

Blood Pressure, Levels of Serum Lipids, Liver Enzymes and Blood Glucose by Aldehyde Dehydrogenase 2 and Drinking Habit in Japanese Men

Sayuri NAKAMURA¹, Yoshinori ITO², Koji SUZUKI² and Shuji HASHIMOTO³

¹Department of Adult Nursing, Fujita Health University School of Health Sciences, Toyoake, Japan

²Department of Public Health, Fujita Health University School of Health Sciences, Toyoake, Japan

³Department of Hygiene, Fujita Health University School of Medicine, Toyoake, Japan

Abstract

Objectives: The association of blood pressure and levels of serum lipids, liver enzymes, blood glucose and aldehyde dehydrogenase 2 (ALDH2) with drinking habit was examined in Japanese men.

Methods: The subjects were 264 men aged 39 to 80 years who were classified into the ALDH2 deficiency or sufficiency group using the ethanol patch test and the Tokyo University ALDH2 Phenotype Screening Test. A self-administered questionnaire including drinking habit was used. Blood pressure and the levels of biochemical markers in groups with ALDH2 sufficiency, ALDH2 deficiency and drinking habit were compared using multiple regression models for adjusting age, smoking habit, physical exercising habit and body mass index.

Results: The levels of serum high-density lipoprotein cholesterol, triglycerides, aspartate aminotransferase (AST) and gamma-glutamyl transpeptidase (γ -GTP) were significantly higher in current drinkers of 20 g of ethanol or more per day than in nondrinkers of the ALDH2 sufficiency group. The levels of serum AST and γ -GTP in current drinkers of 20 g of ethanol or more per day, and fasting blood sugar in current drinkers of less than 20 g of ethanol per day were significantly higher than those in nondrinkers of the ALDH2 deficiency group.

Conclusions: These results suggest that alcohol consumption increases the levels of serum lipids and liver enzymes in ALDH2-sufficient individuals and liver enzymes and blood glucose levels in ALDH2-deficient individuals.

Key words: aldehyde dehydrogenase 2, alcohol, serum lipids, liver enzymes, blood glucose

Introduction

Many epidemiologic studies have shown that a high alcohol consumption affects blood pressure (1–9), levels of serum total cholesterol (2, 8–10) and liver enzymes (2, 8, 11), and glucose tolerance (6, 12, 13). The aldehyde dehydrogenase 2 (ALDH2) enzyme can efficiently detoxify acetaldehyde by converting it into acetic acid, and the activity of ALDH2 may modify the association between alcohol consumption, blood pressure and biochemical markers (14).

Most Caucasians have the active ALDH2 phenotype, whereas many Asians including Japanese do not. About 60% of Japanese have ALDH2 sufficiency, and others have an ALDH2 complete or partial deficiency (15–17).

There is a strong association between the activity of ALDH2 and alcohol consumption. Alcohol consumption is lower in individuals with ALDH2 deficiency than in those with ALDH2 sufficiency (17–19). Thus, the findings on the health effects of alcohol consumption obtained from Western populations might be mainly based on the comparison between ALDH2-sufficient drinkers and nondrinkers, whereas those from Asian populations might be based on the comparison between ALDH2-sufficient drinkers and ALDH2-sufficient or deficient nondrinkers.

In this study, blood pressure and levels of serum lipids and liver enzymes, and blood glucose were compared between groups classified on the basis of ALDH2 sufficiency, deficiency and drinking habit in Japanese men.

Received Oct. 17, 2005/Accepted Jan. 25, 2006

Reprint requests to: Sayuri NAKAMURA

Department of Adult Nursing, Fujita Health University School of Health Sciences, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan

TEL: +81(562)93-9082, FAX: +81(562)93-4595

E-mail: sayuri@fujita-hu.ac.jp

Subjects and Methods

Study subjects

Subjects were inhabitants aged 39–80 years in a town in Hokkaido Prefecture of Japan. Among 1,742 individuals who underwent medical examinations in 2000 and 2001, 634 provided their written informed consent to participate in this study. Of these subjects, 21 individuals with missing data and 20 individuals undergoing medical treatments for liver diseases were excluded. Because most of the 329 women were non-drinkers, we analyzed the data of 264 men. We used the data in 2000 for 24 men who were examined in both 2000 and 2001.

