TISSUE ANGIOTENSIN-CONVERTING ENZYME IN PATIENTS WITH VARIOUS CLINICAL FORMS OF PSORIASIS

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Abstract

Tissue angiotensin-converting enzyme (ACE) was measured in 60 patients with psoriasis and in 20 healthy individuals. According to clinical forms of psoriasis, patients were further divided into three groups: psoriasis with solitary lesions (n=20), psoriasis with multiple disseminated lesions (n=20) and erythrodermic psoriasis (n=20). The tissue ACE activity was determined before and after therapy, by the spectrophotometric method using hippuryl-l-histidyl-l-leucine as a substrate. The enzyme activity is expressed in units: 1 U corresponds to 1 nmol of hippuric acid released by hydrolysis of hippuryl-l-histidyl-l-leucine per minute and 50 mg of the tissue. Before therapy, tissue ACE activity was significantly increased in patients with psoriasis (4,14±0,34; X±SEM) in comparison to healthy individuals (1,86±0,16). The greatest increase in tissue ACE activity was observed in patients with erythrodermic psoriasis (4,72±0,65), followed by those with multiple disseminated lesions (4,24±0,63) and solitary psoriatic lesions (3,47±0,48). After therapy, serum ACE activity was significantly decreased in all clinical forms of the disease. Determination of tissue ACE activity might be a good non-specific parameter for assessment therapeutic effects.

KEY WORDS: angiotensin converting enzyme, psoriasis, tissue, therapy.

Introduction

Angiotensin-I-converting enzyme (ACE, kininase II, EC 3.4.15.1) is a zinc metallopeptidase that catalyses the conversion of angiotensin I into the vasoactive and aldosterone-stimulating peptide angiotensin II. This enzyme is also involved in the inactivation of bradykinin, a potent vasodilator (1). ACE is a membrane bound enzyme in the endothelial cells and several types of epithelial and neuro epithelial cells. Thus, ACE appears to play a key role in the regulation of vascular tone and remodeling as well as in development of atherosclerotic lesions (2). Initially, the elevated plasma ACE level was found in patients with sacroidosis and several other granulomatous diseases-Gaucher's disease, leprosy, berylliosis (3). The association between sarcoidosis and psoriasis was reported about thirty years ago (4,5), which stimulated research on the role of ACE in psoriasis. Raff and co-workers (6) were the first to found an increase of serum ACE in patients with psoriasis, and this was confirmed in other studies (7,8,9,10). Furthermore, it was observed that serum ACE activity decreased after therapy (8,10). In our recent studies we also found the decrease of serum ACE activity after treatment of the disease, and we noticed there was no significant difference response between various forms of treatment (11, 12). Hara and co-workers (13) first found an increase of tissue ACE in theirs study with low number of patients with psoriasis. Recently, we have also found an increase of tissue ACE activity in alteration skin of patients with psoriasis and a decreased of tissue ACE activity after treatment of the disease (14). However, the tissue ACE activity in patients with various forms of psoriasis was not described. Thus, the aim of the present study was to investigate tissue ACE activity in patients with various forms of psoriasis and the possible influence of therapy on tissue ACE activity.

