Changes of Microalbuminuria in Nondiabetic Hypertensive Patients after One Year Follow-Up

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Objective: *The purposes of the present study are to determine the effect of one year usual care of nondiabetic hypertensive patients (non-DM HT patients) at the Hypertension clinic to find conversion rate of MAU to NAU and occurrence rate of NAU to MAU. In addition, to identify factors which affect the regression of MAU to NAU.*
Material and Method: *The present Cohort Study was carried out from February to June 2007, at the Out-patient Department, Siriraj Hospital. Two thirds of those hypertensive patients who underwent MAU detection in the previous study were asked to collect morning urine. They did not have DM or impaired fasting glucose (FPG 100-125 mg/dl), chronic kidney disease (Cr. > 1.5 mg/dl) and leukocyturia (wbc > 5 cells/HPF). MAU was again tested by using Microalbustix test®. They were also asked to answer a short predefined questionnaire used in the previous study and have their BP's measured once after 5 minute rest, including abdominal circumference and body weight.*
Results: *A total of 334 non-DM HT patients, 112 male, were enrolled in the present study. Three of them were excluded due to leukocyturia. After one year, 55 cases out of 69 MAU patients (79.7%) became NAU (p-value < 0.001) and 16 cases out of 262 NAU patients (6.1%) developed MAU (p-value < 0.001).*
Conclusion: *The conversion rate of MAU to NAU was 79.7% and the occurrence rate of MAU from NAU was 6.1%. Annual MAU check up as a continuous monitoring should be carried out in every non-DM HT patients.*

Keywords: *Microalbuminuria, Nondiabetic hypertension*

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Microalbuminuria (MAU) is recognized to be an independent risk factors of renal and cardiovascular diseases both in diabetic patients with or without hypertension (HT) and nondiabetic hypertensive patients (non-DM HT patients)[1-4]. The detection of MAU was recommended in every newly diagnosed diabetes mellitus (DM) because of the high prevalence and being an independent cardiovascular risk[5]. However, there were not many studies on MAU in non-DM HT patients. Recently, a study of MAU in non-DM HT patients without chronic kidney disease (CKD) was carried out in the Division of Hypertension, Department of Medicine, Siriraj Hospital. It was found that the prevalence of MAU and macro-albuminuria (MacAU) were 18.6% and 2.2% respectively[6]. Followings these patients after one year of treatment is performed to observe the changes of those MAU and normoalbuminuria (NAU) group.

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Objective

The purposes of the present study are to determine the effect of one year treatment on MAU conversion to NAU (MAU conversion group) and occurrence rate of NAU to MAU (NAU conversion group) in this group of non-DM HT patients at the Hypertension clinic. In the meantime, the authors wish to identify factors associated with the regression of MAU to NAU. In addition, the authors may find out whether annual MAU check up is needed in every non-DM HT patient.

Material and Method

Study Design

The first cross-sectional study was carried

out from February to March 2006. Non-DM HT patients of both sexes, aged >18 years, attended at Hypertension clinic, the Outpatient Department, Siriraj Hospital were recruited. The major inclusion criteria were those with non-DM HT patients who were already receiving antihypertensive medication. The present study excluded those with impaired fasting glucose (IFG) which fasting plasma glucose (FPG) $\geq$ 100 and < 126 mg/dl, T2DM, CKD which serum creatinine (serum Cr) > 1.5 mg/dl, leukocyturia (wbc > 5/HPF), fever and heavy exercise. Medical records were carefully reviewed whether they had been tested for proteinuria. If their previous urinalysis showed no proteinuria or minimal proteinuria (trace), they were enrolled. After verbal consents were given, each individual eligible volunteer was asked to collect a morning urine sample from home. When they returned with urine samples, questionnaires about their demographic data, smoking status, current medical illnesses, including those of their family and personal history of HT and cardiovascular diseases were filled in by a well trained interviewer. The duration and the onset of HT were also obtained. Simultaneously, the recent lipemic and blood pressure (BP) control including drug treatments for both conditions were also recorded. Every patient was asked to rest in sitting position for 5 minutes before sitting BP was measured with a calibrated digital automatic BP monitor, OMRON® model: HEM-907. Participants were also examined for weight, height and waist circumferences. Body mass index (BMI) was calculated by weight (kg)/height $(m)^2$. Cigarette smoking and coffee drinking were prohibited for at least 30 minutes before BP measurements. To determine urine albumin excretion (UAE), freshly voided morning urine had to be sent to the laboratory room within 2 hours. Collected urine samples were initially tested for MacAU by using Multistix test® (Bayer HealthCare LLC, USA) and for MAU by using Microalbustix test® (Bayer HealthCare LLC, USA). Subjects were then divided into 3 groups: NAU (negative Multistix test® plus negative Microalbustix test®), MAU (negative Multistix test® plus positive Microalbustix test®) and MacAU (positive Multistix test®). Renal function, calculated creatinine clearance (CCr), was evaluated with the Cockroft-Gault formula and adjusted for body surface area (BSA)[7,8]. The present study designs and results were reported elsewhere[6].