Determination of ALDH2 deficiency and sufficiency

The subjects were classified into the ALDH2 deficiency and sufficiency groups using the proposed procedures of the ethanol patch test (20, 21) and the Tokyo University ALDH2 Phenotype Screening Test (TAST) (22) by ASK Human Care Inc., Tokyo. An adhesive plaster with a few drops of 70% ethanol was placed on the inside of the subject's upper arm for 7 minutes and then removed. Ten minutes after the removal, his/her skin reaction was assessed. ALDH2 deficiency (complete and partial deficiency) or sufficiency was determined on the basis of the result. When the result was uncertain, the TAST score for 13 questions on physical symptoms after drinking was used. These tests were performed by an experienced public health nurse. Possible problems in these procedures are discussed later.

Questionnaire

A self-administered questionnaire with items including those on drinking habit, smoking habit, physical exercising habit and medical history was used. The questions on drinking habit included drinking status, age when drinking started, frequency of drinking per week, and the usual amount of alcohol consumed on each occasion. The unit alcohol consumption per occasion was "gou" (Japanese standard unit for an alcoholic beverage "sake"), which can be converted to 23 g of ethanol. A glass of wine, a glass of double whiskey and 2 cans of beer were converted to a gou of sake. The subjects were classified on the basis of their drinking habit, namely, nondrinkers, former drinkers and current drinkers. Nondrinkers included persons who drank less than once a week. For current drinkers, the average daily alcohol consumptions, determined by multiplying the usual amount of alcohol consumed on each occasion by frequency of drinking, were categorized into less than 20 g of ethanol and 20 g or more.

The subjects were also classified on the basis of their smoking habit, namely, never smokers, former smokers and current smokers. Regarding physical exercising habit, the subjects were classified into nonregular and regular exercisers. Regular exercisers exercise more than twice a week for 30 minutes for more than 1 year. Medical history, including medical treatments for hypertension, hyperlipemia and liver diseases, and a history of diabetes mellitus were examined.

Clinical examination

Systolic blood pressure (SBP) and diastolic blood pressure

(DBP) were measured using a mercury sphygmomanometer while subjects were sitting down.

Using fasting blood samples, the levels of serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transpeptidase (γ -GTP) were measured using an autoanalyzer (JCA-RX20, Nihon Denshi Inc.). Fasting blood sugar (FBS) level was measured using a glucose AUTO & STAT GA-1122 kit (Kyoto Daiichi Inc., Kyoto) (23). Serum was separated from blood cells within one hour of collection by centrifugation. Blood hemoglobinA_{1c} (HbA_{1c}) level was measured by high-performance liquid chromatography (24).

Body height and weight were measured. Body mass index (BMI) was calculated as body weight (kg) divided by the square of height (m).

Statistical analysis

The association among ALDH2 sufficiency, ALDH2 deficiency, drinking habit and medical history was tested using the chi-squared test.

Differences in the mean blood pressure, and mean levels of serum lipids, liver enzymes and blood glucose among the groups with ALDH2 sufficiency, ALDH2 deficiency and drinking habit were estimated using multiple regression models. For TG, AST, ALT, γ -GTP and FBS, because their values were log normally distributed, the logarithmically transformed values were used in their models, and their differences in means were converted to ratios of geometric means by the inverse transformation of logarithm. Blood pressure and the levels of serum lipids, liver enzymes and blood glucose were dependent variables. The models included the combination of ALDH2 sufficiency, ALDH2 deficiency and drinking habit as dummy independent variables. The combination had four categories: ALDH2-deficient nondrinkers, ALDH2-deficient current drinkers, ALDH2-sufficient nondrinkers and ALDH2-sufficient current drinkers. Other independent variables were age, smoking habit, physical exercising habit and BMI. Former drinkers were excluded in the above models. The subjects receiving medical treatments for hypertension were excluded in the models with SBP and DBP as dependent variables. Those receiving medical treatments for hyperlipemia were excluded in the models with TC, HDL-C and TG as dependent variables. Those with a history of diabetes mellitus were excluded in the models with FBS and HbA_{1c} as dependent variables.

Blood pressure and the levels of serum lipids, liver enzymes and blood glucose in the groups with ALDH2 sufficiency, ALDH2 deficiency and alcohol consumption were also compared using multiple regression models with alcohol consumption as an independent variable. The combination had six categories: ALDH2-deficient nondrinkers, ALDH2-deficient current drinkers with less than 20 g of ethanol per day, ALDH2-deficient current drinkers with 20 g of ethanol or more per day, ALDH2-sufficient nondrinkers, ALDH2-sufficient current drinkers with less than 20 g of ethanol per day, and ALDH2-sufficient current drinkers with 20 g of ethanol or more per day.

