BLOOD PRESSURE CONTROL AND DIPPING STATUS IN HYPERTENSIVE PATIENTS WITH MILD RENAL DYSFUNCTION

HAFİF RENAL FONKSİYON BOZUKLUĞU OLAN HİPERTANSİF HASTALARDA KAN BASINCI KONTROLÜ VE DİPPİNG DURUMU

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Özet

Renal fonksiyonlarda azalma hipertansiyonun son organ hasarlarından birisidir. Bu çalışmada renal fonksiyonları hafif azalmış hipertansiyon hastalarında kan basıncı kontrolünü ve dipping durumunu inceledik. Altmış yedi hastaya (57.4±11.9, 19 erkek, 48 kadın) 24 saatlik kan basıncı monitorizasyonu yapıldı. Renal fonksiyonlar MDRD formülü ile tahmin edilen Glomerül filtrasyon hızı (GFH) olarak ifade edildi. Diyabeti ve koroner arter hastalığı olanlar çalışmaya alınmadı. GFH 60 ml/dk altında ve üstünde olanlarda 24 saatlik, gündüz ve gece kan basıncı ortalamaları ile dipping durumu karşılaştırıldı. İstatistiki analizler Independent Samples t testi ile SPSS 11.0 kullanılarak yapıldı. 24 saatlik, gündüz ve gece sistolik ve diyastolik kan basınçları GFH<60 ml/dk olan hipertansif hastalarda yüksek izlendi (p>0.05, Tablo 1). Dipping durumu gruplar arasında farklı değildi (Tablo 2). Ancak her iki grupta da non dipping durumunun yüksek olması dikkat çeken bir bulguydu. Kan basıncı kontrolü GFH <60 ml/dk olan hipertansif hastalarda renal fonksiyon bozukluğa gidişi yavaşlatmak için özellikle önemlidir. Bu hastalarda nondipping durumunun baskın olması etkin bir antihipertansif tedavi ile düzeltilmesi gereken bir durumdur. (Anatol J Clin Investig 2009:3(2);123-126).

Abstract

Renal dysfunction is one of the end organ damages induced by hypertension. We aimed to evaluate the blood pressure control and dipping status in hypertensive patients with mild renal dysfunction. Sixty seven patients (57.4±11.9, 19 male, 48 female) were performed 24 hour ambulatory blood pressure monitoring. Renal functions were defined as glomerular filtration rate (GFR) estimated by MDRD Formula. Patients with diabetes and/or coronary artery disease were excluded. Averages of 24 hour, daytime and nighttime systolic and diastolic blood pressures and also dipping status of patients were compared between the groups with GFR under and above 60 ml/min. Statistical analysis were performed by Independent Samples t test using SPSS 11.0. 24 hour, daytime and nighttime systolic and diastolic blood pressures were higher in hypertensive patients with GFR lower than 60 ml/min (p>0.05, Table 1). Distribution of dipping status was not different between groups (Table 2). However predominance of nondipping status in both groups was an alerting finding. Blood pressure control is particularly important in hypertensive patients with GFR <60 ml/min to slow the course of renal dysfunction. Predominance of nondipping in those patients should be overcomed by effective antihypertensive management. (Anatol J Clin Investig 2009:3(2);123-126).

Introduction

Nondipping status of patients with hypertension is characterized with the blunted nocturnal fall of blood pressure. Non dipping feature is clinically important in hypertensive patients. It is a strong predictor for increased cardiovascular morbidity and mortality [1]. Additionally non-dipping pattern is closely related with target organ damage induced by hypertension. In patients with renal insufficiency, loss of nocturnal decrease of blood pressure accelerates the rate of progression of the disease. It is also related with a high incidence of cardiovascular disease in patients with end stage renal disease [2].

Nondipping status could be associated with subsequently decline of glomerular filtration rates (GFR) in the further lifetime unless it was managed [3]. This relationship is independent of baseline renal functions, systolic blood pressure, or other risk factors. Thus nephrosclerosis which clinically manifests by impairment of renal function is one of the end-organ damages induced by hypertension [4]. GFR is an important index of renal functions. Therefore GFR is a useful and routine method used in the management and follow up in clinical course of patients with renal failure, hypertension, and diabetes, etc [5]. MDRD formula which was recently introduced by the study of Modification of Diet in Renal Disease could rapidly and reliably predict and determine the creatinine

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clearance (CrCl) with an accuracy comparable to measured CrCl or GFR [6,7].

