Reduction in Morning Blood Pressure Is a Key Factor for Ameliorating Urinary Albumin Excretion in Patients With Morning Hypertension Irrespective of Treatment Regimen

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Background: The Morning Hypertension and Angiotensin Receptor Blocker/Hydrochlorothiazide Combination Therapy (MAPPY) study has shown that losartan/hydrochlorothiazide (HCTZ) combination is superior to high-dose losartan in not only reducing morning systolic blood pressure (SBP) but also ameliorating urinary albumin excretion (UAE) after 3-month treatment. The purpose of the present study was to investigate factors associated with UAE reduction in on-treatment patients with morning hypertension.

Methods and Results: A total of 95 patients registered in the MAPPY study were analyzed. Patients were treated with either a losartan/HCTZ combination regimen (n=47) or a high-dose losartan regimen (n=48). Three-month treatment significantly reduced morning SBP, evening SBP, and clinic SBP ($P<0.001$, $P<0.05$, and $P<0.01$, respectively). UAE and serum uric acid were significantly decreased ($P<0.01$ for both) without the change in estimated glomerular filtration rate. Multiple linear regression analysis indicated that %morning SBP reduction and baseline UAE were independent determinants of the UAE reduction ($P=0.001$ for both). After adjustments for the reduction in morning-evening SBP difference, baseline UAE, and %uric acid reduction, estimated %UAE reduction level was positively correlated with the tertiles of the increasing %morning SBP reduction level ($P=0.031$ for trend). Moreover, subgroup analysis showed that morning SBP reduction was an independent determinant of UAE reduction in both treatment regimens.

Conclusions: Reduction in morning SBP was a key factor in UAE reduction in patients with morning hypertension, irrespective of treatment regimen. (*Circ J* 2013; **77**: 1551–1557)

Key Words: Albuminuria; Angiotensin II receptor blocker; Diuretics; Home blood pressure measurement; Morning hypertension

Recently, we conducted the Morning Hypertension and Angiotensin Receptor Blocker/Hydrochlorothiazide Combination Therapy (MAPPY) study to compare the efficacy of losartan/hydrochlorothiazide (HCTZ) combination and high-dose losartan in controlling morning hypertension.¹

In the MAPPY study, losartan/HCTZ combination was superior to high-dose losartan in the primary endpoint: morning systolic blood pressure (SBP) reduction after 3-month treatment. Unexpectedly, urinary albumin excretion (UAE) reduction, a secondary endpoint, was significantly greater in patients

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Table 1. Baseline Subject Characteristics and Demographics

Characteristics	
Combination regimen	47 (49.5)
Age (years)	69.5±10.2
Men	41 (43.6)
BMI	24.1±3.5
Morning SBP (mmHg)	149.9±7.9
Evening SBP (mmHg)	138.2±10.9
M-E difference (mmHg)	12.3±12.5
Clinic SBP (mmHg)	146.6±13.2
UACR (mg/g Cre) [†]	62.8 (40.9–84.7)
Uric acid (mg/dl)	5.67±1.56
eGFR (ml·min ⁻¹ ·1.73m ⁻²)	69.9±15.0
K (mmol/L)	4.34±0.40
LDL-C (mg/dl)	115.0±28.4
HDL-C (mg/dl)	59.0±14.8
Triglycerides (mg/dl) [†]	121.6 (110.1–133.1)
Hemoglobin A _{1c} (%)	5.57±0.60
BNP (pg/ml) [†]	47.4 (37.2–57.6)
Comorbidity	
Diabetes	17 (18.1)
Dyslipidemia	36 (48.4)
Coronary artery disease	14 (14.9)
Cerebrovascular disease	7 (7.4)
Smoking	13 (14.6)
Co-prescribed drug	
Ca channel blocker	33 (36.3)
α -blocker	5 (5.3)
β -blocker	14 (15.3)
Loop diuretics	1 (1.1)

Data given as n (%), mean±SD or geometric mean (95% confidence interval). [†]Natural logarithm-transformed data were used for statistical analysis. BMI, body mass index; BNP, B-type natriuretic peptide; Cre, creatinine; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; M-E difference, morning-evening SBP difference; SBP, systolic blood pressure; UACR, urine albumin/creatinine ratio.

receiving losartan/HCTZ combination than those receiving high-dose losartan. The original MAPPY study included some patients lacking one or more data point at the baseline and/or post-treatment assessment. The occurrence of missing data represents a potential source of bias in evaluating the relationship among UAE reduction, morning SBP reduction, and other factors. Accordingly, to investigate factors associated with UAE reduction, this subanalysis included only patients for whom complete data were available.