All statistical analyses were performed using SPSS software (version 12.0, SPSS Japan Inc., Tokyo).

Table 1 Characteristics of study subjects

	No. (%)
Total	264 (100.0)
Age	
39–49 years	51 (19.3)
50–59 years	70 (26.5)
60–69 years	84 (31.8)
70–80 years	59 (22.4)
Drinking habit	
Nondrinkers	93 (35.2)
Former drinkers	22 (8.3)
Current drinkers	149 (56.5)
Smoking habit	
Never smokers	57 (21.6)
Former smokers	94 (35.6)
Current smokers	113 (42.8)
Physical exercising habit	
Nonregular exercisers	213 (80.7)
Regular exercisers	51 (19.3)
Body mass index (kg/m ²)	
<18.5	6 (2.3)
18.5–24.9	173 (65.5)
≥25	85 (32.2)
Medical treatments for hypertension	
No	197 (74.6)
Yes	67 (25.4)
Medical treatments for hyperlipemia	
No	251 (95.1)
Yes	13 (4.9)
History of diabetes mellitus	
No	238 (90.2)
Yes	26 (9.8)

Results

Table 1 shows the characteristics of subjects. Of 264 subjects, the percentages of subjects aged 39–49, 50–59, 60–69 and 70–80 years old ranged from 19.3% to 31.8%. The percentages of non-, former and current drinkers were 35.2%, 8.3% and 56.5%, respectively. Table 2 shows the mean or geometric mean values of blood pressure, serum lipids, liver enzymes and blood glucose. The mean or geometric mean values were 127.7 mmHg of SBP, 80.2 mmHg of DBP, 201.3 mg/dl of TC, 53.0 mg/dl of HDL-C, 105.2 mg/dl of TG, 25.0 IU/l of AST, 23.3 IU/l of ALT, 31.0 IU/l of γ -GTP, 98.0 mg/dl of FBS and 5.06% of HbA_{1c}.

Table 3 shows the association among ALDH2 sufficiency, ALDH2 deficiency, drinking habit and alcohol consumption. The numbers of ALDH2-deficient and ALDH2-sufficient subjects were 80 (30.3%) and 184 (69.7%), respectively. The percentage of current drinkers was significantly lower in the ALDH2 deficiency group than in the ALDH2 sufficiency

Table 3 Association among ALDH2 sufficiency, ALDH2 deficiency, drinking habit and alcohol consumption

	ALDH2 deficiency	ALDH2 sufficiency	p value
	No. (%)	No. (%)	
Drinking habit			
Nondrinkers	46 (57.5)	47 (25.5)	<0.001
Former drinkers	7 (8.7)	15 (8.2)	
Current drinkers	27 (33.8)	122 (66.3)	
Total	80 (100.0)	184 (100.0)	
Alcohol consumption (g of ethanol per day)*			
less than 20	16 (59.3)	38 (31.1)	0.006
20 or more	11 (40.7)	84 (68.9)	
Total	27 (100.0)	122 (100.0)	

* Current drinker.

Table 2 Mean blood pressure and mean levels of serum lipids, liver enzymes and blood glucose

	No.	Mean	Mean minus standard deviation	Mean plus standard deviation
Systolic blood pressure (mmHg) ^{a,1}	197	127.7	112.2	142.7
Diastolic blood pressure (mmHg) ^{a,1}	197	80.2	70.9	89.5
Total cholesterol (mg/dl) ^{b,1}	251	201.3	169.6	233.0
High-density lipoprotein cholesterol (mg/dl) ^{b,1}	251	53.0	36.0	70.0
Triglycerides (mg/dl) ^{b,2}	251	105.2	61.7	179.2
Aspartate aminotransferase (IU/l) ²	264	25.0	18.8	33.2
Alanine aminotransferase (IU/l) ²	264	23.3	14.9	36.4
Gamma-glutamyl transpeptidase (IU/l) ²	264	31.0	15.1	63.5
Fasting blood sugar (mg/dl) ^{c,2}	238	98.0	87.4	109.9
HemoglobinA _{1c} (%) ^{c,1}	238	5.06	4.63	5.49

^a Subjects undergoing medical treatments for hypertension were excluded.

^b Subjects undergoing medical treatments for hyperlipemia were excluded.

^c Subjects with a history of diabetes mellitus were excluded.

¹ Data are presented as mean, mean minus and plus standard deviations.

