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Long-term follow-up of ACE-inhibitor versus β-blocker treatment and their effects on blood pressure and kidney function in renal transplant recipients

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Abstract Hypertension and nephrotoxicity are frequent complications of cyclosporine-induced immunosuppression in renal transplant recipients. Long-term antihypertensive treatment is obligatory for hypertensive transplant patients, to protect allograft function. The use of angiotensin-converting enzyme (ACE) inhibitors in the anti-hypertensive treatment of renal transplant recipients who receive immunosuppression with cyclosporine has long been discussed controversially. The aim of this prospective study, with a duration of 2 years and a follow-up of another 3 years, was to estimate the long-term antihypertensive potential of quinapril compared with that of the β-blocker atenolol and to compare their effects on renal allograft function and proteinuria in 96 hypertensive renal transplant recipients who received cyclosporine A as immunosuppressive therapy. Patients were randomly assigned to receive either quinapril (group Q) or atenolol (group A) as anti-hypertensive treatment. Forty patients of each group completed the 5-year observation period according to protocol. Intention-to-treat and according-to-protocol analyses were performed. With the patients starting at similar baseline blood pressure values, both agents, atenolol and quinapril, decreased systolic and diastolic blood pressure (SBP, DBP) as well as middle arterial pressure (MAP) and pulse pressure (PP) to a similar extent (ΔSBP: group Q: -8 ± 3 vs group A mmHg: -5 ± 3; ΔDBP: -5 ± 2 vs -4 ± 2 mmHg; ΔMAP: -6 ± 2 vs -5 ± 2 mmHg; ΔPP: -2 ± 2 vs -1 ± 3 mmHg; mean ± SEM). Neither serum creatinine levels nor Cockcroft–Gault clearance had changed significantly in either group after the 5-year period (Δcreatinine: 0.1 ± 0.1 vs 0.2 ± 0.2 mg/dl; ΔCockcroft–Gault clearance: 3.9 ± 4.6 vs 2.8 ± 4.3 ml/min; mean ± SEM). Urinary protein excretion remained stable among the quinapril-treated patients, whereas a significant increase was observed in the atenolol group during the 5-year study period (group Q: from 0.52 ± 0.08 to 0.54 ± 0.14 g/24 h; group A: from 0.34 ± 0.03 to 0.72 ± 0.13 g/24 h, $P < 0.02$; mean ± SEM). Albuminuria increased comparably in both groups, while the excretion of α-microglobuline increased slightly in the atenolol group, but decreased slightly in the quinapril group. The difference between the groups failed to be statistically significant (ANOVA, $P < 0.056$). In conclusion, quinapril and atenolol may be considered suitable and safe substances in the long-term treatment of hypertensive renal transplant

recipients, since both agents prove to be effective in anti-hypertensive treatment, and keep allograft function stable over a period of 5 years.

Keywords ACE inhibitors · β-Blockers · Renal transplantation · Allograft function · Hypertension · Proteinuria

Introduction

Hypertension after renal transplantation (RTx) affects more than 50% of allograft recipients [23] and even occurs in 80% of patients treated with cyclosporine A (CYA), as shown in a 5-year follow-up study [21]. Since graft survival is impaired in patients with uncontrolled hypertension [21, 27], effective antihypertensive therapy is required for renal allograft recipients.

The use of angiotensin-converting enzyme (ACE) inhibitors in the anti-hypertensive treatment of kidney transplant recipients is still a point of discussion, since they are known to have dual effects on renal function depending on the setting in which they are administered. In contrast to their renoprotective effects in renal hypertension and diabetic nephropathy, ACE inhibitors may lead to compromised renal function via their intrarenal hemodynamic effects if reduced renal perfusion is present or if used in combination with the renal vasoconstrictor CYA [5, 8]. Meanwhile, many studies have examined the effects of ACE inhibitors on proteinuria and kidney function in renal transplant recipients [16] and have compared ACE inhibitors with other anti-hypertensive substance groups such as β-blockers [10], calcium antagonists [19], and angiotensin-II receptor antagonists [25]. ACE inhibitors may particularly improve long-term graft outcome by decreasing glomerular capillary hydrostatic pressure, leading to a reduction of hyperfiltration [2, 12] and a decreased rate of urinary protein excretion [3, 10]. The reduction of proteinuria has to be considered an important objective in the long-term treatment of transplant recipients since proteinuria correlates with transplant dysfunction and reduced transplant survival [13]. Nevertheless, long-term studies observing the effects of ACE inhibitors on renal allograft function are still lacking.

