

## Changes in plasma kininogen levels associated with rheumatoid activity

P.M. BROOKS, W.C. DICK, J.N. SHARMA  
& I.J. ZEITLIN\*

*University Department of Medicine, Royal Infirmary, Glasgow, The Centre for Rheumatic Diseases and Department of Physiology & Pharmacology, University of Strathclyde, Glasgow*

During a control study it was noticed that some elderly volunteers with untreated rheumatoid inflammation had abnormally raised plasma kininogen levels (Zeitlin, I.J., unpublished observations). This observation has been examined in greater detail.

Seven patients with seropositive rheumatoid arthritis, controlled with indomethacin therapy, participated in the trial. Indomethacin was stopped for 48 h, no other therapy being administered during this time. Cubital vein blood was taken for estimation of plasma levels of kininogen, proteins and indomethacin, and haematocrit. The patients then took oral indomethacin (50 mg, t.d.s.) for 1 week and the measurements were repeated. Plasma kininogen was activated using trypsin and the kinin formed was assayed using the isolated oestrous rat uterus (Brocklehurst & Zeitlin, 1967). Indomethacin was measured in plasma by the method of Emori, Champion, Bluestone & Paulus (1973). Plasma kininogen levels were also measured in a control group of five non-inflamed fracture patients, and in five healthy subjects, before and after ingesting indomethacin (50 mg q.d.s., 2 days).

The mean plasma kininogen concentration

measured in the untreated rheumatoid patients,  $12.9 \pm 1.2 \mu\text{g}$  bradykinin equivalents (Bk Eq)/ml of plasma, was more than three times the mean value measured in fracture patients ( $4.9 \pm 1.2 \mu\text{g}$  Bk Eq/ml plasma) with  $P < 0.01$  (Mann-Whitney U test) and more than twice the mean control value found in the five healthy subjects ( $5.0 \mu\text{g}$  Bk Eq/ml).

Following indomethacin administration to the rheumatoid patients, the plasma level rose to a mean value of  $2.3 \pm 0.6 \mu\text{g/ml}$ . The mean plasma kininogen concentration fell to  $7.2 \pm 1.0 \mu\text{g}$  Bk Eq/ml just over half the untreated level ( $P < 0.01$ ). There was no change ( $P > 0.05$ ) in haematocrit, or in the plasma concentrations of total protein, albumin or globulin. No change was detected in plasma kininogen concentrations in the three healthy volunteers following indomethacin administration.

The raised level of plasma kininogen in untreated rheumatoid arthritis patients is not easily explained. It may possibly reflect augmented synthesis compensating for a chronically increased rate of kinin-formation.

We are grateful to Sandoz Ltd for a generous gift of synthetic bradykinin.

### References

- BROCKLEHURST, W.E. & ZEITLIN, I.J. (1967). Determination of plasma kinin and kininogen levels in man. *J. Physiol. (Lond.)*, 191, 417-426.
- EMORI, H.W., CHAMPION, G.D., BLUESTONE, R. & PAULUS, H.E. (1973). Simultaneous pharmacokinetics of indomethacin in serum and synovial fluid. *Ann. Rheum. Dis.*, 32, 433-435.