Methods

Study Setting

The MAPPY study (Clinical Trials Registration-Unique Identifier: NCT00795847) was a 3-month prospective, randomized, open-labeled, parallel-group, multicenter trial with blinded end-point assessment.¹ The institutional review boards or ethics committees of all participating institutions approved the study protocol. All patients gave written informed consent.

Subjects

The MAPPY study enrolled outpatients who had morning hypertension despite anti-hypertensive medications.¹ Morning hypertension was defined as morning SBP ≥135 mmHg, diastolic blood pressure (DBP) ≥85 mmHg, or both² on 7 different days during the 1-month run-in period. The exclusion criteria were as follows: secondary hypertension, malignant hypertension or uncontrolled hypertension (eg, DBP ≥120 mmHg), uncontrolled diabetes mellitus with HbA_{1c} ≥9.0%, a history of gout or serum uric acid ≥8.0 mg/dl, serum creatinine (Cre) ≥2.0 mg/dl, serum potassium (K) ≥5.5 mmol/L, liver damage (eg, ALT or γ -GTP level >3× the upper normal limit), use of a thiazide diuretic, use of an angiotensin II type I receptor blocker (ARB) or angiotensin-converting enzyme inhibitor (ACEI) exceeding the standard doses approved in Japan, and contraindications for thiazides or ARBs.

This subanalysis included only patients for whom complete data were available. Of 216 patients who were enrolled in the original MAPPY study, a total of 121 were excluded because the patients lacked data for one or more parameters, such as UAE and type B-natriuretic peptide (BNP), at the baseline and/or post-treatment assessment. Accordingly, 95 patients were enrolled in this study.

Study Protocol

The study protocol has been described elsewhere.¹ Briefly, an anti-hypertensive drug was randomly switched to a 50-mg losartan/12.5-mg HCTZ combination tablet (combination regimen) or 100-mg losartan (high-dose regimen) without wash-out period. If patients had been given an ARB or ACEI, the ARB or ACEI was switched to losartan/HCTZ combination or 100-mg losartan. If an ARB or ACEI had not been prescribed, one of the prescribed anti-hypertensives was changed to either of the test drugs. The prescription of anti-hypertensive agents was not changed during the 3-month treatment.

Data Collection and Measurement

The initial evaluation and laboratory tests were performed after written informed consent was obtained. Patients were instructed to perform home blood pressure (BP) self-measurement in the early morning (within 1 h after waking up, after urination, before dosing in the morning, before breakfast, after 1–2-min resting in a sitting position) and in the evening (before bedtime, after 1–2-min resting in a sitting position) every day, according to the Japanese Society of Hypertension Guidelines for the Management of Hypertension 2009 (JSH2009 guidelines).² The first measurement taken each morning and evening were recorded.² The measurements for the last 7 days preceding each clinic visit were averaged for the morning and evening BP. Cuff oscillometry was applied using electronic upper arm-cuff devices. The device type was unknown, but it was certificated that all devices conformed to the Association for the Advancement of Medical Instrumentation standards. Each patient used the same type of home BP monitoring device throughout the study. Clinic BP was recorded at each hospital visit using the sphygmomanometer after 5 min resting in a seated position at 1–2-min intervals. At least 2 measurements were averaged for the clinic BP measurement.² The sum of morning SBP reduction and evening SBP reduction was defined as a parameter of the effects of all-day SBP reduction. Morning-evening SBP (M-E) difference was calculated by subtracting evening SBP from morning SBP.

