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Chitotriosidase and prolidase in tinea pedis: A preliminary study

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Abstract

Dermatophyte infections are superficial fungal infections. Tinea pedis is a dermatophyte infection of the feet and interdigital spaces. An evaluation was made of the chitotriosidase (ChT) concentrations, prolidase activity and the possible association between these biomarkers in tinea pedis. Study subjects were comprised of 42 patients with tinea pedis and 40 healthy subjects. Serum ChT concentrations and prolidase activity were determined in study population. Higher ChT concentrations were found in patients than controls ($p < 0.001$). We did not find any difference between groups in terms of prolidase activity ($p = 0.162$). We also did not found any correlation between ChT and prolidase activity. ChT seems to have roles during the inflammatory conditions in patients with tinea pedis. Whereas prolidase activity is not associated with the tinea pedis.

Keywords: Tinea pedis, chitotriosidase, prolidase, Dermatophyte, Serum, ChT

Introduction

Dermatophyte infections are common fungal disorders. There is an increase in the incidence of the disease during the last decade [1]. The disease is defined as chronic dermatophyte infection of the feet and interdigital spaces [2]. Diagnosis of tinea pedis based on identifying of fungal element with laboratory studies including potassium hydroxide staining and clinical evaluation. Keratinizes and other enzymes are released in this process and therefore host keratinocytes are activated [3]. Inflammation can be activated by the activated keratinocytes via various kinds of inflammatory cells and cytokines such as neutrophil, macrophage, macrophage chemotactic and activating factors in the skin [4,5].

Chitotriosidase (ChT) is an enzyme secreted from activated tissue macrophages. Therefore, ChT is considered as a biomarker of macrophage activation [6]. Human ChT is associated with several infectious and inflammatory diseases [7-8]. Increased ChT expressions have been also indicated in fungal infections [9, 10].

Human prolidase is a widely distributed cytosolic exopeptidase that cleaves imidopeptides residues located at the C-terminal end. Impaired prolidase metabolism and is associated with different disease including skin ulcers and skin infections [11-14].

The hypothesis of this study was that increased serum ChT concentrations and prolidase activity may have role in patients with tinea pedis. Therefore, an evaluation was made of the ChT concentrations, prolidase activity and the possible association between these biomarkers in tinea pedis. To the best of our knowledge, the role of ChT and prolidase in tinea pedis has not been well investigated. Therefore, this study will provide an important opportunity to advance understanding of the role of ChT and prolidase in tinea pedis.

Material and Methods

Determination of ChT concentrations and prolidase activity

The quantitative ELISA kits were used to detect chitotriosidase concentrations (Sunred, Shanghai, China). Test procedures were performed according to kit insert. Prolidase activity was determined by a spectrophotometric method [15,16].

Study population

The diagnosis of tinea pedis was performed based on both clinical and microscopic examinations. All patients had not been receiving any drugs. Patients with chronic disorders such as impaired renal function, diabetes mellitus, rheumatic disease, musculoskeletal disease, skin ulcer, liver disease were excluded from the study. Same exclusion criteria in the study were applied for healthy controls. The protocol was approved by local ethical committee (E-17-02-07). Informed consent was obtained from all individual participants included in the study.

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Samples

Overnight fasting blood samples were collected from all participants into red top tube (Greiner, Austria). Patient samples were taken on the first day after admission. The serum sample tubes were allowed to clot before centrifugation. After centrifugation at 4°C for 15 minutes at 3500 rpm, the serum was aliquoted and immediately frozen at -20°C.

Statistical analysis

Data normality was assessed by Shapiro-Wilk's test. Student's t-test and Mann-Whitney U test were used to compare the differences of ChT and prolidase, respectively. Spearman correlation coefficients were calculated to see the relationship between ChT and prolidase. Analyses were performed by using IBM SPSS software (release 22.0, IBM, SPSS Inc., Chicago, IL, USA) considering $P < 0.05$ as statistically significant.

Results

Study subjects comprised 42 patients with tinea pedis [27 males and 15 females; with ages 27 - 63 years (mean age: 42 ± 16)] and 40 healthy controls [12 males and 28 females; with ages 32 - 53 years (mean age: 40 ± 11)]. Mean values of creatinine, alanine aminotransferase, aspartate aminotransferase, white blood cell count and C reactive protein concentrations were 0.78 ± 0.11 mg/dL, 37.33 ± 4.2 U/L, 28.58 ± 7.4 U/L, 10.31 ± 3.59 10³ mL and 7.60 ± 4.31 mg/L in patients, respectively. Mean ChT levels were found as 112.90 ± 43.93 and 5358 ± 1963.52 pg/mL in controls and patients, respectively ($p < 0.001$) (Figure 1.) Median prolidase activities were found as 364.46 (177.75 - 559.11) and 394.48 (185.00 - 477.90) U/L in controls and patients, respectively ($p = 0.162$) (Figure 2). We also did not find any correlation between ChT concentrations and prolidase activity ($p = 0.368$, $r = -0.226$).

