**ACE Inhibition and Albumin Excretion**

Predictors of Angiotensin-Converting Enzyme Inhibitor–Induced Reduction of Urinary Albumin Excretion in Nondiabetic Patients


**Abstract**—Urinary albumin excretion is a predictor for cardiovascular mortality and morbidity. We investigated which parameters determine baseline urinary albumin excretion in nondiabetic subjects, without renal disease. In addition, we evaluated the parameters that predict the albuminuria-lowering efficacy of an angiotensin-converting enzyme inhibitor. In this substudy of the Prevention of Renal and Vascular Endstage Disease Intervention Trial, 384 microalbuminuric patients were included. Patient and biochemical characteristics were obtained at baseline and after 3 months of double-blinded, randomized treatment (fosinopril 20 mg or placebo). Mean age was 51.1±11.5 years, and 65.6% were male. Median urinary albumin excretion was 22.2 mg per 24 hours. At baseline, mean arterial pressure (βstandardized=0.161; P=0.006), urinary sodium excretion (βstandardized=0.154; P=0.011), and estimated renal function were independently associated with albumin excretion. In these predominantly normotensive to prehypertensive subjects, fosinopril reduced albumin excretion by 18.5% versus a 6.1% increase on placebo after 3 months (P<0.001). Fosinopril use and blood pressure reduction independently predicted the change in urinary albumin excretion. Baseline urinary albumin excretion independently predicted the antialbuminuric effect of fosinopril (βstandardized=−0.303; P<0.001). In conclusion, at baseline, sodium intake and blood pressure were positively associated with urinary albumin excretion. Fosinopril reduced albuminuria more than might be expected from its blood pressure–lowering effect alone, and this effect was more outspoken in subjects with higher baseline albumin excretion. Based on our data, we hypothesize that angiotensin-converting enzyme inhibition may result in superior cardiovascular protection when compared with other blood pressure–lowering agents in subjects with higher baseline levels of albuminuria. (*Hypertension*. 2006; 48:870-876.)

**Key Words:** randomized, controlled trial ■ albumin ■ urine ■ ACE inhibitor ■ hypertension ■ sodium

In patients with primary renal disease and diabetic nephropathy, it has been shown that proteinuria predicts future renal function decline.1 Moreover, it has been shown that a decrease in proteinuria induced by ACE inhibitors in the short-term predicts long-term efficacy of such treatment on renal function outcome.2 The more proteinuria is lowered, the better the prognosis with regard to renal function. These observations have led researchers in clinical practice to pursue a maximal antiproteinuric response on angiotensin-converting enzyme (ACE) inhibitors in renal patients by coprescribing treatments that are known to increase the antiproteinuric efficacy of this class of drugs, for example, sodium-restricted diet and diuretics. Interestingly, it has also been shown that in subjects with diabetes or hypertension, and even in the general population, urinary albumin excretion (UAE) predicts future cardiovascular events.3–5 It was also suggested that in such subjects a short-term decrease in UAE with a renin–angiotensin system blocker predicts long-term cardiovascular outcome.6 Factors that determine the response to ACE inhibitors have been examined mainly in patients with renal disease. In subjects on a low-sodium diet and with a high baseline plasma renin activity, for example, a more pronounced antiproteinuric response is obtained.7,8 Whether this is also the case in microalbuminuric subjects in the general population is yet unknown. The mechanism by which albuminuria originates in patients with renal disease and in subjects from the general population may well be different. Although in patients with renal disease urinary protein loss is the result of specific glomerular damage, in nonrenal patients, microalbuminuria has been mentioned to be a consequence of generalized endothelial dysfunction.9 Also, the efficacy of ACE inhibitors to...
lower urinary protein loss may be different between proteinuric patients with renal disease and microalbuminuric subjects. Although in patients with renal disease it is generally accepted that ACE inhibitors lower UAE more than may be expected from the blood pressure–lowering effect of these drugs alone, this issue is debated in microalbuminuric subjects.16

Given these considerations, we investigated in nondiabetic subjects from the general population, without renal disease, which patient characteristics are associated with UAE in the untreated situation, and which characteristics predict a reduction in UAE after 3 months of ACE inhibitor treatment. Such knowledge may be helpful to optimize treatment for the prevention of cardiovascular disease. For this purpose we used data from the Prevention of Renal and Vascular Endstage Disease Intervention Trial (PREVEND IT).