Circulating biochemistry and UAE were measured in the morning in a fasting state at baseline and after 3 months of treatment. All assays were performed using commercially avail-

Figure 1. (A) Effects of the 3-month treatment on systolic blood pressure (SBP). (B) Effects of the 3-month treatment on urine albumin/creatinine ratio (UACR), serum uric acid, and estimated glomerular filtration rate (eGFR). (◇) Baseline; (◆) after treatment. (A,C,D) Bars, 1 SD; (B) bars, 95% confidence interval. * $P<0.05$, ** $P<0.01$, and *** $P<0.001$ vs. baseline (paired Student's *t*-test).

able laboratory. Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault equation modified for Japanese.² UAE level was determined from a spot urine sample and expressed as urine albumin/Cr ratio (UACR; mg/g Cr).³

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 18.0J (IBM Japan). Data are expressed as mean $\pm$ SD. Because of skewed distributions, geometric mean (95% confidence interval [95% CI]) was used and natural logarithmic transformation was performed for baseline UACR, triglycerides, and BNP. Natural logarithm-transformed data were used for statistical analysis and then reconverted to anti-logarithm. Simple linear regression analysis was performed to investigate the relationships between %UACR reduction and each of the following continuous variables: baseline levels and %reductions of morning SBP, evening SBP, clinic SBP, morning SBP reduction + evening SBP reduction, M-E difference reduction; age, body mass index; baseline UACR; baseline level and %reduction of uric acid; and baseline level and %change of K, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, HbA_{1c}, and BNP. Categorical variables were converted to dummy variables before the analysis. Two-sample *t*-test with equal variance or Welch's *t*-test with possible unequal variance was used to assess the association between %UACR reduction and each of

the categorical variables: treatment (combination regimen), male gender, diabetes, dyslipidemia, coronary artery disease, cerebrovascular disease, and ARB/ACEI use during the run-in period; Ca channel blocker use, β -blocker use, and α -blocker use during the treatment period. Multiple linear regression analysis was performed using the significant variables. Differences for tertiles were evaluated using 1-way ANOVA for continuous variables and chi-square test for categorical variables. Analysis of covariance followed by post-hoc analysis was used to compare estimated %UACR reduction according to tertiles of increasing %morning SBP reduction. $P<0.05$ was considered statistically significant.

Results

Baseline Characteristics and Demographics

This study included 95 patients (41 men; mean age, 69.5 ± 10.2 years) with morning hypertension based on home BP self-measurement (Table 1). At baseline, morning SBP, evening SBP, and clinic SBP were 149.9 ± 7.9 mmHg, 138.2 ± 10.9 mmHg, and 146.6 ± 13.2 mmHg, respectively. Baseline UACR was 62.8 mg/g Cr (95% CI: 40.9 – 84.7 mg/g Cr), and UACR was <300 mg/g Cr (ie, microalbuminuria), in most subjects (94.8%).

Anti-Hypertensive Treatment and Biochemical Parameters

During the run-in period, an ARB or an ACEI was used in 93.7% of the study patients (data not shown). During the

Table 2. Linear Regression Analysis for %UACR Reduction

	Simple		Multiple	
	β	P-value	β	P-value
Baseline UACR [†]	0.300	0.003	0.341	0.001
Morning SBP				
Baseline	−0.056	0.597	—	—
% Reduction	0.335	0.002	0.353	0.001
Evening SBP				
Baseline	−0.054	0.632	—	—
% Reduction	0.093	0.441	—	—
Morning SBP reduction+evening SBP reduction [‡]	0.289	0.025	—	—
M-E difference reduction	0.207	0.112	—	—
Clinic SBP				
Baseline	−0.062	0.579	—	—
% Reduction	0.073	0.482	—	—
% Uric acid reduction	−0.267	0.010	−0.224	0.079
R ² =0.302				

[†]Natural logarithm-transformed data were used for statistical analysis because of skewed distribution. [‡]Omitted from multiple regression analysis because this variable was co-linear with % morning SBP reduction. Abbreviations as in Table 1.

3-month treatment, 49.5% of the patients were treated with the combination regimen (Table 1). Ca channel blocker, β -blocker, α -blocker, and loop diuretics were co-prescribed in 37.9%, 15.3%, 5.3%, and 1.1%, respectively, during the treatment period.

Effects on Home and Clinic BP, UAE, and Biochemical Parameters

The 3-month treatment with the combination regimen or high-dose regimen significantly reduced morning SBP, evening SBP, and clinic SBP ($P<0.001$, $P<0.05$, and $P<0.01$, respectively; Figure 1A). UACR and serum uric acid were significantly reduced after the 3-month treatment ($P<0.01$ for both; Figures 1B,C). There were no differences in eGFR level (Figure 1D) and other parameters, such as M-E difference, HbA_{1c}, lipids, and BNP, between the baseline and post-treatment assessments (data not shown).

