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Short-term course of renal function in accelerated hypertension

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Summary

Thirty-four patients with primary accelerated hypertension were studied regarding the effect of BP on renal function and the association between fundal grade and renal function before treatment; and the changes in renal function on normalization of BP in 12 patients. Mean arterial pressure was negatively correlated with serum creatinine ($r = -0.44$, $P < 0.02$) and there was no significant difference in serum creatinine or in the occurrence of renal failure between patients with grade III (n = 21) and grade IV (n = 13) retinopathy, (P = n.s. and $X^2 = 0.172$ P = n.s. respectively). Twenty-two patients required dialysis at presentation. Serum creatinine rose in 12 other patients on reduction of BP; 7 patients with serum creatinine level ≤ 3.2 mg/dL (283 umol/L) at presentation never required dialysis in the 3 months following reduction of BP while those with levels ≥ 3.6 mg/dL (319 umol/L) did. In accelerated hypertension, renal function is partly maintained by the blood pressure and dialysis may be required soon after presentation or normalization of BP.

Résumé

Trente-quatre malades ayant l'hypertension accélérée ont été étudiés afin de voir l'eflet de la pression sauguine sut le fonctionnement du renale et la relation entre la grade fundale et le fonctionnement due rénale dans la normalisation de la pression sanguine. Le moyen de la pression arteriale a été correlée avec la serum créatinine ($r = -0.44$, $P < 0.02$) et il s'y trouvait aucune différence significative soit à la sérum créatinine soit à l'occurence de la cessation du fonctionnement du rénale entre les malades ayant grade III (n = 21) et grade IV (n = 13) retinopathie (P = n.s. et $X^2 = 0.172$, P = n.s. respectivement). La sérum créatinine a monté chez les malades (n = 12) du a la réduction de la pression sanguine. Sept malades avec un niveau de sérum créatinine ≤ 3.2 mg/dL (283 umol/L) sur présentation n'ont plus besoin de dialyse trois mois suivant une réduction de la pression sanguine tandis que ceuse qui ont les niveaux ≥ 3.6 mg/dL (319 umol/L) en avaient besoin. Quand à l'hypertension accélérée, le fonctionnement du rénale est soutenu eu partie par la pression sanguine et la dialyse deviendra obligatoire en cequi concerne les malades ayant les débuts de la sérum créatinine ≥ 3.66 mg/dL (319 umol/L) auisitôt après da normalisaton de la pression sanguine.

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Introduction

Primary accelerated hypertension differs prognostically from primary benign hypertension principally on account of the severity of the resulting renal dysfunction [1]. Renal function in primary accelerated hypertension can be variable and is correlated with the degree of narrowing of the interlobular arteries [2]. Being commoner and more severe in Blacks than Whites [3], accelerated hypertension may actually run a different course in Blacks, and presumably, affect renal function differently.

In the face of renal arteriolar narrowing resulting from the mucoid intimal proliferation which is characteristic of accelerated hypertension [1,2] the perfusion of the kidney may be maintained by the abnormally elevated blood pressure (BP). Hypertension, especially when severe has however also been associated clearly with increased morbidity from heart failure [4] and cerebrovascular accidents [5]. Achievement of BP control is therefore necessary, but it is likely to be complicated by a reduction in renal perfusion and worsening of renal function [6].

Conceivably, there is a level to which the BP may be safely lowered to preserve renal function in the short term, or a degree of renal function at which reduction of BP is not attended by a precipitous worsening of renal function. The first option is impracticable. We have therefore attempted to describe the course of renal function in accelerated hypertension, its relationship with

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the BP, and also define the setting in which a marked worsening of function may occur following reduction of the BP.

Patients and methods

Patient selection

Accelerated hypertension was defined as hypertension with bilateral retinal haemorrhages and exudates (grade III retinopathy), with (grade IV retinopathy) or without papilloedema [7,8]. The following were considered in determining that the hypertension was primary and not secondary to renal disease, clinical examination and basic screening tests having excluded other probable causes of secondary hypertension: family history of hypertension, identified period of benign hypertension, short duration of identified renal dysfunction, kidney bipolar diameter < 10 cm on ultrasound or intravenous urography, preserved corticomedullary differentiation on ultrasound. Thirty-four patients were entered into the study.