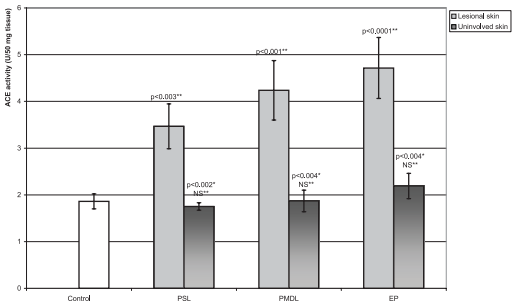
Materials and Methods

Patients with diseases that might influence serum ACE activity (sarcoidosis, arterial hypertension, pulmonary tuberculosis, hepatic disea ses, diabetes mellitus, and others) were excluded from the study. A study group included 60 patients with psoriasis of both sexes, aged 35-45 years, who were medically treated. The diagnosis of psoriasis was made on the basis of clinical examination and biopsy findings at the Department of Dermatology, University Hospital in Sarajevo. The patients with psoriasis received either local therapy (10% ol. candidi, 5%-10% salicyl-vaseline; n=30), photochemotherapy (8-methoxypsoralen as photosensibilizer in a dose of 0,6 mg/kg body weight; n=20) or cytostatic therapy (methotrexate 25 mg per week, total dose 100 mg; n=10). The patients were divided into three groups, according to clinical form of the disease: 20 patients with solitary lesions (10 men and 10 women), 20 patients with multiple disseminated lesions (10 men and 10 women) and 20 patients with erythrodermic psoriasis (10 men and 10 women). A control group consisted of subjects of both sexes (10 male and 10 female), aged 35-45 years, who were healthy according to their subjective and objective findings. Routine laboratory analyses, including erythrocyte and leukocyte counts, erythrocyte sedimentation rate, hematocrit, hemoglobin, urea, uric acid, creatinine, triglycerides, cholesterol, and glucose levels, as well as a complete urine analysis, were performed in each patient. A biopsy of skin was taken in all patients with psoriasis for a pathohystologic analysis. Tissue ACE activity was measured in patients with psoriasis before and after therapy. After biopsy all tissues skin samples were weighed and washed extensively with 0,9% NaCl solution (4°C) for blood elimination. The tissues were placed in the mixture of sodium phosphate buffer (0,065 mol/L, pH 8,3 and 0,5 mol/L NaCl; 50mg/ml) and stored at -20°C. The tissues were homogenized in a Teflon coated Potter-Elvehjem homogenizer, adding one drop of a nonionic surfactant (Nonidet P 40) in each samples. After centrifugation at 4000 g for 30 min, the supernates were frozen at -25°C until determination of ACE activity. Tissue ACE was determined by the spectrophotometric method using hippuryl-l-histidyl-l-leucine (Sigma, St. Louis , Mo. , USA) as a substrate (15), and a Perkin Elmer 550 S spectrophotometer for optical readings. The enzyme activity is expressed in units: 1 U corresponds to 1 nmol of hippuric acid released by hydrolysis of hippuryl-l-histidyl-l-leucine per minute and 50 mg of the tissue. Serum ACE activity is expressed as mean values ± SEM. Differences between the mean values were statistically compared using Student's and paired attest. Probability values of less than 0,05 were considered significant.

Results

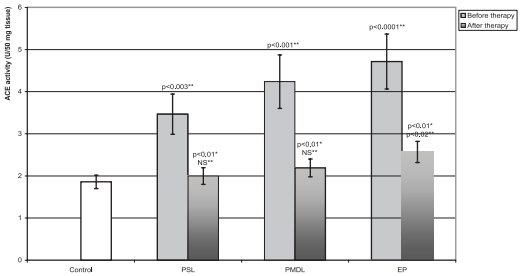
Figure 1 shows that tissue ACE activity was significantly increased in lesional skin of all clinical forms of psoriasis. The highest increase of the enzyme activity was found in the patients with erythrodermic psoriasis, i.e. by 153% higher than in the healthy subjects ($p<0,0001$). A similar increase was found in the patients with multiple disseminated psoriatic lesions (a 128% increase in comparison to the control group; $p<0,001$), and the least one (by about 86%) in the patients with solitary psoriatic

FIGURE 1. Tissue ACE activity (mean ± SEM) in patients with various clinical forms of psoriasis and healthy controls.



Control-group (healthy subjects; n=16);
PSL-psoriasis with solitary lesions (n=20);
PMDL-psoriasis with multiple disseminated lesions (n=20); EP-erythrodermic psoriasis (n=20);
NS - not significant. p – probability

FIGURE 2. Effect of treatment on tissue ACE activity (mean ±SEM) in patients with various clinical forms of psoriasis.



