On the other hand, the groin region has higher 5 α-reductase activity, compared with hair follicles and other parts of the skin (18,23). Moreover, *E. floccosum* is known as the most common agent of tinea cruris throughout the world. These findings suggest that the high level of activity of 5 α-reductase in the groin skin might be a possible reason for the strong tendency of *E. floccosum* for colonization in this region. In addition, the activity of 5 α-reductase in the scalp skin and hair follicle is not as high as in the groin skin and therefore is not adequate to modify the circumstances for *Epidermophytone* growth in the mentioned areas. Hence, testosterone concentration not only plays a role in the pathophysiology of some complications such an acne or hirsutism but it may also be considered a predisposing factor for tinea cruris.

Collectively, we suggested that there might be a relation between the low serum testosterone levels seen in patients with dermatophytosis caused by *E. floccosum* and susceptibility to tinea cruris infection. This hypothesis gained strength because of the fact that serum testosterone level was significantly lower in patients with dermatophytosis caused by *E. floccosum* than in both healthy controls and patients with dermatophytosis due to *T. rubrum*. It remains an open question, however, whether there is a higher 5 α-reductase activity in patients with tinea cruris as compared to healthy individuals.

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