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Reduction of proteinuria by angiotensin converting enzyme inhibition

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Reduction of proteinuria by angiotensin converting enzyme inhibition. The effects of the angiotensin converting enzyme (ACE) inhibitor lisinopril on blood pressure, proteinuria and renal hemodynamics were evaluated in 13 patients with renal disease of different origin. A comparison was made with the effects of conventional antihypertensive therapy. Both drug regimens significantly lowered blood pressure, while only after 12 weeks of treatment with lisinopril, blood pressure was significantly lower than during conventional therapy. Lisinopril reduced proteinuria (by 61 ± 40%), whereas conventional therapy had no significant effect on protein excretion. During the first eight weeks of treatment with lisinopril, there was a comparable degree of blood pressure reduction with both treatment regimens, whereas urinary protein loss was significantly less during ACE inhibition. There was only a nearly–significant positive correlation between the fall in proteinuria during lisinopril and the concomitant decrease in mean arterial pressure. Glomerular filtration rate decreased from 26.3 ± 11.6 to 20.6 ± 9.4 ml/min during treatment with lisinopril. This decrease was not correlated with the fall in proteinuria. A significant positive correlation existed between the fall in urinary protein excretion and both the decrease in overall renal vascular resistance, and the fall in filtration fraction. Although blood pressure lowering by itself could contribute to the antiproteinuric effect of lisinopril, our results suggest that this effect of ACE inhibition is also due to efferent (postglomerular) vasodilation. We conclude that the ACE inhibitor lisinopril effectively reduces blood pressure and proteinuria in renal disease. The latter effect is not only the result of a lower blood pressure, but is probably also due to a fall in intraglomerular capillary pressure.

Angiotensin converting enzyme (ACE) inhibitors are effective antihypertensive agents. Additionally, this group of drugs has been found to induce renal vasodilation. Effective renal plasma flow rises, whereas the glomerular filtration rate remains constant, notwithstanding a fall in blood pressure [1–3]. The concomitant fall in filtration fraction has been interpreted as a fall in efferent (postglomerular) vascular tone. Data on the use of ACE inhibitors in patients with renal function impairment and proteinuria are scarce to date [4, 5]. Animal data suggest that enalapril is able to protract the course of renal function deterioration in the rat renal ablation model [6, 7], and in rats with streptozotocin–induced diabetes mellitus [8, 9]. In these studies ACE inhibitors prevented urinary protein loss [6–9]. Interestingly, the favorable effect on renal function and proteinuria observed after treatment with enalapril was not present [10], or less pronounced [11], after reserpine, hydralazine, and hydrochlorothiazide, or after verapamil [9]. Since only the ACE inhibitor, and not other antihypertensives, caused a fall in glomerular capillary pressure, notwithstanding a similar fall in systemic blood pressure [10], it has been suggested that changes in renal hemodynamics, induced by ACE inhibition, are responsible for this benign effect on renal function [6–10]. Taguma et al recently showed that captopril induced a fall in proteinuria in patients with diabetic nephropathy [12]. We now extend these observations to patients with renal function impairment and proteinuria of various origin. In these patients blood pressure, renal hemodynamics and proteinuria were studied during conventional antihypertensive treatment, during a control period without antihypertensive medication, and during a 12 week course of ACE inhibition with lisinopril, a lysine analogue of enalapril with a more prolonged duration of action.

Methods

Patients

Thirteen patients (7 male, 6 female) were enrolled in this study. Mean age was 43.6 ± 9.4 years. All gave their informed consent and the study was approved by the Ethical Committee of our hospital. All had renal function impairment, hypertension and proteinuria. They used antihypertensive drug therapy, generally a diuretic, beta–blocker, and vasodilator for at least one year. Etiology of their renal disease and the conventional antihypertensive drugs used are summarized in Table 1. In most cases diagnosis was obtained by renal biopsy, except for the patients with diabetic nephropathy ($N = 3$), polycystic kidney disease ($N = 1$) and chronic pyelonephritis ($N = 1$). All patients adhered to a dietary regimen of 3 to 5 g sodium chloride per day. A protein intake of 30 to 40 g/day had been advised to patients with a creatinine clearance of less than 30 ml/min, and 40 to 60 g/day to patients with a creatinine clearance of 30 to 60 ml/min, from at least six months prior to the start of the study. Concomitant medication consisted of iron supplementation, multivitamins, phosphate binders, and vitamin D analogues in most patients with a creatinine clearance less than 30 ml/min. The sodium and protein content of the diet, as well as these concomitant medications, were not changed during the entire study period.

