Int J Clin Exp Med 2020;13(10):7700-7708
www.ijcem.com /ISSN:1940-5901/IJCEM0114924

Original Article

Effect of high alcohol intake on heavy metal levels in the blood, urine cotinine metabolism, and pulmonary function according to the severity of smoking

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Received May 25, 2020; Accepted July 25, 2020; Epub October 15, 2020; Published October 30, 2020

Abstract: The relationship between alcohol intake, heavy metal levels in the blood, urine cotinine (uCot), and pulmonary function in smokers has seldom been studied. This study aimed to investigate the effect of high alcohol consumption on heavy metal levels in the blood, cotinine metabolism, and lung function according to the severity of smoking. A total of 3,262 adult participants were evaluated by measuring heavy metal levels in the blood, uCot, and spirometric indices. The degree of alcohol intake was assessed by the alcohol use disorders identification test (AUDIT) score. In heavy smokers, levels of lead, cadmium, and mercury in the blood were significantly higher in subjects with AUDIT score ≥ 8, than in those with AUDIT score < 8. However, in light smokers, there were no significant differences in heavy metal levels in the blood between the two groups. AUDIT score was significantly associated with mercury level in the blood, whereas uCot was correlated with cadmium levels in the blood. In nonsmokers, men with AUDIT score ≥ 8 demonstrated a significantly higher forced expiratory volume in the first second/forced vital capacity ratio than those with AUDIT score < 8 (0.81 ± 0.09 versus 0.76 ± 0.08, P < 0.001). However, no significant difference was observed in uCot levels between the groups. In conclusion, co-use of cigarette smoking and high alcohol intake leads to elevated heavy metal levels in the blood in heavy smokers. High alcohol consumption has some positive effects on pulmonary function in nonsmokers but has no significant influence on cotinine metabolism.

Keywords: Alcohol consumption, smoking, urinary cotinine, heavy metals in the blood, pulmonary function

Introduction

Smoking is associated with numerous diseases, such as chronic obstructive pulmonary diseases, cardiovascular diseases, and a variety of cancers [1]. Cigarette smoke contains more than 4,000 toxic substances, including nicotine, heavy metals, carbon monoxide, and polycyclic aromatic hydrocarbons [2]. Smoking is an important source of lead and cadmium exposure in the general population [3]. Heavy metals can accumulate in the body, resulting in chronic endogenous exposure. In particular, cadmium is a carcinogenic metal of increasing public health concern [4].

Nicotine is mainly absorbed by the pulmonary system during cigarette smoking. It is metabolized into cotinine by a hepatic enzyme, CYP2A6, which accounts for approximately 75% of nicotine metabolism [5]. Approximately 10-15% of cotinine is excreted in the urine, and the rest is further metabolized to trans-3'-hydroxycotinine and other byproducts [6]. As cotinine has much longer half-life than nicotine, measurement of cotinine is preferred to the measurement of nicotine as a biomarker for cigarette smoking [7]. A study demonstrated that chronic alcohol consumption induces CYP2A6 enzyme activity [8]. However, other studies have reported no significant association between current alcohol consumption and CYP2A6 enzyme activity [9, 10].

Cigarette smoking with excessive alcohol intake is a highly co-morbid behavior. The prevalence of alcohol use disorders is higher in heavy smokers than in the overall population [11]. The

alcohol use disorders identification test (AUDIT) score is the most widely used alcohol screening test for hazardous and harmful drinking. AUDIT score ≥ 8 is generally accepted as the criteria for hazardous drinking [12].

The relationship between cigarette smoking and blood heavy metal levels has been extensively studied. However, few studies have closely examined the effect of co-use of cigarette smoking and drinking alcohol on heavy metal levels in the blood, nicotine metabolism, and pulmonary function in smokers. This study investigated how alcohol intake, measured by AUDIT score, influences heavy metal levels in the blood, spirometric indices, and cotinine metabolism, in conjunction with smoking severity.

