BLOOD RENIN LEVEL IN TERMINAL BRIGHT'S DISEASE TREATED BY HAEMODIALYSIS AND BY RENAL ALLOTRANSPLANTATION

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Arterial hypertension being a common feature of terminal Bright's disease, it was found necessary to assess the role of renin in this type of hypertension, with the hope of defining more clearly the indications for bilateral nephrectomy in the treatment of malignant hypertension in chronic renal insufficiency. As acute hypovolaemia constitutes one of the best stimuli of renin secretion (Brown et al., 1966), the blood renin level was determined in chronic uraemic patients during massive bleeding. In patients bearing a kidney allograft, blood renin levels were determined during acute and chronic graft rejection episodes, as well as after salt deprivation.

MATERIAL AND METHODS

Renin concentration was determined in 514 blood samples collected from 59 patients, 13 to 60 years old, with chronic glomerulonephritis (36 cases), chronic pyelonephritis (13 cases), nephroangiosclerosis (1 case), lupus nephritis (1 case), periarteritis nodosa (1 case) or undetermined renal disease (7 cases). Endogenous creatinine clearance amounted to less than 4 ml/min. in all patients, who were all treated by bi-weekly haemodialysis. Twenty-four of the 59 patients were submitted to 32 renal allotransplantations, from related donors in 5 cases and from cadavers in 27. In 18 patients, the diseased kidneys were removed prior to transplantation; in 2 cases, nephrectomy and transplantation were done on the same day; in 4 patients, nephrectomy followed transplantation.

Plasma renin determinations were performed, with minor modifications, by the method of Brown et al. (1964). In healthy individuals, this method yields values ranging from 4 to 22 U/l (9.4 ± S.D. 5.8), which are close to those of Brown: 2 to 18 U/l (8.2 ± S.D. 2.7).

RESULTS

1. Patients treated by haemodialysis

1. Blood renin level versus type of nephropathy

Mean blood renin levels amounted to 24.4 ± S.D. 22.2 U/l in 31 cases of chronic glomerulonephritis, and 15.3 ± S.D. 12.7 U/l in 12 cases of pyelonephritis. Difference between the two means is not significant, but renin concentration was higher than the upper normal value in 10 out of 31 cases of glomerulonephritis, and in only 1 out of 12 patients with pyelonephritis. The highest value recorded in the whole group of 59 cases was observed in periarteritis nodosa: 221 U/l.

2. Blood renin level versus blood pressure

In Figure 1, 266 blood renin determinations performed in 50 patients are plotted with simultaneously recorded systolic blood pressure readings. The data show plasma renin
concentration to be significantly related to systolic blood pressure ($r = 0.270; P < 0.001$). A similar correlation is observed with diastolic blood pressure ($r = 0.204; P < 0.001$).

The 52 patients suitable for study can be divided into two groups: (1) 20 cases with malignant hypertension and retinal changes rated from III to IV, (2) 32 cases with normal blood pressure or benign hypertension and retinal changes ranging from 0 to II. In the group of severely hypertensive patients, renin was significantly increased in 8 cases, but it was inferior or equal to 22 U/l in 12 cases. In the group of 32 moderately hypertensive patients, renin was normal in 26 cases and increased in 6 cases.

3. **Blood renin level versus natraemia**

Sodium concentration was determined in every plasma sample submitted to renin assay. In Figure 2, renin values are plotted with sodium concentrations: a significant negative correlation ($r = -0.382; P < 0.001$) appears between plasma renin and sodium concentrations, as previously observed by Brown *et al.* (1965).

4. **Blood renin level during haemorrhage**

In 4 patients, plasma renin concentration was measured a few hours to 5 days after massive bleeding (Fig. 3). In 3 cases, during protracted terminal gastrointestinal haemorrhage, renin level amounted to 52, 71 and 128 U/l. In 2 cases, these high figures were isolated but in the third patient, 30 days after bleeding, plasma renin concentration dropped to 19 U/l. In the fourth case, where monthly measurements of plasma renin level ranged from 6 to 25 U/l during 11 months, acute bleeding due to ventricular injury during pericardiotomy was followed 5 days later by a rise of renin to 97 U/l; renin concentration was normal 31 days later.

It should be stressed that in 2 of the 4 cases, high plasma renin concentration was accompanied by marked hyponatraemia: 115 and 124 mEq/l.
**Fig. 2.** Correlation between plasma renin and sodium concentrations in 49 cases of terminal Bright's disease (264 determinations).

5. **Effect of haemodialysis on blood renin level**

On 17 occasions, renin concentration was determined in plasma samples obtained before and after haemodialysis. Mean values were 20.8 U/l before, and 20.8 U/l after dialysis.

