ORIGINAL ARTICLE

Correlation between Alcohol Consumption and Hepatitis B Surface Antigen Related to Hepatocellular Carcinoma

S Liu and Z Sheng

ABSTRACT

Objective: *To describe the epidemiological characteristics of patients with hepatocellular carcinoma (HCC), to gain more knowledge about the relationship among age, dietary habits, behavioural habits, living habits and HCC, and to clarify the risk of causing HCC by alcohol consumption.*

Methods: *A case-control study was utilized. In the form of a questionnaire, 200 cases of patients with HCC were investigated, and their related information was stored in a computer. The patients were divided into experimental and control groups. Meanwhile, the odds ratio and 95% confidence interval were estimated by using logistic multiple regression.*

Results: *A univariate analysis of variance was used to describe the basic characteristics of the two groups of patients. It showed that the factors closely related to the occurrence of HCC were hepatitis B surface antigen (HBsAg) positivity, liver cirrhosis, other chronic liver diseases and schistosomiasis. However, there was no obvious correlation between alcohol consumption and HCC. In addition, further analysis showed no correlation among the number of drinking years, alcohol intake and drinking age. However, HBsAg positivity and a history of chronic liver disease were closely associated with the occurrence of HCC; the HCC incidence in HBsAg-positive patients was significantly higher. In HBsAg-negative subjects, there was no significant correlation (*$p > 0.05$*) between alcohol consumption and the incidence of HCC. In the study of patients with chronic liver disease, the risk of causing liver cancer among alcohol-drinking patients was higher than that among non-alcohol-drinking patients. The risk was higher with higher alcohol consumption.*

Conclusion: *Hepatitis B surface antigen positivity and chronic liver diseases were independent risk factors for HCC. Although drinking alcohol was not an independent risk factor, drinking alcohol would increase the possibility of causing HCC among patients with HBsAg positivity and a history of chronic liver disease and it would be especially noticeable with increased alcohol consumption.*

Keywords: Alcohol, hepatitis B surface antigen, hepatocellular carcinoma, risk factor

From: Department of Gastroenterology, Weinan Central Hospital, Weinan Shaanxi, 714000, China.

Correspondence: Dr Z Sheng, Department of Gastroenterology, Weinan Central Hospital, Weinan Shaanxi, 714000, China. Email: yinghuigezz@163.com

DOI: 10.7727/wimj.2016.253

Correlación entre el consumo de alcohol y el antígeno de superficie de la hepatitis B en relación con el carcinoma hepatocelular

S Liu and Z Sheng

RESUMEN

Objetivo: *Describir las características epidemiológicas de pacientes con carcinoma hepatocelular (CHC) a fin de obtener más conocimientos sobre la relación entre la edad, los hábitos dietéticos, los hábitos de conducta, los hábitos de vida, y el CHC; y aclarar el riesgo del desarrollo del CHC a causa del consumo de alcohol.*

Métodos: *Se utilizó un estudio de casos y controles. Mediante un cuestionario, se investigaron 200 casos de pacientes con CHC, almacenándose la información en una computadora. Los pacientes fueron divididos en dos grupos: experimental y de control. Por otro lado, el odds-ratio y el intervalo de confianza de 95% fueron estimados utilizando el método de regresión logística múltiple.*

Resultados: *El análisis univariante de la varianza se usó con el fin de describir las características básicas de los dos grupos de pacientes. Dicho análisis mostró que los factores estrechamente relacionados con la ocurrencia de CHC fueron la positividad del antígeno de superficie de la hepatitis B (HBsAg), la cirrosis hepática, otras enfermedades crónicas del hígado, y la esquistosomiasis. Sin embargo, no hubo ninguna correlación obvia entre el consumo de alcohol y el CHC. Además, un análisis posterior, no mostró ninguna correlación entre el número de años dedicados a la bebida, la ingestión de alcohol, y la edad del bebedor. Sin embargo, la positividad de HBsAg y una historia de enfermedad hepática crónica se hallaron estrechamente relacionadas con la ocurrencia del CHC. Asimismo, la incidencia del CHC en pacientes positivos al HBsAg fue significativamente mayor. En sujetos negativos al HBsAg, no hubo ninguna correlación significativa (*$p > 0.05$*) entre el consumo de alcohol y la incidencia de CHC. En el estudio de pacientes con enfermedad hepática crónica, el riesgo de cáncer de hígado fue mayor entre los pacientes alcohólicos que entre los pacientes no alcohólicos. A mayor consumo de alcohol, mayor riesgo de cáncer del hígado.*

