－Originals－

Effect of age on urinary excretion of N-acetyl-β-D-glucosaminidase

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Abstract

To examine the relationship between the concentrations of urinary NAG and age, we measured ratios of urinary N-acetyl-β-D-glucosaminidase (NAG) to urinary creatinine (NAG index) in 137 healthy subjects, aged from 19 to 88 years. The study is also designed to evaluate the relationship between urinary NAG and blood pressure. The subjects were divided into 7 subgroups, according to their age (＜30, 30-39, 40-49, 50-59, 60-69, 70-79, 80 or more years). There was a positive correlation between NAG index and age (r=0.36；P<0.001). The regression equation relating NAG index (y) to age (x) was y=0.065 x+0.97. The mean NAG indexes for the 7 subgroups divided by age were significantly different (P<0.01). There was a positive correlation between NAG index and systolic blood pressure (r=0.18；P<0.05), but was not between diastolic blood pressure and NAG index. In multiple regression analysis, age and BUN significantly correlated with NAG index (r=0.32；P<0.01, r=3.3；P=0.07, respectively), although there was no correlation between systolic blood pressure and NAG index.

This cross-sectional study showed a clear elevation in NAG index with age. The rate of elevation was 0.65 per decade. Urinary excretion of NAG may be unrelated to blood pressure. (J Nippon Med Sch 1999；66：33—36)

Key words：N-acetyl-β-D-glucosaminidase, aging, blood pressure

Introduction

Excretion of various enzymes in the urine has been used to evaluate or predict subtle degrees of renal injury[1,2]. N-acetyl-β-D-glucosaminidase (NAG) is hydrolytic enzyme with a molecular weight of 130,000 to 140,000 daltons. It is normally not filtered at the glomerulus. NAG is a widely distributed lysosomal enzymes, located predominantly in the renal proximal tubules[3]. Urinary NAG increases in patients with various glomerlonephritides, tubulointerstitial diseases, renal allograft rejection, toxic renal injury, and diabetes mellitus [1,2,4-8]. But the effect of aging upon urinary excretion of NAG remains uncertain [9-11]. The aim of the present study is to examine whether any correlation exists between the concentrations of urinary NAG and age. The study is also designed to evaluate the relationship between urinary NAG and blood pressure.

Materials and Methods

The present study included 137 healthy subjects, 62 male and 75 female, aged from 19 to 88 years (mean age；59.9 ± 13.5 y old). The subjects were divided into 7 subgroups, according to their age (＜30, 30-39, 40-49, 50-59, 60-69, 70-79, 80 or more years). All of the subjects had normal physical findings. None had clinical evidence of heart disease, cancer, gout, diabetes, liver disease or renal dysfunction in our routine examination, i. e., chest X-ray, a standard 12-lead electro-

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Table 1 Clinical characteristics of the subjects studied

n	137	
Male/Female	62/75	
Age (yr.)	59.9 ± 13.5	(19—88)
BMI (kg/m^2)	22.2 ± 3.3	(14.6—32.5)
Systolic BP (mmHg)	134.6 ± 15.3	(94—177)
Diastolic BP (mmHg)	79.8 ± 9.4	(50—100)
Total cholesterol (mg/dl)	202.4 ± 34.5	(106—294)
Triglyceride (mg/dl)	114.3 ± 59.8	(27—348)
Uric acid (mg/dl)	5.3 ± 1.3	(2.4—8.6)
BUN (mg/dl)	14.9 ± 3.9	(8—36)
Cr (mg/dl)	0.83 ± 0.16	(0.4—1.2)
Urine albumin (mg/g·Cr)	11.5 ± 8.9	(3.6—44.1)

Mean ± SD (range)

cardiogram and determinations of blood count, blood chemistry, and urine protein. None of the subjects had taken any medications. Urinary NAG activity was measured spectrophotometrically with sodio m-cresolsulfonphthleinyl N-acetyl-β-D-glucosaminide as substrate (NAG test Shionogi)[12]. After an overnight fast, blood pressure and body mass index (BMI) were measured and blood was taken for determinations of total cholesterol (TC), triglyceride (TG), uric acid (UA) and BUN. Ratios of urinary NAG to urinary creatinine (NAG index) were calculated from random urine samples collected on two or more separate occasions within three months. Multiple regression analysis was used to investigate the relationship among NAG index and explanatory variables. Explanatory variables were as follows : age, systolic blood pressure, TC, TG, UA, BUN and BMI.