Materials and methods

Subjects

A total of 3,262 subjects were investigated, including 1,801 men and 1,461 women. Their mean age was 43 years, and the age range was 20-87 years. Data were obtained from the Korean National Health and Nutrition Examination Survey. Adult participants aged ≥ 20 years with the following data were included: completed self-reported smoking status, alcohol consumption status, urine cotinine (uCot) test, heavy metal blood assay, and spirometric indices. Exclusion criteria were as follows: (a) those with abnormal renal or hepatic function (to exclude the potential effect on nicotine metabolism), (b) people on nicotine replacement therapy, including a nicotine patch, (c) those with missing values in the health assessment or questionnaires. The study protocol was approved by the institutional review board, and informed consent was obtained from all participants.

Estimation of uCot, CCR, and smoking status

The concentration of uCot was assayed by gas chromatography and mass spectrometry using Perkin Elmer Clarus 600T (PerkinElmer, Turku, Finland). The uCot/creatinine ratio (CCR) was calculated using the following formula; CCR (μg/g) = [uCot (ng/mL)/urinary creatinine (mg/dL)] × 100 [13]. Individuals with uCot > 50 ng/mL were defined as cotinine-verified smokers, and those with uCot < 15 ng/mL were defined as cotinine-verified nonsmokers [14]. Smokers were classified into two groups based on the amount of smoking per day: heavy smokers (> 20 cigarettes/day, n = 415) and light smokers (< 10 cigarettes/day, n = 348).

Measurement of heavy metals in the blood

Blood samples were collected to assess heavy metal levels. Concentration of cadmium and lead were measured by graphite furnace atomic absorption spectrometry with a Zeeman background correction (AAnalyst 600; PerkinElmer, Turku, Finland). For quality assurance, reference materials were used (Lyphochek, Whole Blood Metals Control; Bio-Rad, Hercules, CA, USA). Mercury level was measured by a cold vapor atomic absorption spectrometric method using a mercury analyzer (M-6000A, CETAC Technologies, USA). The detection limits for lead, cadmium, and mercury in the blood in the present study were 0.23 μg/dL, 0.30 μg/L, and 0.36 μg/L, respectively.

Assessment of AUDIT score

Assessment of alcohol intake was assessed by AUDIT, a 10-item screening instrument designed to measure three domains of alcohol use: consumption (items 1-3), dependence (items 4-6), and alcohol-related problems (items 7-10) [15]. The AUDIT score is the sum of scores from all ten AUDIT questions. AUDIT scores fall into four categories: non-drinker (score = 0), non-hazardous drinking (1-7), hazardous drinking (8-14), and harmful drinking (15-40). Smokers were categorized into two groups according to AUDIT score and intensity of smoking: heavy smokers with high alcohol consumption (AUDIT score ≥ 8, n = 294) or low alcohol consumption (AUDIT score < 8, n = 121); light smokers with high alcohol consumption (AUDIT score ≥ 8, n = 206) or low alcohol consumption (AUDIT score < 8, n = 142).

Pulmonary function tests

Pulmonary function tests (PFTs) were performed by a trained expert using a spirometer. Forced vital capacity (FVC) was measured as the volume of air that can forcibly be blown out after full inspiration. Forced expiratory volume in the first second (FEV_1) was measured as the volume of air that can forcibly be blown out in the first 1 second after full inspiration. The