**Fig. 3.** Plasma renin after severe bleeding in 4 chronic uraemic patients undergoing intermittent haemodialysis. H: haemorrhage. P:\textsubscript{Na}: plasma sodium concentration in high renin plasma samples. CGN: chronic glomerulonephritis. Day 0 is the day of first dialysis.
6. Effect of bilateral nephrectomy on blood renin level

Renin concentration was determined in 94 plasma samples of 14 anephric patients. In 35 samples, renin could not be detected, but in 59 samples, renin concentration ranged from 3 to 14 U/l.

If the first 15 postoperative days are excluded, bilateral nephrectomy was followed by a significant fall in blood pressure in only 4 out of 12 patients; 3 of these 4 patients showed high plasma renin levels preoperatively (52, 57 and 112 U/l), while renin concentration was normal in the remaining 9 cases (Verniory et al., 1968).

II. PATIENTS BEARING AN ALLOGRAFT

In 17 patients bearing a renal allograft as sole kidney tissue, 78 plasma renin determinations were obtained 1 to 920 days after transplantation. These data cover 21 distinct grafts.

1. Blood renin level versus creatinine clearance

In Figure 4, plasma renin concentrations are plotted with simultaneous creatinine clearance measurements of the 21 transplants. Plasma renin rises significantly as function of the graft decreases. When creatinine clearance is higher than or equal to 50 ml/min., 22 out of 28 renin determinations are normal, while 28 out of 50 renin levels are higher than 22 U/l for clearance values inferior to 50 ml/min.

\[ r = 0.331 \]
\[ 0.001 < P < 0.01 \]

![Graph](image)

Fig. 4. Correlation between plasma renin level and creatinine clearance in 17 patients with an allograft as sole renal tissue (78 determinations, 21 grafts). Dotted horizontal line represents upper limit of normal plasma renin concentration.

2. Blood renin level versus blood pressure

No significant correlation was observed between plasma renin levels and blood pressure readings (systolic and diastolic). This observation, which contrasts with the significance obtained in patients treated by haemodialysis, may be due to the small number of observations in grafted patients. It should be stressed that, in 1 patient, a sharp rise of renin (100 U/l) occurred during a severe bout of hypertension in an early rejection episode (patient MOE, Fig. 6).
3. Blood renin level versus natraemia

As in the case of blood pressure, no significance was observed in the correlation between plasma renin and sodium concentrations; this may also be explained by the limited data. In 2 patients, however, high plasma renin levels (91 and 111 U/l) followed unsuspected sodium deprivation 18 and 139 days postoperatively, demonstrating the ability of the graft, as the normal kidney (Brown et al., 1965), to increase renin secretion in low salt syndrome (Fig. 5).

4. Blood renin level during graft rejection

Serial plasma renin determinations were obtained in 8 patients during unequivocal early acute rejection episodes (Fig. 6). In 3 cases, renin concentration rose steadily until removal of the graft, while in 3 cases, a transient rise was followed by a sharp fall before transplant removal (2 cases) or after reversion of rejection (1 case). In the remaining 2 patients, no rise in renin level was observed.

In 5 patients undergoing slow chronic rejection of their graft, with rising blood pressure and falling creatinine clearance, 169 to 638 days postoperatively, steady rise in plasma renin concentration was observed in 2 cases, while renin fell in 1 patient, and remained normal in the other 2 cases.

CONCLUSIONS

In the terminal stage of chronic renal failure, blood renin level was elevated in 33% of cases in glomerulonephritis, and in 8% in pyelonephritis. Renin concentrations were significantly related to blood pressure readings, suggesting that renin plays some role in the pathogenesis of hypertension. When high blood renin level and malignant hypertension coexist, bilateral
nephrectomy usually brings blood pressure to normal. Nevertheless, high plasma renin concentration is noted in 19% of cases of Bright’s disease with benign hypertension or with normal blood pressure.

The significant negative correlation observed between plasma renin and sodium concentrations would suggest either that renin induces water retention through an ADH-like activity, or that primary hyponatraemia enhances renin secretion. As water excretion by such diseased kidneys would not respond to hormonal stimuli, the last interpretation is more plausible.

The elevated plasma renin concentrations which follow haemorrhagic hypovolaemia demonstrate the ability of severely damaged kidneys to increase their renin output.

In patients bearing an allograft as sole renal tissue, blood renin level is significantly correlated with function of the transplant: renin concentration is usually normal when clearance is high, and commonly elevated when clearance is poor. Sodium deprivation induced a sharp rise in plasma renin level in transplanted patients. During acute graft rejection, blood renin usually rises but its further evolution is quite variable. Plasma renin level is less consistently modified during slow chronic rejection of the graft.
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REFERENCES