Study protocol

All patients were followed in our out–patient hypertension and nephrology unit. Blood pressure and biochemical parame-

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Table 1. Patient characteristics at entry during therapy with conventional antihypertensive drugs

No.	Sex	Age	Diagnosis	Antihypertensives[a]
1	M	39	Chronic pyelonephritis	furo 40/meto/100/ pra 1.5
2	M	40	Membranoproliferative GN**	meto 100/hydral 75
3	F	49	Polycystic kidney disease	HCT 50/meth 500
4	F	42	Diabetic nephropathy	HCT 50
5	F	51	Diabetic nephropathy	furo 40/clon 450/ hydral 40
6	M	36	Membranoproliferative GN	furo 40/meth 1500/ pra 3
7	F	62	Diabetic nephropathy	furo 80
8	F	45	Local focal glomerulosclerosis	clon 450
9	M	49	Atherosclerosis/ischemia	meto 200
10	F	51	Atherosclerosis/ischemia	meto 200/pra 9/hydral 200
11	M	45	Wegener's granulomatosis	HCT 50
12	M	26	Local focal glomerulosclerosis	meto 100
13	M	32	IgA glomerulopathy	furo 40/meto 100

** GN = glomerulonephritis

[a]furo, furosemide; meto, metoprolol; pra, prazosine; hydral, hydralazine; HCT, hydrochlorothiazide; meth, alphamethyldopa; clon, clonidine. Numbers refer to daily dose in mg.

ters were measured at least three times to obtain stable data during conventional antihypertensive therapy. Thereafter, this medication was withdrawn. They were without antihypertensive therapy for two weeks before starting lisinopril, except for the patients 6 and 10 who started therapy three and five days after withdrawal of previous medication because of clinically symptomatic, high blood pressures. Data obtained before the start of lisinopril will be referred to as control period. Lisinopril was gradually titrated from a starting dose of 2.5 or 5 mg once a day to a maximum of 40 mg o.i.d. The therapeutic goal was a diastolic blood pressure of less than 95 mm Hg. If blood pressure remained elevated notwithstanding this maximum dose of 40 mg lisinopril, a diuretic could be added (furosemide 20 or 40 mg b.i.d.). Lisinopril was administered at 10 a.m., separated by at least two hours from other medications used. At days of out–patient visits, lisinopril was taken only after blood pressure recordings and blood sampling had been carried out. Blood was drawn for serum electrolytes, creatinine and urea. At the control period (the day before lisinopril was started), and at weeks 4, 8, and 12 during lisinopril treatment, blood was also drawn for determination of ACE activity. The day before every out–patient visit 24-hour urine was collected for measurement of 24-hour protein excretion and creatinine clearance. Additionally, the day before the first lisinopril dose and after three months of treatment with the converting enzyme inhibitor, glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were measured with the patients in supine position. After three hours of supine test, blood was drawn for measurement of plasma renin activity (PRA) and plasma aldosterone concentration (PAC).

Table 2. Blood pressure, creatinine clearance and 24-hour protein excretion in the patients at entry during conventional antihypertensive treatment

No.	Blood pressure *mm Hg*	Creatinine clearance *ml/min*	Protein excretion *g/24 hr*
1	134/92	22	2.4
2	146/100	56	0.5
3	156/100	38	0.9
4	162/90	35	12.4
5	232/104	25	7.8
6	126/90	19	4.4
7	186/92	22	3.5
8	162/90	55	0.4
9	150/94	48	3.9
10	170/110	13	1.5
11	170/98	10	2.2
12	148/92	15	6.3
13	134/98	15	2.9

Data are the mean of three measurements.

