Original Article

Clinical Characteristics in Patients with Liver Cirrhosis Induced by HBV Infection and Combined with Mild Alcohol Intake

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Objective To investigate the differences of clinical and biochemical characteristics between patients with liver cirrhosis induced by HBV infection combined with and without mild alcohol intake.

Methods Data of patients with liver cirrhosis who were hospitalized in the First Hospital Affiliated to Xinjiang Medical University were retrospectively analyzed. Patients were divided into three groups: patients with liver cirrhosis induced by HBV infection and combined with mild alcohol intake, patients with HBV-related cirrhosis, and patients with alcohol-related cirrhosis. Biochemical detections including liver function, fasting lipid profiles, lipoprotein, kidney function, glucose, uric acid and regular blood tests were carried out and results were compared among three groups. Data were analyzed through STATA software and co-variant analysis.

Results Total of 2 350 patients with liver cirrhosis were included, 732 patients had cirrhosis induced by HBV infection combined with mild alcohol intake, 1 316 patients had HBV-related liver cirrhosis, 302 patients had alcohol-related cirrhosis. The highest mean level of white cell count, mean corpuscular volume, γ -glutamyltranspeptidase and uric acid were observed in HBV infection combined with mild alcohol intake group. Multivariate regression analysis revealed that HBV infection, excessive alcohol intake, male and age were risk factors for hepatocellular carcinoma (HCC) in patients with liver cirrhosis.

Conclusions HBV infection combined with mild alcoholic-related liver cirrhosis group showed the highest oxidative stress compared with alcoholic liver cirrhosis group, which suggested that mild alcohol intake may increase the incidence of liver cirrhosis in HBV infected patients and may not increase the incidence of HCC.

Key words: Liver cirrhosis; Oxidative stress; Hepatitis B virus; Mild alcohol; Biochemical characteristics

Multiple factors are associated with cirrhosis and hepatocellular carcinoma (HCC), and it is a common clinical issue. HBV, HCV, alcohol intake, male and age are documented as risk factors for HCC development.¹ Few researches focused on synergisms of risk factors in the development of cirrhosis and HCC.²

Mild alcohol intake is considered not a cause for liver cirrhosis but benefits for the health of general population. Whether or not it contributes to the development of liver cirrhosis and HCC among HBV carriers is still an unsettled issue.³ This retrospective

study aimed to observe the clinical and biochemical characteristics of patients with liver cirrhosis induced by HBV infection and combined with mild alcohol intake.

PATIENTS AND METHODS

All patients who were hospitalized in the First Hospital Affiliated to Xinjiang Medical University during January 1, 2001 to June 30, 2009 were enrolled. The inclusion criteria were: a diagnosis of liver cirrhosis based on image character, or typical clinical signs of portal hypertension (splenomegaly, ascites, varices on endoscopy/episodes of variceal bleeding) and liver failure (poor synthetic function

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according to Child-Pugh scores). Patients with HBV infection, HCV infection, HDV infection or excessive alcohol consumption were excluded. The diagnosis of alcohol-related cirrhosis were made based on the history of excessive alcohol consumption (more than 40 g/day of alcohol for man and 20 g/day of alcohol for woman and last for at least 5 years in their life) and excluded primary biliary cirrhosis, AIH related cirrhosis, primary sclerosing cholangitis-related cirrhosis. According to the severity, liver cirrhosis was divided into compensated cirrhosis and decompensated cirrhosis based on whether complications (ascites, variceal bleeding, sepsis) and liver failure (poor synthetic function according to Child-Pugh score) occurred. HBV infection was defined as the presence of circulating HBsAg in serum. Diabetes mellitus was defined on a history of diagnosis or therapy for diabetes mellitus (diet, oral therapy or insulin). All blood detection, image and pathological results were carried out by the First Hospital Affiliated to Xinjiang Medical University.

The conception of HBV infection combined with mild alcohol intake is patients with HBV-related liver cirrhosis and a history as follows: alcohol ingestion of less than 20 g/day of alcohol for men and less than 10 g/day of alcohol for women, a little alcohol ingestion, occasionally alcohol ingestion, or “yes for alcohol”. The cases who have alcohol ingestion for more than 20 g/day or reached alcohol abuse combined with HBV infection were excluded from this group. HBV-related liver cirrhosis group was: HBV-related liver cirrhosis patients who have no alcohol ingestion in their life.