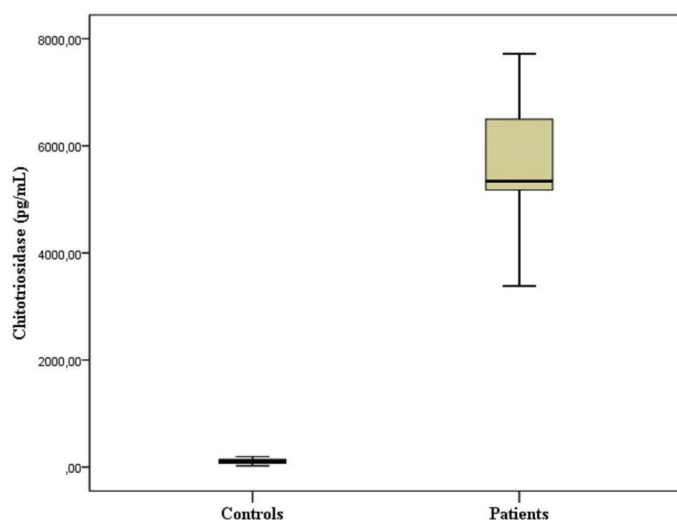


Figure 1. Box plots for chitotriosidase concentrations. The image of each group shows the box with median (horizontal line within the box); the interquartile range (IQR), corresponding to the 25th - 75th percentiles (lower and upper limit of the box); nearest observations within 1.5 IQRs (the whiskers) and outliers (circles within 3 IQR).

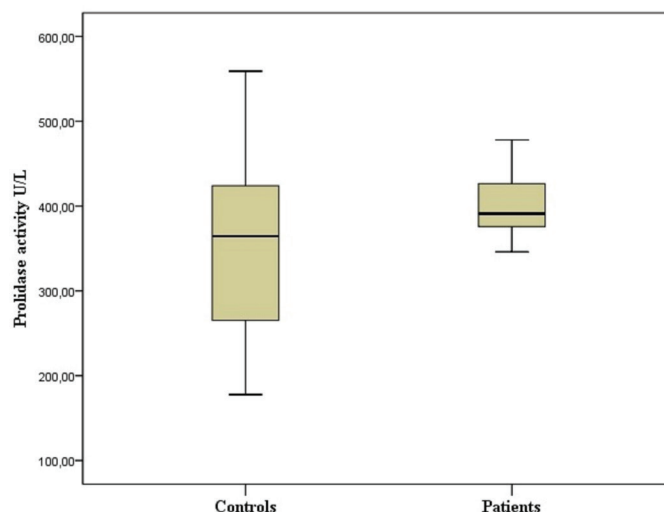


Figure 2. Box plots for prolidase activity. The image of each group shows the box with median (horizontal line within the box); the interquartile range (IQR), corresponding to the 25th - 75th percentiles (lower and upper limit of the box); nearest observations within 1.5 IQRs (the whiskers) and outliers (circles within 3 IQR).

Discussion

Recent in-vivo and in-vitro studies suggest that ChT is involved at multiple points in different inflammatory and infectious diseases [10,17-21] although the molecular mechanism of the ChT is far from being completely resolved in these conditions [10,22]. It was reported increased plasma ChT activity in neonates with fungal infection [10]. In a study made by Overdijk et al. [23] Increased levels of chitinases have been reported in experimental *Aspergillus fumigatus* infection. Neutrophils and monocytes/macrophages play pivotal role in the defense mechanism against fungi, including cutaneous mycoses [24]. ChT is produced, storage and secreted by macrophages and neutrophils [25]. In this study, ChT concentrations were found to be higher in patients than in the healthy control group. We speculate that the reason for increased ChT concentrations can be assumed to be associated with increased activation of neutrophils and macrophage due to tinea pedis and ChT has an important role in the host defense mechanism in response to tinea pedis like dermatophytosis.

Fungal cell wall glucans can increase the activation of different aspects of innate immunity [26]. Additionally, it has been found that glucans can directly modulate the functional activity of human dermal fibroblasts [27]. Prolidase activity has been shown in dermal fibroblasts [28]. The enzyme activity plays an important role in the recycling of proline mostly derived from degradation products of collagen [29]. Wei et al. [30] have been reported that glucan stimulates human dermal fibroblast collagen biosynthesis through a nuclear factor-1 dependent mechanism. In our study, we did not find any difference between patients and controls in terms of prolidase activity. We also did not find any correlation between ChT concentrations and prolidase activity. We believe that the reason for unchanged prolidase can be assumed to be associated with increased activation of glucan associated collagen formation instead of degradation.

Although this research was carefully prepared there were some limitations in the study. First, the study was conducted with the small size of patients. Therefore, to generalize the results for larger groups the study should have involved more participants. Second, we did not group dermatophytes according to their species and therefore we could not examine the effects of different dermatophytes on ChT concentrations.

Conclusion

ChT seems to have roles during the inflammatory conditions in patients with tinea pedis. We also speculate that host chitinase responses may have importance for both diagnostic assays and therapeutic approaches in patients with tinea pedis. However, ChT needs better characterization before becoming a reliable biomarker of tinea pedis evolution. We also believe that prolidase activity is not associated with the tinea pedis.

Ethics

Ethics Committee Approval: This study was approved by local ethical committee (E-17-02-07).

Informed Consent: All participants gave written and verbal informed consent.

Peer-review: Internal peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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