We therefore present the results of a 5-year follow-up study on the effects of quinapril and atenolol on blood pressure and renal allograft function. The 2-year results of part of this study population have been published previously [10].

Patients and methods

Patients

We conducted a prospective, double-blind, randomized study, which had been approved by the local ethical committee. Ninety-six patients aged between 18 and 60 years who had received a renal allograft between September 1990 and January 1995 were enrolled into the study 6–12 weeks after transplantation if the allograft function was stable, if they were under CYA immunosuppression, and if they had developed or aggravated systemic hypertension within 6–12 weeks after renal allografting. Hypertension was defined as a systolic blood pressure (SBP) of greater than 140 mmHg and/or a diastolic blood pressure (DBP) of greater than 90 mmHg in at least three office blood pressure readings on different occasions over a period of 1 month. All patients had given their informed consent.

The exclusion criteria were a serum creatinine concentration of more than 3 mg/dl; a history of allergy to β-blockers, ACE inhibitors, or diuretics; malignant hypertension, myocardial infarction, or cerebrovascular accident in the 6 months preceding the study; insulin-dependent diabetes mellitus; malignancies; severe urological complications; having had three or more RTxs; drug or alcohol abuse; pregnancy; renal artery stenosis. Before inclusion into the study, a Doppler sonography was performed in each patient to rule out renal artery stenosis.

Study design

Anti-hypertensive treatment

We screened all eligible patients during the first 3 months after transplantation to determine whether their allograft function was stable and to control blood pressure. They were then randomly assigned to receive either quinapril (Accupro; Goedecke, Berlin, Germany) or atenolol (Tenormin; AstraZeneca, Wedel, Germany). Patients were treated with a stepwise approach that optimally involved just quinapril or atenolol, but if necessary, were given various antihypertensive drugs to maintain the SBP at or below 140 mmHg and DBP at or below 90 mmHg. Forty-eight patients who had been assigned to the quinapril group initially received 2.5 mg quinapril daily, whereas the 48 patients of the control group were started with an initial dose of 12.5 mg atenolol/day. If the initial dose did not achieve the target blood pressure, a stepwise increase up to 40 mg (range 10–20 mg) of quinapril or up to 100 mg (range 25–50 mg) of atenolol was performed. If target blood pressure was not achieved by maximal doses of quinapril or atenolol monotherapy, we added 40 mg (up to 80 mg if necessary) of furosemide (Lasix; Aventis Pharma, Bad Soden, Germany) or 5 mg (up to 60 mg if necessary) of nifedipine (Adalat; Bayer, Germany). Doxazosin (Cardular; Pfizer, Karlsruhe, Germany; 4–16 mg) or clonidine (Catapresan; Boehringer, Ingelheim, Germany; 75–150 mg) was added in case the double therapy was insufficient. In order to control the patients' compliance, we asked them to bring back their unused medication so that the amount of medication taken could be supervised. All patients were advised to reduce their salt intake to approximately 4–8 g/day, especially those patients under quinapril treatment, since the ACE inhibitor's effect strongly depends on the sodium load [11, 18]. Patients were instructed by a dietician and were asked to follow their diet closely.

Immunosuppressive treatment

The standard immunosuppressive therapy consisted of CYA and prednisolone (5–15 mg/day). The target CYA concentration levels

were between 125 and 150 ng/ml during the first year after transplantation and between 75 and 100 ng/ml thereafter, as measured by high-performance liquid chromatography. However, some patients received a triple drug regimen with CYA, prednisolone, and azathioprine (1–2 mg/day/kg b.w.) or a combination of CYA, prednisolone, and mycophenolate mofetil (500–1500 mg/day).

