Captopril in hypertension after renal transplantation

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Summary

Eight hypertensive renal allograft recipients who had received captopril are presented. Captopril in a maximal daily dose of 250 mg enabled the withdrawal of large doses of beta-blocking agents and vasodilators. Blood pressure was satisfactorily controlled in all except one. No adverse side effects were observed other than the 'first dose' effect which resulted in transient anuria in one patient. Captopril appears to be a useful agent in the management of severe hypertension after renal transplantation.

KEY WORDS: anuria, thrombocytopenia.

Introduction

Hypertension is common after renal transplantation and frequently resistant to conventional antihypertensive therapy including the combination of a beta-blocker, a vasodilator and a diuretic. We report here our experience in the use of captopril, an angiotensin-converting-enzyme inhibitor active by the oral route (Vidt, Bravo and Fouad, 1982), in eight renal allograft recipients for up to 15 months.

Patients and methods

All eight patients had hypertension which could not be adequately controlled by the standard triple therapy, i.e. the combination of a beta-blocker, a vasodilator and a diuretic. A variety of beta-blockers were often tried in the same patient. The vasodilator commonly used was hydralazine. The maximal daily dose of captopril never exceeded 250 mg, and was given in two to three divided doses. The diuretic used was frusemide. In three patients, hydralazine had to

be replaced by minoxidil after maximal doses of the former proved ineffective. In these patients, the blood pressure was reasonably well controlled but hirsutism became intolerable and the patients were switched to captopril. None of the patients had bilateral nephrectomy either before or after renal transplantation. An initial test dose of 25 mg was given in all but one patient who received 6.25 mg. The initial dose effect (i.e. decrease in blood pressure within 2 hr) was apparent in all patients, but in only one of them was hypotension so severe that it resulted in transient anuria. The dose of captopril was adjusted according to the control of blood pressure and was increased weekly or monthly intervals to a maximal dose of 250 mg daily. All patients were maintained on diuretic therapy before and throughout the period of treatment with captopril. The patients were seen weekly and later monthly. Blood pressure was measured by mercury sphygmomanometer. At every visit, blood was taken for haematological tests, liver function and renal function tests and proteinuria was determined in 24 hr urine samples. The clinical and laboratory data of the patients are summarized in Table 1 and Fig. 1.

Results

Good blood pressure control was achieved in all except one patient, D.C., who had severe arterial stenosis of the transplant kidney which had failed to respond to transluminal balloon-catheter dilatation. The patient also had relentless vascular rejection and the allograft had to be removed 3 months after starting captopril. Patient M.K. had accelerated hypertension when she presented with renal failure. Her blood pressure was controlled with captopril while she was on continuous ambulatory peritoneal dialysis. She again became hypertensive shortly after

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TABLE 1. Clinical data of patients who received captopril after renal transplantation

