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Study of Relationship between Testosterone and Dermatophytosis due to *Trichophyton verrucosum*

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Abstract: The inhibitory effect exerted by steroid hormones on the *in vitro* growth characteristics of dermatophytes is poorly understood. As a hypothesis this inhibition could result from fungal adaptation to the human host. Therefore, in this study the susceptibility of *T. verrucosum* to androgenic hormones was done. As a result, testosterone proved to reduce fungal growth whereas hydrocortisone had no such effect. In general, *T. verrucosum* was shown to be more susceptible to steroid hormones. However, since fungal response to hormones consisted of growth inhibition and occurred only at steroid concentrations much higher than present in human, it cannot be assumed to contribute to this adaptation.

Key words: Androgenic hormones, testosterone, dermatophytosis, *Trichophyton verrucosum*, Iran

INTRODUCTION

Dermatophytosis is one of the dermal mycosis that results from the group of fungus actions in the keratinized tissue (such as hair, nail and skin keratinized tissue) that called dermatophytes. Dermatophytes is a group of keratinophilic fungus that known from many years ago. Now a days 41, species of dermatophytes were identified that totally divided into three geniuses (with notice to the asexual phase) with names microsporium, trichophyton, epidermophyton. Dermatophytosis is not contiguous disease and probably specific agents in sufferance to this disease are effective. Physical and chemical agents can be effective in reveals of dermatophytosis pathogenesis in human which some people are sensitive and some other are resistance and might be dermatophytes also shown difference susceptible against of this agent. Of physical effective agents can be refer to temperature, moisture and pH that have difference effects on several dermatophytes. Several chemical factors such as hormones, fatty acids and amino acids in skin can be effective in dermatophytes growth (Xavier *et al*., 2008; Hashemi *et al*., 2004). Androgen, also called androgenic hormone or testoid is the generic term for any natural or synthetic compound usually a steroid hormone that stimulates or controls the development and maintenance of male characteristics in vertebrates by binding to androgen receptors. This includes the activity of the accessory male sex organs and development of male secondary sex characteristics. Androgens were first discovered in 1936 (Singh *et al*., 2006; Sinha-Hikim *et al*., 2004). Androgens are also the original anabolic steroids and the precursor of all estrogens, the female sex hormones. The primary and most well-known androgen is testosterone. A subset of androgens, adrenal androgens includes any of the 19-carbon steroids synthesized by the adrenal cortex, the outer portion of the adrenal gland (zonula reticularis-innermost region of the adrenal cortex) that function as weak steroids or steroid precursors including Dehydroepiandrosterone (DHEA), Dehydroepiandrosterone Sulfate (DHEA-S) and androstenedione. Besides testosterone, other androgens include: first, Dehydroepiandrosterone (DHEA) which is a steroid hormone produced in the adrenal cortex from cholesterol. It is the primary precursor of natural estrogens (Vlahopoulos *et al*., 2005). DHEA is also called dehydroisoandrosterone or dehydroandrosterone. Second Androstenedione (Andro) which is an androgenic steroid produced by the testes, adrenal cortex and ovaries. While androstenediones are converted metabolically to testosterone and other androgens, they are also the parent structure of estrone. Use of androstenedione as an athletic or body building supplement has been banned by the International Olympic Committee as well as other sporting organizations. Third androstenediol is a steroid metabolite and act as main regulatory agent of gonadotropin secretion. Fourth androsterone which is a chemical by-product created during the breakdown of androgens or derived from progesterone that also exerts minor

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masculinising effects but with one-seventh the intensity of testosterone. It is found in approximately equal amounts in the plasma and urine of both males and females. Fifth, Dihydrotestosterone (DHT) which is a metabolite of testosterone and a more potent androgen than testosterone in that it binds more strongly to androgen receptors. It is produced in the adrenal cortex. Physiological mediators of human host that interfere with pathogenic fungi are of particular interest in clinical mycology. An example for such mediators is steroid hormones (Brasch and Gottkehaskamp, 1992; Hashemi and Sarasgani, 2004). For this reason, researchers measured serum level of androgen hormones levels especially testosterone in dermatophytosis patients due to *Trichophyton verrucosum* and in control group in order to determine the effects of sex hormones on dermatophytosis *in vivo*.

MATERIALS AND METHODS

After examination by dermatologists the patients were admitted to the Sina hospital, Tabriz, Iran. The patients were sampled by the scraping of lesions. None of them had taken antifungal agent at least 20 days before sampling. All specimens were examined by KOH 10% and cultured on sabouraud dextrose agar containing cyclohexamide and chloramphenicol. A blood sample was also taking from each patient with dermatophytosis due to *T. verrucosum* as well as control group. The sera was dispersed immediately and then frozen at -20°C in order to keep the serum stability. After the sampling, the frozen sera were defrosted and the levels of androgenic hormones were measured in both groups by means of the Enzyme Linked Immunosorbent Assay (ELISA) Method. Commercially available kits from DRG international, Ins. (New York, N.K., USA) were used. The serum testosterone levels of all groups were compared using student's t-test. The $p<0.05$ were considered significant statistical analysis was done by SPSS Software, Version 8 (Hashemi and Sarasgani, 2004).