² Data are presented as mean, mean minus and plus standard deviations of logarithmic values converted by the inverse transformation of logarithm. A converted mean is a geometric mean.

group. The percentage of subjects that consume 20 g of ethanol or more per day among current drinkers was significantly lower in ALDH2 deficiency than in ALDH2 sufficiency.

Table 4 shows the association between ALDH2 sufficiency, ALDH2 deficiency, drinking habit and medical history. The percentages of those receiving medical treatments for hypertension in each of the four groups of ALDH2-sufficient nondrinkers and current drinkers, and ALDH2-deficient nondrinkers and current drinkers ranged from 17.4% to 29.8%. The percentages of those receiving medical treatments for hyperlipemia in each of these four groups ranged from 4.1% to 7.4%. The percentages of subjects with a diabetes mellitus history were 2.2% in ALDH2-deficient nondrinkers, 0.0% in ALDH2-deficient current drinkers, 12.8% in ALDH2-sufficient nondrinkers and 10.7% in ALDH2-sufficient current drinkers. There were no significant differences among these percentages.

Table 5 shows the differences in means or the ratios of geometric means values in blood pressure, serum lipids, liver enzymes and blood glucose between groups with ALDH2

sufficiency, ALDH2 deficiency and drinking habit adjusted for age, smoking habit, physical exercising habit and BMI. That is the differences in means or the ratios of geometric means indicated in blood pressure and levels of serum lipids, liver enzymes and blood glucose as shown by the 3 comparisons of nondrinkers versus current drinkers among ALDH2 deficiency, nondrinkers versus current drinkers among ALDH2 sufficiency, and ALDH2 deficiency versus sufficiency among nondrinkers. There were no significant differences in SBP, DBP, and levels in serum ALT and HbA_{1c} in the 3 comparisons of nondrinkers versus current drinkers among ALDH2 deficiency, nondrinkers versus current drinkers among ALDH2 sufficiency, and ALDH2 deficiency versus sufficiency among nondrinkers. The mean TC level was significantly lower, and the geometric mean TG level was lower in ALDH2 sufficiency than in ALDH2 deficiency among nondrinkers (p=0.091). The mean HDL-C level was higher in current drinkers than in nondrinkers among those with ALDH2 sufficiency (p=0.057). The geometric mean TG, AST and γ -GTP levels were significantly higher in current

Table 4 Association between ALDH2 sufficiency, ALDH2 deficiency, drinking habit and medical history

Medical history		ALDH2 deficiency		ALDH2 sufficiency		p value
		Nondrinkers	Current drinkers	Nondrinkers	Current drinkers	
		No. (%)	No. (%)	No. (%)	No. (%)	
Medical treatments for hypertension	No	38 (82.6)	21 (77.8)	33 (70.2)	89 (73.0)	0.501
	Yes	8 (17.4)	6 (22.2)	14 (29.8)	33 (27.0)	
Medical treatments for hyperlipemia	No	44 (95.7)	25 (92.6)	45 (95.7)	117 (95.9)	0.901
	Yes	2 (4.3)	2 (7.4)	2 (4.3)	5 (4.1)	
History of diabetes mellitus	No	45 (97.8)	27 (100.0)	41 (87.2)	109 (89.3)	0.077
	Yes	1 (2.2)	0 (0.0)	6 (12.8)	13 (10.7)	

Table 5 Differences in means or ratios of geometric mean values in blood pressure, serum lipids, liver enzymes and blood glucose between groups with ALDH2 sufficiency, ALDH2 deficiency and drinking habit adjusted for age, smoking habit, physical exercising habit and body mass index

	No.	ALDH2-deficient nondrinkers versus ALDH2-deficient current drinkers		ALDH2-sufficient nondrinkers versus ALDH2-sufficient current drinkers		ALDH2-deficient nondrinkers versus ALDH2-sufficient nondrinkers	
		Difference or ratio	p value	Difference or ratio	p value	Difference or ratio	p value
		Systolic blood pressure (mmHg) ^{a,1}	181	-2.1	0.681	2.6	0.472
Diastolic blood pressure (mmHg) ^{a,1}	181	0.4	0.899	1.8	0.405	-0.4	0.363
Total cholesterol (mg/dl) ^{b,1}	231	-11.9	0.219	6.2	0.344	-21.6	0.006
High-density lipoprotein cholesterol (mg/dl) ^{b,1}	231	-4.3	0.339	5.9	0.057	-1.4	0.704
Triglycerides (mg/dl) ^{b,2}	231	0.948	0.733	1.249	0.036	0.811	0.091
Aspartate aminotransferase (IU/l) ²	242	1.068	0.462	1.138	0.034	1.090	0.904
Alanine aminotransferase (IU/l) ²	242	0.988	0.923	1.076	0.396	1.020	0.847
Gamma-glutamyl transpeptidase (IU/l) ²	242	1.908	0.004	1.850	<0.001	1.259	0.190
Fasting blood sugar (mg/dl) ^{c,2}	222	1.100	0.008	1.025	0.331	0.989	0.699
HemoglobinA _{1c} (%) ^{c,1}	222	0.21	0.119	0.03	0.733	-0.07	0.503

^a Former drinkers and subjects undergoing medical treatments for hypertension were excluded.