In this study we grouped the patients with GFR under and above 60 ml/min which was estimated by MDRD formula. Thereafter we evaluated the dipping status and blood pressure control among those groups by means of 24-hour ambulatory blood pressure monitoring.

Material and Method

Sixty seven patients (age 57.4 ± 11.9, 19 male and 48 female) were enrolled to the study. Patients who have been followed up for primary hypertension were recruited for a routine control. Patients voluntarily underwent 24 hour ambulatory blood pressure monitoring and were performed echocardiographic examination. Blood samples for the measurement of serum urea and creatinine levels were obtained at 12 hour fasting state. Patients were informed and signed written informed consent form. Patients with diabetes and coronary artery disease, congestive heart failure, end-stage renal disease, and on haemodialysis therapy, etc. were excluded. All subjects underwent 24-hour ambulatory blood pressure monitoring on a usual daily activity. They were instructed to go on their routine daily activities. An appropriate sized cuff was placed around the non-dominant arm. Measurement of blood pressure at 15-minute intervals throughout the 24-hour study period was planned. All subjects were instructed to rest or sleep between 10:00 PM and 06:00 AM (nighttime) and to maintain their usual activity at 06:00 AM and 10:00 PM. Subjects working at night shift were excluded. Dipping condition was determined by the 10% decrease of blood pressures in the night measurements compared to day measurements. 24 hour, daytime and nighttime systolic and diastolic blood pressures were obtained from the 24 hour measurements.

Estimated renal functions; estimated GFR; were expressed by MDRD formula as ml/min/1.73 m^2. MDRD formula was calculated using the following method [6,8].

MDRD formula=186 x $(P_{cr} \times 0.0113)^{-1.154}$ x $age^{-0.203}$ x (0.742 if female); P_{Cr}; plasma creatinine; is expressed in μmol/l. Unit of mg/dl was converted to μmol/l by the formula of [P_{Cr} (mg/dl) x 88.4=P_{Cr} (μmol/l)]. Age of subjects is expressed in years. N Statistical analysis was performed by Mann Whitney U test and Chi Square test using SPSS 11.0 for Windows.

Results

Patients with estimated GFR <60 ml/min were older than the other group (55,5±13,0 vs 67,6±9,7, p<0.05). BMI was not different between groups. Levels of serum urea and creatinine were significantly higher in patients with GFR <60 ml/min (Table 1). Left ventricular ejection fraction of patients was not different between groups. 24 hour, daytime and nighttime systolic and diastolic blood pressures were higher in patients with GFR <60 ml/min. But the difference was not statistically significant (Table 1). Additionally non dipping status was slightly higher in patients with GFR <60 ml/min (Table 2), but the distribution of dipping and nondipping status was not statistically significant between groups. However we observed that the nondipping status of patients was predominant in both of the groups.

Discussion

Measurement of ambulatory blood pressure gives not only about the daytime and nighttime blood pressure but also diurnal variation and nighttime dipping and nondipping. Nondipping feature of nighttime blood pressures was found to be related to target-organ damage in previous studies [4]. In this study we aimed to evaluate the blood pressure control and nondipping status in hypertensive patients with mildly diminished renal function; expressed as GFR estimated by MDRD<60 ml/min. Since achievement of blood pressure targets is particularly important in patients with mild to moderate renal dysfunction in order to prevent or to prolong the duration resulting with the end stage renal disease. Also non dipping status is a significant factor which promotes the course of renal dysfunction from moderate to end stage.

In the ESC guideline of arterial hypertension it was suggested that lowering blood pressure below 130/80 mm Hg may help preserve renal function in patients with non-diabetic renal disease [9]. It was reported a significant reduction of end stage renal disease in patients with non-diabetic kidney disease that were randomized to blood pressure below 120/80 mm Hg compared to 140/90 mm Hg [10]. In our study we could conclude that the optimal blood pressure could not be achieved in hypertensive patients with GFR <60 ml/min estimated by MDRD formula. Thus those patients were increased at risk for progression to end-stage renal disease and also cerebrovascular and cardiovascular diseases due to uncontrolled blood pressure and additionally being elderly.

Torbjörnsdotter et al. reported that the nondipping status was closely related to renal morphological changes in adolescent patients with type 1 diabetes. Also that relationship was independent of presence of type I diabetes.

