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Habitual alcohol drinking and peripheral blood cell counts in men with diabetes

ABSTRACT

Background. Habitual alcohol drinking has been shown to be associated with incidental diabetes and glycemic status. The aim of this study was to determine the relationships between alcohol drinking and peripheral blood cell counts in patients with diabetes.

Methods. The participants (n = 333) were Japanese male workers with diabetes aged 32–65 years (mean age: 52.9 years). Relationships of frequency of habitual alcohol drinking with peripheral blood cell-related variables were investigated in middle-aged men with diabetes.

Results. Erythrocyte and leukocyte counts were significantly lower in regular drinkers than in nondrinkers, while platelet count, hemoglobin concentration and hematocrit were not significantly different between regular drinkers and nondrinkers. Mean corpuscular hemoglobin and mean corpuscular volume were significantly higher in regular drinkers than in nondrinkers. Both serum γ-glutamyl transpeptidase and HDL cholesterol levels tended to be higher with an increase of frequency of drinking.

Conclusions. There are inverse associations of habitual alcohol drinking with erythrocyte count and leukocyte count but not with platelet count in men with diabetes.

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Keywords: alcohol, diabetes, erythrocytes, leukocytes, platelets

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Introduction

Alcohol drinking has been shown to be associated with incidental diabetes and glycemic status: According to previous meta-analysis studies, light-to-moderate alcohol drinking was shown to be inversely associated with incidence of type 2 diabetes, and there was a U-shaped relationship between amount of alcohol intake and risk of diabetes [1–3]. Alcohol consumption has also been reported to be inversely associated with hemoglobin A1c level in the general population [4–6].

Alcohol is known to influence peripheral blood cell counts. Alcohol use disorder (AUD), including both alcohol abuse and alcohol dependence, causes macrocytic (megaloblastic) anemia due to deficiency of folate [7]. Mean corpuscular volume (MCV), an index of erythrocyte size, is used as a biomarker for screening to detect AUD [8–10]. In addition, ineffective erythropoiesis associated with impaired iron utilization has been reported in bone marrow of patients with AUD [11]. In the general population, erythrocyte count and leukocyte count were reportedly lower in habitual drinkers than in nondrinkers [12, 13]. Platelet count has been shown to be lower in persons with AUD [14, 15] but not to be different in drinkers and nondrinkers in the general population [16].

Although the inverse associations of habitual drinking with erythrocyte and leukocyte counts in the general population were reported in several studies [12, 13, 16], it remains to be clarified whether and how peripheral blood cell counts are influenced by alcohol drinking in patients with diabetes. Patients with diabetes are vulnerable to infectious disease [17], and thrombosis is an important process in the pathophysiology of cardiovascular disease [18], which is the most frequent complication that decides the prognosis of diabetes patients [19]. In addition, anemia is associated with mortality in patients with ischemic heart disease [20–22]. Thus, it would be of interest to know how peripheral blood cell counts of patients with

diabetes are influenced by habitual alcohol drinking, which shows both harmful and beneficial effects on cardiovascular health: the risk of coronary heart disease is lower in light drinkers but is higher in heavy drinkers compared with nondrinkers [23]. The purpose of this concise study was therefore to determine the relationships between habitual alcohol drinking and peripheral blood cell counts in men with diabetes.

Subjects and methods

Subjects

The participants in the original database were Japanese male workers aged 30–65 years (n = 16014) who had received periodic health checkup examinations at workplaces in Yamagata Prefecture in Japan. This study was approved by the Hyogo College of Medicine Ethics Committee (No. 3003 in 2018). Histories of alcohol consumption, cigarette smoking, illness, and therapy for illness were surveyed by questionnaires. Subjects of this study (n = 333) were men with diabetes [age: 32–65 years (mean age: 52.9 years)] who were extracted from the above database according to the criteria for diabetes as described below. Those receiving therapy for anemia were excluded from the subjects of this study.

Frequency of habitual alcohol drinking was asked in the questionnaire as "How frequently do you drink alcohol?" Frequency of weekly alcohol drinking was categorized as "every day" (regular drinkers), "sometimes" (occasional drinkers) and "never" (nondrinkers). The subjects were divided into four groups by average cigarette consumption (nonsmokers; light smokers, ≤ 20 cigarettes per day; heavy smokers, > 20 and ≤ 40 cigarettes per day; very heavy smokers, > 40 cigarettes per day).