^b Former drinkers and subjects undergoing medical treatments for hyperlipemia were excluded.

^c Former drinkers and subjects with a history of diabetes mellitus were excluded.

¹ Data are presented as differences in means and p value.

² Data are presented as the ratios of geometric means and p value.

Table 6 Differences in means or ratios of geometric mean values in blood pressure, serum lipids, liver enzymes and blood glucose between groups with ALDH2 sufficiency, ALDH2 deficiency and alcohol consumption adjusted for age, smoking habit, physical exercising habit and body mass index

	No.	ALDH2 deficiency				ALDH2 sufficiency			
		Nondrinkers versus current drinkers of less than 20 g of ethanol per day		Nondrinkers versus current drinkers of 20 g of ethanol or more per day		Nondrinkers versus current drinkers of less than 20 g of ethanol per day		Nondrinkers versus current drinkers of 20 g of ethanol or more per day	
		Difference or ratio	p value	Difference or ratio	p value	Difference or ratio	p value	Difference or ratio	p value
Systolic blood pressure (mmHg) ^{a,1}	181	-7.9	0.338	-3.2	0.480	1.4	0.792	3.2	0.405
Diastolic blood pressure (mmHg) ^{a,1}	181	1.2	0.720	-1.2	0.802	0.7	0.810	2.4	0.278
Total cholesterol (mg/dl) ^{b,1}	231	-3.6	0.752	-26.7	0.061	16.8	0.087	3.2	0.646
High-density lipoprotein cholesterol (mg/dl) ^{b,1}	231	-6.9	0.197	0.3	0.963	4.0	0.380	6.5	0.048
Triglycerides (mg/dl) ^{b,2}	231	0.859	0.407	1.133	0.582	1.069	0.668	1.296	0.020
Aspartate aminotransferase (IU/l) ²	242	0.949	0.617	1.313	0.038	1.053	0.551	1.170	0.013
Alanine aminotransferase (IU/l) ²	242	0.912	0.550	1.132	0.515	1.057	0.663	1.091	0.346
Gamma-glutamyl transpeptidase (IU/l) ²	242	1.357	0.221	3.508	<0.001	1.338	0.160	2.136	<0.001
Fasting blood sugar (mg/dl) ^{c,2}	222	1.106	0.019	1.089	0.108	1.032	0.400	1.023	0.400
HemoglobinA _{1c} (%) ^{c,1}	222	0.10	0.505	0.37	0.058	0.09	0.514	0.01	0.899

^a Former drinkers and subjects undergoing medical treatments for hypertension were excluded.

^b Former drinkers and subjects undergoing medical treatments for hyperlipemia were excluded.

^c Former drinkers and subjects with a history of diabetes mellitus were excluded.

¹ Data are shown as differences in means and p value.

² Data are shown as the ratios of geometric means and p value.

drinkers than in nondrinkers among those with ALDH2 sufficiency. The geometric mean γ -GTP and FBS levels were significantly higher in current drinkers than in nondrinkers among those with ALDH2 deficiency.

Table 6 shows the differences in means or the ratios of geometric means values in blood pressure, serum lipids, liver enzymes and blood glucose between groups with ALDH2 sufficiency, ALDH2 deficiency and alcohol consumption adjusted for age, smoking habit, physical exercising habit and BMI. There were no significant differences in SBP, DBP and ALT level in the 4 comparisons of nondrinkers versus current drinkers of less than 20 g of ethanol per day among those with ALDH2 deficiency, nondrinkers versus current drinkers of 20 g of ethanol or more per day among those with ALDH2 deficiency, nondrinkers versus current drinkers of less than 20 g of ethanol per day among those with ALDH2 sufficiency, and nondrinkers versus current drinkers of 20 g of ethanol or more per day among those with ALDH2 sufficiency. The mean HDL-C level and geometric mean TG, AST and γ -GTP levels were significantly higher in current drinkers of 20 g of ethanol or more per day than in nondrinkers among those with ALDH2 sufficiency. The mean TC level was higher in current drinkers of less than 20 g of ethanol per day than in nondrinkers among those with ALDH2 sufficiency (p=0.087). The geometric mean AST and γ -GTP levels were significantly higher in current drinkers of 20 g of ethanol or more per day than in nondrinkers among those with ALDH2 deficiency. The mean TC level was lower, and the mean HbA_{1c} level was higher in current drinkers of 20 g of ethanol or more per day than in nondrinkers among those with ALDH2 deficiency, but the differences were not significant (p=0.061 and 0.058, respectively). The geometric