Measurements

Patients were examined every month during the first 3 months of treatment by a physician who was unaware of the group assignment, and then every 3 months. The study period was 2 years with a follow-up period of 3 years. At each examination, heart rate and blood pressure were measured with the patient in a sitting position shortly before ingesting the anti-hypertensive agent. A 24-h blood pressure monitoring was conducted at least once a year. Pulse pressure was calculated as the difference between SBP and DBP. Hemoglobine concentration, serum creatinine level, and 24-h urinary proteine, albumine, and α-microglobuline excretion, were determined. Total urinary proteine was estimated with Coomassie Brilliant Blue stain, and other proteins were determined by SDS-PAGE electrophoresis. Renal function can be evaluated reliably by the Cockcroft–Gault algorithm, which can estimate the glomerular filtration rate [4]. The Cockcroft–Gault clearance is defined as

$$(140 - \text{age}) \times \text{body weight (kg)} / \text{serum creatinine concentration} \times 72$$

for men and as

$$(140 - \text{age}) \times \text{body weight (kg)} / \text{serum creatinine concentration} \times 85$$

for women, respectively.

Statistical analysis

We used the computer software Excel (Microsoft) for statistical analysis. Data are expressed as mean ± SEM. After testing data for normality, we used Student's paired *t*-test or the Wilcoxon signed-rank test, as well as analysis of variance (ANOVA) for repeated measurements, to compare the two groups. A *P* value below/equal to 0.05 was considered statistically significant.

Results

Ninety-six renal transplant recipients with different causes of renal failure were included in the study. The underlying primary renal diseases were chronic glomerulonephritis in 37 patients, rapid progressive glomerulonephritis in eight, diabetic nephropathy in ten, polycystic kidney disease in nine, chronic pyelonephritis in 15, renal vascular disease in five, hemolytic uremic syndrome in two, Alport's syndrome in one, medullary sponge kidney in one, and unknown in eight patients.

Forty-eight patients were assigned to receive quinapril, and 48 were randomly selected to receive atenolol. 40 patients of each group completed the study according to protocol. Five patients died (two in the quinapril group: one of septicemia, the second of myocardial infarction; two in the atenolol group died of malignancies and one of lung embolism), five patients (two in the quinapril group, three in the atenolol group) had their immunosuppressive treatment changed from CYA to FK506 because of gingiva hyperplasia and hypertrichosis, and six patients (three in each group) had their study medication altered (three for cough and three for development of hyperglycemia).

The data from all 96 patients were subjected to an intention-to-treat analysis. For those patients who did not complete the 5-year study or whose study medication had been changed, data were censored and an according-to-protocol analysis of data of the remaining patients was performed. In this study, we depict data of the according-to-protocol analysis at the point of entry into the study (E0: 6–12 weeks after RTx), 1 year ± 2 months after RTx (E1), 2 years ± 2 months after RTx (E2), 4 years ± 2 months after RTx (E4), and 5 years ± 5 months after RTx (E5).

Demography and immunosuppression

The demographic characteristics of the two randomized groups were similar (Table 1). Patients in the two groups were well matched for gender, height, initial weight, initial body mass index (BMI), duration of hemodialysis, and age at transplantation. There were no significant differences between the groups.

Neither CYA whole-blood levels (106.8 ± 7.0 vs 112.6 ± 9.6 ng/ml) nor prednisolone dosage (12.7 ± 0.8 vs 13.1 ± 1.0 ng/ml) differed significantly between the groups at inclusion into the study. Throughout the 5 years, patients of both groups were able to reduce sig-

Table 1 Demographic data of the study population. Data given as mean ± SEM. *NS* not significant

Variable	Intention-to-treat analysis			According-to-protocol analysis		
	ACE inhibitor ($n=48$)	β-blocker ($n=48$)	*P* (Q/A)	ACE inhibitor ($n=40$)	β-blocker ($n=40$)	*P* (Q/A)
Gender: male/female	33/15	35/13	NS	28/12	28/12	NS
Age (years)	44 ± 2	42 ± 2	NS	43 ± 2	43 ± 2	NS
Duration of hemodialysis (months)	41 ± 5	33 ± 4	NS	44 ± 6	36 ± 5	NS
Height (cm)	172 ± 2	174 ± 2	NS	172 ± 2	174 ± 2	NS
Weight (kg)	68 ± 2	70 ± 2	NS	67 ± 2	69 ± 2	NS
Initial BMI (kg/m^2)	23 ± 1	23 ± 1	NS	23 ± 1	23 ± 1	NS

Table 2 Hemodynamic data of the groups treated either with quinapril or with atenolol, according-to-protocol analysis (Δ difference between baseline and last value)