Methods

Population

The study population was selected from the PREVEND IT study, an investigator-initiated, randomized trial performed between November 2000 and February 2004 that used a 2-by-2 factorial design to compare the effect of statin therapy (40 mg of pravastatin orally per day) and placebo therapy and of ACE inhibitor therapy (20 mg of fosinopril orally per day) and placebo on UAE and the risk of cardiovascular events in microalbuminuric patients. In total, 864 subjects who presented with persistent microalbumuria during the screening phase (once a urinary albumin concentration >10 mg/L in a first morning void urine sample and at least once 15 to 300 mg per 24 hours in 2 subsequent 24-hour urines) and who provided written informed consent were enrolled. Exclusion criteria were: hypertension and hypercholesterolemia, as defined according to prevailing guidelines for Dutch general practitioners at the design of the study (respectively, systolic blood pressure [SBP] ≥160 mm Hg, diastolic blood pressure [DBP] ≥100 mm Hg, or use of antihypertensives and a total cholesterol ≥8 mmol/L or ≥5 in case of a previous myocardial infarction), as well as known diabetes. Details of the study design have been presented previously.11,12 Of note, subjects with known renal disease were excluded from participation, as well as subjects with UAE ≥300 mg per 24 hours, because this might indicate the presence of a primary renal disease. As part of the protocol, fasting blood samples were obtained at randomization. Plasma samples were stored at −80°C until assayed. For these laboratory assessments that were not part of the initial protocol of the PREVEND IT, we used plasma obtained at baseline, before subjects were randomly assigned to treatment, and for albuminuria also after 3 months of double-blind treatment, a period assumed to be adequate for the effect of ACE inhibitor therapy on this variable to be established. For logistic reasons, we decided to restrict the analysis to plasma samples of 400 participants of the total cohort (from all 4 of the randomly assigned groups, we used the samples of the final 100 patients who were included) who had a plasma sample available at both baseline and 3-month visit. Because the patients were randomly assigned to each treatment arm, this methodology guarantees that proper random assignment is maintained and that the results will not be biased. Because we wanted to study a nondiabetic population, all of the subjects not previously known with diabetes, but with a baseline fasting plasma glucose ≥7.0 mmol/L, were excluded from this analysis. Thus, 384 patients were eligible for the present study. All of the participants gave written, informed consent. The PREVEND IT was approved by the local medical ethics committee and was conducted in accordance with the guidelines of the Declaration of Helsinki.

Laboratory Methods

Urinary albumin concentration was determined using nephelometry (BNII, Dade Behring). Plasma glucose, serum cholesterol, and serum creatinine were determined by Kodak Ektachem dry chemistry (Eastman Kodak). A validated assay was used to determine plasma renin activity.13 Urinary sodium and urea measurements were done with a MEGA clinical chemistry analyser (Merck). Sodium was determined by indirect potentiometry and urea by a photometric test with the urease-glutamate dehydrogenase method. Urinary albumin, sodium, and urea are given as the mean of two 24-hour collections. At baseline, before study medication was started, each subject collected 2 sets of two 24-hour urine samples. To avoid spurious associations between dependent and independent variables, urinary sodium and urea were determined in the first 2 collections, whereas urinary albumin concentration was determined in the last two 24-hour urine collections.

Definitions and Calculations

SBP and DBP measurements were calculated as the mean of the last 2 of 10 consecutive measurements with an automatic Dinamap XL model 9300 series device (Johnson-Johnson Medical Inc). Mean arterial pressure (MAP) was calculated as (1/3 × SBP + 2/3 × DBP). Renal function was estimated using the simplified Modification of Diet in Renal Disease formula: estimated glomerular filtration rate (mL/min/1.73 m²) = 186.3 × (serum creatinine)−1.154 × (age)−0.203 × (0.742 if female).14 Body mass index (BMI) was calculated as the ratio of weight and square of height (kilograms per meter squared). Protein intake was estimated using the method proposed by Maroni.15