Methods

Blood pressure was measured with a standard mercury sphygmomanometer. Measurements were performed in triplo after 10 minutes of supine rest. The mean of three readings, differing not more than 10 mm Hg, was recorded. Mean arterial pressure (MAP) was calculated as the diastolic blood pressure plus one third of the difference between systolic and diastolic pressure. Serum and urinary electrolytes, creatinine, and urea were measured by a standard auto–analyzer technique. Urinary protein was determined by biuret method in aliquots of 24-hour urine collections. Serum angiotensin converting enzyme was determined using a HPLC-assisted assay [13]. PRA and PAC were measured by radioimmunoassay [14, 15]. GFR and ERPF were measured simultaneously by constant infusion of ^{125}I-iothalamate and ^{131}I-hippuran, respectively [16]. Both parameters were corrected for standard body surface area (1.73 m^2). Filtration fraction (FF) is given as the quotient of GFR and ERPF. Renal vascular resistance (RVR) is calculated as the quotient of MAP and ERPF. Statistical analysis was performed using Wilcoxon's test for paired data, since the parameters involved (especially those on proteinuria) appeared to be non-normally distributed. Data are given as mean ± SD, unless otherwise indicated.

Results

Data on blood pressure, creatinine clearance, and 24-hour protein excretion during conventional antihypertensive therapy are given in Table 2. Creatinine clearance varied from 10 to 56 ml/min and 24-hour protein excretion ranged from 0.4 to 12.4 g/24 hr. Although a nephrotic range proteinuria (>5 g/24 hr) was present in three patients, only one had a serum albumin content of less than 30 g/liter.

After withdrawal of the antihypertensive drugs, systolic blood pressure increased from 160 ± 27 to 176 ± 32 mm Hg ($P < 0.01$) and diastolic blood pressure rose from 96 ± 6 to 110 ± 10 mm Hg ($P < 0.01$). Proteinuria was 3.8 ± 3.4 g/24 hr on conventional therapy and 4.2 ± 3.2 g/24 hr without antihypertensive drugs. Although daily protein excretion during conventional therapy was lower compared to control values in 10

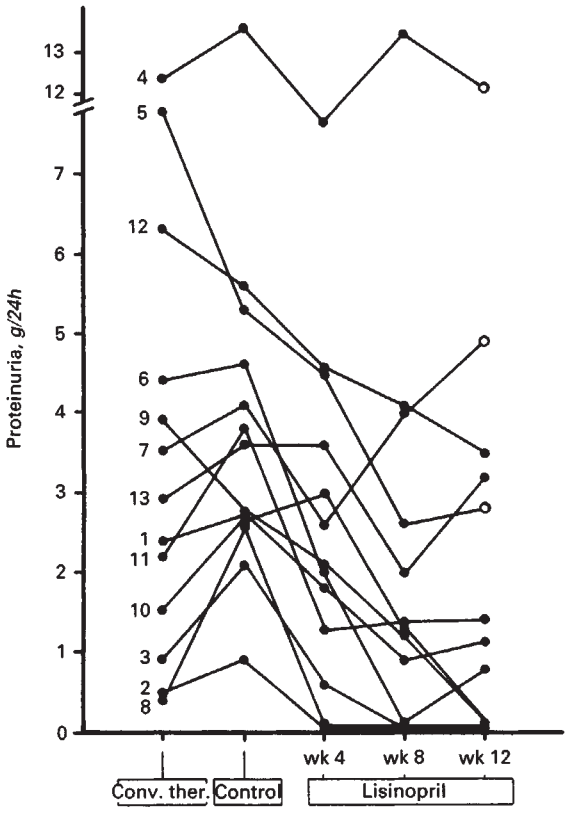

Fig. 1. *Urinary protein excretion per 24 hours in the 13 patients during conventional therapy (conv. ther.), the control period (control), and after 4, 8, and 12 weeks of treatment with lisinopril.* Open circles refer to the patients who also received furosemide on week 12. The different patients are identified by their number.

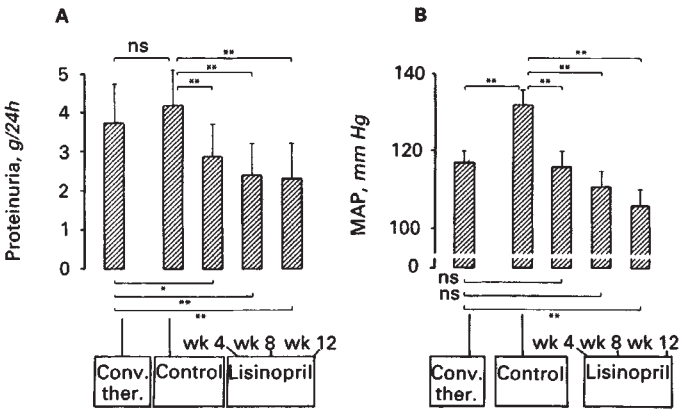

Fig. 2. *Mean and SEM of proteinuria* (**A**) *and mean arterial pressure (MAP,* **B**) *during conventional antihypertensive drugs (con. ther.), after withdrawal of these drugs (control), and during lisinopril.* The significance of the difference compared to control is given at the top, and the significance of the difference compared to the value during conventional therapy is given at the bottom. * = $P < 0.05$ and ** = $P < 0.01$.

out of 13 patients (Fig. 1), the difference appeared to be not statistically significant.