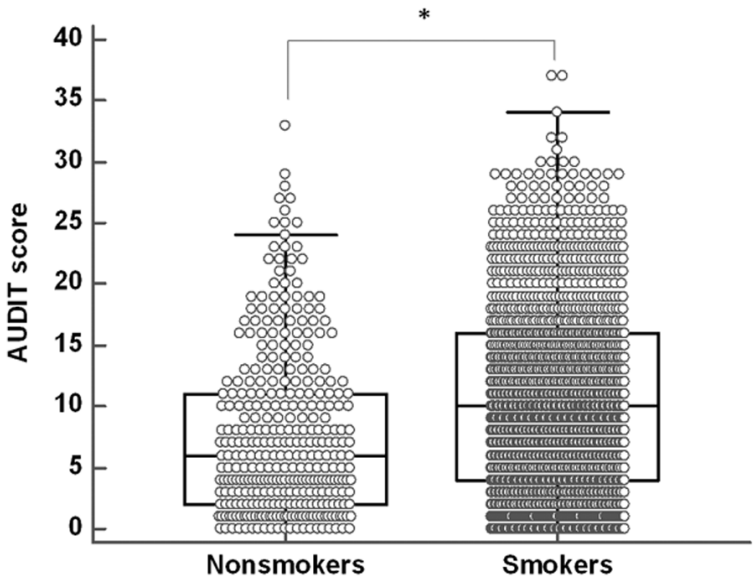

Figure 1. Comparison of alcohol intake between current smokers and nonsmokers. AUDIT scores are significantly higher in current smokers (n = 825) than nonsmokers (n = 330) in men. *; P < 0.001.

FEV_1/FVC ratio was calculated by dividing the value of FEV_1 with the value of FVC.

Physical activity

To exactly evaluate spirometric indices, physical activity was measured as an influencing factor of PFTs. Participants were asked about their physical activity each week. Vigorous exercise was defined as performing physical activities for at least 30 minutes/day, such as running, climbing, cycling fast, swimming fast, football, basketball, jumping rope, playing squash, and playing singles tennis. Moderate exercise was defined as performing physical activities for at least 30 minutes/day, such as walking fast, swimming slowly, playing doubles tennis, and volleyball [16].

Seafood consumption

To assess possible exposure to heavy metals from seafood consumption, the frequency of fish or shellfish consumption was evaluated. Information about the frequency of seafood consumption was obtained from the nutrition survey. The consumption frequency of at least one type of fish or shellfish was counted on the basis of a nutrition survey checklist. Subjects were categorized into two groups based on fish and shellfish consumption frequency of at least once per week or less than once per week.

Statistical analysis

Data were presented as mean ± standard deviation (SD) if normally distributed and as median (range) if non-normally distributed. The normality of data distribution was confirmed by a Kolmogorov-Smirnov's one-sample test. Categorical variables were expressed as frequencies and proportions. A Mann-Whitney U test and a Student's t-test were used to analyze data between the two groups. The relationship between heavy metal concentrations in the blood, uCot, CCR, and AUDIT scores was assessed by multivariate regression analysis after adjustment for potential confounders, including age, sex, body mass index (BMI), and frequencies of physical activity and seafood consumption. Data were analyzed using SPSS software (IBM SPSS Statistics for Windows, version 19.0. Armonk, NY, USA). A value of $P < 0.05$ was considered statistically significant.

Results

Alcohol intake and smoking status in subjects

AUDIT scores were significantly higher in current smokers than nonsmokers in men (11.5 ± 7.5 versus 7.8 ± 6.7, P < 0.001) (**Figure 1**). Of the 330 male and 1,261 female self-reported nonsmokers, 6 males (1.8%) and 59 females (4.7%) were cotinine-verified smokers (uCot > 50 ng/mL). In contrast, 2.2% (18/825) of men and 5.7% (5/88) of women who self-reported as smokers were classified as uCot-verified nonsmokers (uCot < 15 ng/mL) (**Table 1**).

AUDIT score, heavy metals, and spirometric indices

In male heavy smokers, lead, cadmium, and mercury levels in blood in subjects with AUDIT score ≥ 8 were 3.30 ± 1.81 μg/dL, 1.56 ± 0.62 μg/L, and 6.47 ± 5.19 μg/L, respectively; which were significantly higher than the values in those with AUDIT score < 8 (2.84 ± 1.02 μg/dL, 1.37 ± 0.65 μg/L, and 4.90 ± 2.68 μg/L;

