

Risk factors for alcoholic liver disease in China

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Abstract

AIM: To examine the association of daily alcohol intake, types of alcoholic beverage consumed, drinking patterns and obesity with alcoholic liver disease in China.

METHODS: By random cluster sampling and a 3-year follow-up study, 1 270 alcohol drinkers were recruited from different occupations in the urban and suburban areas of Xi'an City. They were examined by specialists and inquired for information on: Medical history and family medical history, alcohol intake, types of alcoholic beverage consumed, drinking patterns by detailed dietary questionnaires. Routine blood tests and ultrasonography were done.

RESULTS: Multivariate analysis showed that: (1) The risk threshold for developing alcoholic liver disease was ingestion of more than 20 g alcohol per day, keeping on drinking for over 5 years in men. The highest OR was at the daily alcohol consumption ≥ 160 g, the occurrence rate of ALD amounted to 18.7% ($P < 0.01$). No ALD occurred when ingestion of alcohol was less than 20 g per day. (2) 87.9% of all drank only at mealtimes. The cumulative risk of developing ALD was significantly higher in those individuals who regularly drank alcohol without food than in those who drank only at mealtimes, especially for those who regularly drank hard liquors only and multiple drinks ($P < 0.05$). (3) The alcohol consumption in those with BMI ≥ 25 was lower than in those with BMI < 25 , but the risk increased to 11.5%, significantly higher than that of general population, 6.5% ($P < 0.01$). (4) Abstinence and weight reduction could benefit the liver function recovery.

CONCLUSION: In the Chinese population the ethanol risk threshold for developing ALD is 20 g per day, and this risk increases with increased daily intake. Drinking 20 g of ethanol per day and for less than 5 years are safe from ALD. Drinking alcohol outside mealtimes and drinking hard liquors only and multiple different alcohol beverages both increase the risk of developing ALD. Obesity also increases the risk. Abstinence and weight reduction will directly affect the prognosis of ALD. Doctor's strong advice might influence the prognosis indirectly.

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INTRODUCTION

Alcoholic liver disease (ALD) is a major health and economic problem in the Western world^[1-5]. Over 14 million Americans are alcohol abusers or alcohol dependent. The problem in China is not as serious as that in Western world. But in recent years, along with the improved living standard and increased alcohol consumption, the morbidity of ALD has risen quickly. Among drinkers, the morbidity has reached 6.1%^[6]. Therefore, ALD has become an increasingly serious disease risk in health care. However, not all drinkers are ALD patients, and there is different susceptibility to damage by alcohol in individuals^[5]. As a common problem, some of its risk factors have been reported in Western countries, but recent analyses have confirmed that geographic and racial variations are evident. In China, however, there is no such study to confirm the main risk factors of ALD, such as cumulative alcohol intake, drinking patterns, types of alcoholic beverage ingested and obesity. In the present study, we aimed to analyze these factors according to random cluster sampling data and a 3-year follow-up study.

MATERIALS AND METHODS

Subjects

We recruited 1 270 drinkers from different occupations in the urban and suburban areas of Xi'an City by random cluster sampling. Every participant was examined by medical staff and received detailed inquiry at his or her home. The medical staff members were trained before the beginning of the study in order to be able to administer the questionnaire uniformly. The questions included: (1) An extensive medical history, including previous diagnosis of chronic liver disease and family medical history. (2) Evaluation of alcohol intake, including detailed questions on the use of alcoholic beverages, types of alcoholic beverage consumed, drinking patterns, the duration of use and the time of drinking (at mealtimes or without food). All the questions were also validated by cross-checking with family members. (3) A detailed physical examination, the body mass index (BMI) and ultrasonography were also performed and recorded. (4) Blood samples were taken to check serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), γ -glutamyl transferase (GGT), hepatitis B (HBsAg) and anti-hepatitis C virus (anti-HCV). (5) Three years later, all the patients were investigated again, including detailed inquiry about their relevant diseases and alcohol intake in the past 3 years. Meanwhile, the BMI, ultrasonography and blood samples were taken again.

Diagnosis

The diagnosis of ALD was confirmed according to the published data^[6].

Statistical analysis

Statistical analysis was performed with SPSS 10.0 statistical

package. A logistic-regression model was used in the multivariate modeling of associations. All the factors for which the *P* value of univariate and discriminant analysis was less than 0.05 were entered in the model. Odds ratios (ORs) and 95% confidence intervals (CI) were also calculated.

RESULTS

Study population

Of the 1 270 drinkers, 83 were ALD patients including 72 cases of alcoholic fatty liver, 6 cases of alcoholic hepatitis, and 4 cases of alcoholic cirrhosis. Only one woman was excluded from the study. None of the patients took any medicine in latest 3 mo. Anti-HCV and HBsAg were all negative. Three years later, 66 of 82 ALD subjects were reinvestigated, constituting 80.5% of all. Of the 66 ALD, 19 subjects had BMI \geq 25 and 47 subjects had BMI less than 25.