Statistical Analysis

Baseline characteristics are given as mean ± SE. In case of a skewed distribution, the median (interquartile range) was used. Differences between groups were tested for continuous data by Student t test or a Mann–Whitney rank test in the case of skewed distribution. Differences in prevalence or incidence were tested with a χ² test. We initially used Pearson correlation coefficients to evaluate the relationship between UAE and other parameters at baseline. In case of a skewed distribution, values were log-transformed for an optimal residual analysis. To explore the association between UAE and patient characteristics in detail, stepwise backward multivariate linear regression analysis was used with UAE as the dependent variable. Which patient characteristics are associated with ACE inhibitor–induced changes in UAE after 3 months of treatment was studied using the same statistical methods. For these latter analyses, we corrected for assignment to pravastatin or placebo. To examine a possible nonlinear relationship between dependent and independent variables, we also entered quadratic terms of each of the independent variables into each model and these quadratic terms for statistical significance. Models were furthermore tested for interaction of independent variables by entering product terms into the regression equation. Interactions were considered significant if P < 0.10. All of the P values were 2-tailed. All of the analyses were performed using SPSS version 11.5 software.

Results

Population

Table 1 shows the mean baseline patient characteristics of the whole group and of both groups when stratified according to fosinopril use or placebo to which they were randomly assigned. Other than a significant difference in serum total cholesterol and low-density lipoprotein levels, no differences were found between the 2 groups that later during the study were to receive fosinopril or matching placebo. Of note, our population consisted of subjects that are assumed to be relatively healthy, as can be concluded from their average blood pressure (MAP: 94.6 ± 11.6 mm Hg), serum cholesterol level (5.87 ± 1.04 mmol/L), and the fact that only 2 patients had a medical history showing a myocardial infarction, 4 had a stroke, and 4 patients had peripheral vascular disease.
Subjects were excluded from participation in the PREVEND IT if they had known diabetes, hypertension, or hypercholesterolemia. For the latter 2 criteria, cutoffs were as defined in prevailing guidelines for Dutch general practitioners at the design of the study (see Methods section). However, when expressed as categories according to the present Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure classification, it seemed that, in our population, 138 patients were normotensive, 16.2% were found to be hypertensive.16 Of our patients, 16.2% were prehypertensive, and 123 patients seemed that, in our population, 138 patients were normotensive, 123 patients were hypertensive, and or hypercholesterolemia. For the latter 2 criteria, cutoffs were as defined in prevailing guidelines for Dutch general practitioners at the design of the study (see Methods section). However, when expressed as categories according to the present Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure classification, it seemed that, in our population, 138 patients were normotensive, 16.2% were found to be hypertensive.16 Of our patients, 16.2% were prehypertensive, and 123 patients were hypertensive.16

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*P<0.05 vs placebo.

Variables Associated With Baseline UAE

The results of the univariate and multivariate linear regression analyses are shown in Table 2. Only 3 baseline variables remained statistically significant in the multivariate model. MAP and urinary sodium excretion were positively associated with UAE (P=0.006 and 0.011, respectively), implying that higher baseline blood pressure and sodium intake are associated with higher levels of albuminuria. A negative association was found between estimated glomerular filtration rate and UAE (P=0.018). Of the other variables, BMI and CRP reached near statistical significance (P=0.076 and 0.077, respectively). Estimated protein intake (as well as urinary urea excretion) did not univariately affect baseline UAE but exhibited strong colinearity with urinary sodium excretion. Therefore, this term was removed from the multivariate model. Of note, when estimated protein intake (or urinary urea excretion) was forced into the definite multivariate model while deleting urinary sodium excretion, again no significant association was found between baseline estimated protein intake and UAE.