All patients were given usual care which included lifestyle modification advice and antihypertensive drugs. Those who had MAU were treated by adding or substituting an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB). Low doses of ACEI/ARB were initiated among those who were not given those before. In the meantime, higher doses were given if ACEI/ARB was already given or the same doses were maintained.

The authors prospectively investigated the changes of MAU. All of the studied patients were approached and the authors convinced as many as the authors could to participate the second study, which is a follow-up study. It was carried out from February to June 2007 using the same method as the first study. The present study was started after permission was granted by the Ethics Committee of the hospital. Every patient has to give an inform consent before enrollment.

Adequacy of BP control was defined according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, the JNC 7 Report[9]. Metabolic syndrome was defined according to the International Diabetes Federation consensus worldwide definition of metabolic syndrome (IDF 2005 guidelines)[10]. Hyperlipidemia and the adequacy of lipemic control were defined according to the Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (ATP-III)[11]. Obesity and overweight were defined according to the WHO Guidelines[12].

Modifications of patients' characteristics were searched for *i.e.* changes in BMI, waist circumference (WC), systolic blood pressure (SBP) level, diastolic blood pressure (DBP) level from the previous study. Changes of biochemical findings were also noted, *i.e.*, decreases in levels of fasting plasma glucose (FPG), serum creatinine (Cr), adjusted creatinine clearance (CCr), serum total cholesterol (chol), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C).

Statistical analyses

Results were demonstrated as mean $\pm$ standard deviation (SD) or percent (%) where appropriate. Statistical analyses were performed using Statistical Packages for Social Sciences (SPSS 9.0). Student's t-test and Chi-square test were used to compare the continuous and categorical data between the NAU and MAU, respectively. A p-value of less than 0.05 was considered statistically significant.

Results

Out of 505 non-DM HT patients from the

previous study, 334 patients (66.1%) agreed to participate the present study. Three patients were excluded due to leukocyturia (wbc > 5 cells/HPF). Therefore, 331 non-DM HT patients (aged 59.5 ± 10.0 years, range 27-82 years); 262 cases with NAU (aged 59.0 ± 9.9 years) and 69 cases with MAU (aged 61.2 ± 10.6 years) (p = 0.11) could be recruited. Of the 69 non-DM HT patients with MAU, 38 females and 31 males, were enrolled. They had the mean BMI of 26.4 ± 3.8 kg/m^2 (range 18.5-35.9 kg/m^2), 25.2 ± 2.7 kg/m^2 in males and 27.3 ± 4.4 kg/m^2 in females. The rest, 262 cases, were the non-DM HT patients with NAU, 181 females and 81 males, were enrolled. They had the mean BMI of 26.8 ± 4.1 kg/m^2 (range 17.5-40.3 kg/m^2), 27.4 ± 4.5 kg/m^2 in males and 26.5 ± 3.9 kg/m^2 in females.