Significant Factors for UAE Reduction

To determine the factors associated with UAE reduction, simple linear regression analysis was performed for continuous variables. A significant relationship was found between %UACR reduction and %morning SBP reduction, morning SBP reduction+evening SBP reduction, baseline UACR, or %uric acid reduction (negatively), whereas %UACR reduction did not have a significant correlation with %evening SBP reduction, M-E difference reduction, %clinic SBP reduction, and other variables (Table 2). In categorical variables, only the combination regimen produced a significant difference in UAE reduction ($P=0.016$).

Multiple linear regression analysis using %morning SBP reduction, baseline UACR, and %uric acid reduction as variables showed that baseline UACR and %morning SBP reduction were independent determinants of %UACR reduction ($P=0.001$ for both; Table 2).

Morning SBP Reduction and UAE Reduction

To investigate correlation between morning SBP reduction and UAE reduction, we divided the patients into tertiles of increasing %morning SBP reduction level (Table 3). There

were significant differences in combination regimen, morning SBP reduction+evening SBP reduction, M-E difference reduction, %UACR reduction, and %uric acid reduction among the tertiles ($P<0.001$, $P<0.001$, $P<0.001$, $P=0.001$, and $P=0.001$, respectively). After adjustments for M-E difference reduction and %uric acid reduction as covariates (model 1), estimated %UACR reduction was significantly correlated with %morning SBP reduction (Figure 2A). Estimated %UACR reduction was greater in the highest tertile than in the lowest tertile ($P<0.05$). Similar results were obtained even when baseline UACR was added into the covariates (model 2; Figure 2B).

Effect of Treatment Regimen on UAE Reduction

To investigate the effects of the difference in anti-hypertensive regimens on UAE reduction, subgroup analysis stratified by treatment regimen was performed. The combination regimen produced greater %morning SBP reduction, greater morning SBP reduction+evening SBP reduction, and greater %UACR reduction, as compared with the high-dose regimen ($P<0.001$, $P<0.01$, and $P<0.05$, respectively). In contrast, the high-dose regimen produced greater %uric acid reduction ($P<0.001$). Multiple linear regression analysis showed that baseline UACR and %morning SBP reduction were independent determinants of %UACR reduction in both subgroups (Table 4).

Discussion

Morning hypertension is an independent risk for cardiovascular events, such as stroke and myocardial infarction.^{4–8} On home BP self-measurement, morning hypertension was observed in >60% of patients receiving anti-hypertensive drugs.⁹ It was suggested that the reduction in morning SBP reduced UAE and improved renal function in patients with diabetic and non-diabetic nephropathy.^{10,11} Standard treatment for morning hypertension, however, has not been established. An ARB/HCTZ combination has complementary mechanisms of action leading to enhanced BP reduction,¹² whereas high-dose ARB exhibits cardiovascular and renal protective effects.¹³ Both treatments are well tolerated in hypertensive patients.¹⁴ Thus, we conducted the MAPPY study to compare the effi-