**TABLE 1. Baseline Characteristics of All Patients and of Patients Allocated to Placebo and Fosinopril Treatment**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total Group (n=384)</th>
<th>Fosinopril (n=192)</th>
<th>Placebo (n=192)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>51.1±11.5</td>
<td>50.9±11.7</td>
<td>51.3±11.3</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>252 (65.6)</td>
<td>128 (66.7)</td>
<td>124 (64.6)</td>
</tr>
<tr>
<td>White, %</td>
<td>369 (96.1)</td>
<td>179 (93.2)</td>
<td>190 (99.0)</td>
</tr>
<tr>
<td>Current smokers, %</td>
<td>123 (32.0)</td>
<td>65 (33.9)</td>
<td>58 (30.2)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.4±4.3</td>
<td>26.5±4.3</td>
<td>26.4±4.2</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>131.3±18.4</td>
<td>130.7±17.7</td>
<td>131.9±19.1</td>
</tr>
<tr>
<td>DBP</td>
<td>76.3±9.7</td>
<td>76.3±9.6</td>
<td>76.3±10.0</td>
</tr>
<tr>
<td>Lipids, mmol/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>5.87±1.04</td>
<td>5.98±1.06*</td>
<td>5.75±1.01</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>4.15±0.94</td>
<td>4.25±0.98*</td>
<td>4.05±0.90</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.03±0.31</td>
<td>1.01±0.32</td>
<td>1.05±0.29</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.55±1.06</td>
<td>1.60±1.01</td>
<td>1.50±1.11</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>90.3±14.0</td>
<td>91.4±14.3</td>
<td>89.2±13.6</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73 m²</td>
<td>94.3±23.3</td>
<td>93.2±23.7</td>
<td>95.4±22.9</td>
</tr>
<tr>
<td>UNa/24 hours, mmol/24 hours</td>
<td>155.0 (45.0 to 386.9)</td>
<td>157.5 (56.2 to 372.9)</td>
<td>154.9 (45.5 to 386.9)</td>
</tr>
<tr>
<td>UUrea/24 hours, mmol/24 hours</td>
<td>404.3 (144.2 to 739.5)</td>
<td>410.9 (144.2 to 739.5)</td>
<td>393.3 (173.4 to 727.9)</td>
</tr>
<tr>
<td>UAE</td>
<td>22.2 (2.8 to 251.6)</td>
<td>23.2 (3.5 to 251.6)</td>
<td>20.2 (2.8 to 237.62)</td>
</tr>
<tr>
<td>β-Blocking agent, %</td>
<td>1.6</td>
<td>0.5</td>
<td>2.6</td>
</tr>
<tr>
<td>Nitrate, %</td>
<td>0.5</td>
<td>1.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Diuretic, %</td>
<td>0.5</td>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>Digoxin, %</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Antiplatelet agent, %</td>
<td>1.8</td>
<td>1.0</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Values are shown as mean±SD or as percentage, when appropriate. UNa/24 hours, UUrea/24 hours, and UAE are shown as median (range). eGFR indicates estimated glomerular filtration rate; UNa/24 hours, 24-hour urinary sodium excretion; UUrea/24 hours, 24-hour urinary urea excretion; LDL, low-density lipoprotein; HDL, high-density lipoprotein. *P<0.05 vs placebo.
found, and no curved relationships between dependent and independent variables were identified.

UAE Reduction by ACE Inhibitor Relation With Blood Pressure

After 3 months of treatment, we observed a median UAE reduction of 18.5% in patients using fosinopril, whereas in patients assigned to placebo, a 6.1% increase was observed (P<0.001). In the placebo-treated patients, MAP decreased by −0.7 mm Hg, whereas with the ACE inhibitor, a decrease in MAP of −5.0 mm Hg was observed (P<0.001). Both fosinopril use (βstandardized = −0.185; P<0.001) and change in MAP after 3 months (βstandardized = 0.151; P=0.004) were independent predictors of change in UAE after bivariate linear regression analysis. Both remained significant after multivariate analysis, correcting for age and gender.

Baseline Predictors of Response to ACE Inhibitor

The results of the multivariate linear regression analysis are shown in Table 3. Both in univariate and multivariate regression analysis, baseline UAE seemed to be the only independent predictor of the change in UAE: the higher baseline albuminuria, the more the percentage decrease in UAE with ACE inhibition. Again, no significant interactions were found, and no curved associations were identified.

Discussion

In the present study, we demonstrate that in a nondiabetic population without renal disease, baseline UAE is associated with mean arterial blood pressure, renal function, and, interestingly, urinary sodium excretion. Furthermore, we found that ACE inhibition decreased UAE more than might be expected from blood pressure reduction alone and that higher baseline UAE predicted a more outspoken albuminuria lowering response to ACE inhibition.