Variable	Quinapril ($n=40$)			Atenolol ($n=40$)		
	Baseline	5-year value	Δ	Baseline	5-year value	Δ
SBP (mmHg)	143 ± 2	134 ± 3*	−8 ± 3	142 ± 2	135 ± 3*	−8 ± 3
DBP (mmHg)	88 ± 2	83 ± 2*	−5 ± 2	89 ± 1	85 ± 2*	−4 ± 2
MAP (mmHg)	106 ± 2	100 ± 2*	−6 ± 2	107 ± 1	102 ± 2*	−5 ± 2
PP (mmHg)	55 ± 2	51 ± 2	−2 ± 2	53 ± 2	50 ± 2	−4 ± 3
Heart rate (beats/min)	78 ± 3	70 ± 2*	8 ± 3	75 ± 1	71 ± 1*	−4 ± 4

*$P < 0.05$ comparing initial with final values within one group

Table 3 Hemodynamic data, intention-to-treat analysis (Δ difference between baseline and last value)

Variable	Quinapril ($n=48$)			Atenolol ($n=48$)		
	Baseline	5-year value	Δ	Baseline	5-year value	Δ
SBP (mmHg)	145 ± 2	135 ± 3*	−8 ± 4	143 ± 2	135 ± 3*	−9 ± 3
DBP (mmHg)	90 ± 2	85 ± 2*	−5 ± 2	91 ± 1	85 ± 2*	−6 ± 2
MAP (mmHg)	108 ± 2	102 ± 2*	−6 ± 3	108 ± 1	102 ± 2*	−7 ± 2
PP (mmHg)	55 ± 2	50 ± 2	−3 ± 3	53 ± 2	50 ± 2	−3 ± 3
Heart rate (beats/min)	82 ± 2	70 ± 2*	−12 ± 3	75 ± 1	72 ± 2*	−2 ± 4

*$P < 0.05$ comparing initial with final values within one group

nificantly the daily dose of prednisolone ($P < 0.01$ in both groups) and of CYA ($P < 0.02$ in both groups) while maintaining a stable cyclosporine whole-blood level. The additional immunosuppressive treatment with azathioprine or mycophenolate mofetil was comparable in both groups.

Among the 80 patients of the according-to-protocol population, 19 cases of intermittent increase (more than 10%) of serum creatinine were observed in the quinapril group, 23 cases in the atenolol group. All rejection episodes were treated with steroid pulse therapy and ameliorated under this treatment.

Blood pressure and anti-hypertensive therapy

Patients followed their anti-hypertensive medication closely, as we observed a compliance rate of 98%. We analyzed the mean values from the 24-h blood pressure monitoring. As the according-to-protocol analysis showed, baseline values of SBP, DBP, and MAP were very similar in both groups. In both groups, SBP (group Q: from 143 ± 2 to 134 ± 3 mmHg, $P = 0.03$; group A: from 142 ± 2 to 135 ± 3 mmHg, $P = 0.03$), DBP (group Q: from 88 ± 2 to 83 ± 2 mmHg, $P = 0.02$; group A: from 89 ± 1 to 85 ± 2 mmHg, $P = 0.01$), and MAP (group Q: from 106 ± 2 to 100 ± 2 mmHg, $P = 0.01$; group A: from 107 ± 1 to 102 ± 2 mmHg, $P = 0.01$; mean ± SEM) decreased significantly over the observed 5 years. In both groups, blood pressure values were successfully lowered below the values defining hypertension. Pulse pressure decreased slightly in both groups, while heart rate was significantly lowered in both groups throughout the study period (Table 2). There were no statistically significant differences between the groups in blood pressure or heart rate at any time. Data from blood pressure and heart rate of the intention-to-treat analysis were very similar and are depicted in Table 3.

The average number of anti-hypertensive drugs required to control blood pressure increased during the study in the quinapril group from 1.3 ± 0.3 drugs/patient at baseline to 2.2 ± 0.1 drugs/patient after 5 years and in the atenolol group from 1.7 ± 0.2 to 2.2 ± 0.2 drugs/patient, respectively. The detailed distribution of the anti-hypertensive treatment is depicted in Table 4.

Hemoglobine concentrations

Hemoglobine concentrations increased significantly in both groups (group Q: from 11.9 ± 0.3 at E0 to 12.9 ± 0.4 g/dl at E5, $P < 0.02$; group A: from 12.2 ± 0.3 to 13.2 ± 0.4 mg/dl, $P < 0.01$). There was no difference in hemoglobine concentrations between the groups at any time.