The average dose of lisinopril was 8.9 ± 4.2 mg per day at week 4, 20.8 ± 14.7 mg per day at week 8, and 22.6 ± 15.9 mg per day at week 12. From week 8 through 12 the patients 4, 5, and 7 also needed a diuretic (furosemide 20 or 40 mg b.i.d.) to be added to the lisinopril treatment, because the goal diastolic blood pressure was not met. Systolic blood pressure fell from 176 ± 32 to 150 ± 32 ($P < 0.01$), 147 ± 30 ($P < 0.01$), and 143 ± 35 ($P < 0.01$) mm Hg at the 4th, 8th, and 12th week of lisinopril, respectively. Diastolic blood pressure decreased from 110 ± 10 to 99 ± 10 ($P < 0.01$), 94 ± 10 ($P < 0.01$), and 88 ± 5 mm Hg ($P < 0.01$), at week 4, 8, and 12 of lisinopril, respectively. Both systolic and diastolic pressure were not significantly different at week 4 and 8 of lisinopril treatment compared to conventional therapy. However, at week 12 of lisinopril treatment systolic ($P < 0.05$) and diastolic ($P < 0.01$) blood pressure were lower compared to conventional treatment. In the patients 4, 5, and 7, who also received a diuretic from week 8 through 12, blood pressure was 174/104, 170/100, and 214/96 mm Hg at week 8, and 136/84, 216/96, and 222/94 mm Hg at week 12, respectively.

Already four weeks after the start of lisinopril, ACE activity had decreased by 80 to 90 percent from 30.5 ± 9.5 to 4.6 ± 3.5 U/liter ($P < 0.01$), and remained stable at this low level during the further course of lisinopril treatment. PRA had increased significantly from 1.35 ± 1.23 to 20.1 ± 19.7 nmol AI/liter/hr ($P < 0.01$) and PAC had fallen from 1.30 ± 0.67 to 0.71 ± 0.53 nmol/liter ($P < 0.01$) during lisinopril.

The changes in urinary protein excretion in the individual patients during lisinopril treatment are shown in Figure 1. Except for the patients 4, 7, and 13, there was a considerable decrease in proteinuria. The changes in mean daily protein excretion are given in Figure 2A. Proteinuria decreased significantly during lisinopril treatment from 4.2 ± 3.2 to 2.9 ± 2.9 g/24 hr ($P < 0.01$), 2.4 ± 3.6 g/24 hr ($P < 0.01$), and 2.3 ± 3.4 g/24 hr ($P < 0.01$) after 4, 8, and 12 weeks, respectively, thus resulting in a total fall of 61 ± 40% compared to control. Comparing the daily protein excretion during conventional therapy with the values of week 4, 8, and 12 of lisinopril treatment, the differences appear to be statistically significant at all periods ($P < 0.05$, $P < 0.01$ and $P < 0.01$, respectively).

Figure 2B depicts the mean values of mean arterial pressure (MAP) in the 13 patients at different study periods. Conventional antihypertensive therapy, as well as lisinopril, lowered blood pressure significantly. Although lisinopril in this particular study design appeared to be more effective at week 12 of treatment compared to conventional treatment ($P < 0.01$), the blood pressure effect of both regimens was not significantly different at weeks 4 and 8 of lisinopril therapy. Thus, with a comparable degree of blood pressure reduction on both antihypertensive regimens during these periods, proteinuria was significantly lower during ACE inhibition. There was a positive correlation between the individual percentage of decrease in proteinuria after 12 weeks of lisinopril therapy and the percentage of fall in MAP. This correlation however, was just not statistically significant ($r = 0.52$, $0.05 < P < 0.10$).