Table 1. Smoking status and uCot levels in subject populations

Self-reported smoking	Subjects (n = 3,262)	Age (years)	Smoking history		uCot level (ng/mL)	
			Duration (years)	Cigarettes/ day	< 15 uCot-verified nonsmoker	> 50 uCot-verified smoker
Men						
Current smokers	825	43 (20-83)	26.2 ± 13.9	17.1 ± 8.3	18 (2.2)[a]	763 (92.5)[a]
Past smokers	646	53 (20-85)	20.7 ± 14.1	17.3 ± 11.4	552 (85.4)	55 (8.5)
Nonsmokers	330	37 (20-76)	NA	NA	291 (88.2)	6 (1.8)
Women						
Current smokers	88	43 (20-86)	19.6 ± 14.2	9.9 ± 5.9	5 (5.7)[a]	81 (92.0)[a]
Past smokers	112	38 (20-87)	6.7± 8.8	7.3 ± 6.6	84 (75.0)	15 (13.4)
Nonsmokers	1,261	44 (20-77)	NA	NA	1,108 (87.9)	59 (4.7)

Data are expressed as mean ± SD, median (range), or frequency (%). [a]Significant (P < 0.05), compared to corresponding groups of nonsmokers. AUDIT: alcohol use disorders identification test; uCot: urine cotinine; NA: not applicable.

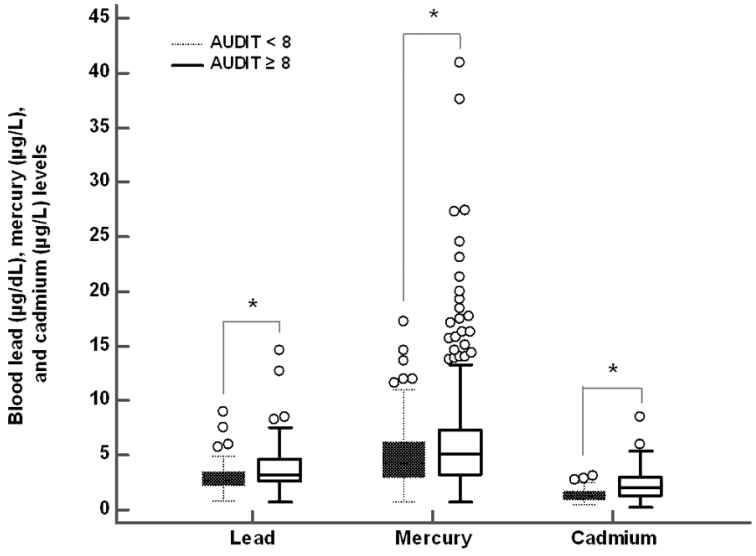

Figure 2. Heavy metal levels in the blood in relation to alcohol consumption in male heavy smokers. Lead, cadmium, and mercury levels in the blood in subjects with AUDIT score ≥ 8 (n = 294) are significantly higher than the values in those with AUDIT score < 8 (n = 121). *; P < 0.05.

respectively, P < 0.05) (**Figure 2**). However, there were no significant differences in heavy metal levels in the blood between the two groups of light smokers. In nonsmokers, men with AUDIT score ≥ 8 displayed a significantly higher FEV_1/FVC ratio than those with AUDIT score < 8 (0.81 ± 0.09 versus 0.76 ± 0.08, P < 0.001). However, in light and heavy smokers, the spirometric indices did not differ between groups based on AUDIT score (**Table 2**).

Heavy metals and PFTs in former smokers

The influence of past smoking on heavy metal levels in the blood and spirometric indices was investigated. To assess the effect of past smoking in the same condition, former smokers with uCot level < 15 ng/mL were compared to age-matched nonsmokers with uCot < 15 ng/mL. Mean AUDIT score of former smokers was not different from that of nonsmokers (9.5 ± 7.3 versus 9.1 ± 6.8, P = 0.532). Cadmium levels in the blood were significantly higher in former smokers than in nonsmokers (0.76 ± 0.33 μg/L versus 0.68 ± 0.31 μg/L, P = 0.006). However, there were no significant differences in spirometric indices and lead and mercury levels in the blood between the two groups (**Table 3**).