Conclusión: *La positividad del antígeno de superficie de hepatitis B y las enfermedades hepáticas crónicas fueron factores de riesgo independientes en la ocurrencia del CHC. Aunque el consumo de alcohol no fue un factor de riesgo independiente, el beber alcohol aumentaba la posibilidad de CHC en pacientes con positividad HBsAg y una historia de enfermedad hepática crónica, y se hacía especialmente notable con un aumento en el consumo de alcohol.*

Palabras claves: Alcohol, antígeno de superficie de la hepatitis B, carcinoma hepatocelular, factor de riesgo

West Indian Med J 2016; 65 (4): 644

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the 10 most commonly occurring solid cancers worldwide and is the second cause of death from malignancy. The most recent data indicate that its incidence is still increasing in many countries whereas the most effective way of reducing mortality due to HCC is prevention (1). The highest rates occur in Eastern Asia. The lowest rates are in Northern Europe and North America. The results of the latest research are mainly explained on the basis that two of the risk factors for HCC, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, are largely prevalent in Eastern Asia. In Italy, for example, HBV-related HCC is now rapidly declining, in comparison to HCV-related HCC, because of the introduction of mass HBV vaccination several years ago (2, 3).

Alcohol intake, smoking, diet, environmental pollution and other factors play an important role in the

occurrence and development of HCC, even a coordinating role between the various factors (4, 5). Consistent with its significant role in cirrhosis, alcohol consumption contributes to 15–45% of HCC cases in developed countries (6). Many studies have demonstrated a significant link between heavy alcohol intake (> 50–70 g/d for several years) and HCC, where males tend to consume more alcohol than females. The annual incidence of HCC due to alcoholic cirrhosis is 1–4% (7–9).

In contrast to American and European countries, alcohol consumption plays a minor role in HCC development in Asia. This is more so for Middle Eastern countries, where the consumption of alcohol is lower than in Southeast Asia. This study describes the epidemiology of newly diagnosed hepatocellular carcinoma, explores the relationship between drinking alcohol, schistosomiasis, genetic and other factors, and HCC and also investigates the relationship between alcohol consumption and the risk and clinical characteristics of HCC.

SUBJECTS AND METHODS

Subjects

We selected a total of 200 patients with HCC pathologically confirmed and who were treated in the Henan Provincial People's Hospital of Zhengzhou University. They comprised 160 male and 40 female patients aged between 29 and 72 years. The study was approved by the Ethics Committee of Zhengzhou University, and participants signed an informed consent form. There were two groups of patients.

Information was collated on gender, ethnicity, age, economic status and educational level of the two groups of patients, but there was no significant difference ($p > 0.05$). In accordance with the provisions of international standardization, all patients were divided into *never* drinkers − alcohol consumption < 22 g/week, *mild* drinkers − alcohol consumption 22–199 g/week; *moderate* drinkers − alcohol consumption 200–399 g/week; *heavy* drinkers − alcohol consumption > 400 g/week.

Table 1: The association between four factors with hepatocellular carcinoma

Factors	Case group	Control group	OR	95% CI
HBsAg-positive	160	20	16.25	5.88, 38.88
Liver cirrhosis	59	9	11.12	4.26, 30.06
Chronic liver disease	50	4	12.65	7.12, 88.32
Shistosomiasis	19	1	6.16	1.89, 13.03
Drinking alcohol	96	86	0.94	0.41, 1.36

Questionnaire design and data collection

The questionnaire contained a total of five modules: the basic module, diet module, bad habits modules, life behaviour module and health module. All information was received and documented by the doctors working in our hospital who were trained for this job. The survey involved face-to-face questions and each questionnaire required less than 30 minutes for completion. All contents must be completed for authenticity.

Statistical analysis

The analysis was performed by using univariate and multivariate unconditional logistic regression analysis *via* SPSS17.0. At the same time, the statistical results were analysed by using odds ratios (OR) and 95% confidence intervals (CI) to assess the relative risk.

RESULTS

Univariate analysis was taken to describe the basic characteristics of the two groups. We found that the closely related factors associated with HCC were: HbsAg positivity, liver cirrhosis, other chronic liver diseases and schistosomiasis. There was no significant correlation between alcohol consumption and HCC. In a further analysis, we did not find a significant correlation between the amount of drinking, alcohol intake, drinking age and other factors (Table 1).