UAE has been shown to be an early risk marker of cardiovascular morbidity and mortality18,19 and is thought to reflect widespread endothelial damage.6 For that reason, reduction of UAE may be interpreted as a recovery of endothelial function, which is in line with the observation that lowering UAE by blocking the renin–angiotensin system improves cardiovascular prognosis in high-risk patients.20 The PREVEND IT demonstrated that fosinopril reduced UAE effectively in microalbuminuric subjects.12 In addition, fosinopril treatment was associated with a trend in reducing cardiovascular events in this population. As biological covariates of UAE, it is not surprising to see MAP and baseline renal function arise as being independently associated with baseline UAE, because these factors are widely acknowledged to be causally related to UAE.21,22 Only a few studies have mentioned an association between UAE and sodium intake.23,24 This is an important finding, because urinary sodium excretion is a reflection of sodium intake, which is, of course, modifiable. The strength of this finding is the fact that urinary sodium excretion was calculated as the mean of 24-hour collections, and UAE was calculated as the mean of 2 different 24-hour collections. This excludes the possibility that the observed association between baseline UAE and urinary sodium excretion is spurious and based on artifacts in 24-hour urine collections.

In addition to identifying independent predictors of baseline UAE, we also demonstrate that the use of fosinopril and the change in MAP are independent predictors of the change in UAE after 3 months of treatment. This observation supports the view that blood pressure lowering obtained by intervention in the renin–angiotensin system has an additive albuminuria-lowering effect over reduction of blood pressure alone. The superior antiproteinuric effects of ACE inhibitors have been acknowledged for a long time. Only in diabetic patients and in patients with renal disease has this characteristic of
ACE inhibitors have been shown to be independent of blood pressure reduction.\textsuperscript{25–27} Our data suggest that in nondiabetic, nonrenal subjects, the antialbuminuric effect of blockade of the renin–angiotensin system cannot completely be attributed to the reduction in arterial blood pressure.

Other than these 2 important findings discussed so far, we also identified baseline UAE as the only independent predictor of the change in UAE after 3 months of fosinopril treatment. Before conclusions can be drawn, it is important to investigate whether the association that we found was biased. For instance, a similar association can be found in case regression to the mean plays a role. Subjects were included in case they had a baseline UAE $\geq 15$ mg per 24 hours. Because of applying a cutoff value, it is to be expected that during follow-up, on average, a decrease in UAE will take place, because of regression to the mean. We analyzed whether such bias may have played a role. In Figure A, we depicted changes in UAE at 3 months of follow-up separately for ACE inhibitor– and placebo-treated subjects, with these subjects divided into tertiles of baseline UAE. This figure shows that in placebo-treated subjects at higher levels of UAE, a reduction in UAE was observed. The reduction in ACE inhibitor-treated subjects was, however, more outspoken. Adding the changes induced by placebo and ACE inhibitor in each tertile of baseline UAE, thereby correcting for the placebo effect, indicates that at higher baseline UAE levels, ACE inhibition induces more reduction in albuminuria. In addition, a sensitivity analysis was conducted to evaluate the robustness of our findings and to eliminate the possibility of spurious associations because of urine collection errors. Therefore, we repeated the above analysis after exclusion of all of the subjects in whom 24-hour urinary creatinine excretions at baseline and after 3 months of treatment differed by $>20\%$. This analysis shows that the association between baseline UAE- and ACEi-induced changes in UAE remained (Figure 1B). This sensitivity analysis was done based on the assumption that the within-person day-to-day 24-hour creatinine excretion is nearly constant. Thus, our findings that subjects with higher baseline UAE will experience more benefit from fosinopril treatment seems quite robust and not spurious.

Interestingly, our data on a baseline UAE-dependent beneficial effect of ACE inhibitors seem in line with studies in different populations and with different outcome parameters. In patients with nondiabetic renal disease, it has been suggested that the extra renoprotective effect of ACE inhibitors over other blood pressure–lowering agents depends on baseline proteinuria.\textsuperscript{28} A post hoc analysis of the Heart Outcomes Prevention Evaluation Study, which was performed in subjects at high risk for cardiovascular disease, shows that the cardioprotective effect of ACE inhibition was larger in subjects with microalbuminuria compared with subjects without microalbuminuria, both with respect to absolute, as well as to relative, risk reduction.\textsuperscript{20,29} In analogy, Asselberg et al\textsuperscript{12} noted that in PREVEND IT, fosinopril reduced the incidence of cardiovascular events by 29\% (from 5.1\% to 3.6\%) in subjects with an albuminuria level below 50 mg per 24 hours but by 60\% in subjects with a higher albumin excretions. Our data, in combination with these data from the literature, suggest that ACE inhibition may confer a beneficial effect on renal and cardiovascular end points beyond the effect that may be expected from blood pressure lowering alone that depends on baseline albuminuria levels.