After a year of follow-up (range 12-17 months), there were 55 non-DM HT patients out of 69 cases (79.7%) who initially had MAU became NAU (MAU conversion group) and 14 cases still had MAU (MAU persistent group). There were 16 cases out of 262 nondiabetic HT patients (6.1%) who were initially NAU developed MAU (NAU conversion group) and 246 cases still had NAU (NAU persistent group). There was a significant higher in number of participants in the MAU conversion group as compared to that of the MAU persistent group (p < 0.001). The number of participants in the NAU persistent group was also significantly higher than that of the NAU conversion group (p < 0.001). No patient with MAU became MacAU and DM. Records of the family history of cerebrovascular disease (CVD), coronary artery disease (CAD), HT, CKD, DM, including patients' history of the metabolic syndrome (MS), CAD, CVD and congestive heart failure (CHF) did not change when compared those MAU conversion group with those of the MAU persistent group (data not shown).

In comparative studies between MAU persistent group and those MAU conversion group, there were no significant differences in the baseline characteristics of age, number of female, duration of hypertension, SBP and DBP levels (Table 1). However, there was a higher BMI (p = 0.04) and a trend to find a higher WC (p = 0.06) among those MAU persistent group as compared to those of the MAU conversion group. When compared those NAU persistent group with those NAU conversion group, no differences of all parameters mentioned above were found (Table 2).

In addition, there were no significant differences in the medical records of smoking and MS between NAU persistent group and NAU conversion group. According to personal history, there were only 2 cases of CVD in each group. There were 3 cases of CAD and 3 cases of CHF in the NAU persistent group but there were none in the NAU conversion group. There were no significant differences in the levels of FPG, serum Cr, adjusted CCr, Chol, TG, HDL-C, LDL-C, and antihypertensive drug regimens between the two groups (data not shown).

After one-year medical intervention, it is interesting to note whether changes of the patients' characteristics had any influences on MAU conversion to NAU. There were no significant differences from baseline in the patients' BMI, WC, but there was a significant ΔSBP level in both MAU conversion group and MAU persistent groups and ΔDBP level in MAU persistent group only (Table 3). However, there were no significant differences on number of cases who had a reduction in these parameters between

Table 1. Clinical characteristics of those non-DM HT patients with MAU conversion and those with MAU persistence

Parameter	Mean ± SD or n (%)		p-value
	MAU conversion group (n = 55)	MAU persistent group (n = 14)	
Age (years)	62.2 ± 9.5	57.6 ± 13.9	0.15
Female	32 (58.2)	6 (42.9)	0.30
Duration of HT (years)	8.2 ± 5.0	9.9 ± 4.6	0.36
BMI (kg/m^2)	25.9 ± 3.8	28.3 ± 3.5	0.04*
Waist circumference (cm)	86.0 ± 13.4	93.1 ± 8.7	0.07
SBP (mmHg)	123.2 ± 12.1	127.1 ± 13.2	0.29
DBP (mmHg)	70.9 ± 8.0	74.6 ± 7.9	0.13

MAU = microalbuminuria, n = number, HT = hypertension, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, BP = blood pressure, *p-value considered significant at < 0.05

Table 2. Clinical characteristics of non-DM HT patients with persistent NAU and those with NAU conversion

Parameter	Mean ± SD or n (%)		p-value
	NAU persistent group (n = 246)	NAU conversion group (n = 16)	
Age (years)	57.9 ± 9.9	59.7 ± 8.6	0.65
Female	168 (68.3)	13 (81.3)	0.21
Duration of HT (years)	6.6 ± 5.1	7.1 ± 4.0	0.45
BMI (kg/m^2)	26.5 ± 4.1	26.7 ± 3.5	0.76
Waist circumference (cm)	87.4 ± 10.7	86.6 ± 7.8	0.21
SBP (mmHg)	128.7 ± 12.4	124.6 ± 19.6	0.22
DBP (mmHg)	74.7 ± 9.0	71.4 ± 10.4	0.15

NAU = microalbuminuria, n = number, HT = hypertension, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, BP = blood pressure, *p-value considered significant at < 0.05

Table 3. Changes of patients' characteristics of non-DM HT patients with MAU conversion and those with MAU persistence

