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Original article

Impact of alcohol intake on the relationships of uric acid with blood pressure and cardiac hypertrophy in essential hypertension

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ABSTRACT

Background: Hyperuricemia, which is frequently associated with hypertension, can be caused by alcohol intake. To date, limited data have shown the link between alcohol intake and hyperuricemic hypertension.
Methods: We retrospectively examined the influence of alcohol intake on the relationship between the uric acid level and blood pressure or cardio-metabolic parameters in 171 untreated non-failing hypertensive patients (mean 59.3 ± 10.7 years).

Cross-sectional analysis was separately performed in regular alcohol drinkers (more than 25 g/day ethanol, $n = 74$, 82.4% men) and non-drinkers ($n = 97$, 33.0% men).
Results: Diastolic blood pressure was significantly higher in drinkers than in non-drinkers (101.6 ± 11.5 mmHg vs. 96.8 ± 8.2 mmHg, $p < 0.01$). Estimated glomerular filtration rate (80.4 ± 14.7 mL/min/1.73 m^2 vs. 80.0 ± 17.8 mL/min/1.73 m^2) and body mass index (BMI, 24.7 ± 4.4 kg/m^2 vs. 24.8 ± 4.2 kg/m^2) were similar in the two groups. In the drinker group, the uric acid level (mean 6.3 ± 1.7 mg/dL) was positively correlated with both systolic and diastolic blood pressures ($r = 0.270$/$p = 0.020$ and $r = 0.354$/$p = 0.0020$, respectively), and with the markers of cardiac hypertrophy, including electrocardiographic voltage ($V_1S + V_5R$, $r = 0.244$/$p = 0.042$) and echocardiographic left ventricular mass index ($r = 0.270$/$p = 0.026$). These correlations were also observed in the male drinker sub-group. In the non-drinkers, the uric acid level (mean 5.0 ± 1.4 mg/dL) was positively correlated with BMI ($r = 0.369$/$p = 0.0002$) but not with blood pressure or the markers of cardiac hypertrophy.
Conclusions: The results suggest that the role of uric acid in blood pressure might differ between hypertensive drinkers and non-drinkers. In regular alcohol drinkers, there was a positive association of uric acid level with blood pressure and the severity of cardiac hypertrophy. In non-regular drinkers, an increased uric acid level is likely to be closely associated with increased BMI.

Introduction

Hyperuricemia is frequently associated with hypertension, and it is thought to be a risk factor for cardiovascular disease (CVD) [1–4]. Several epidemiological studies have suggested that hyperuricemia predicts the development of hypertension [5,6] and that uric acid levels have a positive correlation with blood pressure (BP) in cross-sectional analysis [3,5–9]. Whether hyperuricemia is an independent causal factor for hypertension remains controversial; and the mechanism of hyperuricemia-induced hypertension is still unclear. Studies of basic research have shown that increased uric acid might cause hypertension via reducing nitric oxide [10], activation of renin-angiotensin system [11] and smooth muscle proliferation [12]. Even in untreated patients, there is some difficulty in assessing the relationship between uric acid and BP because several factors, and drinking status, in particular, may affect both the uric acid level and BP. Alcohol intake itself is an important and strong risk factor for the development of not only hyperuricemia [13] but also hypertension [14–16].

Several mechanisms related to the increase in uric acid have been clarified, such as excess purine or alcohol intake [13], obesity [17], renal dysfunction [18], and genetic alterations [19]. Some of these factors are also related to the development of hypertension. Alcohol drinking has also been shown to relate to cardiovascular

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diseases, such as heart failure [20], arrhythmia [21], and stroke [22]. However, the role of alcohol intake in the clinical significance of hyperuricemic hypertension remains unclarified.

Since the clinical features of hyperuricemia may differ in drinkers and non-drinkers, comparison of the differences in clinical profiles can facilitate clarification of the role of uric acid in cardiovascular disease and also provide a basis for the development of tailor-made hypertension treatment. To date, there have been limited data on the relationship between uric acid and BP with regard to alcohol intake.

We investigated the influence of reported alcohol intake on the relationship between uric acid level and BP or cardio-metabolic parameters to clarify the contribution of hyperuricemia to BP. We directly compared these parameters in untreated hypertensive patients who were regular drinkers and non-regular drinkers. The outpatients were not taking any medications confounding the association between uric acid and BP.

Methods

We retrospectively examined the serum uric acid levels and various clinical parameters including echocardiographic assessment in 171 untreated hypertensive patients (mean age: 59.3 years; 93 men and 78 women). Outpatient clinic subjects without overt cardiovascular complications who were sequentially recruited between 2004 and 2012 were included.

Hypertension was defined as a systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg in the sitting position. The exclusion criteria included ischemic heart disease, congestive heart failure, atrial fibrillation, chronic renal insufficiency (serum creatinine >1.3 mg/dL), and a history of stroke.

Ischemic heart disease was defined as >75% organic stenosis of a major coronary artery on angiography or a history of myocardial infarction or percutaneous coronary intervention. A diagnosis of heart failure was made based on a history of dyspnea or exercise intolerance associated with signs of pulmonary congestion or peripheral edema.

Cardiac enlargement or dysfunction shown by chest radiography or echocardiography (UCG) was also a diagnostic criterion.