Serum creatinine, serum urea and creatinine clearance were not significantly different on conventional therapy compared to control (Table 3). During treatment with lisinopril a gradual but not statistically significant rise in serum creatinine was observed. Serum urea increased ($P < 0.01$) and creatinine clearance decreased ($P < 0.05$) during therapy with this ACE inhibitor. More accurate renal function studies were performed in 11 patients during the control period, and after 12 weeks of

Table 3. Biochemical parameters during previous antihypertensive medication, the control period, and during treatment with lisinopril

	Conventional therapy	Control	Lisinopril		
			Week 4	Week 8	Week 12
Serum sodium *mmol/liter*	140.7 ± 2.4	139 ± 3.7	139 ± 3.5	139 ± 2.7	138 ± 2.3
Serum potassium *mmol/liter*	4.9 ± 0.8	4.7 ± 0.6	5.3 ± 0.5[b]	5.4 ± 0.6[b]	5.1 ± 0.5[b]
Serum uric acid *mmol/liter*	0.45 ± 0.12	0.45 ± 0.13	0.42 ± 0.12	0.42 ± 0.12	0.45 ± 0.14
Serum creatinine *μmol/liter*	339 ± 147	377 ± 226	395 ± 248	409 ± 249	422 ± 272
Creatinine clearance *ml/min*	28.7 ± 16.1	28.2 ± 17.2	28.0 ± 15.5	26.6 ± 15.7	24.5 ± 12.8[a]
Serum urea *mmol/liter*	17.1 ± 6.5	15.1 ± 6.5	17.3 ± 6.4[b]	19.1 ± 8.2[b]	21.9 ± 14.4[b]
Urinary urea *mmol/24 hr*	271 ± 88	248 ± 94	253 ± 84	248 ± 90	263 ± 93

[a] $P = <0.05$
[b] $P = <0.01$

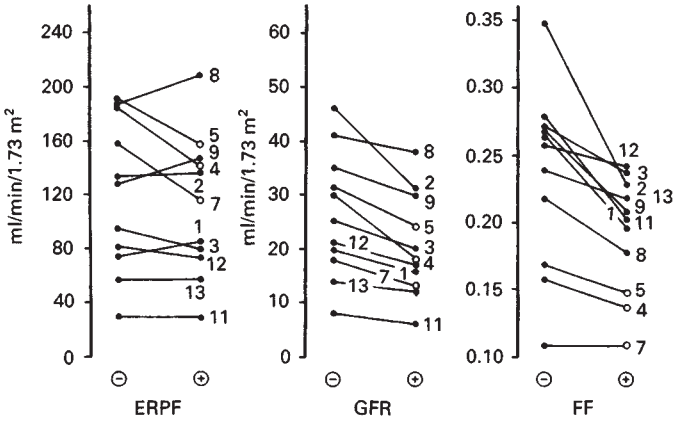

Fig. 3. *Changes in effective renal plasma flow (ERPF, by hippuran clearance) and glomerular filtration rate (GFR, by iothalamate clearance) in ml/min/1.73 m², and in filtration fraction (FF), during therapy with lisinopril.* Individual data of 11 patients (identified by their number) are given at the control period (−) and after 12 weeks of treatment with lisinopril (+). Open circles represent the values of the patients who additionally received furosemide.

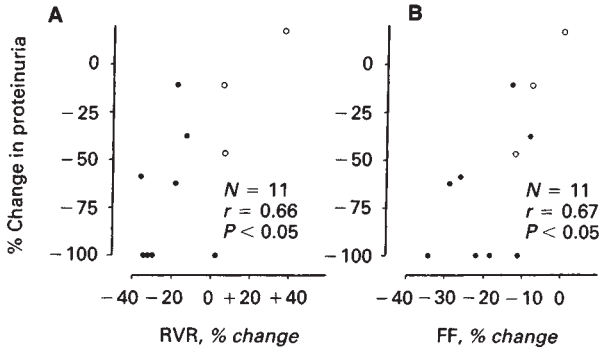

Fig. 4. *The relation between the percentual fall in proteinuria and the percentage change in renal vascular resistance* (RVR, **A**) *and filtration fraction* (FF, **B**). Open circles represent the values of the patients who also received furosemide.