Parameter	Mean ± SD or n (%)		p-value
	MAU conversion group (n = 55)	MAU persistent group (n = 14)	
ΔBMI level (kg/m^2)	-0.07 ± 0.83	-0.39 ± 0.86	0.21
Decrease in BMI	30 (54.5)	4 (28.6)	0.09
Δwaist circumference (cm)	1.32 ± 10.04	-0.81 ± 2.32	0.44
Decrease in waist circumference	23 (41.8)	3 (21.4)	0.16
ΔSBP level (mm Hg)	6.0 ± 15.0**	8.7 ± 14.7**	0.55
Decrease in SBP level	31 (56.4)	11 (78.6)	0.13
ΔDBP level (mm Hg)	1.5 ± 10.5	4.9 ± 8.4***	0.27
Decrease in DBP level	30 (54.5)	10 (71.4)	0.25
Uncontrolled BP ≥ 140/90 mm Hg	6 (10.9)	1 (7.1)	0.56
BP ≥ 135/85 mm Hg	12 (21.8)	7 (50.0)	0.04*

MAU = microalbuminuria, BP = blood pressure, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, HT = hypertension, Δ = value of this study-value of previous study, n = number of patient, *p < 0.05, independent sample t-test, compared between MAU conversion and MAU persistent groups, **p < 0.05, Paired sample t-test, compared between the first and the last BP level within studied group, ***p = 0.05, Paired sample t-test, compared between the first and the last BP level within studied group

groups as well, except the number of cases who could not control BP < 135/85 mmHg was significantly higher in MAU persistent group than those MAU conversion group (p = 0.04). There were no differences in the changes of the levels of FPG, chol, TG and HDL, serum Cr, adjusted CCr from baseline and when compared between MAU conversion group and MAU persistent group as well (data not shown).

Comparative study was carried out between last year (baseline) parameters and those found in the present study among NAU persistent group and NAU conversion group. There were also no significant differences in the patients' BMI, WC, but there were significant lower SBP (128.7 ± 12.4 vs. 123.8 ± 11.5 mm Hg; p < 0.01) and lower DBP (74.7 ± 9.0 vs. 71.0 ± 8.6 mm Hg, p < 0.01) from baseline only in NAU persistent group (data not shown).

When comparing those parameters between NAU persistent group and NAU conversion group, there was a trend in ΔSBP level *i.e.* lower SBP level in

the former than the latter (-4.9 ± 13.9 vs. 1.8 ±12.9 mm Hg; p = 0.07) (Table 4). Moreover, a significantly lower number of cases had a decrease SBP level in the former than in the latter (62.6 vs. 31.3%, p = 0.01, OR = 0.27, 95% CI = 0.1-0.8). Last year (baseline) BP controlled rate were 78.8% (< 140/90 mmHg) and 60.6% (< 135/85 mmHg). After one year, BP controlled rate were 87.7% and 76.7%, respectively.

However, there was a significant difference in the changes of antihypertensive regimen found between the MAU conversion group and the MAU persistent group (Table 5). Those who stopped using of β-blocker (61.8 vs. 9.1%, p = 0.002, OR = 16.2, 95%CI = 1.9-141.3) and those who had been prescribed with angiotensin receptor blocker (ARB) (58.7 vs. 23.1%, p = 0.02, OR = 4.7, 95%CI = 1.2-19.6) during the follow-up were noted. Also, there was a lesser decline in the estimated glomerular filtration rate (GFR) among those who stopped using β-blocker compared to those who continue using it (2.8 ± 6.2 vs. 13.7 ± 21.5 ml/min/1.73 m^2, p < 0.01) (data not shown). However, those who started ARB do not have a significant change in the rate of decline of estimated GFR compared to those who do not have it (3.3 ± 9.1 vs. 4.4 ± 17.2 ml/min/1.73 m^2, p = 0.11) (data not shown). No significant changes were observed after changes of the other antihypertensive drugs *i.e.* diuretic, α-blocker, calcium channel blocker (CCB), angiotensin converting enzyme inhibitor (ACE inhibitor). Changes in the number of drug items or drug dosages were also not significantly associated with a better chance of becoming NAU at the end of the presented study.

However, those in the NAU persistent group and the NAU conversion group had a significant increase of serum Cr level, decrease of adjusted CCr and decrease of LDL-C levels from last year (baseline) values.