Measurements

Height and body weight were measured with light clothes at the health checkup. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured at the navel level according to the recommendation of the definition of the Japanese Committee for the Diagnostic Criteria of Metabolic Syndrome. [24]. Visceral obesity was evaluated by the ratio of waist circumference (cm) to height (cm). Fasted blood was collected from each subject in the morning and immediately transferred to a 2-mL glass tube containing 3.8 mg EDTA-2K. An automatic hematology analyzer (Sysmex XE-2100, Sysmex Corp., Kobe, Japan) was used for the following measurements of blood cell-related variables. Erythrocyte count and platelet count were measured by the electric resistance detecting method, and leukocyte count was measured by flow cytometry (with a red laser at 633 nm). Hemoglobin concentration and hematocrit were measured by the sodium lauryl sulfate (SLS) hemoglobin method and cumulative pulse height method, respectively. A part of the blood was collected into a plastic tube to obtain serum, and serum gamma-glutamyl transpeptidase (GGT) and HDL cholesterol concentrations were measured by enzymatic methods using commercial kits, pureauto S GGT and cholestest N-HDL (Sekisui Medical Co., Ltd, Tokyo, Japan), respectively. Hemoglobin A_{1c} was measured by the NGSP (National Glycohemoglobin Standardization Program)-approved technique using the latex cohesion method with a commercial kit (Determiner HbA_{1c}, Kyowa Medex, Tokyo, Japan). Since the standards of hemoglobin A_{1c} used for measurement are different in the NGSP method and the JDS (Japan Diabetes Society) method, hemoglobin A_{1c} values were calibrated by using a formula proposed by the JDS [25]: hemoglobin A_{1c} (NGSP) (%) = 1.02 × hemoglobin A_{1c} (JDS) (%) + 0.25 (%). Participants with diabetes were defined as those receiving drug therapy for diabetes and/or those showing high hemoglobin A_{1c} levels (≥ 6.5%).

Statistical analysis

Statistical analyses were performed using a computer software program (SPSS version 16.0 J for Windows, Chicago IL, USA). Mean levels of each quantitative variable were compared using analysis of variance (ANOVA) followed by Scheffé's F-test in univariate analysis and analysis of covariance (ANCOVA) followed by Student's t-test after Bonferroni correction in multivariate analysis. GGT levels did not show a normal distribution and were thus non-parametrically analyzed by using the Kruskal-Wallis test followed by the Steel-Dwass test as a post-hoc test in univariate analysis. Comparison of the percentages of each categorical variable between groups was performed using the chi-square test for independence. Age, history of smoking, BMI, GGT and hemoglobin A_{1c} were used as other explanatory variables in ANCOVA. Probability (p) values less than 0.05 were defined as significant.

Results

Table 1 shows the characteristics of the subjects. The variables were compared among non-, occasional and regular drinker groups by univariate analyses. There were no significant differences among non-, occasional and regular drinkers in age, proportion of smokers, proportion of participants receiving medical therapy for diabetes and level of hemoglobin A_{1c}. Obesity-related indices including BMI, waist circumference and waist-to-height ratio were not significantly different in non-, occasional and regular drinkers. GGT

Table 1. Characteristics of each drinking group and overall subjects with diabetes