C ontrol group (healthy subjects; n=20);
PSL - psoriasis with solitary lesions (n=20);
PMDL-psoriasis with multiple disseminated lesions (n=20);
EP - erythrodermic psoriasis (n=20);
*Compared with the values before therapy;
**Compared with the control group (healthy subjects);
NS - not significant. p - probability

lesion (p<0,003). However, there were no significant differences in lesional skin tissue ACE activity among various clinical forms of psoriasis. Also, there were no significant differences in the tissue ACE activity between uninvolved skin of patients with different clinical forms of psoriasis and skin in healthy subjects.

As shown in Figure 2, tissue ACE activity decreased after therapy in all patients with psoriasis in comparison with the values recorded before therapy. The highest therapeutic decrease of the enzyme activity was observed in the patients with multiple disseminated lesions (48%; p<0,01), as compared with the decrease in erythrodermic psoriasis (46%; p<0,01) and solitary lesions (42%; p<0,01). After the treatment, there were no significant differences in tissue ACE activity among both subgroups of patients with solitary lesions and subgroups of multiple disseminated lesions and control groups of subjects, but the difference was only significant in the patients with erythrodermic psoriasis (p<0,02).

Discussion

Our study clearly showed that tissue ACE activity was significantly increased in lesional skin of all patients with different forms of psoriasis in comparison with value determined in skin of the control group. The highest increase of the enzyme activity was found in patients with erythrodermic psoriasis. Furthermore, a less increase was found in patients with multiple disseminated psoriatic lesions and the least one in patients with solitary psoriatic lesion. However, there were no significant differences in lesional skin tissue ACE activity among various clinical forms of psoriasis. Recently, we have also found that the serum ACE activity was increased in patients with psoriasis and there were no significant differences ACE activity in serum among various clinical forms of psoriasis (12). These observations indicate that the determination of the tissue ACE activity cannot be helpful for a differentiation of the clinical forms of psoriasis. Furthermore, we have not found the significant differences in the tissue ACE activity between uninvolved skin of patients with various clinical forms of psoriasis and skin in healthy subjects. Since tissue ACE activity was significantly increased only in lesional skin, it could be suggested that ACE may be involved in the development of psoriatic lesions. The mechanism responsible for the increase in tissue ACE activity in psoriasis is not clear. Consideration that physiology role of renin angiotensin system in skin has not sufficient explained, it is very difficulty to explain causes and mechanisms increase this enzyme in skin of patients with psoriasis on the basis our results. We believe that ACE, via proteolytic cleavage of peptide mediators and growth factors, represent important control factors for the inflammatory response in skin of patients with psoriasis. In the present study, we also investigated effects of therapy on tissue ACE activity in patients with psoriasis. Our results showed that the tissue ACE activity significantly decreased in patients with various clinical forms of pso-

riasis after therapy in comparison with values recorded before therapy. The highest therapeutic decrease of the enzyme activity was seen in the patients with multiple disseminated lesions (48%), followed in erythrodermic psoriasis (46%) and solitary lesions (42%). These findings suggest that therapy have similar effects on tissue ACE activity in all forms of psoriasis, implying that tissue ACE level might be one of the discriminators to assess the effects of therapy. In our recent studies we also found the decrease of serum ACE activity after treatment of the disease, and we noticed that there was no significant difference response of treatment between various forms of psoriasis (11, 12). Subtract the sample of blood is less invasive method in comparison with biopsy of the tissue and we believe that the serum ACE level might be better to used for monitoring effects of the therapy. However, the determination of the tissue ACE activity might be useful for monitoring effects of the therapy only in patients with psoriasis without increase of the serum ACE activity. Although the reason for higher values tissue ACE activity in skin of patients with erythrodermic psoriasis after therapy than in the healthy subjects is not clear, this finding appears to deserve father investigations.

Conclusion

These observations indicate that the determination of the tissue ACE activity cannot be helpful for a differentiation of the clinical forms of psoriasis, but might be a good non-specific parameter for assessment therapeutic effects.

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