Assessment of renal function

Renal function at presentation was assessed by serum creatinine level. It was not practicable to measure glomerular filtration rate in many of the patients as they were anuric at presentation.

Management of the hypertension

The aim of treatment was to reduce the diastolic blood pressure (DBP) to 95–90 mmHg over a week unless acute pulmonary oedema or hypertensive encephalopathy was complicating, when immediate reduction of BP was undertaken with parenteral drugs. Commonly used oral drugs were frusemide, methyldopa, propranolol hydrallazine and occasionally, captopril, nifedipine, minoxidil, in varying doses. Parenteral anti-hypertensives were usually hydrallazine or methyldopa. Some patients required dialysis according to the usual criteria, and it was additive to anti-hypertensive treatment.

Effect of reduction on BP on renal function

At normalization of BP, serum creatinine was again measured and this was repeated after 3 months of maintaining normal BP. The values for those patients who required dialysis were not used for this particular analysis.

Analysis and statistics

Mean arterial pressure (MAP) was calculated as DBP + ⅓ (systolic blood pressure (SBP) – DBP).

Data was presented as mean ± standard error (SE) and absolute values. Linear regression analysis was carried out using Pearson product-moment correlation. Comparisons between groups were made by the Mann-Whitney U-test and Yates' chi-square test as appropriate.

Significance was achieved at $P < 0.05$.

Results

The MAP and serum creatinine stratified according to grade of retinopathy are summarised in Tables 1 and 2. Mean MAP did not differ significantly between patients with grade III and grade IV retinopathy (P = n.s.), and neither did mean serum creatinine (P = n.s. Mann-Whitney U-test).

There was no difference in the frequency of occurrence of renal failure defined as serum creatinine > 3 mg/dL (266 umol/L) between patients with grade III and grade IV retinopathy ($\chi^2 = 0.172$, P = n.s.).

MAP was correlated negatively with serum creatinine at presentation ($r = -0.44$, $P < 0.02$). This suggested that renal function was generally better in those with higher pressures (Fig. 1).

Table 1: Mean arterial pressure (MAP) and serum creatinine stratified according to retinal grade

	Mean ± S.E.
M.A.P. (mmHg)	171 ± 3
Grade III (n = 21)	169 ± 3
Grade IV (n = 13)	175 ± 3
Serum Creatinine (mg/dL) (n = 34)	13.4 ± 1.9
(umol/L)	1186 ± 168
Grade III (n = 21)	14.8 ± 2.8 (1310 ± 248)
Grade IV (n = 13)	11.3 ± 2.7 (1310 ± 239)

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Table 2: Frequency of renal failure in patients with grades III and IV retinopathy

	No. of patients
Serum creatinine <3 mg/dL (<266 umol/L)	
Grade III	5
Grade IV	3
Serum creatinine >3 mg/dL (>266 umol/L)	
Grade III	15
Grade IV	11

$X^2 = 0.172$, P = n.s.

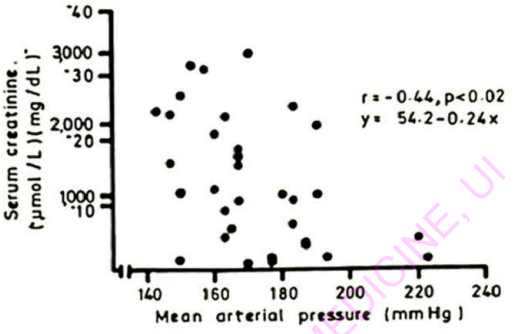

Fig. 1: Relationship between mean arterial pressure and serum creatinine.