Allograft function

In the following, results of only the according-to-protocol analysis are depicted, since the results of the in-

Table 4 According-to-protocol analysis of anti-hypertensive treatment scheme of both groups (*E0* inclusion time point 6–12 weeks after RTx, *E5* 5 years after RTx)

Time point	Antihypertensive therapy	Quinapril ($n=40$)		Atenolol ($n=40$)	
		n	Additional substances	*n*	Additional substances
E0	Mono	20		7	
	Double	7	Furosemide ($n=5$) Nifedipine ($n=2$)	17	Furosemide ($n=11$) Nifedipine ($n=6$)
	Triple	13	Furosemide + nifedipine ($n=8$) Furosemide + clonidine ($n=5$)	16	Furosemide + nifedipine ($n=12$) Nifedipine + doxazosin ($n=4$)
E5	Mono	21		8	
	Double	10	Furosemide ($n=7$) Nifedipine ($n=3$)	18	Furosemide ($n=11$) Nifedipine ($n=7$)
	Triple	9	Furosemide + nifedipine ($n=7$) Furosemide + clonidine ($n=2$)	14	Furosemide + nifedipine ($n=7$) Furosemide + doxazosin ($n=3$) Nifedipine + doxazosin ($n=4$)

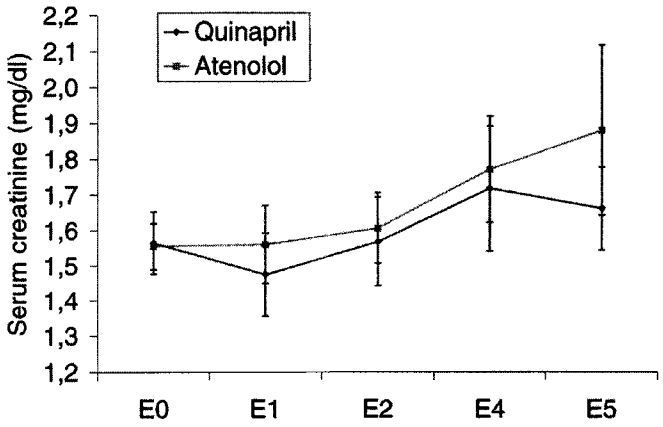

Fig. 1 According-to-protocol analysis of the time-dependent effects of quinapril and atenolol on serum creatinine levels. Data given as mean ± SEM. *E0* entry into the study, 6–12 weeks after RTx, *E1* 1 year after RTx, etc.)

tention-to-treat analysis were very similar. At entry into the study, patients' serum creatinine concentrations did not differ significantly between the atenolol- and quinapril–treated groups (Fig. 1). During the 5-year observation period, serum creatinine concentration increased slightly in both groups. Among the quinapril-treated patients, we observed an elevation in serum creatinine concentration from the mean baseline value of 1.6 ± 0.1 to 1.7 ± 0.1 mg/dl, a difference of 0.1 ± 0.1 mg/dl over 5 years. The use of atenolol led to an increase in serum creatinine concentration from baseline values of 1.6 ± 0.1 to 1.9 ± 0.2 mg/dl, an increase of 0.2 ± 0.2 mg/dl. There were no statistically significant differences in serum creatinine levels between the groups (ANOVA, $P=0.18$). In both groups, the Cockcroft–Gault clearance increased significantly ($P<0.01$) during the first year, namely from 64.4 ± 3.2 to 74.2 ± 4.2 ml/min among the quinapril-treated patients and from 64.8 ± 3.7 to 73.4 ± 6.2 ml/min in the atenolol group. Afterwards, values fell constantly in both groups. Nevertheless, after 5 years the clearance was still higher than that shortly after transplantation (group Q: ΔCockcroft–Gault clearance = 3.9 ± 4.6 ml/min; group A: ΔCockcroft–Gault clearance = 2.8 ± 4.3 ml/min). No statistically significant differences between the groups were found.

