Total Plasma Kininogen in Psoriasis and Atopic Dermatitis

R. K. WINKELMANN

Department of Dermatology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota, USA


Total plasma kininogen was measured in 75 normal individuals and in patients with extensive dermatoses. Elevated levels were found in 20 of 30 hospitalized patients with atopic dermatitis. Elevated levels were observed in 33 psoriasis patients. Nine atopic patients responded to intravenous calcium gluconate with elevated levels during three hours of observation in contrast to no response to control injections or in control individuals. Extensive chronic inflammatory skin disease correlates with elevated total plasma kininogen. (Received November 27, 1983.)

R. K. Winkelmann, Department of Dermatology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55905, USA.

The kinin forming system is related to many other mediator systems and could reflect relationships to disease. Elevated total kininogen values were reported in patients with pruritus and Hodgkin’s disease (1). A patient with Hodgkin’s disease studied here by the same method showed an elevated value also. It seemed appropriate to study a large group of normal individuals and also a group of hospitalized psoriasis and atopic dermatitis patients. Extensive inflammatory skin disease appears to be related to increased total plasma kininogen values.

METHODS

The method of Diniz and Carvalho was used for total kininogen (2). The blood was drawn from normal individuals and patients in an a.m. fasting state into heparinized plastic syringes and placed in plastic tubes for centrifugation. The method uses trypsin to release bradykinin from total plasma kininogen. One unit of kininogen releases one unit of bradykinin (0.05 µg of synthetic bradykinin). The results of the bioassay are expressed as µg/ml equivalents of synthetic bradykinin activity. No distinction is possible in this assay between high molecular and low molecular weight bradykininogen. Blood was drawn from patients on their first morning before systemic therapy was begun.

RESULTS

Plasma kininogen values on 75 normal individuals ranged from 0.8 µg/ml to 15 µg/ml of bradykinin. The mean and standard deviation is 4.09±1.9 µg/ml. A comparison of the 60 females with the 15 males revealed a slight difference (4.6±2 µg/ml = females, 2.9±1.4 µg/ml: male), Fig. 1. Separation by age group of the females revealed no differences (0–30 (31 females): 4.4±2.8 µg/ml, 30–50 (29 females): 4.6±1.9 µg/ml). Repeat weekly examinations in 17 females revealed one of the values elevated above the mean in all but 3. These changes did not correlate with the menstrual cycle. Only two of seven males had such elevated values in one of the two samples.

Plasma kininogen values of 30 hospitalized patients with atopic dermatitis gave a range from 0.8 to 40 µg/ml of bradykinin. The mean value was 14.3±13 µg/ml. Ten of the atopic patients had plasma kininogen values within normal range, Fig. 2. No sex difference in atopic patients were noted. One patient was studied weekly during hospitalization and the value of plasma kininogen fell from 12 to 0.4 µg/ml in 8 days of active local treatment and bedrest.
Thirty-three patients with psoriasis who were hospitalized for Goeckerman therapy studied for plasma kininogen values showed a mean value of total plasma kininogen of the psoriasis patients was elevated at $16.7 \pm 11 \mu g/ml$. This level may be compared to normal, atopic and other dermatoses values in Fig. 3. Eight patients with severe generalized contact dermatitis for which they were hospitalized had mean plasma kininogen values of $12.9 \pm 7 \mu g/ml$. Five patients hospitalized for leg ulcers were found to have essentially normal values ($5.4 \pm 2 \mu g/ml$).

One case each of pityriasis rubra pilaris, scleroderma, and erythema multiforme gave elevated values of 8 $\mu g/ml$ of plasma kininogen expressed as bradykinin equivalents. One case of polycythemia vera, one case of mycosis fungoides, and one case of Hodgkin’s disease gave values of 4, 8, and 16 $\mu g/ml$ respectively. Three cases of pruritus including

---

**Fig. 1.** Normal plasma kininogen.

**Fig. 2.** Plasma bradykininogen values in atopic dermatitis.

**Fig. 3.** Mean plasma kininogen values.
one case of pruritus with lymphoma gave values of 4, 8, and 2.4 µg/ml. The two cases of
lichen planus studied gave high values of 24 and 40 µg/ml.

The response of the higher atopic plasma kininogen values to intravenous calcium
 gluconate was an initial slight or no depression followed by a marked rise in nine atopic
 patients followed at 30 min and hourly for 3 h. No change in the elevated plasma kininogen
 occurred in atopic patients treated with intravenous saline as controls or in 5 normal
 individuals given either intravenous saline or calcium gluconate.

**DISCUSSION**

Kininogen is synthesized in the liver and is found in the blood in high and low molecular
 weight forms. Total plasma kininogen is increased in pregnancy (3) and has been found by
 Zeitlin et al. (4) to be increased to twice normal values in rheumatoid arthritis.

This subject suggests that inflammatory skin disease may show consistently increased
 values of circulating total kininogen. Grebennikov (5) found that resistant cases of dissemi­
 nated neurodermatitis had repeated high values of plasma kininogen. This author noted an
 increase in kininogen with a flare of dermatitis. The patients reported here did not all have
 elevated values though all were hospitalized for atopic dermatitis. The increase of the
 plasma levels with intravenous calcium gluconate may reflect the type of response that
 could be noted with a flare of the dermatitis. It is particularly interesting that one atopic
 patient had progressively lower values during symptomatic control of the disease. Total or
 fractional kininogen values may correlate with response to therapy and help predict the
 chronic, relapsing difficult cases.

The patients with psoriasis had elevated total plasma kininogen values. Wolf et al. (6)
 studied eleven psoriasis patients and found that all patients had elevated values of plasma
 prekallikrein, although in only half was the plasma kallikrein also elevated. It is possible
 that in some patients all components of the kinin pathway are altered or elevated.
 Salicylates have been demonstrated to lower total plasma kininogen (4) and perhaps those
 occasional psoriasis or atopic dermatitis patients helped by salicylates may follow this
 mechanism rather than the inhibition of the better recognized prostaglandin pathways.

It should be noted that many generalized inflammatory dermatoses showed elevated
 levels of circulating total plasma kininogen. It is probable that this level is a response to
 chronic mediator release and cutaneous inflammation similar to the elevation of plasma
 fibrinogen, also synthesized in the liver, which occurs with chronic coagulation. While it
 does not seem to be related to pruritus, specifically, it does seem to be related to chronic
 extensive skin disease. Total or fractional plasma kininogen values may provide a means
 to monitor responses of extensive dermatologic disease to therapy.

**REFERENCES**

2. Diniz CR, Carvalho IF. A micromethod for determination of bradykininogen under several
    conditions. Am NY Acad Sci 1963; 104: 77-84.
3. Wiegertahausen B, Hennighausen G, Paegelow L, Klausch B. Kininogen content of plasma in
    man and animal during gestation in bradykinin and related peptides. In: Sienteri F, Roche e Silva M &
4. Zeitlin IG, Skarma JN, Brooks PM, Dick WC. Raised plasma kininogen levels in rheumatoid
    1975: 335-43.
5. Grebennikov VA. Investigation of blood bradykininogen in patients with disseminated neuroder­
    Biomedicine 35: 77-8.