Statistical analysis was carried out using the chi-squared, Student t test and one way analysis of variance. The correlation was evaluated using the linear regression analysis. Backward stepwise multiple regression analysis was used to investigate the relationship among NAG index and explanatory variables. Data in the text, tables and figures were expressed as mean ± SD.

Results

Table 1 shows the clinical characteristics of the subjects.

Fig 1 shows the relationship between NAG index and age. There was a positive correlation between NAG index and age (r=0.36 ; P<0.001). The regression equation relating NAG index (y) to age (x) was y=0.065 x+0.97. The mean NAG indexes for the 7 subgroups divided by age were significantly different (P <0.01) (**Fig. 2**). Variability of NAG index tended to increase with aging.

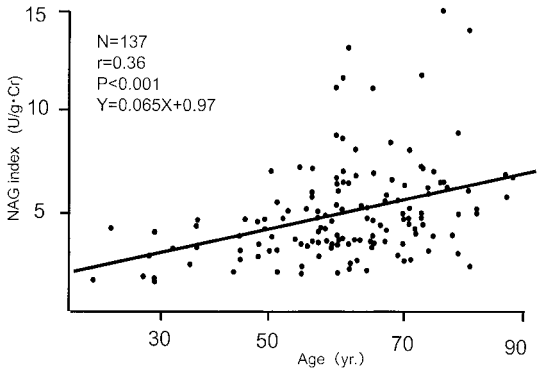

Fig. 1 Correlation between NAG index and age

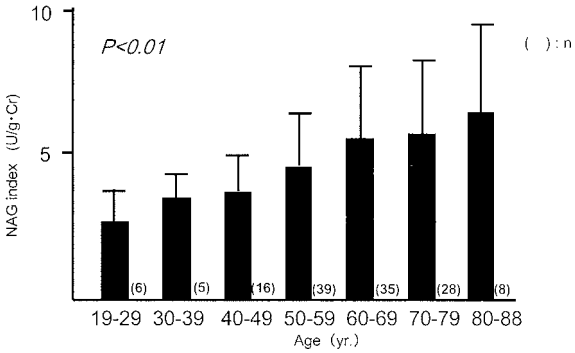

Fig. 2 Mean NAG indexes for the subgroups divided by age

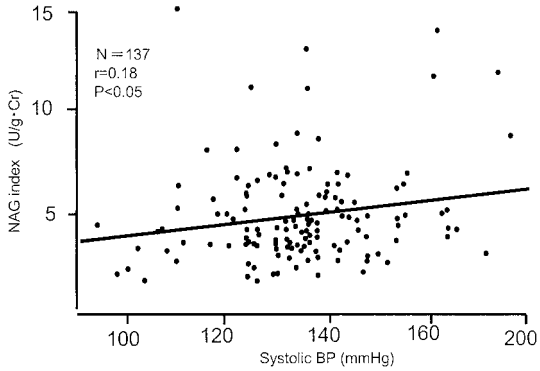

Fig. 3 Correlation between NAG index and systolic blood pressure

Fig 3 shows the relationship between systolic blood pressure and NAG index. There was a positive correlation between NAG index and systolic blood pressure (r=0.18 ; P<0.05).

Fig 4 shows the relationship between diastolic blood pressure and NAG index. There was no correla-

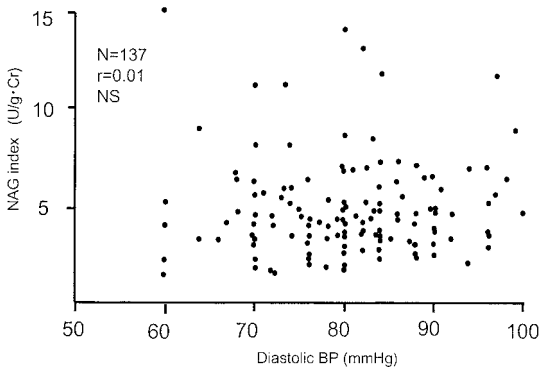

Fig. 4 Correlation between NAG index and diastolic blood pressure

Table 2 Standardized partial correlations (r) between NAG index and explanatory variables in backward stepwise multiple regression analysis (Fvalue ≧ 2.0)

Explanatory variables	r	F value	P
Age	0.32	10.5	< 0.01
Systolic BP	−		
Total cholesterol	−		
Triglyceride	−		
Uric acid	−		
BUN	0.19	3.3	0.07
BMI	−		

tion between them.