lisinopril treatment (Fig. 3). Lisinopril did not induce a significant change in ERPF, which was 120 ± 56 ml/min during control, and 111 ± 52 ml/min after 12 weeks of lisinopril treatment (NS). In contrast however, GFR fell in all subjects, with a mean decrease of 21 ± 10% (from 26.3 ± 11.6 to 20.6 ± 9.4 ml/min, $P < 0.01$). Consequently, also a fall in FF was observed (from 0.24 ± 0.07 to 0.19 ± 0.04, a decrease of 16.5 ± 10.3%, $P < 0.01$). At the time of the second renal function measurements, the patients 4, 5, and 7 also received diuretic treatment. Interestingly, these three patients, in whom blood pressure had not decreased significantly with lisinopril only, had the lowest initial filtration fraction. These three subjects, who all had diabetic nephropathy, responded with a fall in ERPF. Two out of these three patients showed no fall in proteinuria, not even after addition of furosemide. In the overall group of patients, there was no correlation between the individual percentual fall in GFR and the percentual fall in urinary protein excretion ($r = -0.22$, NS). The patients with the highest FF during the control period showed the most pronounced fall in FF during lisinopril ($r = 0.82$, $P < 0.01$), as well as the most pronounced decrease in proteinuria ($r = 0.72$, $P < 0.01$). As a consequence of the fall in MAP, with the stable ERPF, overall renal vascular resistance (RVR) fell in most patients, although RVR increased in the three patients using furosemide. We found a significant positive correlation between the fall in protein excretion and the fall in total RVR (Fig. 4A). A similar positive correlation was observed between the fall in proteinuria and the fall in FF (Fig. 4B). Thus, in the patients with the most exaggerated fall in total RVR, as well as in FF (an index of postglomerular vascular resistance), protein excretion fell most.

Biochemical parameters were not different between conventional therapy and control (Table 3). Serum sodium did not change during treatment with lisinopril, whereas serum potassium increased significantly. In fact, in five out of the 13 patients a rise in serum potassium of more than 1.0 mmol/liter occurred, and in eight patients serum potassium levels of more than 5.8 mmol/liter were observed. With additional dietary advice regarding potassium containing foods, acceptable potassium levels could be obtained. Serum uric acid did not change. According to 24-hour urinary sodium excretion, mean sodium intake was approximately 2 g higher than the dietary prescription, and according to urea excretion protein intake was approximately 10 g higher than advised. Sodium and urea excretions during lisinopril treatment were comparable to the excretions during conventional therapy (Table 3). Serum albumin had not changed during lisinopril treatment (38.2 ± 5.3 g/liter at control and 38.2 ± 5.0 g/liter at week 12 of lisinopril therapy).

Discussion

Lisinopril effectively lowered ACE activity with a concomitant rise in plasma renin activity and a fall in plasma aldosterone concentration. This resulted in a significant reduction of blood

pressure. During conventional antihypertensive therapy, blood pressure was also significantly lower compared to control. Only after 12 weeks of treatment with lisinopril, blood pressure was significantly more reduced than during conventional therapy. At weeks 4 and 8 of lisinopril treatment, however, the degree of blood pressure lowering was not significantly different from conventional antihypertensive treatment.

In most patients, urinary protein excretion was lower during conventional therapy compared to control. However, this difference was not statistically significant. In contrast, lisinopril significantly lowered proteinuria, compared to control, as well as compared to conventional therapy. There appeared to be only a nearly–significant positive correlation between the fall in urinary protein excretion and decrease in MAP during lisinopril. Moreover, during the first eight weeks of treatment with lisinopril, there was a comparable degree of blood pressure lowering on both therapeutic regimens, whereas proteinuria was significantly more reduced during ACE inhibition. Thus, although blood pressure lowering by itself could partially explain the fall in proteinuria during lisinopril, we argue that our observations are in consonant with a more specific antiproteinuric effect of ACE inhibitors. This is in agreement with the data of Taguma et al, who showed the proteinuria lowering effect of captopril in patients with diabetic nephropathy without a concomitant fall in blood pressure [12].

It is likely to attribute these changes in protein leakage to an interference of lisinopril with angiotensin-II–mediated effects on the kidney. Indeed, in animal experiments infusion of angiotensin II caused a rise in urinary protein loss [17, 18]. This angiotensin-II–induced proteinuria has been attributed both to changes in the permeability properties of the glomerular capillary wall [17, 19], and alternatively to hemodynamic changes with a concomitant rise in filtration fraction [18]. Also in man, renin induced proteinuria has been described in cases of renal artery stenosis [20–23]. Nephrectomy of the ischemic kidney [21, 22], or treatment with captopril [23], has been found to lower proteinuria in those conditions. Although we did not systematically exclude the possibility of renal artery stenosis in our patients, no clinical evidence of renovascular disease was found.