We collected baseline data of blood sampling, electrocardiogram (ECG), chest radiography, and UCG using a SONOS-2500 (Hewlett Packard, Palo Alto, CA, USA) or SSD 2200 (ALOKA, Tokyo, Japan). The end-diastolic dimensions were measured to calculate the left ventricular mass index (LVMI) [23]. For evaluation of diastolic function, Doppler flow recordings were obtained to measure the peak velocity of early diastolic left ventricular (LV) inflow (E-wave) and that after atrial contraction (A-wave), their ratio (E/A ratio), and the deceleration time of the E-wave (DcT).

Patients were divided into drinker (more than 25 g/day ethanol) and non-regular drinker (non-drinker) groups according to their alcohol intake habits. Ex-drinkers were included in the non-drinker group. None of the patients were taking medications for hyperuricemia or anti-hypertensive agents. All study procedures were carried out in accordance with the institutional and national ethical guidelines for human studies (approved by the Ethics Committee of The Jikei University School of Medicine: 25-010 7145).

Statistical analysis

All data are presented as the mean ± standard deviation. Comparisons were performed by Student's *t*-test, while regression coefficients were calculated by linear regression analysis. When univariate regression analysis showed significant differences, multivariate regression analysis was performed to determine the independence of variables. The chi-square test was used to assess differences of percentages. Analyses were performed with SAS software for Macintosh (StatView version 5.0, SAS Institute Inc., Cary, NC, USA), and $p < 0.05$ was considered to indicate statistical significance.

Results

Table 1 shows the comparison of clinical parameters in all patients. In patients from the drinker group (mean uric acid: 6.3 ± 1.7 mg/dL), the following several parameters pointed to more advanced disorder compared to those from the non-drinker group (mean uric acid: 5.0 ± 1.4 mg/dL): higher DBP, ECG voltage ($SV_1 + RV_5$: Sokolow-Lyon voltage) and serum creatinine level. SBP was slightly higher in the drinker group than in the non-drinker group but it was not statistically significant. More than half of this study population did not meet the criteria of hyperuricemia as defined by the clinical guideline (more than 7.0 mg/dL). Because of gender difference, a higher but normal creatinine level and greater LV end-diastolic diameter may have reflected in part the higher percentage of men in the drinker group. This group also had a significantly higher gamma-glutamyltransferase (γGTP) level compared with the non-drinker group.

However, body mass index (BMI), estimated glomerular filtration rate (eGFR), cardiac function (LV ejection fraction or DcT on UCG), and the prevalence of metabolic syndrome were

Table 1
Clinical characteristics of all subjects.

	Drinker	Non-drinker
General		
Number (men)	74 (61)	97 (32)*
Age (years)	56.3 ± 10.7	61.7 ± 10.1**
SBP (mmHg)	167.0 ± 17.7	164.6 ± 13.3
DBP (mmHg)	101.6 ± 11.5	96.8 ± 8.2**
Heart rate (bpm)	73.5 ± 14.0	73.2 ± 12.2
BNP (pg/mL)	32.1 ± 37.7	34.8 ± 40.7
Aldosterone (pg/mL)	82.7 ± 26.5	80.0 ± 41.3
Noradrenaline (pg/mL)	342.6 ± 165.3	379.8 ± 167.1
Renin (ng/mL/h)	1.46 ± 1.72	0.93 ± 0.76*
Uric acid (mg/dL)	6.3 ± 1.7	5.0 ± 1.4***
Creatinine (mg/dL)	0.77 ± 0.17	0.67 ± 0.18***
eGFR (mL/min/1.73 m^2)	80.4 ± 14.7	80.0 ± 17.8
CTR (%)	47.4 ± 4.6	48.6 ± 4.3
$SV_1 + RV_5$ (mV)	3.54 ± 1.15	3.13 ± 1.01*
Metabolic parameters and the prevalence of metabolic syndrome		
BMI (kg/m^2)	24.7 ± 4.4	24.8 ± 4.2
FPG (mg/dL)	102.1 ± 12.0	99.8 ± 12.3
LDL cholesterol (mg/dL)	116.1 ± 30.7	133.6 ± 32.8**
HDL cholesterol (mg/dL)	56.8 ± 14.1	55.2 ± 12.6
TG (mg/dL)	137.2 ± 78.1	120.2 ± 57.8
γGTP (IU/mL)	84.1 ± 115.6	29.8 ± 22.3***
Metabolic syndrome (%)	37.8	33.0
Echocardiographic findings		
EF (%)	69.8 ± 7.5	70.6 ± 6.7
IVS (mm)	10.8 ± 2.1	10.3 ± 2.0+
LVPW (mm)	10.8 ± 1.7	10.3 ± 1.8+
LVDd (mm)	48.0 ± 5.5	45.5 ± 5.4**
LVMI (g/m^2)	110.0 ± 28.7	102.5 ± 28.1
E/A ratio	0.93 ± 0.28	0.79 ± 0.24**
DcT (ms)	222 ± 38	225 ± 42

SBP, systolic blood pressure; DBP, diastolic blood pressure; BNP, B-type natriuretic peptide; CTR, cardiothoracic ratio; BMI, body mass index; FPG, fasting plasma glucose; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglyceride; γGTP, gamma-glutamyltransferase; EF, ejection fraction; IVS, interventricular septal thickness; LVPW, left ventricular posterior wall thickness; LVDd, left ventricular end-diastolic diameter; LVMI, left ventricular mass index; DcT, deceleration time.
+ $p < 0.1$.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$ drinker vs. non-drinker.

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