	Nondrinkers	Occasional drinkers	Regular drinkers	Overall subjects
Number	80	125	128	333
Age [years]	51.5 (49.5 ~ 53.5)	52.7 (51.3 ~ 54.1)	54.0 (52.8 ~ 55.2)	52.9 (52.1 ~ 53.8)
Smokers [%]	48.8	47.2	50.8	48.9
Therapy for diabetes [%]	55.0	55.2	47.7	52.3
Body mass index [kg/m^2]	25.7 (24.8 ~ 26.7)	25.2 (24.4 ~ 26.0)	24.5 (23.9 ~ 25.1)	25.1 (24.6 ~ 25.5)
Waist circumference [cm]	88.3 (86.0 ~ 90.7)	87.9 (86.3 ~ 89.6)	86.2 (84.6 ~ 87.7)	87.3 (86.3 ~ 88.4)
Waist-to-height ratio	0.523 (0.510 ~ 0.536)	0.519 (0.509 ~ 0.529)	0.512 (0.503 ~ 0.520)	0.517 (0.511 ~ 0.523)
Hemoglobin A_{1c} [%]	7.14 (6.74 ~ 7.53)	6.90 (6.56 ~ 7.23)	6.89 (6.56 ~ 7.22)	6.95 (6.75 ~ 7.15)
GGT [U/dL]	37.0 (22.5, 48.0)	43.0 (31.0, 84.0)**	57.5 (37.5, 95.0)**, †	46.0 (30.0, 80.5)
HDL cholesterol [mg/dL]	44.8 (42.8 ~ 46.8)	50.2 (48.2 ~ 52.2)*	57.1 (54.4 ~ 59.8)**,††	51.5 (50.1 ~ 53.0)
Erythrocytes [x10^4/μL]	500.2 (491.4 ~ 509.1)	498.5 (491.7 ~ 505.3)	485.2 (478.6 ~ 491.7)*,†	493.8 (489.6 ~ 498.0)
Hemoglobin [g/dL]	15.2 (14.9 ~ 15.5)	15.4 (15.2 ~ 15.6)	15.4 (15.2 ~ 15.5)	15.3 (15.2 ~ 15.4)
Hematocrit [%]	45.6 (44.8 ~ 46.4)	46.4 (45.8 ~ 47.0)	46.0 (45.5 ~ 46.6)	46.1 (45.7 ~ 46.4)
MCH [pg]	29.9 (29.5 ~ 30.3)	30.4 (30.1 ~ 30.7)	31.3 (31.0 ~ 31.5)**,††	30.6 (30.4 ~ 30.8)
MCV [fL]	91.3 (90.3 ~ 92.2)	93.3 (92.4 ~ 94.2)*	95.1 (94.3 ~ 95.9)**,†	93.5 (93.0 ~ 94.0)
Leukocytes [/μL]	7531 (7037 ~ 8026)	6880 (6546 ~ 7214)	6438 (6168 ~ 6707)**	6866 (6662 ~ 7071)
Platelets [× 10^4/μL]	23.0 (21.7 ~ 24.3)	22.5 (21.6 ~ 23.5)	22.6 (21.6 ~ 23.6)	22.7 (22.1 ~ 23.3)

Shown are numbers of subjects, frequencies, and means with 95% confidence intervals in parentheses and medians with 25 and 75 percentile values in parentheses of each variable. BMI — body mass index; GGT — γ-glutamyltransferase; HDL — high-density lipoprotein; MCH — mean corpuscular hemoglobin; MCV — mean corpuscular volume. Each variable was compared among the groups by univariate analyses. Asterisks denote significant differences from nondrinkers (*$p < 0.05$; **$p < 0.01$) and occasional drinkers (†$p < 0.05$; ††$p < 0.01$)

and HDL cholesterol levels were significantly higher in occasional and regular drinkers than in nondrinkers and were significantly higher in regular drinkers than in occasional drinkers. Erythrocyte count was significantly lower in regular drinkers than in nondrinkers and occasional drinkers [mean with 95% confidence interval of erythrocyte count (× 10^4/μL): 500.2 (491.4–509.1) in nondrinkers *vs* 498.5 (491.7–505.3) in occasional drinkers *vs* 485.2 (478.6–491.7) in regular drinkers], while hemoglobin concentration and hematocrit were not significantly different among the three drinking groups [hemoglobin (g/dL): 15.2 (14.9–15.5) in nondrinkers *vs* 15.4 (15.2–15.6) in occasional drinkers *vs* 15.4 (15.2–15.5) in regular drinkers; hematocrit [%]: 45.6 (44.8–46.4) in nondrinkers *vs* 46.4 (45.8–47.0) in occasional drinkers *vs* 46.0 (45.5–46.6) in regular drinkers]. Mean corpuscular hemoglobin (MCH) and mean corpuscular volume (MCV) were significantly higher in regular drinkers than in nondrinkers [MCH (pg): 29.9 (29.5–30.3) in nondrinkers *vs* 31.3 (31.0–31.5) in regular drinkers; MCV (fL): 91.3 (90.3–92.2) in nondrinkers *vs* 95.1 (94.3–95.9) in regular drinkers]. MCH and MCV were also significantly higher in regular drinkers than in occasional drinkers [MCH (pg): 30.4 (30.1–30.7): MCV (fL) 93.3 (92.4–94.2) in occasional drinkers]. Leukocyte count was significantly lower in regular drinkers than in nondrinkers [leukocyte count (/μL): 7531 (7037–8026) in nondrinkers *vs* 6438 (6168–6707) in regular drinkers], while platelet count was not significantly different among the three drinking groups [platelet count (× 10^4/μL): 23.0 (21.7–24.3) in nondrinkers *vs* 22.5 (21.6–23.5) in occasional drinkers *vs* 22.6 (21.6–23.6) in regular drinkers].