Relationship between heavy metals in the blood, uCot, and AUDIT score

To assess the relationship between heavy metals in the blood, uCot-related parameters, and AUDIT scores, multivariate regression analysis was conducted. After adjusting for potential confounders, the uCot concentration was closely associated with cadmium levels (r = 0.265, P < 0.001), and AUDIT score was positively correlated with mercury and cadmium levels (r = 0.142 and r = 0.154, respectively, P < 0.001). Lead levels were significantly associated with CCR (r = 0.201, P < 0.001), but not with uCot levels (**Table 4**). An example of scatter plots showing the correlations between

Table 2. Physical activity and spirometric indices in relation to AUDIT score in light and heavy smokers

Parameters	uCot-verified male smokers (n = 763)						uCot-verified male nonsmokers (n = 291)		
	Heavy smokers (n = 415)			Light smokers (n = 348)					
	AUDIT ≥ 8 (n = 294)	AUDIT < 8 (n = 121)	*p* value	AUDIT ≥ 8 (n = 206)	AUDIT < 8 (n = 142)	*p* value	AUDIT ≥ 8 (n = 119)	AUDIT < 8 (n = 172)	*p* value
Demographic variables									
Age (years)	44.5 ± 11.7	44.7 ± 12.6	0.412	39.5 ± 13.9	42.7 ± 15.0	0.072	40.7 ± 14.5	41.3 ± 15.9	0.740
BMI (kg/m^2)	24.4 ± 2.9	24.2 ± 3.7	0.342	23.7 ± 2.9	23.1 ± 2.8	0.065	24.5 ± 3.1	23.5 ± 3.2	0.106
Smoking status									
Smoking (cigarettes/day)	23.1 ± 6.2	22.6 ± 6.4	0.166	7.7 ± 2.9	7.8 ± 2.7	0.891	NA	NA	NA
Duration (years)	20 (1.5-62)	20 (1.0-64)	0.726	3 (0.5-12)	2.5 (1.0-15)	0.203	NA	NA	NA
uCot (ng/mL)	1866.2 ± 1008.4	1841.8 ± 1004.3	0.855	917.8 ± 848.6	985.7 ± 780.6	0.490	4.64 ± 3.59	3.92 ± 3.49	0.094
CCR	1301.4 ± 982.8	1339.2 ± 1019.6	0.775	703.5 ± 780.2	725.0 ± 812.7	0.524	3.25 ± 4.85	2.62 ± 3.39	0.191
Alcohol intake									
AUDIT score	16.2 ± 6.1	2.9 ± 2.4	< 0.001	14.8 ± 5.9	3.8 ± 2.2	< 0.001	14.5 ± 5.3	3.1 ± 2.2	< 0.001
Physical activity (frequency/week)									
Vigorous exercise	2.3 ± 1.9	2.2 ± 2.0	0.318	2.4 ± 1.8	2.0 ± 1.7	0.062	2.5 ± 1.9	2.4 ± 1.8	0.247
Moderate exercise	2.5 ± 2.1	2.3 ± 1.9	0.153	2.3 ± 1.9	2.1 ± 1.8	0.332	2.4 ± 1.7	2.3 ± 1.6	0.309
Seafood intake ≥ 1/week (n, %)	67 (22.8)	25 (20.6)	0.325	43 (20.8)	28 (19.7)	0.462	28 (23.5)	42 (24.4)	0.407
Spirometric indices									
FVC (%)	93.8 ± 12.5	90.1 ± 9.6	0.063	91.2 ± 13.2	93.1 ± 11.3	0.431	91.6 ± 9.9	90.1 ± 11.3	0.488
FEV_1 (%)	89.8 ± 12.4	86.4 ± 10.6	0.098	88.0 ± 12.8	90.4 ± 12.9	0.345	90.6 ± 10.2	89.2 ± 10.5	0.537
FEV_1/FVC ratio	0.76 ± 0.08	0.74 ± 0.08	0.112	0.75 ± 0.09	0.76 ± 0.08	0.492	0.81 ± 0.09	0.76 ± 0.08	< 0.001

Data are expressed as mean ± SD, median (range), or frequency (%). BMI: body mass index; uCot: urine cotinine; CCR: uCot/creatinine ratio; AUDIT: alcohol use disorders identification test; FVC: forced vital capacity; FEV_1: forced expiratory volume in first second; NA: not applicable.