Discussion

Follow-up studies of non-DM HT patients with MAU are infrequent and information about contributing factors other than the effect of BP reductions on the change of UAE over time is limited[13-16]. A decrease in BP levels during follow-up is a documented determinant that could cause a regression of UAE[17]. In addition, a decrease in UAE in non-DM HT patients, either drug induced or BP reduction, is associated with a lowered risk for cardiovascular disease[18]. Furthermore, short-term drug-induced BP reductions in UAE predicted long-term renal outcome in nondiabetic renal disease[19,20]. Therefore, an attempt to decrease BP's in these patients with MAU is crucial in the decreasing of UAE and improving their cardiovascular/renal outcomes. After one-year of medical interventions in the 69 non-DM HT patients with MAU, lower BMI, WC and DBP level were associated with MAU conversion. The present study revealed that 79.7% of these patients with MAU

Table 4. Changes of patients' characteristics of non-DM HT patients with persistent NAU and those with NAU conversion

Parameter	Mean ± SD or n (%)		p-value
	NAU persistent group (n = 246)	NAU conversion group (n = 16)	
ΔBMI level (kg/m^2)	-0.12 ± 2.0	0.09 ± 0.8	0.69
Decrease in BMI	134 (54.5)	7 (43.8)	0.41
Δwaist circumference (cm)	0.08 ± 3.5	0.75 ± 3.4	0.46
Decrease in waist circumference	96 (39.0)	5 (31.3)	0.54
ΔSBP level (mm Hg)	-4.9 ± 13.9**	1.8 ± 12.9	0.07
Decrease in SBP level	154 (62.6)	5 (31.3)	0.01*
ΔDBP level (mm Hg)	-3.7 ± 10.3**	0.5 ± 10.1	0.11
Decrease in DBP level	160 (65.0)	10 (62.5)	0.84
Uncontrolled BP ≥140/90 mm Hg	30 (12.2)	4 (25.0)	0.14
BP ≥135/85 mm Hg	55 (22.4)	4 (25.0)	0.51

NAU = normoalbuminuria, BP = blood pressure, BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, Δ = value of this study-value of previous study, n = number of patient, HT = hypertension, *p < 0.05, independent sample t-test, compared between NAU persistent and NAU conversion groups, **p < 0.05, Paired sample t-test, compared between the first and the last BP level within studied group

Table 5. Changes of antihypertensive drugs of non-DM HT patients with MAU conversion and those with MAU persistence

Parameter	Mean ± SD or n (%)		p-value
	MAU conversion group (n = 55)	MAU persistent group (n = 14)	
Diuretic			
Stop using	5 (12.2)	0	0.44
Adding on	6 (25.0)	0	0.18
α-blocker			
Stop using	6 (26.1)	0	0.38
Adding on	3 (6.4)	1 (7.7)	0.63
β-blocker			
Stop using	21 (61.8)	1 (9.1)	< 0.01*
Adding on	2 (5.0)	0	0.79
CCB			
Stop using	5 (11.4)	1 (8.3)	0.62
Adding on	1 (5.9)	0	0.85
ACE-inhibitor			
Stop using	1 (20.0)	0	0.31
Adding on	2 (4.3)	0	0.67
ARB			
Stop using	0	0	NA
Adding on	27 (58.7)	3 (23.1)	0.02*
Increase in number/dosage of anti-hypertensive drugs used	2.67 ± 0.8	2.50 ± 0.7	0.84

MAU = microalbuminuria, n = number, NA = not applicable, α-blocker = alpha blocker, CCB = calcium channel blocker, β-blocker = beta blocker, ACE-inhibitor = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker, *p-value considered significant at < 0.05

became NAU.