Table 2 shows a comparison of each variable of peripheral blood cells and HDL cholesterol in multivariate analysis (ANCOVA) with adjustment for age, history of smoking, BMI, GGT and hemoglobin A_{1c}. Erythrocyte count tended to be lower in regular drinkers than in non- and occasional drinkers, although not significant [erythrocyte count (× 10^4/μL): 497.6 (489.4–505.9) in nondrinkers *vs* 498.2 (491.8–504.6) in occasional drinkers *vs* 487.1 (480.6–493.5) in regular drinkers]. There were no significant differences in hemoglobin concentration and hematocrit in non-, occasional and regular drinkers [hemoglobin (g/dL): 15.2 (14.9–15.4) in nondrinkers *vs* 15.4 (15.2–15.6) in occasional drinkers *vs* 15.4 (15.2–15.6) in regular drinkers; hematocrit (%): 45.7 (44.9–46.4) in nondrinkers *vs* 46.4 (45.9–47.0) in occasional drinkers *vs* 46.0 (45.4–46.5) in regular drinkers]. MCH and MCV were significantly higher in regular drinkers than in nondrinkers [MCH (pg): 30.0 (29.7–30.4) in nondrinkers *vs* 31.2 (30.9–31.5) in regular drinkers; MCV (fL): 91.9 (90.9–92.8) in nondrinkers *vs* 94.6 (93.8–95.4) in regular drinkers], and

Table 2. Comparisons of variables related to peripheral blood cells and HDL cholesterol among the drinking groups of subjects with diabetes by multivariate analysis

	Nondrinkers	Occasional drinkers	Regular drinkers
Erythrocytes [$\times 10^4/\mu$L]	497.6 (489.4 ~ 505.9)	498.2 (491.8 ~ 504.6)	487.1 (480.6 ~ 493.5)
Hemoglobin [g/dL]	15.2 (14.9 ~ 15.4)	15.4 (15.2 ~ 15.6)	15.4 (15.2 ~ 15.6)
Hematocrit [%]	45.7 (44.9 ~ 46.4)	46.4 (45.9 ~ 47.0)	46.0 (45.4 ~ 46.5)
MCH [pg]	30.0 (29.7 ~ 30.4)	30.4 (30.1 ~ 30.7)	31.2 (30.9 ~ 31.5)**,†
MCV [fL]	91.9 (90.9 ~ 92.8)	93.4 (92.6 ~ 94.2)*	94.6 (93.8 ~ 95.4)**
Leukocytes [/μL]	7476 (7073 ~ 7880)	6922 (6607 ~ 7238)	6431 (6113 ~ 6748)**
Platelets [$\times 10^4/\mu$L]	22.8 (21.6 ~ 24.0)	22.5 (21.6 ~ 23.5)	22.7 (21.8 ~ 23.7)
HDL cholesterol [mg/dL]	45.6 (42.9 ~ 48.3)	50.3 (48.2 ~ 52.4)*	56.5 (54.4 ~ 58.6)**,†

Shown are means with 95% confidence intervals in parentheses of each variable after adjustment for age, history of smoking, BMI, GGT, and hemoglobin A_{1c} in analysis of covariance. MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume. Symbols indicate significant differences from nondrinkers ($^*p < 0.05$; $^{**}p < 0.01$) and occasional drinkers ($^\dagger p < 0.01$). HDL cholesterol is known to be sensitive to the amount of alcohol consumption [28]