Urinary protein excretion fell significantly in the quinapril group during the first year (from 0.52 ± 0.08 to 0.31 ± 0.03 g/24 h, $P<0.03$; $\Delta 0-1 = -0.2 \pm 0.07$ g/24 h), increased to baseline values until the second year, and then remained stable over the rest of the 5-year study period (Fig. 2). Proteinuria was stable in the atenolol group during the first year (from 0.34 ± 0.030 to 0.3 ± 0.04 g/24 h). There was a significant difference in Δ0–1 between the groups ($P<0.04$). Although urinary protein excretion was lower in the atenolol group than in the quinapril group at baseline, it increased significantly over the 5 years (from 0.34 ± 0.03 to 0.72 ± 0.13 g/24 h, $P<0.01$) and finished at a higher level than in the quinapril group. Δ0–5 failed to be statistically significant between the groups ($P=0.06$; Fig. 2).

In both groups, excretion of albumine increased throughout the observation period, in the atenolol group slightly stronger than in the quinapril group ($\Delta 0-5 = 45.9 \pm 28.0$ vs $\Delta 0-5 = 36.9 \pm 29.2$ g/24 h). Urinary excretion of α-microglobuline, a marker of proximal tubule damage [7], decreased slightly ($\Delta 0-5 = -8.3 \pm 5.0$ g/24 h) in the quinapril group and increased slightly ($\Delta 0-5 = 7.4 \pm 10.9$ g/24 h) in the atenolol group. The difference between the groups failed to be statistically relevant (ANOVA, $P=0.06$).

Discussion

The maintenance of allograft function is the major point of interest in the treatment of renal transplant recipients. There is no doubt that hypertensive renal transplant recipients need an efficient anti-hypertensive treatment

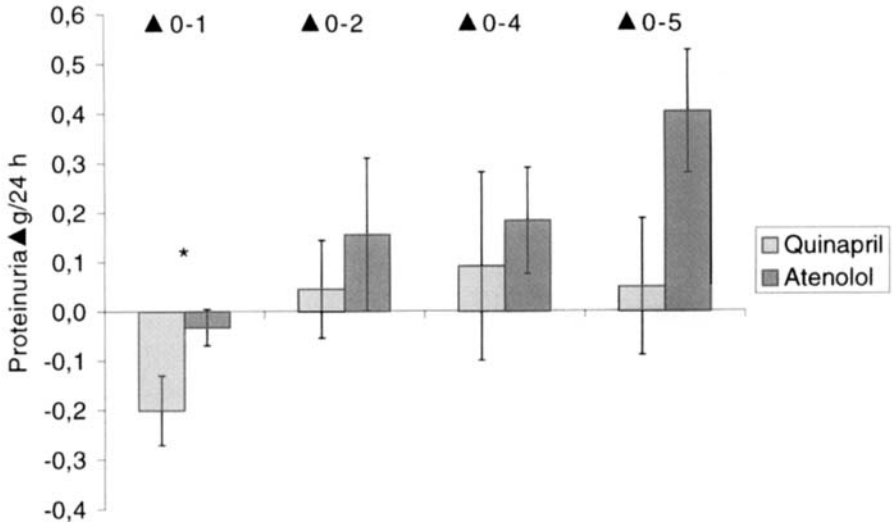

Fig. 2 Changes in urinary protein excretion (Δ) from baseline values to any given time point in quinapril- and atenolol-treated patients. (Δ0–1 difference in proteinuria from inclusion into the study 6–12 weeks after RTx until 1 year after RTx, etc.). Data given as mean ± SEM.
* Significant difference between the atenolol and quinapril group

in order for the allograft to be protected. The use of ACE inhibitors in RTx is still a point of discussion. Deterioration of allograft function may occur due to the combination of CYA-induced vasoconstriction of the afferent glomerular arteriole [24] and ACE inhibitor-induced vasodilator action at the efferent glomerular arteriole [14], resulting in a decrease in glomerular pressure. In fact, deterioration of allograft function induced by captopril has been described in cyclosporine-treated patients [1]. On the other hand, some authors did not observe deterioration of renal allograft function under immunosuppressive treatment with CYA and ACE inhibitor treatment [19, 25]. Mourad et al. hypothesized that the stable renal function they observed may have been due to relatively low CYA levels, which in their study were kept below 150 ng/ml.