mean FBS level was significantly higher in current drinkers of less than 20 g of ethanol per day than in nondrinkers among those with ALDH2 deficiency.

Discussion

There was no statistically significant association between blood pressure and drinking habit among subjects with an ALDH2 deficiency and those with an ALDH2 sufficiency. Previous studies showed that a high blood pressure is associated with alcohol consumption, not with ALDH2 activity (25, 26). We failed to detect a positive association between blood pressure and alcohol consumption in part because our analysis would not have sufficient power. Thus our results provide no information on the association between blood pressure and ALDH2 activity.

The levels of serum HDL-C and TG were significantly higher in current drinkers of 20 g of ethanol or more per day than in nondrinkers with ALDH2 sufficiency. This result confirms the positive association between serum lipid level and alcohol consumption reported by a previous study of western populations where most individuals were ALDH2-sufficient (2). However, this similar positive association between serum lipid level and alcohol consumption was not observed among subjects with ALDH2 deficiency. The associations between serum lipid level, alcohol consumption and ALDH2 activity seemed unclear in both the present and a previous study (26).

The association between liver function and alcohol consumption has been well known (2, 8, 11). In the present study, the levels of serum AST and γ -GTP were significantly higher in current drinkers of 20 g of ethanol or more per day

than in nondrinkers with ALDH2 sufficiency and in those with ALDH2 deficiency. In ALDH2-deficient persons, blood acetaldehyde level increases after drinking, which is more likely to cause liver injury. However, the finding that the effect of alcohol consumption on liver function is greater in current drinkers with ALDH2 deficiency than in those with ALDH2 sufficiency was not observed in either the present or a previous study (27).

A higher FBS level in current drinkers of less than 20 g of ethanol per day, and a higher blood HbA_{1c} level in those consuming 20 g of or more of ethanol per day than in nondrinkers having ALDH2 deficiency were observed, whereas there were no differences in these levels between current drinkers and nondrinkers with ALDH2 sufficiency. The specific reasons for these results remain unknown. Previous studies showed that light to moderate alcohol consumption is associated with glucose tolerance, and that heavy alcohol consumption is inversely associated with glucose tolerance (12, 28). Previous studies showed no difference in blood glucose level between individuals with ALDH2 deficiency and those with sufficiency (26, 29). However, blood glucose level was reportedly higher in light to moderate drinkers than in nondrinkers with ALDH2 deficiency in type2 diabetes mellitus subjects (29). A previous study showed that ethanol and acetaldehyde inhibit insulin action (30). Our results suggest that moderate alcohol consumption was inversely associated with glucose tolerance in those with ALDH2 deficiency. Further research is necessary to clarify this issue.

The present study has some limitations and problems. The subjects were limited to inhabitants who underwent medical examination and agreed to participate in this study. Because most of the women had no drinking habit, we analyzed the data of men only. Drinking habit information was obtained using a self-administered questionnaire. ALDH2 deficiency or sufficiency was determined using the proposed procedures of ethanol patch test and TAST. Although these procedures have been used in several studies (20, 21, 25, 31, 32), the accuracy of

their determinations could be lower than that of determination base on genetic polymorphism (33, 34). The proportion of agreement between these determinations from the previous study would be from 80% to 90% (33, 34).

The percentage of ALDH2 sufficiency in the present study was 69.7%, which was higher than the near 60% in previous studies of Japanese subjects. The participation rate in our study would be higher among individuals with ALDH2 sufficiency than among those with ALDH2 deficiency. The percentage of current drinkers was low in ALDH2 deficiency because some symptoms such as facial flushing, pulsation, headache and nausea in ALDH2-deficient individuals are induced by an elevation in the blood acetaldehyde level after drinking. Our data might not have sufficient power for analyzing the health effects of drinking in ALDH2 deficiency. Our analysis included adjusting for age, smoking habit, physical exercising habit and BMI. Further adjustment for other potential confounders such as diet might be important. Although our study design was cross-sectional, our findings would provide useful information for evaluating the health effects of alcohol drinking among those with ALDH2 sufficiency and deficiency. A longitudinal study would provide a more accurate evaluation.