Patient	Sex/Age (yrs)	Time captopril introduced post-transplant (months)	Antihypertensive drugs immediately before captopril	Daily dose of immunosuppressives	Follow-up (months)	Final antihypertensive regime
M.B.	M/19	18	Oxprenolol, 640 mg Minoxidil, 20 mg Frusemide 80 mg	P, 12.5 mg A, 50 mg	15	Captopril, 150 mg (2.5 mg/kg) Oxprenolol, 160 mg Frusemide, 80 mg
D.R.	M/9	5	Oxprenolol, 320 mg Minoxidil, 10 mg Frusemide, 40 mg	P, 9 mg A, 50 mg	15	Captopril, 50 mg (1.5 mg/kg) Frusemide, 40 mg
N.H.	M/20	40	Oxprenolol, 280 mg Frusemide, 160 mg Minoxidil, 40 mg Spironolactone, 100 mg Methyldopa, 2 g	P, 8 mg A, 50 mg	15	Captopril, 150 mg (3 mg/kg) Oxprenolol, 160 mg Frusemide, 80 mg
P.T.	M/15	12	Oxprenolol, 320 mg Frusemide, 160 mg Minoxidil, 15 mg	P, 15 mg A, 150 mg	12	Captopril, 50 mg (0.8 mg/kg) Frusemide, 80 mg
C.E.	F/14	2	Propranolol, 160 mg Frusemide, 80 mg Hydralazine, 150 mg	P, 35 mg A, 75 mg C, 25 mg	3	Captopril, 18 mg (0.5 mg/kg) Frusemide, 80 mg
D.C.	F/50	9	Propranolol, 320 mg Frusemide, 80 mg Hydralazine, 200 mg Nifedipine, 30 mg Methyldopa, 1 g	P, 14 mg A, 100 mg	2	Captopril, 100 mg (1.9 mg/kg) Frusemide, 160 mg
M.K.	F/48	1	Atenolol, 100 mg Frusemide, 40 mg Hydralazine, 100 mg	P, 30 mg A, 150 mg	6	Captopril, 100 mg (1.7 mg/kg) Frusemide, 240 mg
G.T.	F/52	13	Nadalol, 320 mg Bumetanide, 2 mg Hydralazine, 200 mg	P, 30 mg A, 75-100 mg	15	Captopril, 100 mg (1.6 mg/kg) Nadalol, 160 mg Bumetanide, 8 mg

P = prednisolone; A = azathioprine; C = cyclophosphamide

FIG. 1. Change in clinical and biochemical parameters after captopril treatment in renal allograft recipients. The closed circles represent the mean values and the vertical bars the s.e.m. In parenthesis are the numbers of patients receiving captopril.

renal transplantation and captopril was re-introduced after a short trial of beta-blockers and hydralazine. Patient G.T. who had chronic vascular rejection and whose blood pressure initially proved resistant to captopril had transient episodes of mild thrombocytopenia (platelet count $70 \times 10^9/\text{litre}$) which reverted to normal when the dose of azathioprine was reduced. Her platelet count 15 months after commencement of captopril was $135 \times 10^9/\text{litre}$. Captopril was reduced from a maximal dose of 250 mg to 100 mg daily. Haematological indices, liver function tests and plasma urate did not show any consistent trend.

Mean 24 hr urinary protein excretion was 0.86 g when captopril was started, but fell to 0.08 g after 12 weeks of treatment. No proteinuria was detected after either 12 or 15 months of captopril.

Discussion

Early reports of leucopenia/agranulocytosis in patients treated with captopril must have caused great anxiety and concern over the use of this drug in hypertensive renal allograft recipients. Only 16

patients who were treated with captopril because of hypertension after renal transplantation have been reported (Elijovich and Krakoff, 1980; Aurell, Delin and Herlitz, 1980; Kirchertz *et al.*, 1981; Hamilton *et al.*, 1981). One patient who received 450 mg of captopril daily had granulocytopenia (Elijovich and Krakoff, 1980). The fact that no leucopenic episodes were experienced although all our patients received azathioprine and captopril concurrently must be related to the small dose of captopril used. The average dose was 89 mg daily, whereas the doses used in patients who developed severe leucopenia and agranulocytosis often exceeded 200 mg daily (Vidt *et al.*, 1982). No proteinuria occurred *de novo* in our patients. Indeed as the blood pressure came under control and renal function improved, proteinuria frequently subsided. No clinical or biochemical evidence of hepatotoxicity due to captopril was detected in our study.

We conclude that captopril is extremely useful in the treatment of severe hypertension after renal transplantation. Recognizing the potential additive effects of azathioprine and captopril (Kirchertz *et al.*, 1981), we have not ventured beyond a maximal daily dose of 250 mg. Since the first dose effect can be very dramatic as was evident in one patient who had transient hypotension and anuria, patients are best admitted into hospital for observation at the commencement of captopril therapy. Captopril is mainly excreted in the kidney (Vidt *et al.*, 1982) and the dose must be appropriately adjusted according to the renal function. With more experience, it may even prove the drug of choice since many hypertensive renal allograft recipients have high plasma renin activities.

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