Effects of Sodium, Potassium, ACTH and Nephrectomy on Adrenal Renin

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In 1967 Ryan first reported a renin-like enzyme in rabbit adrenal glands. Since then, other investigators have observed adrenal renin in cattle, dogs, rats, and humans. In 1974 Ganten et al. showed that adrenal renin increased after sodium and potassium depletion. Naruse and Inagami recently reported the presence of renin in the adrenal glands of SHR and Wistar-Kyoto rats. The concentration of renin was higher in SHR and increased markedly post-nephrectomy. This adrenal renin was inactivated by specific kidney renin antibodies. Despite these observations, the physiological role of adrenal renin still unclear.

To clarify the physiological role, we compared renin concentrations in the rat adrenal glomerulosa and adrenal fasciculata-medullary portions during alterations in sodium and potassium balance and after nephrectomy.

We also studied the effect of ACTH on adrenal renin using hypophysectomized rats, and correlated adrenal renin with aldosterone concentration in all experiments.

Sprague-Dawley female rats weighing 180–210g were used. The rats were decapitated and the adrenals flushed with normal saline through the aorta. The adrenals were then removed and the capsules separated from the fasciculata-medullary portions. The separated portions were 0.1 M Tris acetate buffer pH 7.4 at 4°C, and centrifuged for 30 minutes at 1800 x g 4°C. The supernatant was aspirated and renin activity was measured at pH 7.4 in Tris acetate buffer using naphysectomized rat plasma as substrate. Aldosterone in the supernatant was measured by radioimmunoassay. The protein concentration was measured method. Three different sodium diets were used: a high sodium diet prepared by adding 1% sodium chloride to the drinking water; a sodium-free diet (low sodium); and a normal sodium diet consisting of regular Purina rat. All the diets were given for five days. Potassium loaded rats received 0.3 M KCl + 0.015 M NaCl in 5% glucose in the drinking water. Control rats received 5% glucose in the drinking water. Nephrectomy was performed under pentobarbital anesthesia (30 mg/kg) 20 hours before decapitation. Hypophysectomized rats were used for experiments four days after operation and maintained by 5% glucose water. ACTH (H.P. Acthar Gel: 10 U/day) was subcutaneously injected into the hypophysectomized rats, starting two days before nephrectomy. The molecular weight of adrenal renin was estimated by Sephacryl-S-200 column (Pharmacia), using bovine serum albumin, ovalbumin, chymotrypsinogen A, and ribonuclease A as the molecular weight standards (Pharmacia). The results of the experiments are expressed as the mean ± the standard error. Statistical analysis was performed by the Student’s t-test. Significance was defined as a P value of less than 0.05.

The molecular weight of adrenal renin was approximately 40,000. This enzyme generated angiotensin I from natural renin substrate at pH 7.4 indicating that it was not cathepsin D. Changes in the sodium diet induced changes in the adrenal glomerulosa renin concentration (high Na: 2.21 ± 0.34, normal Na: 4.34 ± 0.53, low Na: 13.19 ± 1.67 ngAl/mg-protein/hr) but had no effect on the concentration of renin in the fasciculata-medullary portion (high Na: 1.25 ± 0.12, normal Na: 1.19 ± 0.11, low Na 1.25 ± 0.12 ngAl/mg-protein/hr). Adrenal glomerulosa aldosterone concentration also varied with the sodium diet (high Na: 15.57 ± 2.52, normal Na: 26.00 ± 3.29, low Na: 40.95 ± 4.34 ng/mg-protein). The high potassium diet
increased adrenal glomerulosa renin concentration from 5.27 ± 0.33 to 39.78 ± 5.68 ngAI/mg-protein/hr. The increase of adrenal renin in the high potassium diet was much larger than the increase in the low sodium diet.

The high potassium diet did not change the concentration of renin in the fasciculata-medullary portion.

Adrenal aldosterone increased from 26.78 ± 1.78 in the normal diet to 54.56 ± 5.12 ng/mg-protein in the high potassium diet whereas plasma renin concentration decreased from 7.28 ± 0.63 in the normal diet to 5.05 ± 0.60 in the high potassium diet. These data suggested a possibility that potassium stimulated the production of aldosterone via adrenal renin. Bilateral nephrectomy had a profound effect on the renin concentration of the adrenal glomerulosa portion, which increased from 4.34 ± 1.49 before nephrectomy to 71.5 ± 10.6 ngAI/mg-protein/hr 20 hours post-nephrectomy. However, nephrectomy did not affect the fasciculata-medullary renin.

Adrenal glomerulosa aldosterone concentration in the nephrectomized rats was significantly increased from 26.0 ± 3.28 to 71.9 ± 5.51 ng/mg-protein. Plasma renin concentration was undetectable at 20 hours after nephrectomy. These results suggested that the adrenal renin worked independently of the kidney renin and stimulated the aldosterone production after nephrectomy.

The adrenal renin concentration in hypophysectomized rats (6.95 ± 1.06 ngAI/mg-protein/hr) was the same level as that in normal rats (5.27 ± 1.83 ngAI/mg-protein/hr). However, the addition of ACTH (20 unit/2 day) to hypophysectomized rats increased the adrenal renin concentration to 40.54 ± 6.78 ngAI/mg-protein/hr. We also studied the effect of ACTH on the response of adrenal renin post-nephrectomy. Hypophysectomy prior to nephrectomy blunted the adrenal renin response to nephrectomy (hypophysectomy + nephrectomy: 10.37 ± 1.16 ngAI/mg-protein/hr) and giving an ACTH supplement to hypophysectomized rats re-increased the adrenal renin response (hypophysectomy + ACTH + nephrectomy: 120.26 ± 20.62 ngAI/mg-protein/hr). ACTH may therefore be necessary for the adrenal renin response after nephrectomy.

Finally, we correlated the adrenal renin and aldosterone in all experiments and found a positive correlation (r = 0.07, p < 0.001) between adrenal renin and aldosterone.

In summary, we have confirmed the presence of adrenal renin and have shown that the preferential localization of adrenal renin is the zona glomerulosa.

The renin concentration of the glomerulosa portion was influenced by changes in sodium and potassium balance and by nephrectomy, in contrast to the renin concentration the fasciculata-medullary portion. Adrenal renin is concerned with the regulation of blood volume and blood potassium and may act locally to help regulate aldosterone production.

REFERENCES

7. NARUSE M, INAGAMI T: Marked elevated specific renin levels in the adrenal in genetically hypertensive rats. Proceeding of the National Academy of Science, USA 79: 3295, 1982