Table 3. Heavy metal levels in the blood and spirometric indices in past smokers

Parameters	Past smokers (males; n = 552)	Nonsmokers (males; n = 164)	*p* value
Demographic parameters			
Age (years)	53.2 ± 11.3	52.1 ± 15.3	0.775
BMI (kg/m^2)	24.3 ± 2.8	23.9 ± 3.2	0.253
Smoking status			
Smoking (cigarettes/day)	23.0 ± 11.5	NA	NA
Duration of smoking (years)	13.3 ± 12.6	NA	NA
Cotinine-related parameters			
uCot (ng/mL)	3.93 ± 3.45	4.21 ± 3.54	0.374
CCR	2.49 ± 2.55	2.87 ± 4.05	0.213
Heavy metals			
Lead (μg/dL)	2.52 ± 0.91	2.45 ± 1.34	0.442
Mercury (μg/L)	5.34 ± 3.58	5.01 ± 4.03	0.315
Cadmium (μg/L)	0.76 ± 0.33	0.68 ± 0.31	0.006
Spirometric indices			
FVC (%)	92.5 ± 11.8	92.1 ± 10.3	0.783
FEV_1 (%)	89.9 ± 13.5	91.0 ± 11.0	0.486
FEV_1/FVC ratio	0.77 ± 0.09	0.77 ± 0.08	0.681
Alcohol intake			
AUDIT score	9.5 ± 7.3	9.1 ± 6.8	0.532
Physical activity (frequency/week)			
Vigorous exercise	2.5 ± 1.8	2.3 ± 1.7	0.227
Moderate exercise	2.7 ± 2.1	2.4 ± 1.8	0.063
Seafood intake ≥ 1/week (n, %)	132 (23.9)	42 (25.6)	0.297

Data are expressed as mean ± SD or frequency (%). BMI: body mass index; AUDIT: alcohol use disorders identification test; uCot: urine cotinine; CCR: uCot/creatinine ratio; FVC: forced vital capacity; FEV_1: forced expiratory volume in first second; NA: not applicable.

Table 4. Relationship between heavy metals in the blood, uCot-related parameters, and AUDIT scores in 763 uCot-verified male smokers

	Cadmium (μg/L)	Lead (μg/dL)	Mercury (μg/L)
Univariate			
uCot (ng/mL)	0.314 (< 0.001)	0.072 (0.124)	-0.021 (0.566)
CCR	0.263 (< 0.001)	0.241 (< 0.001)	-0.033 (0.425)
AUDIT score	0.176 (< 0.001)	0.058 (0.096)	0.213 (< 0.001)
Multivariate*			
uCot (ng/mL)	0.265 (< 0.001)	0.053 (0.137)	-0.017 (0.642)
CCR	0.237 (< 0.001)	0.201 (< 0.001)	-0.029 (0.431)
AUDIT score	0.154 (< 0.001)	0.023 (0.516)	0.142 (< 0.001)

Data are expressed as standardized β (*p* value). *Adjusted for age, BMI, and frequencies of physical activity and seafood consumption. uCot: urine cotinine; CCR: uCot/creatinine ratio; AUDIT: alcohol use disorders identification test.

uCot concentrations, AUDIT scores, and cadmium and mercury levels in the blood is illustrated in **Figure 3A** and **3B**.