MCH and MCV were also significantly higher in regular drinkers than in occasional drinkers [MCH(pg): 30.4 (30.1–30.7); MCV (fL): 93.4 (92.6–94.2) in occasional drinkers]. Leukocyte count was significantly lower in regular drinkers than in nondrinkers and tended to be lower with an increase in the frequency of alcohol drinking [leukocyte count (/μL): 7476 (7073–7880) in nondrinkers *vs* 6922 (6607–7238) in occasional drinkers *vs* 6431 (6113–6748) in regular drinkers], while platelet count was not significantly different among the three drinking groups [platelet count ($\times 10^4/\mu$L): 22.8 (21.6–24.0) in nondrinkers *vs* 22.5 (21.6–23.5) in occasional drinkers *vs* 22.7 (21.8–23.7) in regular drinkers]. HDL cholesterol was significantly higher in occasional and regular drinkers than in nondrinkers and was significantly higher in regular drinkers than in occasional drinkers [HDL cholesterol (mg/dL): 45.6 (42.9–48.3) in nondrinkers *vs* 50.3 (48.2–52.4) in occasional drinkers *vs* 56.5 (54.4–58.6) in regular drinkers].

Discussion

This study showed for the first time the relationships of habitual alcohol drinking with peripheral blood cell counts in men with diabetes. Erythrocyte count was lower in regular drinkers than in nondrinkers and occasional drinkers, and MCH and MCV were higher in regular drinkers than in nondrinkers, while hemoglobin concentration and hematocrit were not significantly different among the drinking groups. Since MCH and MCV are calculated by hemoglobin and hematocrit, respectively, with being divided by erythrocyte count, higher MCH and MCV in regular drinkers may reflect lower erythrocyte count in regular drinkers than in nondrinkers. Leukocyte count was also lower in regular drinkers than in nondrinkers, while platelet counts were comparable in the three drinking groups. Therefore, it is concluded that in persons with diabetes, erythrocyte count and leukocyte count are inversely associated with regular alcohol drinking, while there is no association between alcohol drinking and platelet count.

The significance of lower erythrocyte count and lower leukocyte count in habitual drinkers with diabetes remains unknown. Although the difference in erythrocyte count between drinkers and nondrinkers was small, there was a considerable difference (about 1000/μL) in leukocyte count of regular drinkers and nondrinkers. Lower leukocyte count is suspected to be related to the risks of infection and cardiovascular disease in patients with diabetes. There is a possible significance of lower leukocyte count in regular drinkers with diabetes as a reason for their vulnerability to infection. Another possibility is that lower leukocyte count reflects the anti-atherosclerotic action of alcohol that results in suppression of inflammatory responses in atherosclerotic lesions [26]. In fact, men who consumed alcohol three to four or five to seven days per week have been shown to have decreased risks of myocardial infarction compared with the risks in men who consumed alcohol less than once per week [27]. However, it is not possible to conclude the changes in peripheral blood cell counts by alcohol in patients with diabetes since this study is a cross-sectional study. Therefore, future prospective studies using a larger population of subjects are needed to clarify causal relationships between alcohol drinking and peripheral blood cell counts in patients with diabetes. There is also a limitation of this study: comparisons of blood cell counts were performed only in the groups of subjects with different frequencies of drinking and were not performed in groups of subjects with different amounts of alcohol drinking since the numbers of subjects in subgroups with different amounts of alcohol intake were not large enough for

statistical analysis. GGT and HDL cholesterol are known to be sensitive to the amount of alcohol consumption [28]. In the present study, there are clear associations of frequency of alcohol drinking with GGT and HDL cholesterol levels (Table 1), implying considerable differences in the amounts of alcohol intake of non-, occasional and regular drinkers. Therefore, it is easily expected that amount of alcohol intake is also inversely associated with erythrocyte count and leukocyte count.

Conclusions

There are inverse associations of regular drinking with erythrocyte and leukocyte counts in men with diabetes. Clinical significance of lower erythrocyte and leukocyte counts in habitual drinkers with diabetes remains to be elucidated.

Conflict of interest

The author declares that there are no competing interests regarding this paper.

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