In conclusion, this study suggest that alcohol consumption increases the levels of serum lipids and liver enzymes in individuals with ALDH2 sufficiency, and increases liver enzymes and blood glucose levels in those with ALDH2 deficiency in Japanese men.

Acknowledgements

The authors wish to thank all the subjects for their participation in our study. We are also grateful to Dr. Kunio Aoki, Professor Emeritus, Aichi Cancer Center, and the staff of the medical examination program for residents in the town in Hokkaido, Japan. This study was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

References

- Ueshima H, Shimamoto T, Iida M, Konishi M, Tanigaki M, Doi M, et al. Alcohol intake and hypertension among urban and rural Japanese populations. *J Chronic Dis.* 2001;37:585–592.
- Hoffmeister H, Schelp FP, Mensink GB, Dietz E, Böhning D. The relationship between alcohol consumption, health indicators and mortality in the German population. *Int J Epidemiol.* 1999;28:1066–1072.
- Fuchs FD, Chambless LE, Whelton PK, Nieto FJ, Heiss G. Alcohol consumption and incidence of hypertension: the atherosclerosis risk in communities study. *Hypertension.* 2001;37:1242–1250.
- Nakanishi N, Yoshida H, Nakamura K, Suzuki K, Tataru K. Alcohol consumption and risk for hypertension in middle-aged Japanese men. *J Hypertens.* 2001;19:851–855.
- Xin X, He J, Frontini MG, Ogden LG, Motsamai OI, Whelton PK. Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension.* 2001;38:1112–1117.
- Taniguchi Y, Hayashi T, Tsumura K, Endo G, Fujii S, Okada K. Serum uric acid and the risk for hypertension and type 2 diabetes in Japanese men: The Osaka Health Survey. *J Hypertens.* 2001;19:1209–1212.
- MacMahon S. Alcohol consumption and hypertension. *Hypertension.* 1987;9:111–121.
- Hashimoto Y, Futamura A, Nakarai H, Nakahara K. Relationship between response of γ -glutamyl transpeptidase to alcohol drinking and risk factors for coronary heart disease. *Atherosclerosis.* 2001;158:465–470.
- Sakurai H, Yamaguchi H. Alcohol and cardiovascular disease. *Rinsho Eiyo.* 1996;89:607–613. (Article in Japanese)
- Johansen D, Andersen PK, Jensen MK, Schnohr P, Gronbaek M. Nonlinear relation between alcohol intake and high-density lipoprotein cholesterol level: results from the Copenhagen City heart study. *Alcohol Clin Exp Res.* 2003;27:1305–1309.