Discussion

Smoking is known to increase heavy metal levels in the blood [17]. In this study, we assessed the effect of alcohol intake on heavy metal levels in the blood according to severity of smoking. In heavy smokers, lead, cadmium, and mercury levels in the blood were higher in subjects with AUDIT score ≥ 8, than in those with AUDIT score < 8. However, no significant differences in heavy metal levels in the blood were observed between groups of light smokers. To assess the potential effect of seafood consumption on heavy metal concentrations, the frequency of fish or shellfish consumption was evaluated. There were no significant differences in the frequency

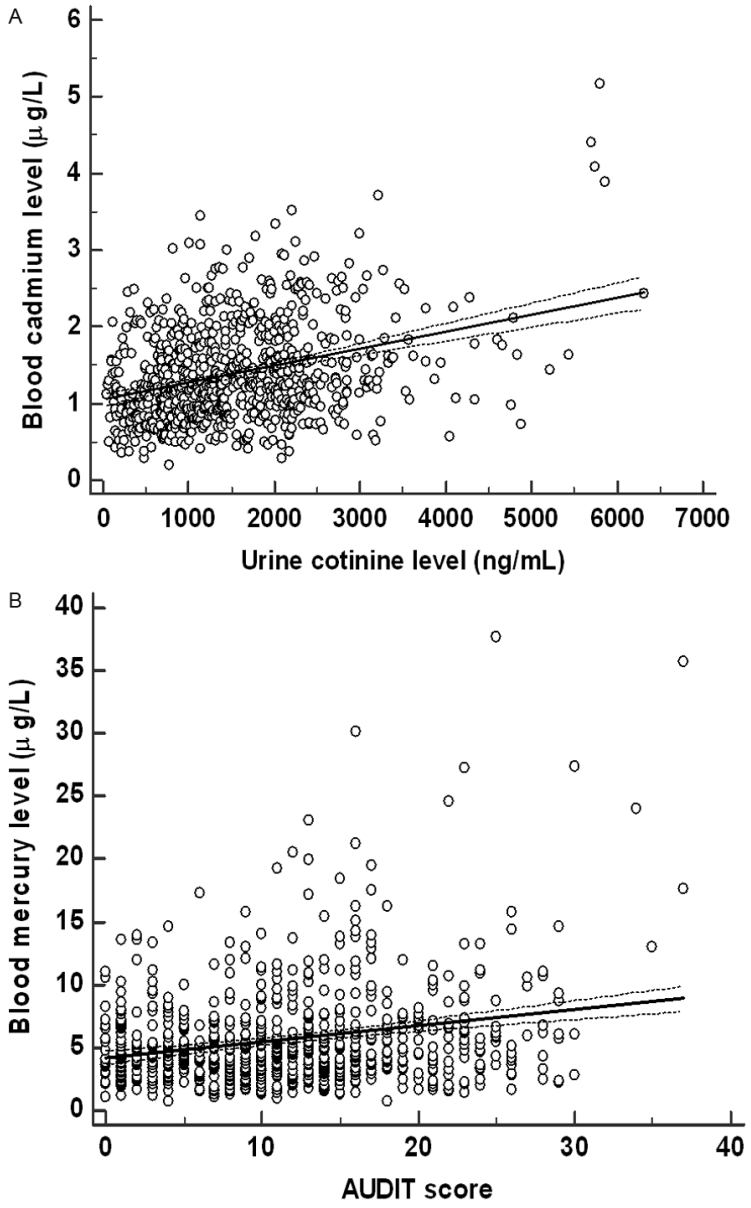

Figure 3. Scatter plots showing the relationship between uCot concentrations and cadmium levels (A) and between AUDIT scores and mercury levels (B) in uCot-verified male smokers (n = 763). Cadmium levels in the blood are significantly associated with uCot concentrations ($y = 0.0002x + 1.047$, $r = 0.314$, $P < 0.001$) and AUDIT scores are closely correlated with blood mercury levels ($y = 0.127x + 4.189$, $r = 0.213$, $P < 0.001$).

of seafood consumption between subjects with AUDIT score ≥ 8 and those with AUDIT score < 8. Therefore, elevated heavy metal levels in the blood are attributable to high alcohol consumption in conjunction with heavy smoking. Alcoholic beverage drinking may facilitate absorption of heavy metals from cigarette smoke. These results suggest that the effect of alcohol consumption on heavy metal levels in the blood differs according to intensity of smoking. In addition, heavy metal levels in the blood are intensified when high alcohol intake is combined with heavy smoking.