The present results were supported by many studies. A large-scale study of 6,000 non-DM HT patients showed that MAU can be reversed in many cases when treated by antihypertensive drugs[17]. Brantsma and coworkers had studied general population in the Gronigen city, Netherlands from 1997 to 2003, the Prevention of REnal and Vascular ENd-stage Disease (PREVEND) cohort. Of the 812 non-DM participants who initially had baseline urinary albumin concentration (UAC) from the morning urine samples at 30-300 mg/dl (MAU) with BP's of 140 ± 23/79 ± 11 mmHg, 19.0% could have UAE < 30 mg/dl (NAU) after a median follow-up of 4.2 years[21]. Pascual and coworkers had shown that the average BP levels of the treated Spanish non-DM HT patients with MAU, studied during 1998-2000, could be lowered from 146.0/84.1 mmHg to 139.3/78.4 mmHg. Their UAE had been decreased by more than half in 44.8% at 18 months and 75% at 25.8 months[22]. Fesler and coworkers had presented a 5.8 years follow-up study in 132 French who had non-DM HT; their initial BP levels could be lowered from 163 ± 17/98 ± 11 mm Hg to 138 ± 15/81 ± 9 mmHg. The number of volunteers presenting with MAU could be significantly decreased from 28% to 18% (p = 0.007) which confirmed the present study[23]. In addition, a two-year follow-up in the MARPLE cohort study carried out in Germany on 832 treated cases who had non-DM HT with MAU, supported the present study. Their average BP levels could be lowered from 160.4/93.2 mmHg to 142.0/83.2 mmHg. Normalized protein excretion could be observed in 30.6% of studied patients. Therefore, adequate BP reduction in non-DM HT with MAU is beneficial. The present study showed that MAU as an early marker of renal dysfunction is reversible[2].

However, the higher rate of participants with MAU who became NAU after one-year treatment that was obtained in the present study could be due to at least 2 reasons. Firstly, antihypertensive treatment given among the MAU conversion group in the present study could achieve lower BP levels, 123.2 ± 12.1/70.9

± 8.0 mmHg, when compared to the Spanish report[22]. BP levels achieved in the present study were lower than that of the 'regressors' group (139.3 ± 59.4/78.4 ± 10.7 mmHg) in the Spanish study ($p = 0.0485$ for SBP and $p < 0.01$ for DBP)[22]. Secondly, the baseline kidney function of participants enrolled in the present study was also much better. The initial adjusted CCr in the present study (83.5 ± 25.4 ml/min per 1.73 m^2) among the MAU conversion group (data not shown) was higher than that of the 'regressors' group of the MAU participants (69.4 ± 19.4 ml/min per 1.73 m^2) in that study ($p < 0.01$)[22]. These finding implied a better kidney function and a lower grade of target organ damage in our studied group. BP levels achieved in the present study were also lower than that of the 'regression' group (137.0 ± 24.0/78.0 ± 12.0 mmHg) reported by Brantsma et al ($p < 0.01$ for both of the SBP and DBP)[21]. However, initial adjusted CCr levels in the present study were not different from that of the MAU participants (78 ± 15 ml/min per 1.73 m^2) of that study ($p = 0.66$)[21]. Again, BP levels achieved in the present study were lower than that demonstrated by Fesler and coworkers (138.0 ± 15.0/81.0 ± 9.0 mmHg) ($p < 0.01$ for both SBP and DBP)[23]. Unfortunately, estimated GFR in the 'regressors' group among treated MAU participants was not mentioned in their report[23].

The higher BMI and WC may impede the regression of albuminuric status in treated non-DM HT, the MAU persistent group. Therefore, to encourage these patients to lose more weight may promote the regression of albuminuric status in treated nondiabetic HT with MAU. This was supported by the previous studies on the impact of weight change on albuminuria[24,25].

After one year follow-up of those non-DM HT patients with NAU, there were 16 cases who had MAU later. Therefore, the incidence of MAU was 6.1/100 patients/year. However, it is comparable to the 4.4/100 patients/year of the Spanish report[16]. Generally, a reduction in albuminuria could be translated to reduction in cardiovascular events in hypertensive patients[18]. Non-DM HT with NAU should be managed with multiple modalities to prevent the occurrence of microalbuminuria. A population-based cohort, 250 non-DM HT patients with NAU, aged 50-70 years, were followed prospectively for 6.1 ± 0.7 years. The cumulative incidence of microalbuminuria was 14.0% (95%CI = 9.7-19.3)[26]. Also, in the 2.7 ± 1.2 years studied on the 187 treated essential hypertensive Spanish with NAU, 22 patients (11.7%) still developed MAU in spite of their attempt to reach a goal BP of 130/85 mmHg[16]. To prevent its appearance, modalities that helped should be implemented in the routine practice.

