SHORT COMMUNICATION

Renal kallikrein content of spontaneously hypertensive rats

S. FAVARO, B. BAGGIO, A. ANTONELLO, A. ZEN, G. CANNELLA, S. TODESCO AND A. BORSATTI
Istituto Patologia Medica dell'Universita di Padova, Padova, Italia

(Received 28 January 1975)

Summary

1. The kallikrein content of kidneys from spontaneously hypertensive and normal rats at birth and at age 37 days was determined.
2. Kallikrein values were significantly lower in the hypertensive rats.
3. It is suggested that the lowered kallikrein may be related to the development of hypertension.

Key words: blood pressure, bradykinin, kallikrein, sodium, spontaneously hypertensive rats.

Introduction

Since kallikrein seems to be in some way related to sodium excretion (Adetuyibi & Mills, 1972; Marin & Grez, Cottone & Carretero, 1972), we have assayed the kidney kallikrein content in SH rats of the strain developed by Dr G. Bianchi in Milan (Bianchi, Fox & Imbasciati, 1974).

Material and methods

Spontaneously hypertensive and normotensive rats were selectively bred from a single Wistar strain by Dr G. Bianchi in Milan (Bianchi, Fox & Imbasciati, 1974). Four groups of six rats were examined: newborn SH, newborn normotensive, SH(1) rats at 37 days (mean systolic blood pressure 153±3 mmHg ± 1.05 SEM) and normotensive rats at 37 days (mean systolic blood pressure 125±8 mmHg ±1.5). The rats were killed with a blow on the neck and the kidneys were removed, decapsulated, washed in NaCl solution (154 mmol/l) and stored at −20°C. The kidneys were then cut in small pieces with a razor blade, washed three times with sucrose (250 mmol/l) and disrupted in a Waring Blender operating at medium speed. The homogenate was centrifuged at 3000 rev./min for 10 min in a Sorvall centrifuge, the precipitate was discarded and the supernatant liquid was analysed. Protein was determined by the method of Lowry, Rosebrough, Farr & Randall (1951) with bovine serum albumin used as a standard. Kallikrein was assayed by its esterolytic activity at alkaline pH (8.5) on the substrate benzoyl-L-arginine ethyl ester.

(1) Abbreviations: SH, spontaneously hypertensive; BAEE, benzoyl-L-arginine ethyl ester.
(BAEE) according to the enzymatic ethanol assay described by Trauthschold (1970) with Padutin (Bayer) as a standard; results were expressed in units/mg of protein.

Kidney protein and kallikrein values for each rat were taken to be the mean of triplicate estimations on each. The significance of the difference between the mean values of kidney protein and kallikrein in normotensive and SH rats was assessed by Student’s t-test. Except where stated, results are expressed as mean values ± SEM.

Results
The mean kidney protein content at birth was 29.1 ± 1.6 mg in normotensive rats and 30.4 ± 2.3 in newborn SH rats. The difference between the two groups was not statistically significant (t = 0.46; P > 0.05). The mean kidney protein content of rats at 37 days of age was 45.1 ± 3.1 mg in normotensive and 38.5 ± 5.1 in SH rats. Again, the difference between the two groups was not statistically significant (t = 1.10; P > 0.05).

The mean kidney kallikrein concentration at birth was 495 ± 21 munits/mg of protein in normotensive rats and 325 ± 27 in SH rats. The difference between the two groups was statistically significant (t = 4.98; P < 0.005). Kidney kallikrein concentration at 37 days of age was 353 ± 14 munits/mg of protein in normotensive and 287 ± 11 in SH rats. Again, the difference between the two groups was statistically significant (t = 4.84; P < 0.005). Mean values for kallikrein concentration of each animal are shown in Fig. 1.

Discussion
The technique employed here does not directly assay the kallikrein present in renal tissue. However, since kininogenetic activity in urine and kidney homogenate and BAEE esterase activity at alkaline pH (8.5) cannot be distinguished (Nustad, 1970; Nustad & Rubin, 1970), BAEE esterase activity can be taken to reflect tissue kallikrein concentration.

Our data show that the kidneys of our strain of SH rats contain significantly less kallikrein than those of controls. It is possible that other strains of SH rats behave in a different way since Margolius, Geller, De Jong, Pisano & Sjoerdsma (1972) have demonstrated an enhanced urinary kallikrein excretion in SH rats of the Japanese strain. However, a hypertensive role for the kidney in Japanese SH rats has not yet been reported.

The decreased tissue kallikrein concentration observed in SH rats cannot be produced by high blood pressure since it is present in newborn animals before the development of hypertension.

Kallikrein exerts a potent natriuretic action through its end product bradykinin (Webster & Gilmore, 1964; Barraclough & Mills, 1965; Willis, Ludens, Hook & Williamson, 1969). Moreover bradykinin releases prostaglandin-like substances from the kidney (MacGiff, Terragno, Malik & Lonigro, 1972), and recently it has been suggested that the intrarenal release of kinins could be a physiological mediator of prostaglandin secretion (Miller, MacGiff & Nasjletti, 1973). Thus it is possible that anomalies in sodium handling observed in kidneys of SH rats might be related to a lowered renal kallikrein concentration.

Acknowledgment
We thank Dr G. Bianchi for kindly supplying us with the kidneys of his SH rats.

References
Renal kallikrein in hypertensive rats