Table 2 shows standardized partial correlation coefficients (r) between NAG index and explanatory variables in the results of the relationship backward stepwise multiple regression analysis (F value≧2.0). Age and BUN significantly correlated with NAG index (r=0.32 ; P<0.01, r=0.19 ; P=0.07, respectively), although there was no correlation between systolic blood pressure and NAG index.

Discussion

The broad clinical implications of changes in renal function with age require careful consideration in the management of geriatric patients, particularly those with multiple medical problems. Careful, noninvasive measurement of the important modalities of renal function should be performed routinely in the elderly. Since serum creatinine may be a poor indicator of glomerular filtration rate (GFR) in the aged patients, the endogenous creatinine clearance is of much more value [13]. However, it may sometimes be difficult to obtain the necessary 24-hour urine collections in the elderly [14]. With regard to the outpatient group, it is evident that the patients could not have been bringing in consistently complete 24-hour urine collections. Measurement of GFR is too cumbersome for use in everyday clinical circumstances.

It has been established that NAG activity in the urine increases with various renal diseases, so NAG index has been used to evaluate or predict subtle degrees of renal injury [1,2,4-8]. NAG index for random specimens provides a useful, convenient measurement of daily NAG excretion and avoids many of the problems of 24-hour collections. Study by Ellis and associates[8] found that correlation coefficient for NAG index in random early morning urine samples versus 24-hour NAG excretion was 0.80 in diabetic children.

This cross-sectional study showed a clear elevation in NAG index with age. The rate of elevation in this carefully screened study group was 0.65 per decade. At present, there are few reports examining the age-related effects upon urinary NAG. Watanabe et al[11], reported that age-related elevation in urinary NAG in non-insulin dependent diabetes mellitus (NIDDM). However, Hosoya et al.[10] found no correlation between age and concentration of urinary NAG and there were wide variations in value among the patients. Their subjects were 329 inpatients who were presumably free of renal disease or water-electrolyte imbalance or exposure to any drugs that affect the kidney function. Cause of this discrepancy in results is unknown. In humans, it is difficult to differentiate between age-induced changes and changes caused by past renal disease. Hence, we have investigated urinary NAG in a group carefully selected and screened to exclude all conditions which can produce disease-related effects upon urinary NAG which could be misperceived as age-related.

In the populations of almost all developed countries, both systolic and diastolic pressures rise with age up to the seventh decade. Thereafter, systolic blood pressure continues to rise while diastolic pressure begins to decrease in advanced age. The effect of blood pressure upon urinary excretion of NAG remains uncertain. Schnoell et al.[15] reported that urinary NAG index did not differ significantly in hypertensive versus normotensive diabetics. Alderman et al.[9] reported that the urinary NAG level was elevated in many patients with high blood pressure even though there is no

other evidence of renal damage and declined after drug-induced reduction of blood pressure. On the other hand, Sano et al[16] found that NIDDM patients with persistent microalbuminuria, the ACE inhibitor enalapril reduced urinary albumin excretion in both normotensive patients and well-controlled hypertensive patients, whereas urinary NAG was not lowered in both groups. Our results showed a weak association of elevated NAG index and systolic blood pressure. However, in multiple regression analysis, age and BUN significantly correlated with NAG index, but there was no correlation between systolic blood pressure and NAG index.

Our results suggest that the function of proximal tubule cells deteriorates with age. Both excretory and reabsorptive capacities of the renal tubules decrease as age increases. The decrease in tubular secretion of diodrast and para-amino-hippuric acid in the aged reveals a decrease in tubular function[17]. The reduction in the number of functioning nephron units appears to be the most important factor causing deterioration in the physiologic function of the renal tubules. Other factors may also play a role, including primary tubular cell aging, changes in cardiac output and renal blood flow [13]. Electron microscopic studies reveal increases in thickness of both glomerular and tubular basement membranes with increasing age[18, 19].

The authors hope that in the future studies age-specific reference values on NAG index be established and used in clinical practice.

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