The short-term effect of changing antihypertensive drug within one year had been studied. Levey and coworkers had previously demonstrated that starting β-blocker was associated with a greater GFR decline than stopping it[27]. Similarly, our result has supported that stopping β-blocker is associated with a better chance to have a NAU after one year. A lesser decline in the estimated GFR was found in those who stopped using of β-blocker compared to those who continued using it. This could due to alteration in the hemodynamic determinants of GFR[28]. However, this can be simply explained by replacement of a β-blocker by an ARB which has antiproteinuric effect (Table 5).

The present study on the effect of therapy with ARB compared to the number of comparators on proteinuria of all nondiabetic kidney disease outcome trials that demonstrated a reduction in proteinuria was scarce[29]. Mostly, they included treated hypertensive patients presenting with frank proteinuria[30]. Only a few studies reported on the effect of antihypertensive treatment of the non-DM HT patients with MAU are available. Among these studies, only Nutahara and coworkers could demonstrate the sustained antiproteinuric effect of ARB in the adult hypertensive patients after one year of treatment[31].

In the present study, adding of an ARB in the treatment regimens is associated with a better chance to have MAU conversion at the end of the present study period compared to those who do not have it. However, it is unlikely to be due to GFR manipulation by 'adding' of an ARB. A non-significant difference in the decline of GFR between those who received an ARB or not was noted. It conforms to a previous systemic review and meta-analytic study which has shown a non significant benefit on CKD slowing and on a decreasing of GFR with the used of ARB in patients with GFR above 70 ml/min/1.73 m^2, or on those who did not have proteinuria (urine albumin < 300 mg/d)[29]. Moreover, only a small magnitude of reduction of MAU after one year treatment with ARB can be expected. De Alvaro and coworkers had shown the magnitude of MAU reduction after one year irbesartan added treatment with an average dose of 250.7 ± 60.3 mg/day in 855 nondiabetic HT Koreans presenting with albuminuria[32]. They were small but significant reduction of albuminuria from 276 ± 28 mg/day to 152 ± 18 mg/day. Notably, the reductions mostly remained within the range of 30-300 mg/day.

Among the antihypertensive drugs other

than β-blocker and ARB used in the present study, the Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT) had confirmed that diuretics, CCBs and ACE inhibitors had no specific benefit other than BP lowering for patients with nondiabetic kidney disease[33]. Moreover, the ONTARGET study in which 25,600 cases with cardiovascular disease were enrolled comparing the effect of ramipril with telmisartan also supported that increase in UAE was found less with ARB than with ACE inhibitor[34]. Therefore, adding or stopping of any other antihypertensive drugs might not be helpful in the reduction of MAU aside from the direct effect of BP reduction.

Microalbuminuria assessment is recommended in the risk stratification strategy for hypertension management. The 2007 ESH/ESC guidelines recommend screening for MAU in all patients with hypertension[35]. The JNC-7 report stated that 'the presence of albuminuria, including MAU, even in the setting of normal GFR, is also associated with an increase in CV risk and recommended that annual screening for MAU in high-risk groups, such as those with diabetes or renal disease and as an option in other hypertensive patients[9]. American Kidney Foundation recently supported the notion that proteinuria might be a cause of progressive kidney damage and suggested that the reduction of UAE in non-DM HT patients may be a useful indicator of therapeutic response[36]. Therefore, a failure to regress MAU may result from the inadequacy of intervention. Microalbuminuria should be checked annually in every hypertensive patient and every 6 months within the first year of treatment to assess the impact of antihypertensive therapy[37].

Conclusion

The conversion rate of MAU to NAU was 79.7%. Factors that associated with regression of UAE in non-DM HT patients with MAU were lowering BP intensively, stopping β-blockers and adding ARBs. The incidence of recent onset MAU was 6.1% per year. Annual MAU check up should be carried out in every non-DM HT patients[18].

Potential conflicts of interest

None.