Importantly, baseline plasma renin activity was not associated with baseline UAE and did not predict the fosinopril-induced reduction in albuminuria independently. Thus, a patient with an activated circulating renin–angiotensin system does not necessarily have higher baseline UAE, nor does he experience a greater antialbuminuric reaction when using an ACE inhibitor. An association between plasma renin activity and UAE has been suggested previously in hypertensive patients,\textsuperscript{30} but our findings do not support the existence of such an association in a predominantly normotensive to prehypertensive population. In addition, we specifically questioned whether an interaction between sodium intake and activation of the RAS might play a role in the association between sodium intake and albuminuria. However, this was not the case.

The positive association between baseline UAE (divided into tertiles) and the change in UAE after 3 months of treatment with placebo (**) or fosinopril (**). Furthermore, the effect of fosinopril corrected for placebo is shown (**). The association between baseline UAE and change in UAE after 3 months of treatment was more obvious in fosinopril users than in subjects using placebo (A). To test the robustness of this observation, we repeated the analysis after exclusion of all subjects in whom urinary creatinine excretion in the 24-hour collections differed by $>20\%$ (B).
To appreciate the value of the current study, a few limitations need to be considered. First, our results should be interpreted with caution, because this is a post hoc analysis of prospective data. The data provided should, therefore, be regarded as only hypothesis generating. Second, biological variability in terms of within-subject variability of UAE remains an issue. The variation of this biological marker can be as high as 40%. Misclassification because of variability may have caused underestimation of some of the observed associations. Third, our results with respect to sodium intake should be seen in the context that the subjects under study remained on their usual diet. Whether the antialbuminuric response to ACEi might be augmented by coprescription of a salt-restricted diet can, therefore, not be excluded. Fourth, the PREVEND IT was performed in a predominantly white and normotensive-to-prehypertensive population. Whether our observations hold true for other populations, therefore, needs corroboration.

Perspectives

We found that mean arterial blood pressure, urinary sodium excretion, and low renin function are independently associated with UAE. Because albuminuria has been shown to be a strong risk marker for future cardiovascular events, we hypothesize that in nondiabetic, microalbuminuric patients without renal disease, reduction of sodium intake may be a sensible first approach. However, this hypothesis needs to be evaluated in prospective investigations.

Controversy exist as to whether ACE inhibitors in subjects without renal disease reduce UAE more than might be expected from their blood pressure–lowering action alone. Our analysis demonstrates that fosinopril reduces UAE, partially independent of its antihypertensive effects. The only baseline variable that independently predicts the antialbuminuric effect of fosinopril in this study was found to be baseline UAE. These latter findings have 2 consequences, when one takes into consideration that recent investigations demonstrated that a short-term change in albuminuria after initiation of blood pressure–lowering treatment predicts long-term cardiovascular outcome. On the one hand, it is reassuring, because it suggests that ACE inhibition will be cardioprotective in a broad population, irrespective of age, gender, or any other biological characteristic. On the other hand, these data suggest that ACE inhibition may result in superior cardiovascular protection when compared with other blood pressure–lowering agents in subjects with higher baseline levels of albuminuria. This intriguing hypothesis has to be tested, however, in prospective trials studying the cardioprotective effect of an ACE inhibitor compared with that of other blood pressure–lowering agents in which participating subjects are grouped into strata according to baseline albuminuria.

Conclusions

In nondiabetic patients without renal disease, the main predictors of baseline UAE are arterial blood pressure, renal function, and sodium intake. ACE inhibition effectively lowers UAE. This antialbuminuric effect is found to be more than may be expected from blood pressure lowering alone, especially in patients with higher baseline levels of albuminuria.

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Disclosures

None.

References


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