Plasma Renin Activity (PRA) and Plasma Aldosterone (PA) in Hypertensive Kidney Allograft Recipients

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Summary

Basal and stimulated plasma renin activity (PRA) and plasma aldosterone (PA) were measured in 13 hypertensive and 16 normotensive patients with kidney allografts one to nine years after transplantation. In both groups no significant differences were observed between mean basal and stimulated PRA and PA values. Therefore, we conclude that abnormal renin secretion might not be the main factor causing hypertension in renal allograft recipients. Other mechanisms seem to be involved in the pathogenesis of hypertension in these patients.

Introduction

A considerable number of renal allograft recipients suffer from some degree of hypertension in the late post-transplant period. The pathogenesis of hypertension in these patients is unclear. Corticosteroid therapy, the presence of the recipients own kidneys, renal artery stenosis, intrarenal vascular or parenchymal disease, and inadequate sodium intake have been proposed as possible mechanisms. The data in the literature about the role of renin and aldosterone, the former being related to vasoconstriction, the latter to extracellular volume expansion, are contradictory. (Nielsen et al, 1970; Roguska et al, 1971, Cooke et al, 1973; Sampson et al, 1973; Beckerhoff et al, 1974; Bennett et al, 1974; Chrysant et al, 1974; McDonald et al, 1974).

PATIENTS

The study concerns 16 normotensive and 13 hypertensive patients; 28 of 29 patients had been bilaterally nephrectomised; all had an unrestricted dietary
intake of sodium; kidney function revealed serum creatinine levels lower than 1.9 mg/100 ml (m ± SD : 1.22 ± 0.27 mg/100 ml in normotensive patients; 1.25 ± 0.22 mg/100 ml in hypertensive patients); immunosuppressive therapy included 10 mg of prednisone and 100 - 200 mg azathioprine per day. In the hypertensive patients diuretic and antihypertensive drugs were withdrawn for one week before the study. Serum potassium was more than 3.8 mEq/L in all but one patient, in whom it was 3.3 mEq/L. One of 13 hypertensive patients had systolic blood pressure values between 160 and 180 and diastolic values between 120 and 140 mmHg without antihypertensive therapy. Twelve patients had a systolic pressure below 170 and a diastolic pressure between 95 and 115 mmHg. However, in every patient hypertension was absent under appropriate antihypertensive therapy. All patients were studied while visiting the outpatient clinic; they arrived at 8am. Blood samples for PRA and PA measurements were drawn from the cubital vein after one hour of recumbency (basal values) and one hour later after continuous walking (stimulated values).

METHODS

PRA was determined by radioimmunoassay for angiotensin I (Haber et al, 1969). The normal basal range of our laboratory after one hour recumbency and under normal sodium intake (120 - 150 mEq/day) is 0.3 - 3.0 ng/ml.3hr, the normal stimulated range after one hour upright position 3 - 10 ng/ml.3hr. PA was measured by radioimmunoassay as described by Vetter et al (1973). The normal basal range is 20 - 120 pg/ml, the normal stimulated range 100 - 300 pg/ml.

RESULTS

Twelve out of 26 patients, who had been hypertensive before nephrectomy and transplantation, remained hypertensive after transplantation, 14 became normotensive. From three patients, who had been normotensive prior to transplantation, two remained normotensive and one became moderately hypertensive after transplantation.

Figure 1 shows supine PRA and urinary sodium excretion for normotensive and hypertensive subjects. One normotensive and one hypertensive patient had a sodium excretion of less than 100 mEq/day. When the PRA values obtained in this study were related to urinary sodium excretion, three normotensive patients had high and eight had normal PRA values. In the hypertensive group three patients had high, one low, and six normal PRA values (one of the latter group was studied twice).

Figure 2 shows basal and stimulated PRA in both normotensive and hypertensive patients. In normotensive patients PRA did not increase in response to
Figure 1. Plasma renin activity in renal transplant recipients.

Figure 2. Plasma renin activity in renal transplant recipients.
upright posture in five patients. When sodium excretion was measured in some of them, the lack of stimulation could not be related to high urinary sodium. The PRA values in the hypertensive group cover a broad spectrum: four patients had low basal PRA, which could not be stimulated by the upright position, three of them showed high urinary sodium excretion, one patient had low PRA, which could be stimulated, five patients had high basal PRA, also when studied repeatedly. All but one of them showed an increase in PRA. Three hypertensive patients had normal PRA, which could not be stimulated in two of them. Basal and stimulated mean PRA values were not significantly different in patients with and without hypertension.

A renal artery murmur could be heard in two normotensive and five hypertensive patients. Two of the latter had low, one had normal, and two had high PRA.

In normotensive patients, basal PA (Figure 3) was normal in all but two patients, who had relatively high values, when related to actual sodium excretion (236 and 309 mEq/day respectively). One of the two high PA-patients had high,
one normal PRA. In the hypertensive group only one patient had an abnormally high basal PA. In six normotensive and three hypertensive patients PA did not increase after upright posture. The mean basal and stimulated PA was not significantly different between normotensive and hypertensive patients.

Figure 4 shows the lack of correlation between PRA and PA in normotensive and in hypertensive subjects. There were several hypertensive subjects with low PRA and normal PA and several with high PRA and normal PA.

COMMENT

In this study no significant differences of PRA were observed between normotensive and hypertensive renal transplant recipients. Thus an increased secretion of renin might not be the main factor causing hypertension in these patients. The same conclusion can be drawn for adrenal aldosterone release. Two of our hypertensive patients with elevated PRA and renal artery murmurs might suffer from renal artery stenosis. No angiography has been performed in them until now, because hypertension is mild and easily controlled with antihypertensive drugs. Some patients with low PRA showed high sodium excretion. We suppose therefore, that extracellular volume expansion might be related to their hypertension, although measurements of plasma volume have not been performed.

Our results concerning the stimulation of PRA during the late post-transplant period can not be interpreted conclusively as being due to variable urinary sodium excretion.

A lack of correlation between basal PRA and PA has also been observed by Sampson et al (1973). It is consistent with the view that renin is not the only factor regulating aldosterone biosynthesis. The same frequency of post transplant hypertension and normotension in patients with high blood pressure before transplantation indicates that arterial pressure before kidney transplantation is not necessarily related to hypertension afterwards.
There was no correlation between post-transplant hypertension and kidney disease before kidney grafting.

Some authors (Popovtzer et al, 1973; Sampson et al, 1973) have suggested that the immunosuppressive therapy with glucocorticoids may play an important role in the development of hypertension. It is very unlikely that prednisone therapy is the main cause of hypertension in our patients, because all of them, normotensives and hypertensives, received the same low dose of 10 mg prednisone per day.

References

Sampson, D, Kirdani, R Y, Sandberg, A A and Murphy, G P (1973) *British Journal of Surgery*, 60, 819

Open Discussion

DUFRESNE (Montreal) Is patency of the A-V fistula a factor in blood pressure control after transplantation? One of our patients became hypertensive after closure of his forearm fistula.

DUTZ (Berlin) In 150 consecutive cadaveric kidney transplants we found a significant correlation between HLA matching and post-transplant hypertension between one and five years after transplantation. The borderline between high and low incidence of hypertension was at a net histocompatibility ratio (NHT) of 0.36.