In this prospective randomized study conducted on CYA-treated renal transplant recipients, it was demonstrated for the first time that the ACE inhibitor quinapril was a safe substance in the antihypertensive treatment of renal allograft recipients over a period of 5 years. Renal function, assessed by levels of serum creatinine and Cockcroft–Gault clearance, remained stable throughout the first 4 years and increased slightly less in the quinapril group than in the control group treated with atenolol during the last year of observation. Interestingly, both groups showed an increase in Cockcroft–Gault clearance after 1 year. This may be due to the fact that body weight increased significantly in both groups at that time. Nevertheless, these results suggest that the ACE inhibitor quinapril is as safe as the β-blocker atenolol and may be successfully used in the anti-hypertensive treatment of CYA-treated renal allograft recipients, keeping allograft function stable over the long term. At this point it should be noted that calcium channel blockers (CCBs) were more frequently used in the atenolol-treated group. These drugs, however, affect renal function in CYA-treated renal transplant recipients favorably [22].

ACE inhibitors have shown beneficial effects on the progression of renal insufficiency in different renal diseases [9, 17]. In clinical practice, the reduction of systemic and/or intraglomerular pressure might contribute to the anti-proteinuric/anti-albuminuric effect of ACE inhibitors, which has been observed in patients with different renal diseases [15, 20] and in renal transplant recipients [3]. β-Blockers have been shown to reduce proteinuria in different renal diseases as well [6, 26]. In this study, we observed a significant reduction in urinary protein excretion during the first year, with an increase in the following 3 years and, again, a slight decrease in the last year in the quinapril group. In the atenolol group, the minimum of proteinuria was reached after the first year as well. However, proteine excretion increased continuously from the second to the fifth year in the atenolol group, resulting in a significant overall rise in urinary protein excretion in the atenolol group throughout the 5-year study period. Urinary albumine excretion increased comparably in both groups, whereas the urinary excretion of α-microglobuline, which decreased in the quinapril group, showed a marked, yet insignificant increase among the atenolol-treated patients during the 5-year study period. In contrast to this observation, the 2-year results of our previous study showed a significantly lower albumin excretion in patients treated with quinapril. The previous study, however, was performed with a lower number of participants. Furthermore, the study population was not completely identical, and only according-to-protocol data are presented. Finally, urinary excretion of proteins was not related to urinary creatinine excretion, which would allow a more valid interpretation of proteine patterns. Long-term treatment with quinapril shows a tendency to lead to a more beneficial outcome concerning proteinuria and the excretion of α-micro-

globuline than does the regimen with atenolol in renal transplant recipients. This tendency was also seen in the 2-year results of our previous study [10]. The favorable outcome of quinapril regarding proteinuria, especially during the first year, can be explained by the ACE inhibitor-induced vasodilation of the efferent arteriole, which reduces intraglomerular pressure and therefore contributes to reduced excretion of proteins. Reduced filtration of proteins might lead to a reduced deposit of proteins in the tubular system. The amelioration of tubular damage might be indicated by the decrease of tubular marker protein α-microglobuline. It should be noted that all participants in this study were on a low-salt diet (4–8 g/day). However, salt excretion was not monitored. This point may be of special interest, since salt uptake may influence blood pressure and protein excretion, especially in ACE inhibitor-treated patients.

ACE inhibitors and β-blockers have been proven to have comparable anti-hypertensive potential. In this study, SBP, DBP, and MAP were reduced significantly in both groups of patients treated with either quinapril or atenolol. Also, heart rate decreased significantly in both groups. The observation that the decrease in heart rate was comparable between patients treated with quinapril and those treated with atenolol might be explained by the additional anti-hypertensive treatment: some patients in the quinapril group were treated with clonidine, an α_2-receptor agonist which reduces heart rate, while some patients of the atenolol group received an α_1-antagonist, which increases heart rate. The similarity of heart rate might therefore result from slightly different additional anti-hypertensive medication. The comparable decrease in heart rate can also be explained by a similar increase in hemoglobine concentration in both groups. There was no difference in the effects on blood pressure and heart rate between patients under a regimen with quinapril and those with atenolol.

Taken together, our results might indicate that the use of quinapril or atenolol in the treatment of cyclosporine-treated renal transplant recipients does not differ significantly concerning the effects on blood pressure, renal function, and urinary excretion. Quinapril as well as atenolol decreased blood pressure and kept renal allograft function stable over a 5-year time period. Both agents may therefore be considered safe and well tolerated in the long-term treatment of cyclosporine-treated renal allograft recipients.

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