Table 3. Baseline Characteristics vs. Increasing %Morning SBP Reduction

	T1 (≤6.1%)	T2 (6.2–12.9%)	T3 (≥13.0%)	P-value
n	32	31	32	—
Combination regimen	6 (18.8)	20 (64.5)	21 (65.6)	0.000
Age (years)	67.8±10.7	71.2±11.5	68.7±8.1	0.461
Men	13 (40.6)	18 (58.1)	13 (40.6)	0.230
BMI	24.1±2.9	23.6±3.4	24.7±4.1	0.577
Morning SBP				
Baseline (mmHg)	150.1±9.3	149.2±6.8	150.5±7.5	0.821
Evening SBP				
Baseline (mmHg)	138.5±9.9	136.9±11.7	137.7±11.6	0.884
% Reduction	4.4±8.3	8.8±7.4	10.0±9.9	0.096
Morning SBP reduction+evening SBP reduction (mmHg)	4.2±12.3	26.4±9.0	39.6±14.6	0.000
M-E difference				
Baseline (mmHg)	12.9±12.5	11.8±12.0	12.1±13.4	0.848
Reduction (mmHg)	−8.3±13.7	1.5±8.9	11.2±14.3	0.000
Clinic SBP				
Baseline (mmHg)	147.1±13.2	147.8±12.9	146.3±13.4	0.915
% Reduction	7.2±11.0	11.4±9.8	6.1±10.4	0.148
UACR				
Baseline (mg/g Cre) [†]	75.5 (30.9–120.1)	64.3 (28.6–116.2)	48.6 (25.4–62.8)	0.194
% Reduction	−30.9±70.2	12.8±60.2	28.1±48.8	0.001
Uric acid				
Baseline (mg/dl)	5.64±1.53	5.71±1.60	5.18±1.02	0.316
% Reduction	15.2±17.7	−3.5±20.9	−2.1±22.8	0.001
eGFR (mL·min ^{−1} ·1.73 m ^{−2})	70.2±17.8	68.7±15.9	70.7±11.5	0.879
K (mmol/L)	4.3±0.5	4.4±0.5	4.4±0.5	0.496
LDL-C (mg/dl)	116.6±33.6	113.7±25.1	116.5±27.9	0.919
HDL-C (mg/dl)	59.1±18.6	60.4±12.0	59.2±15.0	0.947
Triglycerides (mg/dl) [†]	146.3 (120.9–171.7)	103.1 (84.7–121.6)	120.9 (103.5–138.3)	0.140
Hemoglobin A _{1c} (%)	5.5±0.6	5.5±0.6	5.7±0.6	0.227
BNP (pg/ml) [†]	45.4 (29.1–61.8)	53.2 (31.1–75.3)	45.3 (28.3–62.3)	0.784
Comorbidity				
Diabetes	4 (12.5)	6 (19.4)	7 (21.9)	0.542
Dyslipidemia	16 (50.0)	7 (22.6)	13 (40.6)	0.055
Coronary artery disease	6 (18.8)	4 (12.9)	4 (12.5)	0.558
Cerebrovascular disease	3 (9.4)	1 (3.2)	3 (9.4)	0.827
Smoking	6 (18.8)	3 (9.7)	4 (12.5)	0.159
Co-prescribed drug				
Ca channel blocker	11 (34.3)	10 (32.2)	12 (37.5)	0.899
α-blocker	3 (9.4)	2 (6.5)	5 (15.6)	0.229
β-blocker	12 (37.5)	7 (22.6)	10 (31.3)	0.594
Loop diuretics	0 (0.0)	1 (0.3)	0 (0.0)	0.363

Data given as n (%), mean ± SD or geometric mean (95% confidence interval). [†]Natural logarithm-transformed data were used for statistical analysis. Abbreviations as in Table 1.

cacy of these treatments in patients with morning hypertension.¹ The MAPPY study has shown that a losartan/HCTZ combination induces a greater morning SBP reduction, the primary endpoint, than high-dose losartan (−18 mmHg vs. −8 mmHg, $P<0.001$). With regard to the secondary endpoints, the combination regimen decreased UAE ($P<0.05$), whereas the high-dose regimen lowered serum uric acid ($P<0.001$). Either treatment did not change eGFR. Accordingly, we investigated the factors associated with the reduction in UAE, a surrogate marker of cardiovascular events, in patients with morning hypertension.

The most important finding of this study was that the reduc-

tion in morning SBP and baseline UACR were independent determinants of UAE reduction in patients with morning hypertension (Table 2). This observation was consistent with a previous study showing that morning BP was a stronger predictor for UAE than clinic BP.¹⁵ It is interesting to note that morning SBP reduction was significantly correlated with UAE reduction even after adjustment for baseline UACR and other confounding factors (Figure 2). Moreover, the subgroup analysis showed that morning SBP reduction is an independent determinant of UAE reduction in both the combination regimen and high-dose regimen. Thus, it is suggested that morning SBP reduction is important for UAE reduction, irrespec-

Figure 2. Estimated urine albumin/creatinine ratio (UACR) reduction vs. tertiles of increasing %morning systolic blood pressure (SBP) reduction. **(A)** Model 1 was adjusted for morning-evening SBP (M-E) difference reduction and %uric acid reduction as covariates. **(B)** Model 2 was adjusted for M-E difference reduction, %uric acid reduction, and baseline UACR as covariates. Tertile (T) 1, %morning SBP reduction ≤6.1%; T2, 6.2–12.9%; T3, ≥13.0%. Bars, 95% confidence interval. * $P < 0.05$ vs. T1 (analysis of covariance followed by Bonferroni test). Because of skewed distributions, the natural logarithm-transformed baseline UACR data were used for statistical analysis and then reconverted to anti-logarithm.