Cadmium has a biological half-life of more than 20 years in the body. Once taken up, cadmium accumulates in liver, kidneys, and bone [18]. Only a small portion of the total body burden of cadmium is eliminated per day via the urine. Low fractional excretion determines the cumulative effects of cadmium on renal, neurologic, and cardiovascular diseases [19, 20]. A study reported that cadmium levels in the blood were two- to five fold higher in smokers than in nonsmokers [21]. In our study, the uCot concentration was more strongly associated with cadmium level than lead and mercury levels in the blood. To strictly assess cadmium level in the same conditions, former smokers with uCot < 15 ng/mL were compared to age-matched nonsmokers with uCot < 15 ng/mL. Cadmium level was significantly higher in former smokers than in nonsmokers, although the uCot level of former smokers did not differ from that of nonsmokers. Interestingly, no significant differences were observed in lead and mercury levels in the blood and spirometric indices between the two groups. The results suggest that cadmium accumulates more easily in the body than lead and mercury and also that past smoking does not necessarily decrease lung function.

Fluid intake can influence uCot levels by affecting urine volume. Urinary CCR has been used to overcome this problem [22]. A previous study demonstrated that the use of CCR is better than the use of uCot alone [23]. In our study,

uCot levels were correlated with cadmium level in the blood alone, but CCR was correlated with lead and cadmium levels. Because CCR is calculated by considering urine creatinine content, it may lessen the potential influence of kidney function on lead levels in the blood. This is a possible explanation for why lead levels were significantly associated with CCR but not with uCot in our study.

A study reported that alcohol consumption is associated with improved lung function [24, 25]. However, another study demonstrated that excessive alcohol intake has a detrimental effect on pulmonary function [26]. Studies on the effect of alcohol intake accompanied by cigarette smoking on spirometric indices are limited. In the present study, the effect of alcohol consumption on pulmonary function was assessed in relation to smoking. In smokers, spirometric indices did not differ between subjects with AUDIT score ≥ 8 and those with AUDIT score < 8. However, in male nonsmokers, subjects with AUDIT score ≥ 8 exhibited higher FEV_1/FVC ratio than those with AUDIT score < 8. In our study, physical activity and anthropometric parameters were evaluated as potential confounders of PFTs. There were no significant differences in confounding factors between the two groups. These results imply that high alcohol consumption may have a positive effect on lung function, although this effect is limited to nonsmokers. In smokers, the beneficial effect of alcohol intake on spirometric indices seems to be counterbalanced by the negative effect of cigarette smoking on pulmonary function.

Alcohol ingestion reportedly increases CYP2A6 enzyme activity, which is associated with nicotine metabolism [27]. If alcohol intake enhances CYP2A6 activity, cigarette smoking would be underestimated in alcohol drinkers when cotinine is used as a biomarker of smoking. This study investigated whether alcohol consumption influences nicotine metabolism in smokers. There was no significant difference in uCot levels between smokers with AUDIT score ≥ 8 and those with AUDIT score < 8. These findings are consistently observed in light and heavy smokers. Based on these results, the co-use of alcohol consumption and cigarette smoking has no significant effect on the cotinine level in urine.

This study has several limitations. The relationship between AUDIT score and smoking in women was not investigated because of the small sample size of women who were both cigarette smokers and alcohol drinkers in our study population. Heavy metal levels in the blood could not be evaluated in serial samples to assess disease progression. Despite these limitations, this study has important significance. In the present study, the effect of alcohol intake on heavy metal levels in the blood and spirometric indices was evident only when subjects had hazardous drinking exhibited by AUDIT score ≥ 8.

In conclusion, this study demonstrates that high alcohol consumption accompanied by cigarette smoking significantly increases heavy metal levels in the blood, particularly in heavy smokers. Alcohol consumption has some beneficial effect on pulmonary function, although the effect is limited to nonsmokers. High alcohol intake does not seem to affect cotinine metabolism in smokers.

Acknowledgements

This study was supported by a research grant from Inha University Hospital.

Disclosure of conflict of interest

None.

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