In order to analyze the risk factors of HCC in patients with liver cirrhosis, stepwise multivariate logistical regress analysis were performed based on factors such as HBV infection, excessive alcohol intake, HBV infection combined with mild alcohol intake, age, sex, diabetes mellitus and ethnicity (Han, Uygur and others).

All statistical analysis were performed by STATA software. Student's *t* test and univariate ANOVA were performed to compare means between or among groups. Transformations were performed to obtain approximately normal distribution if data were not

normally distributed. Categorical variables among different types of liver cirrhosis were compared by Chi-square tests. The risk factors related to the development of HCC were analyzed by multivariate logistic analysis, after adjusting age, sex, ethnicity, type 2 diabetes, HBV and alcohol consumption. And $P < 0.05$ were considered as statistically significant.

RESULTS

Patients demographics

Total of 2 350 patients with liver cirrhosis were enrolled in this study, 78.6% were male, aged 7-88 years (average age 52 years old), 79.9% were Han people, 11.1% were Uygur, 9.0% were other minorities. About 65% of the liver cirrhosis cases were decompensated, the incidence of HCC was 25.3%, 9.0% of patients died during hospitalization, the incidence of diabetic mellitus was 8.7% in liver cirrhosis patients. Clinical comparisons and primary outcome were shown in Table 1. The risk factors of HCC included older age ($OR = 1.04$, 95% CI 1.03-1.05; $P < 0.001$), male ($OR = 1.83$, 95% CI 1.43-2.34; $P < 0.001$), HBV infection ($OR = 8.36$, 95% CI 4.87-14.34; $P < 0.001$) and excessive alcohol consumption ($OR = 1.26$, 95% CI 1.03-1.54; $P = 0.024$). Among these factors, HBV infection was the most important indicator of HCC. While mild alcohol intake was not related to HCC (Table 2).

Biochemical characteristics of patients with liver cirrhosis induced by HBV infection combined with mild alcohol intake

Total of 2 048 patients had HBV-related cirrhosis, 732 were induced by HBV infection combined with mild alcohol intake, 1 316 patients with HBV-related liver cirrhosis and no alcohol consumption (only HBV cirrhosis group). There were no significant differences in age, incidence of diabetes mellitus and liver cirrhosis among HBV infection combined with mild alcohol intake group, HBV-related cirrhosis group and excessive alcohol consumption cirrhosis group. The highest level of white cell count, corpuscular volume, γ 0 and uric acid were observed in HBV infection combined with mild alcohol intake group ($P < 0.01$), no significant

Table 1. Clinical data of liver cirrhosis in different patient groups

	Total	HBV infection combined with mild alcohol intake	HBV infection	Alcoholic cirrhosis
Number of patients	2 356	732	1 322	302
Age (mean $\pm$ SD) (average, range)	50 $\pm$ 13 50 (7 - 88)	50 $\pm$ 13 50 (7 - 83)	50 $\pm$ 13 50 (9 - 88)	52 $\pm$ 12 52 (26 - 82)
Male (n, %)	1 851 (78.6)	559 (76.4)	995 (75.3)	297 (98.3)
Ethnicity				
Han (n, %)	1 883 (79.9)	609 (83.2)	1 091 (82.5)	183 (60.6)
Uygur (n, %)	262 (11.1)	69 (9.4)	129 (9.8)	64 (21.2)
Other minority (n, %)	211 (9.0)	54 (7.4)	102 (7.7)	55 (18.2)
Cirrhosis stage				
Compensated	830	242	472	116
Decompensated (n, %)	1 520 (65.0)	490 (66.9)	844 (64.1)	186 (62.0)
Diabetes (n, %)	209 (8.7)	61 (8.3)	111 (8.4)	37 (12.3)
HCC (n, %)	596 (25.3)	226 (30.9)	352 (26.6)	18 (6.0)
Males with HCC (n, %)	490 (26.5)	185 (33.1)	287 (28.8)	18 (6.1)
Females with HCC (n, %)	106 (21.0)	41 (23.7)	65 (19.9)	0 (0.0)
Mortality rate (%)	9.0	10.0	8.3	8.9

Table 2. Risk factors of HCC by stepwise Logistic regression analysis

Variables	Standard error	Wald	<i>P</i>	<i>OR</i>	95% CI
Age	0.004	88.075	< 0.001	1.04	1.03 - 1.05
Sex	0.126	23.099	< 0.001	1.83	1.43 - 2.34
HBV infection	0.275	59.536	< 0.001	8.36	4.87 - 14.34
Alcohol intake	0.102	5.060	0.024	1.26	1.03 - 1.54
Constant	0.391	203.683	< 0.001	0.004	

difference for fast glucose and lipoprotein metabolism were observed among the three groups ($P > 0.05$) (Figure 1, 2, 3 and 4).