In order to accurately investigate the combined effect of each variable, multi-factor non-conditional logistic regression analysis was used, for effective control of confounding factors that may interfere with the results, such as gender, age, education and alcohol and other single factors. The results showed that the major risk factors for HCC were chronic liver disease and HbsAg positivity ($p < 0.001$), Table 2.

In analysing the relationship between alcohol consumption and HCC after adjusting for gender, age and educational level, it was found that in HBsAg-positive patients, those with alcohol consumption had an increased incidence of HCC but in the HbsAg negative patients, there was no significant correlation between

Table 2: The risk factors of hepatocellular carcinoma *via* non-conditional logistic multifactor regression analysis

Factors	Parameter estimation	Standard error	$\chi 2$	p	OR	95% CI
HBsAg-positive	1.925	0.453	36.235	0.006	9.125	3.175, 15.252
Chronic liver disease	1.918	0.885	8.554	0.000	16.678	1.987, 29.902
Cirrhosis	10.985	531.215	0.003	0.057	4.665	0.548, 7.432
Schistosomiasis	3.024	1.125	4.325	0.098	3.125	1.788, 5.512

alcohol consumption and HCC incidence ($p > 0.05$). The possibility of HCC onset in HBsAg-positive patients who drank alcohol was significantly higher than in non-drinkers, and this difference increased with the amount of alcohol. It reminds us that in HBsAg-positive population, alcohol consumption will increase the possibility of HCC (Table 3).

Table 3: The association among drinking, hepatitis B surface antigen and liver cancer

Factors	HBsAg	Case group	Control group	OR	95% CI
No drinking	–	21	99	1.000	
Mild drinking	–	9	45	0.908	0.598, 2.612
Moderate drinking	–	7	35	1.401	0.875, 2.453
Heavy drinking	–	3	1	1.412	0.902, 2.106
No drinking	+	83	83	8.952	4.614, 16.326
Mild drinking	+	20	20	7.992	5.214, 12.385
Moderate drinking	+	35	35	12.120	9.654, 22.851
Heavy drinking	+	22	22	11.978	7.654, 29.365

According to the presence or absence of chronic liver disease, the relationship between alcohol consumption and liver cancer after adjusting for gender, age and education level was analysed. The results showed that whether drinking or not, the risk of HCC was significantly higher in patients with chronic liver disease. In non-drinking patients with chronic liver disease, there was no significant difference in the incidence of HCC. Compared with patients with non-chronic liver disease, in the drinkers with chronic liver disease, the risk of HCC was significantly increased and with an increase in alcohol consumption, the risk rose proportionately (Table 4).

Table 4: The association among drinking, chronic liver disease and liver cancer

Factors	HBsAg	Case group	Control group	OR	95% CI
No drinking	–	103	111	1.000	
Mild drinking	–	30	48	1.245	0.648, 4.712
Moderate drinking	–	12	37	1.402	1.225, 2.618
Heavy drinking	–	5	12	8.687	5.643, 18.314
No drinking	+	1	3	14.625	4.614, 16.326
Mild drinking	+	4	0	14.004	7.915, 23.142
Moderate drinking	+	30	0	18.216	8.658, 30.323
Heavy drinking	+	15	1	16.918	9.318, 35.226

DISCUSSION

There is no doubt that liver cirrhosis, chronic hepatitis, chronic HBV and HCV infections, and intoxication by alcohol, schistosoma and aflatoxin-B1 all play a major role in causing HCC (10–13). Whether alcohol consumption is an independent risk factor for hepatocellular carcinoma is not yet determined, but what is certain is that there is a significant correlation between heavy alcohol consumption and hepatocellular carcinoma (14–16). The mechanism may be as follows (17). Firstly, large amounts of alcohol can cause liver cell fibrosis, cirrhosis and then eventually lead to the occurrence of HCC; secondly, large amounts of alcohol can serve as an exogenous carcinogen involved in HCC; and thirdly, after drinking a lot, alcoholic liver disease can result with superimposed hepatitis B and hepatitis C virus infections.

Alcoholism is an important risk factor for HCC because it causes fatty liver, necro-inflammation, fibrosis, liver cirrhosis and malnutrition, especially when it is associated with HCV infection. Alcohol abuse is the most important risk factor for HCC in North America and Northern Europe. Alcohol is a risk factor with a high predictive value for HCC incidence, especially among moderate to heavy alcoholics [> 30 g/d] (18).

