Accelerated hypertension in the rat: relation between renin, renal vascular lesions, salt intake and blood pressure

SAWALUCK CHUSILP, A. S. P. HUA AND PRISCILLA KINCAID-SMITH
Department of Nephrology and University Department of Medicine,
The Royal Melbourne Hospital, Victoria, Australia

Summary
1. Complete ligation of the aorta between the origins of the two renal arteries in the rat produces a predictable form of accelerated hypertension. Changes in the blood pressure, plasma renin activity and renal histological lesions have been studied.

2. Group 1 rats and their control group (group 2) received tap water, and group 3 and its control group (group 4) received sodium chloride solution (0.154 mol/l) in place of tap water, for 4 weeks before aortic ligation. In the experimental groups 1 and 3, complete ligation was carried out. In groups 2 and 4 the aorta and renal arteries were exposed, but not ligated. Interlobular artery lesions were studied on a blind basis and graded 0-4 according to severity.

3. Groups 1 and 3 developed severe hypertension. In group 1 the raised mean arterial pressure showed a significant correlation with increased plasma renin activity. Both mean arterial pressure and plasma renin activity also showed a significant correlation with changes in interlobular arteries. In group 3 the raised mean arterial blood pressure did not show a significant correlation with the depressed plasma renin activity, or with changes in interlobular arteries. A significant correlation was, however, found between plasma renin activity and interlobular artery lesions in group 3.

4. These results suggest that the renin–angiotensin system may influence renal vascular lesions through some mechanism independent of the blood pressure.

Key words: malignant hypertension, renal hypertension, renin.

Introduction
Plasma renin activity has been implicated as a potential risk factor in hypertension in man (Laragh, Baker, Brunner, Bühler, Sealey & Vaughan, 1972). Although the severity of hypertension has traditionally been linked with the height of the blood pressure, patients with marked elevation of blood pressure may have surprisingly few changes in morphology (Kincaid-Smith, 1975). This study was designed to examine the relationship between plasma renin activity, the level of blood pressure and morphology of vascular lesions during the development of severe hypertension in the rat. Salt loading was used to depress renin concentrations.

Methods
Sprague-Dawley rats weighing 200–300 g were fed on standard rat cubes. Two groups of rats (group 1, n = 34; group 2, n = 11) received tap water ad libitum. Two groups (group 3, n = 20 and group 4, n = 10) received NaCl solution (0.154 mol/l) ad libitum in place of tap water, commencing 4 weeks before the start of the experiment and maintained throughout the experimental period. In groups 1 and 3 hypertension was induced by complete aortic ligation between the origins of the two renal arteries. The control groups 2 and 4 were subjected to sham operations in which aorta and renal arteries were exposed but not ligated.

The method of Rojo-Ortega & Genest (1968) was used for aortic ligation. After tying the ligature the colour of the right kidney was noted to ensure that the blood supply to the right kidney was intact.

Blood pressure measurements were made by direct cannulation of the left carotid artery under...
light ether anaesthesia via a plastic catheter (SV 35, Dural Plastics), transducer and recorder. Light ether anaesthesia was maintained during the blood pressure recording.

Blood for plasma renin activity was drawn by retro-orbital puncture under light ether anaesthesia. Anticoagulant (0.05 ml), pH 7.4, was used for 0.5 ml of blood. Estimation of plasma renin activity was determined by the rate of angiotensin I production as estimated by radioimmunoassay (Johnston, Mendelsohn & Casley, 1969). Plasma renin activity, which was determined at the same time as blood pressure measurement, was used in the evaluation of results.

The rats were killed from 2 to 41 days after aortic ligation. Kidney tissue was stained with Haematoxylin and Eosin and by the periodic acid-Schiff methods. Interlobular arteries in the right kidney were graded on a blind basis 0–4 according to the severity of the lesions.

Results
In groups 1 and 3 mean arterial blood pressure, plasma renin activity and vascular lesions were all significantly different from those in respective control groups 2 and 4 (P < 0.01). The relations between the blood pressure, plasma renin activity and vascular lesions were analysed by linear regression analysis. Groups 1 and 3 developed severe hypertension. In group 1 the mean arterial pressure (144.4 mmHg, SD 30.5, n = 34) correlated with increases in plasma renin activity (15.53 ng h⁻¹ ml⁻¹, SD 9.0, n = 34) (r = 0.743, P < 0.01). Mean arterial pressure showed a significant correlation with the grade of lesions in interlobular arteries (r = 0.845, P < 0.01). Plasma renin activity also showed a significant correlation with changes in interlobular arteries (r = 0.666, P < 0.01). In group 3 the mean arterial blood pressure (154.58 mmHg, SD 25.5, n = 20) did not correlate with mean plasma renin activity (7.87 ng h⁻¹ ml⁻¹, SD 5.0, n = 20) (r = -0.016, P > 0.1). No correlation could be established between the mean arterial pressure and the changes in interlobular arteries (r = -0.295, P > 0.1). A positive and significant correlation was, however, found between plasma renin activity and interlobular artery lesions in this group (r = 0.741, P < 0.01) (Fig. 1).

Discussion
It has been suggested that the renin–angiotensin system may be responsible for the elevation of blood pressure in renovascular hypertension (Peart, 1965).

Plasma renin activity was elevated in association with marked 'hypertensive' vascular lesions in both groups studied, but the elevation of plasma renin was less marked in rats receiving saline. There was no significant correlation between the blood pressure and the vascular lesions in rats which received saline.

The increase in vascular permeability attributed to renin (Cuthbert, Asscher & Jones, 1966) may be important in the evolution of vascular lesions through permitting penetration of plasma protein and fibrinogen into the arterial wall, resulting in deposition of hyaline and fibrinoid material. These were prominent in this study.

There are many factors which may bring about the vascular lesions associated with high renin levels. Infusion of angiotensin leads to irregular constriction and dilatation in blood vessels (Kincaid-Smith, Hobbs, Friedman & Mathews, 1972). These are associated with evidence of endothelial damage and thrombosis (Kincaid-Smith et al., 1972). Similar changes develop in the blood vessels of the
rat when the aorta is ligated by the method used in this study (Hobbs, Chusilp, Hua, Kincaid-Smith & McIver, 1976).

The significance of our observations in rats in relation to the observations of Laragh et al. (1972) must remain speculative, but the present work does suggest that the influence of renin on vascular lesions may, under certain circumstances, be independent of the blood pressure.

Acknowledgment

Angiotensin antibody and radioactively labelled angiotensin used in the assay were kindly provided by Professor C. I. Johnston, who also made his laboratory facilities available for validation estimations of plasma renin activity in the early stages of this study.

References