Daily alcohol consumption and ALD

Analysis of the data showed that the risk of having ALD was significant with a daily alcohol intake higher than 20 g (Table 1) and the mean duration of drinking longer than 5 years. Above this threshold, the OR for ALD increased proportionally with daily alcohol consumption. The highest OR (10.7, $P < 0.01$) occurred when daily consumption exceeded 160 g. At this highest level of alcohol intake, the percentage of subjects with ALD was 18.7%, significantly higher than that of the lowest level of alcohol intake of less than 20 g/d. Among these subjects whose daily alcohol consumption was less than 20 g and the duration of drinking was less than 5 years, no ALD occurred. So we can assume that daily intake of 20 g alcohol for 5 years is the risk threshold. With longer duration of drinking (more than 10-15 years), a few cases occurred even though the daily intake was less than 20 g, but the morbidity was very low, only 2.2%.

Table 1 Average daily alcohol intake and duration of drinking

Alcohol intake (g/d)	<i>n</i>	<5 yr	\geq 5-9 yr	\geq 10-14 yr	\geq 15-19 yr	\geq 20 yr	Total	OR (95% CI)
<20	780	0	1	3	5	8	17 (2.2%)	—
\geq 20-39	217	1	2	6	6	10	25 (11.4%)	5.5 (2.9-12.3)
\geq 40-79	149	1	6	4	3	6	20 (13.5%)	7.1 (3.5-13.6)
\geq 80-159	76	1	3	2	1	4	11 (14.6%)	8.4 (4.1-17.3)
\geq 160	48	1	1	2	1	4	9 (18.7%)	10.7 (5.2-23.4)
Total	1 270	4 (1.5%)	13 (4.4%)	17 (6.9%)	16 (11.3%)	32 (9.4%)	82 (6.5%)	

$P < 0.01$, vs group of alcohol intake < 20 g/d.

Table 2 Different drinking habits and types of alcoholic beverage

Type of beverage	<i>n</i>	With meals only			At any time			χ^2
		Daily intake (g)	<i>n</i> (%)	Patients (%)	Daily intake (g)	<i>n</i> (%)	Patients (%)	
Beer	390	6.1 \pm 3.7	351 (90.0)	2 (0.57)	8.9 \pm 4.3	39 (10.0)	0 (0.00)	
Wine	132	10.8 \pm 5.3	118 (89.4)	1 (0.84)	19.2 \pm 9.6	14 (10.6)	1 (7.1)	3.32
Hard liquor	491	45.2 \pm 15.9	417 (84.9)	46 (11.0)	67.7 \pm 21.1	74 (15.1)	14 (18.9)	3.65
Multiple	257	29.4 \pm 11.5	231 (89.9)	14 (6.1)	42.8 \pm 13.2	26 (10.9)	4 (15.4)	3.12
Total	1 270		1 117 (87.9)	63 (5.6)		153 (12.1)	19 (12.4)	

$P < 0.05$, vs Beer.

Table 3 Relationship between BMI and ALD

BMI	<i>n</i>	ALD	Years	Daily intake (g)	OR	<i>P</i>
\geq 25	203	24	13.5 \pm 6.2	26.4 \pm 13.7	5.6 (3.02-6.21)	< 0.01
< 25	1 067	58	16.3 \pm 5.8	35.7 \pm 18.1		

Drinking habits and ALD

In our population, beer or wine drinkers were 41.1%, and their alcohol daily intake was less than others. Rural people tended to drink hard liquors. Multiple drinkers were 20.2%, 87.9% of the drinkers consumed alcohol only at mealtimes, the daily alcohol intake was significantly lower than that of alcohol consumed at any time (with and without food) ($P < 0.05$). Daily alcohol intake of only hard liquors, also without food was significantly higher than that of all other categories of drinkers, the morbidity of ALD was also the highest, 2.7 times that of drinkers who drank only wine or beer at mealtimes (Table 2).

Obesity and ALD

Among the 1 270 drinkers, 203 had BMI more than 25. Although their average daily alcohol intake was lower than those with BMI less than 25, the ALD morbidity was 11.5%, more than twice that of normal body mass, significantly higher than the average 6.5%. There were no significant differences in drinking habits between the two groups. Multivariate analysis of the data showed that obesity was a risk factor for ALD, (OR: 5.6, $P < 0.01$). The difference was significant (Table 3).

Retrospective results

A 3-year follow-up indicated that among 19 cases with BMI \geq 25, only 3 cases had a body mass of 20% higher than before, and an increased BMI. Their serum ALT and AST were more than twice the upper normal level. The ultrasonography of the liver also indicated typical alcoholic fatty liver. In 9 of the 19 cases with a significant loss of body weight, their BMI also reduced to below 25. The ultrasonography of liver in several cases also became nearly normal. ALT and AST level was below the upper normal level. Of the remaining 7 subjects, their BMI was the same as before, the "liver function" became nearly normal. Ultrasonography findings became normal in 2 of 7 cases, and

remained the same in the other 5. All these 19 subjects except 3 who drank a little occasionally have already abstained.