Table 4. Linear Regression Analysis for %UACR Reduction vs. Treatment Regimen

	Combination regimen (n=47)				High-dose regimen (n=48)			
	Simple regression		Multiple regression		Simple regression		Multiple regression	
	β	P-value	β	P-value	β	P-value	β	P-value
Baseline UACR†	0.400	0.005	0.383	0.006	0.321	0.026	0.346	0.022
Morning SBP								
Baseline	-0.300	0.088			0.203	0.176		
% Reduction	0.433	0.005	0.440	0.002	0.298	0.040	0.297	0.048
Evening SBP								
Baseline	-0.172	0.275			0.085	0.601		
% Reduction	0.138	0.436			0.241	0.150		
Morning SBP reduction+evening SBP reduction	0.152	0.440			0.275	0.127		
M-E difference								
Baseline	-0.031	0.851			0.018	0.917		
Reduction	-0.355	0.064			0.031	0.865		
Clinic SBP								
Baseline	-0.102	0.496			-0.228	0.119		
% Reduction	0.073	0.625			0.080	0.587		
				$R^2=0.335$				
								$R^2=0.187$

†Natural logarithm-transformed data were used for statistical analysis because of skewed distribution. Abbreviations as in Table 1.

tive of treatment regimen.

We have to consider other factors. The use of diuretics might be a possible factor affecting UAE change, because diuretics deplete the circulating volume and decrease renal blood flow, which may reduce glomerular filtration. This, however, was not the case in the present study, because eGFR was not changed during the 3-month treatment (**Figure 1D**).¹ The present findings may be pertinent from the point of view that UAE not only reflects early renal damage, but is also a marker of endo-

thelial dysfunction.¹⁶ Moreover, increased UAE level, even within the normal range, is a surrogate marker of cardiovascular events in both hypertensive patients and apparently healthy subjects.^{17,18}

Morning SBP reduction+evening SBP reduction was significantly associated with %morning SBP reduction on the basis of simple linear regression analysis (**Table 2**) and was significantly different among the tertiles of increasing %morning SBP reduction (**Table 3**). Because morning SBP reduction+

evening SBP was co-linear with %morning SBP reduction, this variable was omitted from multiple regression analysis in **Table 2** and from adjustment of %UACR reduction in **Figure 2**. Also, there was a significant difference in %uric acid reduction between the high-dose and combination regimens: the high-dose regimen, but not the combination regimen, decreased uric acid (%uric acid reduction, $14.1 \pm 17.4\%$ vs. $-7.5 \pm 18.8\%$, respectively; $P < 0.001$), suggesting that %uric acid reduction was associated with anti-hypertensive regimen. This might be related to the fact that losartan has a dose-dependent effect on the renal uric acid transporter-1 inhibition to reduce uric acid level.¹⁹ Thus, we used %uric acid reduction, but not combination regimen, as a significant variable for multiple linear regression analysis (**Table 2**) and a covariate for adjusting %UACR reduction (**Figure 2**).

This study has several limitations. The number of patients studied was small. Because this study was a subanalysis of the MAPPY study, the balance of treatment regimen was not matched among the tertiles of %morning SBP reduction. Next, care must be taken in interpreting the results of the subanalysis stratified by treatment regimen. The size of each subgroup was substantially small and the statistical power was not sufficient. Finally, the combination of ARB and Ca channel blocker is another alternative option for treatment of morning hypertension.²⁰ Future studies should compare the effects on morning SBP and UAE between ARB/HCTZ combination and ARB/Ca channel blocker combination.

Conclusions

Reduction in morning SBP was an independent determinant of UAE reduction in patients with morning hypertension. Thus, it is suggested that UAE reduction by morning BP reduction would be important for renal and cardiovascular protection in patients with morning hypertension.

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Disclosures

None.

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