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การเปลี่ยนแปลงของไมโครแอลบูมินนูเรียในผู้ป่วยความดันโลหิตสูงภายหลังการติดตามการรักษาหนึ่งปี

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วัตถุประสงค์*: การศึกษานี้มีจุดมุ่งหมายที่จะดูผลของการรักษาในผู้ป่วยโรคความดันโลหิตสูงที่ไม่ได้เป็นโรคเบาหวานที่คลินิกความดันโลหิตสูงตามปกติต่อเนื่อง อัตราการเปลี่ยนแปลงจากที่พบไมโครแอลบูมินนูเรียมาเป็นปัสสาวะปกติและอุบัติการณ์ของการเปลี่ยนแปลงจากปัสสาวะปกติมาเป็นตรวจพบไมโครแอลบูมินนูเรีย สิ่งที่จะได้เพิ่มเติมคือหาปัจจัยซึ่งมีผลต่อการเปลี่ยนจากการตรวจพบไมโครแอลบูมินนูเรียกลับมาเป็นปรกติ*

วัสดุและวิธีการ*: การศึกษาติดตามเริ่มในเดือนกุมภาพันธ์ถึงเดือนมิถุนายน พ.ศ. 2550 ที่แผนกผู้ป่วยนอกโรงพยาบาลศิริราช 2 ใน 3 ของผู้ป่วยความดันโลหิตสูงที่ได้รับการตรวจหาไมโครแอลบูมินนูเรียในการศึกษาที่แล้วจะได้รับการร้องขอให้เก็บปัสสาวะในตอนเช้า ผู้ป่วยเหล่านี้ไม่มีโรคเบาหวานหรือมีระดับน้ำตาลในเลือดขณะงดอาหารผิดปรกติ (100–125 มิลลิกรัม/เดซิลิตร) โรคไตวายเรื้อรัง (ระดับครีแอทินินในเลือดสูงกว่า 1.5 มิลลิกรัม/เดซิลิตร) และการตรวจพบเม็ดเลือดขาว ในปัสสาวะมากผิดปรกติ (เม็ดเลือดขาวมากกว่า 5 เซลล์/HPF) การตรวจพบไมโครแอลบูมินนูเรียจะทดสอบด้วย Microalbustix® เช่นเดิม ผู้ป่วยจะได้รับการร้องขอให้ตอบแบบสอบถามซึ่งใช้ในการศึกษาที่แล้วและได้รับการวัด ความดันโลหิต 1 ครั้งหลังจากนั่งพัก 5 นาที รวมทั้งการวัดเส้นรอบเอว และน้ำหนักตัว*

ผลการศึกษา*: ผู้ป่วยความดันโลหิตสูงที่ไม่เป็นโรคเบาหวานทั้งหมด 334 ราย เป็นผู้ชาย 112 ราย เข้าร่วมการศึกษานี้ 3 ราย ถูกตัดออกไปเพราะมีเม็ดเลือดขาวในปัสสาวะมากผิดปรกติ หลัง 1 ปี ผู้ป่วย 55 ราย จากผู้ป่วย 69 ราย (ร้อยละ 79.7) ซึ่งเคยตรวจพบไมโครแอลบูมินนูเรียเปลี่ยนมาเป็นปัสสาวะปกติ (ค่า $p < 0.001$) และผู้ป่วย 16 ราย จากผู้ป่วย 262 ราย (ร้อยละ 6.1) ซึ่งเคยมีปัสสาวะปกติเกิดตรวจพบไมโครแอลบูมินนูเรีย (ค่า $p < 0.001$)*

สรุป*: อัตราการเปลี่ยนการตรวจพบไมโครแอลบูมินนูเรียเป็นปัสสาวะปกติพบร้อยละ 79.7 และการตรวจพบไมโครแอลบูมินนูเรียจากปัสสาวะปกติพบร้อยละ 6.1 ควรทำการตรวจหาไมโครแอลบูมินนูเรียทุกปีเพื่อเป็นการติดตามอย่างต่อเนื่องในผู้ป่วยโรคความดันโลหิตสูงที่ไม่ได้เป็นโรคเบาหวานทุกราย*