

## Increased Concentrations of Plasma Endothelin-1 and Fibronectin in Psoriasis

Sir,

In the present study, plasma endothelin-1 (ET-1) and fibronectin concentrations were measured in psoriatic patients ( $n=24$ ) and matched controls ( $n=20$ ), since a possible relationship was thought to exist between the plasma ET-1 and fibronectin concentrations and the aetiopathogenic mechanism in psoriasis, in which an increased vascular capillary angiogenesis is seen. Fibronectin is an  $\alpha_2$  surface-binding opsonin protein that is mainly produced by endothelial cells. ET-1 is a very potent vasoconstrictor peptide, consisting of 21 amino acids, and is produced not only by endothelial cells but also by many other cell types. The patient group had higher plasma ET-1 and fibronectin concentrations than those of the controls. Alteration of receptors to fibronectin has been reported in psoriasis (1).

ET-1 is produced not only by vascular endothelial cells but also by a variety of other cell types, such as epithelial cells and keratinocytes (2). In the present study we aimed at investigating plasma concentrations of fibronectin and ET-1 in psoriatic patients and at comparing these parameters with those of the control group.

### MATERIALS AND METHODS

Twenty-four psoriatic patients (12 males, 12 females), who applied to our hospital, were included in the study. Their age ranged from 5 to 50 years, with an average of 32 years. Mean duration of disease was 7.5 years (1–15 years). Of 24 patients, 6 had very severe clinical signs and the other 18 patients had moderately severe clinical signs. None of them had diabetes mellitus, hypertension, or renal or lung disease, all these being conditions related to increased plasma ET-1 concentrations. None of the patients received any medication except local corticosteroid use. Control plasma samples were obtained from age-matched healthy subjects (14 males, 6 females, mean age 36 years, age range from 20 to 53 years).

In order to determine the plasma concentrations of ET-1 and fibronectin, blood samples were drawn from the subjects in the morning in supine position. Five ml of blood were collected into tubes containing 100  $\mu$ l EDTA/ml (EDTA 1 mg/ml) and 40 kallikrein inhibitor units/ml aprotinin (Trasylo<sup>®</sup>). Blood samples were then centrifuged at 4°C for 10 min at 2,000 g. Plasma samples were stored at -20°C until assayed.

Plasma ET-1 was measured by a radioimmunoassay method in acidified plasma samples after extraction with Amprep C2 columns (code RPN 1913, Amersham), which were preequilibrated with methanol and water. Endothelin was eluted with 5 ml of 0.1% trifluoroacetic acid in water and 80% acetonitrile in water plus 0.1% trifluoroacetic acid. The radioimmunoassay of plasma endothelin was performed using a commercially available kit (Endothelin 1-21 specific [<sup>125</sup>I] assay system, Amersham UK). Plasma fibronectin was determined by

an immunoturbidimetric method (Boehringer Mannheim, Cat. No. 401218, Germany).

Values are presented as mean  $\pm$  standard deviation. For statistical evaluation, Student's *t*-test and regression analysis were performed. A *p* value <0.05 was considered statistically significant.

### RESULTS

Mean plasma ET-1 concentrations were  $4.3 \pm 1.3$  (range: 2.3–7.1) pg/ml and  $3.3 \pm 1.4$  (range 1.4–5.6) pg/ml in the patient and control groups, respectively. There was a statistically significant difference between the groups ( $p < 0.05$ ). Mean plasma fibronectin concentrations were  $315.1 \pm 70.6$  (range: 214.1–424.5)  $\mu$ g/ml in the psoriatic patients and  $232.4 \pm 98.4$  (range: 131.8–436.6)  $\mu$ g/ml in the controls. Plasma fibronectin concentrations were significantly higher in the psoriatic patients than in the control group ( $p < 0.01$ ).

In correlation analysis, there was no statistically significant correlation between ET-1 and fibronectin values either in the patients or the controls ( $p < 0.05$  for both groups, Fig. 1). Age and sex had no influence on ET-1 and fibronectin either in the patients or the healthy subjects. Nor was there any correlation between the disease activity and plasma ET-1 and fibronectin values.

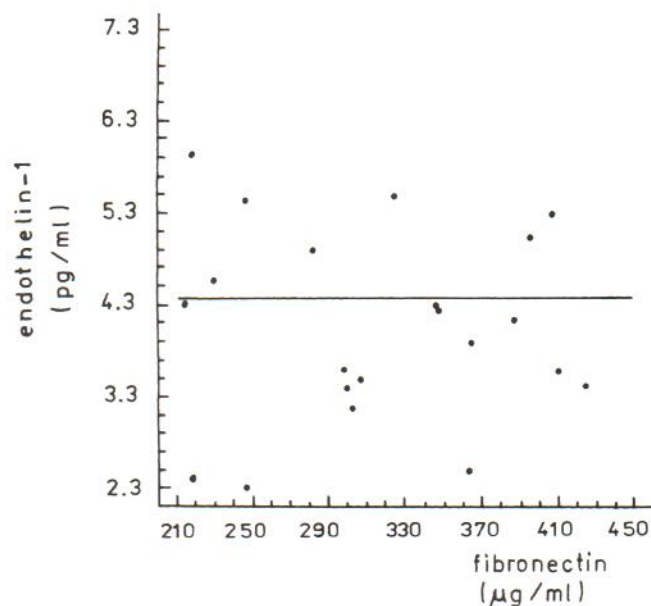


Fig. 1. Lack of correlation between ET-1 and fibronectin values.

## DISCUSSION

The adhesive machinery involving integrin receptors is altered in psoriatic keratinocytes (1). In addition, it has been reported that synthesis of fibronectin in psoriatic epidermis increased (3, 4). Our findings of higher plasma fibronectin concentrations than in the controls is consistent with the previous results (5–7). It could be explained by a high synthetic rate by the endothelial cells of microvessels, which are affected in psoriasis (8). However, it is not clear whether increased fibronectin is a consequence or one of the causes of the disease.

The increased plasma ET-1 concentration found in psoriatic patients was consistent with earlier findings (9, 10), but also our ET-1 levels were lower. This discrepancy may be due to the different kits used for ET-1 determination. The increased concentrations of both ET-1 and fibronectin were independent of the extent of the disease, which is also in agreement with previous reports (6, 7).

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