Creatinine clearance gradually decreased during treatment with lisinopril. Also glomerular filtration rate, measured as the clearance of iothalamate, fell by 21% in our patients. The fall in urinary protein excretion, however, was more pronounced (61%). Thus fractional protein excretion also decreased. Since no correlation existed between the fall in proteinuria and the fall in GFR, we suggest that also other mechanisms are involved in the antiproteinuric effect of lisinopril. ACE inhibitors are known to induce renal vasodilation. In healthy volunteers and in patients with essential hypertension and normal renal function, both captopril and enalapril induce a rise in ERPF [1–3]. We found no change in ERPF in our group of patients with renal function impairment. This difference in response between patients with normal and with impaired renal function is probably due to the renal disease itself. It may well be that these diseased kidneys are unable to compensate for the fall in pressure with a rise in flow. As a consequence, GFR and thus filtration fraction fell. This is compatible with an efferent arteriolar (postglomerular) vasodilation. Efferent vascular tone mainly is dependent on angiotensin II [24]. Thus, after ACE inhibition efferent vasomotor tone will decrease. We observed a significant correlation between the fall in urinary protein excretion and both the fall in overall renal vascular resitance and the fall in filtration fraction. This suggests that the fall in proteinuria is related to the decrease in renal vascular resistance, particularly of postglomerular arteriolar vessels. Such a postglomerular vasodilation will result in a fall in intraglomerular capillary pressure. Filtration of proteins consequently will decrease even more than the filtration of the smaller molecular weight molecules like creatinine or the GFR-marker iothalamate. This is in agreement with the effect of enalapril in the rat renal ablation model [7] and in streptozotocin–induced diabetes mellitus in the rat [8]. In the latter study, the development of glomerulosclerosis and progressive albuminuria was prevented by normalizing glomerular capillary pressure, as a consequence of the reduction of systemic blood pressure as well as of postglomerular arteriolar resistance.

It should be noted that the patients with the lowest filtration fraction before lisinopril, especially the three patients with diabetic nephropathy who also used furosemide at week 12, had the smallest decrease in filtration fraction during ACE inhibition. This indicates an inability to dilate the efferent arteriole in these patients. In fact, these three subjects showed a decrease in ERPF, as well as a rise in renal vascular resistance. This could have influenced the correlations plotted in Figure 4. The different responses of these three patients may be explained by the fact that they were less sensitive to ACE inhibition. Not only blood pressure response was insufficient (which necessitated the combination with a diuretic), but also renal vascular resistance, filtration fraction, and proteinuria responded less favorably compared to the other patients. The reason for this insensitivity, especially where it seems to be related to the underlying renal disease (diabetic nephropathy), remains unclear. On this point, our results are not in agreement with the favorable effects of ACE inhibition on proteinuria in diabetic nephropathy, observed by Taguma et al [12].

Restriction of dietary protein intake can also lower proteinuria [25]. In our patient group, however, the diet was not changed with respect to protein intake from at least six months before the study till the end. Moreover, urinary urea excretion, which can be used as an estimate of protein intake, was approximately stable during the entire observation period. Therefore, we believe this did not significantly influence our results.

Treatment with ACE inhibitors in patients with renal function impairment bear the risk of a rise in serum potassium concentration. We indeed found a significantly–higher serum potassium during lisinopril, which, however, could be adjusted acceptably with further dietary potassium restriction. Changes in other biochemical parameters (Table 3) were not of clinical importance. Finally, serum albumin did not rise, notwithstanding the fall in urinary protein loss. One should however realize that in most patients no hypoproteinemia existed before therapy.

We thus conclude that converting enzyme inhibition results in a fall in urinary protein excretion in patients with renal function impairment. This antiproteinuric effect is not only due to the antihypertensive effect of the drug, since a comparble degree of blood pressure lowering with conventional drugs was not accompanied by a similar decrease in urinary protein loss.

We argue that this antiproteinuric effect likely is the consequence of renal vasodilation, particularly of the efferent arteriole, resulting in a fall in intraglomerular capillary pressure. Whether these changes in intraglomerular pressure will also contribute to protract the course of progressive renal failure cannot be evaluated from our study, and has yet to be established.

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