Additionally they suggested that nondipping status might be an early predictor of later nephropathy [11]. Thus non dipping status is extremely important in the development and progression of hypertension related renal injury in patients. Similarly we excluded the diabetic patients to avoid the diabetes related renal changes in our patients. Since diabetes could be accounted for reduced dipping of blood pressure via autonomic nervous abnormalities, our findings were far from the diabetes associated nondipping status. So we can conclude that predominance of nondipping in patients with GFR<60 ml/min should be an alerting finding in the management of older hypertensive patients. Estimation of renal functions either by MDRD formula or Cockcroft-Gault formula is important in the management of outpatient with hypertension. Estimation of nondipping patients who are at risk for cardiovascular complications and renal dysfunction should alert the physician for the optimal blood pressures achievement and more effective treatment directed to nondipping.

In this study we excluded obese hypertensive patients because obesity is one of the factors which challenge the blood pressure control and also induce nondipping status in hypertensive patients [12,13]. Additionally patients with end-stage renal disease (GFR<30 ml/min) were excluded from the study. Thus exclusion of patients with end-stage renal failure provided an objective comparison because end-stage renal failure is closely associated with uncontrolled blood pressure and high nondipping rates in patients high probably due to volume overload [14]. Limited number of patients in our study group may be one of the limitations of study however those important findings should be studied and reviewed in large populated studies.

ACE inhibitors and angiotensin receptor blockers are the antihypertensive agents of which renoprotective effects were documented and proven. Also those agents act in part by blocking sympathetic nervous system which was one of the accounted mechanisms for nondipping status [15]. It may be suggested that cutting that vicious cycle from the point of nondipping may prolong the time period required by the renal complications to exist. Also beta blockers treatment is secondarily underused due to the fear of adverse hemodynamic and metabolic effects in patients with diabetes. However beta blocker could be an appropriate treatment because increased cardiovascular complications and hypertension mainly depends on sympathetic overactivity in patients with chronic kidney disease [16,17]. Bakris and Kalaitzidis insist on recommendation of beta blocker treatment to achieve optimum blood pressures and to slow the progress of chronic kidney disease in hypertensive patients with chronic kidney disease [18]. Predominance of nondipping status in hypertensive patients with estimated GFR <60 ml/min in our study supports those recommendation, because either nondipping status or uncontrolled blood pressure adversely contributes the course of kidney disease in hypertensive patients.

Conclusion

Blood pressure control and nondipping status are particularly important in the management of hypertensive patients with GFR <60 ml/min estimated by MDRD formula. MDRD or Cockcroft-Gault formula is the easiest and reliable way of determination of renal functions and patients at risk for chronic kidney disease. Both the effective drug therapy and combination antihypertensive therapy are essential to avoid the consequences of uncontrolled blood pressure and nondipping.

Table 1. Comparisons of 24 hour, daytime and nighttime systolic and diastolic blood pressures between the patients with GFR above and below 60 ml/min; estimated by MDRD formula

	GFR >60 (n=53)	**GFR< 60 (n=14)**	**P value**
Age (years)	55,5±13,0	67,6±9,7	<0.05
BMI (kg/m^2)	26,1±2,1	26,1±2,1	>0.05
Blood Urea level (mg/dl)	27,5±5,9	35,8±7,9	<0.05
Creatine level (mg/dl)	0,86±0,2	1,10±0,3	<0.05
LV ejection fraction (%)	63,9±4,6	64,4±5,8	>0.05
Estimated GFR (ml/min)	85,2±20	53,7±9	<0.05
24 hour SBP (mm Hg)	131.8±14.9	134.7±13.4	>0.05
24 hour DBP (mm Hg)	79.7±11.0	85.1±11.0	>0.05
Daytime SBP (mm Hg)	134.5±15.4	137.1±11.8	>0.05
Daytime DBP (mm Hg)	81.2±9.9	88.1±12.1	>0.05
Nighttime SBP (mm Hg)	126.7±16.4	130.6±18.3	>0.05
Nighttime DBP (mm Hg)	77.2±13.7	79.8±10.9	>0.05

DRD, Modification of Diet in Renal Disease formula; GFR, glomerular filtration rate; BMI, body mass index, LV, left ventricle; SBP, systolic blood pressure; DBP, diastolic blood pressure

Table 2. Distribution of dipping condition between patients with GFR above and below 60 ml/min which was estimated by MDRD

	GFR>60 (n=53)	**GFR<60 (n=14)**	**P value**
Nondipping status	40 (% 75,4)	11 (%78,5)	
Dipper status	13 (% 24,6)	3 (%21,5)	>0.05

MDRD, Modification of Diet in Renal Disease formula; GFR, glomerular filtration rate

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