- (11) Takahashi H. Alcohol and liver disease: alcoholic liver disorder. In: Shirakura K, Sawayama T editor. *Alcohol Medical Treatment Introduction*. Tokyo: Shinkou Igaku Shuppan; 2003. P. 30–35. (Article in Japanese)
- (12) Kao WH, Puddey IB, Boland LL, Watson RL, Brancati FL. Alcohol consumption and the risk of type 2 diabetes mellitus: atherosclerosis risk in communities study. *Am J Epidemiol*. 2001;154:748–757.
- (13) Maruyama K, Yokoyama A. Alcohol and metabolic disease: diabetes mellitus, gout. In: Shirakura K, Sawayama T editor. *Alcohol Medical Treatment Introduction*. Tokyo: Shinkou Igaku Shuppan; 2003. P. 41–44. (Article in Japanese)
- (14) Okuyama K. The absorption and metabolism of alcohol. In: Shirakura K, Sawayama T editor. *Alcohol Medical Treatment Introduction*. Tokyo: Shinkou Igaku Shuppan; 2003. P. 12–18. (Article in Japanese)
- (15) Harada S. Genetic polymorphism of aldehyde dehydrogenase and its physiological significance to alcohol metabolism. In: Oggita Z, Market CL editor. *Isozymes: Structure, Function, and Use in Biology and Medicine*. New York: Wiley-Liss; 1990. P. 289–294.
- (16) Mizoi Y, Tatsuno Y, Adachi J, Kogame M, Fukunaga T, Fujiwara S, et al. Alcohol sensitivity related to polymorphism of alcohol-metabolizing enzymes in Japanese. *Pharmacol Biochem Behav*. 1983;18:127–133.
- (17) Higuchi S, Muramatsu T, Shigemori K, Saito M, Kono H, Dufour MC, et al. The relationship between low Km aldehyde dehydrogenase phenotypes and drinking behavior in Japanese. *J Stud Alcohol*. 1992;53:170–175.
- (18) Takeshita T, Mao XQ, Morimoto K. The contribution of polymorphism in the alcohol dehydrogenase β subunit to alcohol sensitivity in a Japanese population. *Hum Genet*. 1996;97:409–413.
- (19) Morimoto K, Takeshita T. Low Km aldehyde dehydrogenase (ALDH2) polymorphism, alcohol-drinking behavior, and chromosome alterations in peripheral lymphocytes. *Environ Health Perspect*. 1996;104:175–179.
- (20) Muramatsu T, Higuchi S, Shigemori K, Saito M, Sasao M, Harada S, et al. Ethanol patch test—a simple and sensitive method for identifying ALDH phenotype. *Alcohol Clin Exp Res*. 1989;13:229–231.
- (21) Higuchi S, Muramatsu T, Saito M, Sasao M, Maruyama K, Kono H, Niimi Y. Ethanol patch test for low Km aldehyde dehydrogenase deficiency. *Lancet*. 1987;1:629.
- (22) Yamada K, Asaka A, Norioka T, Takeshita T. Questionnaire for detecting the phenotype of low Km ALDH (ALDH2). In: Kuriyama K, Takeda A, Ishii H editor. *Biomedical and Social Aspects of Alcohol and Alcoholism*. Amsterdam: Elsevier Science Publishers; 1988. P. 481–484.
- (23) Shima K. Laboratory of blood glucose. In: Yamanaka K, Kawai T, Miyai K editor. *Standard Textbook of Laboratory Medicine*. Tokyo: Igakushoin; 1987. P. 103–104. (Article in Japanese)
- (24) Klenk DC, Hermanson GT, Kronhn RI, Fujimoto EK, Mallia AK, Smith PK, et al. Determination of glycosylated hemoglobin by affinity chromatography: comparison with colorimetric and ion-exchange methods, and effects of common interferences. *Clin Chem*. 1982;28:2088–2094.
- (25) Okayama A, Ueshima H, Yamakawa M, Kita Y. Low-km aldehyde dehydrogenase deficiency does not influence the elevation of blood pressure by alcohol. *J Hum Hypertens*. 1994;8:205–208.
- (26) Hashimoto Y, Nakayama T, Futamura A, Omura M, Nakarai H, Nakahara K. Relationship between genetic polymorphisms of alcohol-metabolizing enzymes and changes in risk factors for coronary heart disease associated with alcohol consumption. *Clin Chem*. 2002;48:1043–1048.
- (27) Takeshita T, Yang X, Morimoto K. The ADLH2 genotype, alcohol intake, and liver-function biomarkers among Japanese male workers. *Hum Genet*. 2000;106:589–593.
- (28) Lu W, Jablonski KA, Resnick HE, Jain AK, Jones KL, Gottlieb AM, et al. Alcohol intake and glycemia in American Indians: the strong heart study. *Metabolism*. 2003;52:129–135.
- (29) Murata T, Suzuki Y, Muramatsu T, Taniyama M, Atsumi Y, Matsuoka K, et al. Inactive aldehyde dehydrogenase 2 worsens glycemic control in patients with type 2 diabetes mellitus who drink low to moderate amounts of alcohol. *Alcohol Clin Exp Res*. 2000;24:5S–11S.
- (30) Flario L, Mohammad AK, Paresch D. Ethanol and its novel metabolites inhibit insulin action on adipocytes. *Diabetes*. 1988;37:912–915.
- (31) Matsuka Y, Wang DH, Suganuma N, Imai K, Ikeda S, Taketa K, et al. Differential responses of serum gamma-gultamyltransferase to alcohol intake in Japanese males. *Acta Med Okayama*. 2003;57:171–178.
- (32) Watanabe H, Nasu I. Relationship between ethanol patch test and problem drinkers among dental students. *Jpn J Alcohol & Drug Dependence*. 2002;37:153–162. (Article in Japanese)
- (33) Takeshita T. Gene-environmental interactions in alcohol-related health problems: contributions of molecular biology to behavior modifications. *Jpn J Hyg*. 2003;58:254–259. (Article in Japanese)
- (34) Takeshita T. Genetic factors which regulate alcohol drinking behavior and their effects on health status. *Jpn J Hyg*. 1999; 54:450–458. (Article in Japanese)