Among 47 cases with BMI<25, their body mass did not change significantly. Eleven of them who kept on drinking had ALT and AST more than twice the upper normal level. The ultrasonography of liver revealed no improvement. Of the remaining who abstained from drinking, more than 85% of them had nearly normal "liver function", and better ultrasonographic findings. The percentage of "liver function" recovery was significantly higher than those who went on drinking ($P<0.01$).

DISCUSSION

Alcohol abuse has been claimed as one important factor leading to chronic liver diseases, as known in other diseases^[7-12]. The natural history of alcoholic liver disease ranges from asymptomatic indolent to end stage liver disease. Most patients lack specific clinical features^[13,14]. Diagnosis of alcoholic fatty liver and alcoholic steatohepatitis, like non-alcoholic fatty liver, without confirmatory laboratory tests, may involve the history of drinking, ultrasonography and liver biopsy^[15-18].

ALD is not only associated with genetic factors, but also involves other factors such as sex, body weight, BMI, the type and pattern of alcoholic beverage consumed, the habit of drinking hard liquors and of consuming alcohol without food, the duration of drinking^[19-21]. Yet, as to the risk threshold, in terms of daily alcohol intake and years of duration that can induce alcohol liver damage, there is no uniformed conclusion: with the wide range between 30 g/d and 80 g/d^[13]. Great differences between Western and Eastern countries exist: geographic variations must be present^[22,23], especially in China.

Our data suggested that the risk threshold of daily alcohol intake was 20 g; the duration was 5 years for Chinese men. Below the threshold, drinking seldom induced liver damage. If the daily intake exceeded 40 g and the duration was longer than 5 years, the liver damage occurred more frequently. However, with a daily intake higher than 160 g, in some cases the prevalence of alcoholic liver disease was only 18.7%. It means there is significantly different susceptibility among different individuals^[24]. It is commonly believed that prevalence of ALD in general population is up to about 15%, and rises with increased alcoholic intake. Our result was a little higher than that, maybe because our subjects were all men. In China, women drinkers are few, and their alcohol consumption is low, so few women develop ALD. There was only one woman case in our data. In spite of that, we believe that there is a great hepatic susceptibility to damage by alcohol in women.

The types of alcoholic beverage and the different drinking and dietary habits are closely related with ALD. Yet, a dose-effect relation between alcohol intake and alcohol-induced hepatic and other organ functional impairment has been demonstrated.

We were able to demonstrate for the first time in China that the habit of drinking hard liquors without food and the consumption of multiple types of drinks were risk factors of alcohol-induced liver damage. Those who drank only wine and beer were at lower risk for ALD. Fortunately, 90% of the Chinese drink wine or alcohol at mealtimes with food. Drinking without food might differentially affect the intragastric metabolism of ethanol by decreasing gastric alcohol dehydrogenase and hepatic glutathione and by accelerating gastric emptying, as it occurs in rats.

Recent studies confirm that the prevalence of alcohol-induced liver disease in obesity is high and serious. Obesity may be a co-risk factor for ALD and accelerate liver damage^[25,26]. It is reported that if the body weight is 20% above normal, the risk for ALD will be twice as great as in normal weight one. This is similar to our result. Among those obese patients whose

weight was above normal for more than 10 years, the risk for ALD was 2.5-3 times higher. At the same time, the liver damage increases with the increased BMI^[27,28]. However, the mechanism is not clear.

All of the patients in this study whose Anti-HCV and HBsAg were negative and with no recent medication history were "pure" ALD. Multivariate analysis showed that each factor was independent of the other variables.

Besides abstaining, which directly affects the prognosis of ALD^[29], BMI can also affect the progress of ALD^[30]. For the overweight cases, weight loss is an important treatment^[31]. Our data have another indication that "education" is also very important for changing patients' lifestyle^[32]. Because all the subjects with BMI \geq 25 had been told that alcohol and overweight would cause bad prognosis of ALD and strongly recommended complete alcohol abstinence and weight reduction, none of these cases went on drinking heavily. On the other hand, among the men with BMI<25, some did not take the risk of drinking seriously, nearly 15% of them went on drinking during the 3 years, resulting in progress of their ALD.

From the present data we can conclude that the minimum alcohol intake and the duration of years associated with a significant increase in the prevalence of alcohol-related liver disease was 20 g per day and 5 years for men. This risk increases in a dose-related pattern. However, the most striking result is that not only the quantity of alcohol consumed, but also the patterns of drinking are an important determinant of the risk of having ALD. Drinking only hard liquors or multiple types of alcoholic beverages without food, independent of the amount, is associated with an increased prevalence of alcohol-related liver disease. Obesity is also an independent risk factor for ALD. Abstinence and weight loss directly affect the prognosis of ALD. Therefore, we suggest reducing alcohol intake, avoiding drinking outside of mealtimes and consuming only wine or beer, especially for obese people.

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