DISCUSSION

About 35% of HBsAg positive patients with liver cirrhosis have alcohol intake according to the data, which indicated that HBV infection combined with alcohol intake is common, but few researches have reported the clinical characteristics of liver cirrhosis patients with HBV infection combined with mild alcohol intake. It is interesting that there was no significant difference in mean age nor the liver cirrhosis severity between HBV-related liver cirrhosis group and HBV infection combined with mild alcohol intake group ($\chi^2 = -0.822$, $P = 0.411$; $\chi^2 = 1.620$, $P = 0.203$), but significant differences were observed among the three groups in white cell count, mean corpuscular volume (MCV), γ -glutamyltranspeptidase (γ -GGT) and uric acid in serum, which all implied

oxidative stress⁴ and are common biochemical characteristics in alcoholic liver disease.⁵ Our data showed that the highest level of these markers were in HBV infection combined with mild alcohol intake group, while the lowest in HBV-related liver cirrhosis group. No significant differences were observed in lipoprotein and glucose metabolism among the groups, showing that HBV infection combined with mild alcohol intake has little effects on metabolic disorder of the patients.

Oxidative stress and oxygen deficit play an important role in alcoholic liver disease.⁶ Increase of MCV, γ -GGT and uric acid in serum were common biomarkers in alcoholic liver disease before cirrhosis developed.⁷ Liver cirrhosis patients with HBV infection combined with mild alcohol intake showed a higher level of oxidative stress and oxygen deficit, which implied HBV infection may increase the sensitivity of alcoholic damage to liver and mild alcohol intake may increase cirrhosis development in HBV infected population.⁸

Figure 1. Comparison of white cell counts among the three groups.

Notes: The white cell count in HBV infection combined with mild alcohol intake liver cirrhosis group was the highest (7.20 ± 5.48), while that of HBV group was the lowest (5.87 ± 4.22), and that in alcohol-related cirrhosis group was 5.87 ± 4.22 ($\chi^2 = 51.79$, $P < 0.001$).

Figure 2. Comparison of mean corpuscular volume among the three groups.

Notes: The mean corpuscular volume in HBV infection combined with mild alcohol intake liver cirrhosis group was the highest (96.01 ± 15.637), while that in HBV group was the lowest (93.86 ± 12.93), and that in alcohol-related cirrhosis group was 94.55 ± 18.54 ($\chi^2 = 15.28$, $P < 0.001$).

Limitations of the observation: to quantify alcohol intake in the study is impossible.

Mild alcohol intake won't increase the incidence of HCC according to stepwise Logistic regression analysis, though it seemed higher in HBV infection combined with mild alcohol intake group (30.9 vs 26.7, $P = 0.04$, $\chi^2 = 4.20$). The phenomenon may result from the sex bias: males are more likely to have alcohol intake in China.

In this study, it can be concluded that mild

alcohol intake may increase the risk of liver cirrhosis but may not increase the risk of HCC development.

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Figure 3. Comparison of γ-glutamyltranspeptidase among the three groups.

Notes: The γ-glutamyltranspeptidase in HBV infection combined with mild alcohol intake liver cirrhosis group was the highest (122.96 ± 173.32), while that in HBV group was the lowest (99.57 ± 141.74), and that in alcohol-related cirrhosis group was 118.51 ± 170.81 ($\chi^2 = 14.7$, $P = 0.001$).

Figure 4. Comparison of uric acid among the three groups.

Notes: The uric acid in HBV infection combined with mild alcohol intake liver cirrhosis group (272.01 ± 114.73) was almost the same with that in alcohol-related cirrhosis group (273.36 ± 116.20), while that in HBV group was the lowest (254.52 ± 111.65) ($\chi^2 = 18.3$, $P < 0.001$).

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