RESULTS

The patient group comprised of 50 patients, 30-45 years old with confirmed dermatophytosis caused by *T. verrucosum*. The control group consisted of 30 age matched male volunteers with no pervious history of dermatophytosis. The serum concentration of the tested hormones is shown in Table 1.

The results show that progesterone, testosterone andestradiol proved to reduce fungal growth whereas, hydrocortisone had no such effect.

Table 1: Mean serum concentration of testosterone in dermatophytic patients and healthy individuals

Groups	Testosterone
T. verrucosum	5.12±1.28
Control group	6.42±1.64

± values are shown as Mean±SD

DISCUSSION

The results shown that testosterone proved to reduce fungal growth whereas hydrocortisone had no such effect. In one study carried out by Hashemi and Sarasgani (2004), revealed that testosterone level of serum in patients with dermatophytosis due to *E. floccosum* without androgenic disorder was significantly lower than those of normal individuals. That is compatible with the research results. In one other study were done by Brasch and Gottkehaskamp (1992) obtained that in agar dilution assays progesterone, testosterone and andestradiol proved to reduce fungal growth whereas hydrocortisone had no such effect. That is compatible with the research results. Androgenic hormones are present within the pilosebaceous units of human skin have different inhibitory effects on the growth of some dermatophytes (Stevens, 1989). On the other hand, these hormones are metabolized within human follicular tissue, therefore it may be speculated that they might influence the colonization of hair follicles by dermatophytes (Takayasus *et al*., 1980).

In one study by Brasch and Flader (1996), they stated that all dermatophytes responded in a dose-dependent manner with reduced diameters of thalli. Growth of *T. rubrum* and *E. floccosum* was completely or strongly suppressed by 10 (2) mg 1 (-1) androstenedione and androstanedione. A minor inhibition of all strains was obtained with 10 (1)-10 (2) mg 1 (-1) testosterone, dehydroepiandrosterone and 5-alpha-dihydro testosterone, the last being least inhibitory for all species. *Trichophyton mentagrophytes* and *M. canis* were least responsive to most hormones. The high susceptibility of *T. rubrum* and *E. floccosum* to intrafollicular androstenedione and androstanedione could be one reason why these two species are unable to cause tinea capitis. Receptor-mediated effects and an unspecific interference with fungal sterol metabolism are discussed as mechanisms of fungal inhibition by steroidal hormones.

Hashemi *et al.* (2004) measured the levels of testosterone androstendione and Dehydroepian derosterone 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.

Schar *et al.* (1986) showed that progesterone inhibited growth in a dose-responsive manner with a 50% inhibition concentration of 5.5×10(-6) M. Partial recovery from inhibition occurred after 24-48 h; inhibition could be enhanced by dividing the amount of added progesterone every 24 h. In the same rank order as was their relationship to each other and progesterone in binding studies, deoxycorticosterone and dihydro testosterone were less effective inhibitors; other steroid hormones that were tested showed no consistent effect. They hypothesized that the binder described acting as a hormone receptor is the molecular site of action for the functional effect of the hormone. The functional effect may be related to the observed resistance of females to dermatophytosis.

Phillips *et al.* (1986) also said that the most frequent causes of hair loss in pediatric patients include tinea capitis, alopecia areata, traction alopecia and trichotillomania. In the adult population, causes to be considered are alopecia areata and hair loss associated with systemic disease and hormonal influence. The clinician must be able to separate the types and causes of hair loss into those that reflect primary dermatologic conditions and those that represent reaction to systemic disease.

Shankland and Richardson (1989) research on dermatophytosis and they evaluated mentagrophytes in a blind study to investigate the advantages of incorporating hydrocortisone with bifonazole for the treatment of dermatophytosis. In that study, one group contained the untreated animals and the other groups were treated daily with: bifonazole alone, hydrocortisone alone, bifonazole/hydrocortisone combination or vehicle alone. The mycological, clinical and histopathological progression of the disease was monitored for 3 weeks. The two groups receiving the antifungal were the most impressive clinically. This was confirmed mycologically and although there was evidence of fungus on histological examination, the stratum corneum showed signs of recovery. In the three groups not receiving antifungal therapy the infection did not resolve by the end of the treatment period. Animals from these groups were mycologically positive throughout the treatment period and histological examination showed proliferation of the fungus. The groups were ranked in descending order as bifonazole/hydrocortisone combination, bifonazole alone, hydrocortisone alone, vehicle alone untreated control.

CONCLUSION

Therefore, it can be concluded that androgenic hormones especially testosterone have inhibitory effect on dermatophytosis due to *T. verrucosum*.

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