Table 3: Changes in serum creatinine of 12 patients

Serum Creatinine	Patient											
(mg/dL)	4	6	7	8	9	10	15	21	25	26	29	34
At presentation	1.6	1	6.7	1.3	1.6	3.2	1.2	0.8	6.1	4.4	3.6	4.9
At normalization of BP	6.7	5.8	10.1	6.1	5.9	6.7	2.9	3.4	12.3	8.1	9.9	12.1
At 3 months	4.9	5	—	3.5	4.8	6.1	2.7	2.8				

To convert to umol/L, multiply by 88.5

Twenty-two patients required dialysis at presentation. The 12 other patients were managed conservatively initially. Their serum creatinine levels at normalization of BP and after 3 months are shown in Table 3. Serum creatinine rose in all 12 patients on normalization of BP such that 5 more patients required dialysis. Of the 7 other patients, serum creatinine dropped over the rest of the 3 month period such that dialysis was never required during the period. Patients with serum creatinine level of 3.2 mg/dL (283 umol/L) or less at presentation, never required dialysis while those with levels of 3.6 mg/dL (319 umol/L) or more, required dialysis during the 3 months.

It was possible to manage 7 of the 27 patients who had received dialysis by conservative measures at the end of 3 months, but 12 others remained dialysis dependent. The remaining 8 patients died during the period. Patients who died had generally been underdialysed due to lack of resources, and differed from the others principally on account of the amount of dialysis received.

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Discussion

The fair degree of negative correlation between MAP and the serum creatinine translates to a positive correlation between MAP and renal function. This suggests that the renal function in untreated accelerated hypertension is partly maintained by the high blood pressure, a point that had not been emphasised in previous works, though its corollary had: reduction of BP may lead to worsening of renal function, at least in the short term in some patients [6,7,9].

We have not found the grade of retinopathy to be of any predictive value regarding the severity of the blood pressure or renal dysfunction at presentation. This in passing, perhaps restates the current trend of regarding patients with grade III and grade IV retinopathy as belonging to the same entity with similar characteristics and prognosis. [7]

Though elevated BP may maintain renal function in accelerated hypertension, the situation is clearly an abnormal one that exists at heavy cost. Thus the hypertension leads to a progressive damage of renal vasculature [10,11] and inevitable renal failure over a variable length of time [6]. Therefore, to reduce overall morbidity and mortality the blood pressure should be controlled.

Twenty-two of our patients required dialysis at presentation implying perhaps that severe destruction of the kidneys had occurred. Five more required immediate dialysis on normalization of the BP; the immediate need for dialysis in these patients having been caused by a reduction of renal perfusion. The implication of these events is that some patients with accelerated hypertension would require dialysis as part of their management very early in the disease. The need for dialysis was based on the usual criteria, one of which was serum creatinine level above 8 mg/dL (708 umol/L). As has been shown, patients who had better renal function at presentation with serum creatinine 3.2 mg/dL (283 umol/L) or less did not require dialysis immediately following the normalization of BP, but there were only 7 of such patients. Perhaps these patients would not require dialysis until the natural progression of the kidney disease brings about its need. Even of those patients who required dialysis at presentation, subsequent adequate control of blood pressure may preserve renal function [12].

Our experience contrasts with that of Gudbrandsson [7] in Sweden, who in over 5 years from 1975, did not see any patient with malignant essential hypertension presenting with severely impaired renal function. The most likely explanation for this disparity is early detection and management of benign essential hypertension in Sweden and indeed in many parts of the more developed world.

We cannot comment now on the long term prognosis of the patients including those who were dialysed at presentation, nor tell what the situation might have been had more gradual reduction of BP been undertaken. The study continues and follows up patients who were dialysed at a point, to determine long-term renal function. Isles and co-workers [13] reported a potential for recovery in malignant hypertension that may last many years. In their series, initial serum creatinine under 300 umol/L was associated with a better prognosis. It is also of note that in a 3 year study of Nigerians with hypertension complicated by renal insufficiency, Ojogwu and Anah [14] reported a better prognosis in patients with initial serum urea under 13.3 umol/L. In this latter study however, it was not stated whether the patients had accelerated or benign hypertension, except in one of 63 patients.

Our study may suffer from relatively small numbers and diagnostic criteria not based on kidney histology, though with careful considerations patients with essential and renal causes of hypertension can often be differentiated on clinical and laboratory findings. We had selected patients without underlying renal disease in order to avoid the confounding effects of the natural progression of the renal disease.

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