Mori *et al* in a prospective study in Japan showed that alcohol consumption and the combined effect of HBV and HCV infection increased HCC (19). Serum anti hepatitis C virus rate for liver cancer patients in developed countries was more than 50% while those in developing countries was between 48% and 58%. In developed countries, in the non-cancer liver tissue of patients with liver cancer, HBsAg-positive rate was less than 40%, while in developing countries, it was more than 50%. Hepatitis B virus and HCV infection are still considered a major risk factor for liver cancer. This is consistent with our findings.

In our study, we found that HBsAg positivity, a history of chronic liver disease and drinking alcohol will increase the possibility of HCC occurrence. This study argues that HBsAg positivity and chronic liver disease are an independent risk factor for HCC. Drinking alcohol is not one of the risk factors for HCC, but in people with the HBsAg positivity and a history of chronic liver disease, drinking behaviour will increase HCC possibility, and it may become more evident with the increase of alcohol intake.

In summary, there is very little evidence to support that drinking alcohol is an independent carcinogen for HCC. Epidemiological studies have indicated that drinking plays an important role in the development of HCC when there is combined cirrhosis and hepatitis B infection, but in different countries and regions, the results are not consistent. Further studies are needed.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; **136:** E359–86.
2. McGlynn KA, Petrick JL, London WT. Global epidemiology of hepatocellular carcinoma: an emphasis on demographic and regional variability. Clin Liver Dis 2015; **19:** 223–38.
3. Mele A, Stroffolini T, Zanetti AR. Hepatitis B in Italy: where we are ten years after the introduction of mass vaccination. J Med Virol 2002; **67:** 440–3.
4. Khan KN, Yatsuhashi H. Effect of alcohol consumption on the progression of hepatitis C virus infection and risk of hepatocellular carcinoma in Japanese patients. Alcohol Alcohol 2000; **35:** 286–95.
5. Corrao G, Tbrchio P, Zambon A, Ferrari PA, Aricò S, di Orio F. Exploring the combined action of lifetime alcohol intake and chronic hepatotropic virus infections on the risk of symptomatic liver cirrhosis. Collaborative Groups for the Study of Liver Disease in Italy. Eur J Epidemiol 1998; **14:** 447–56.
6. El-Serag HB, Rudolph KL. Hepatocellular carcinoma: epidemiology and molecular carcinogenesis. Gastroenterology 2007; **132:** 2557–76.
7. Raga C, La Vecchia C, Negri E, Franceschi S. Attributable risks for hepatocellular carcinoma in northern Italy. Eur J Cancer 1997; **33:** 629–34.
8. Donato F, Tagger A, Chiesa R, Ribero ML, Tomasoni V, Fasola M et al. Hepatitis B and C virus infection, alcohol drinking, and hepatocellular carcinoma: a case control study in Italy. Brescia HCC Study. Hepatology 1997; **26:** 579–84.
9. Jepsen P, Ott P, Andersen PK, Sørensen HT, Vilstrup H. Risk for hepatocellular carcinoma in patients with alcoholic cirrhosis: a Danish nationwide cohort study. Ann Intern Med 2012; **156:** 841–7.
10. Khurana S, Dubey ML, Malla N. Association of parasitic infections and cancers. Indian J Med Microbiol 2005; **23:** 74–9.
11. Abdel-Rahim AY. Parasitic infections and hepatic neoplasia. Dig Dis 2001; **19:** 288–91.
12. Aydın M, Aydın S, Bacanlı M, Başaran N. Aflatoxin levels in chronic hepatitis B patients with cirrhosis or hepatocellular carcinoma in Balıkesir, Turkey. J Viral Hepat 2015; **22:** 926–35.
13. El-Tonsy MM, Husseain HM, Helal TE, Tawfik RA, Koriem KM, Hussein HM. Schistosoma mansoni infection: is it a risk factor for development of hepatocellular carcinoma? Acta Trop 2013; **128:** 542–7.
14. Corrao G, Arico S, Zambon A, Torchio P, Lepore AR, Busellu G et al. Is alcohol a risk factor for liver cirrhosis in HBsAg and HCV negative subjects? Collaborative Groups for the Study of Liver Disease in Italy. J Hepatol 1997; **27:** 470–6.
15. Voigt MD. Alcohol in hepatocellular cancer. Clin in Liver Dis 2005; **9:** 151–69.
16. Schutte K, Bornschein J, Malfertheiner P. Liver cancer: descriptive epidemiology and risk factors other than HBV and HCV infection. Cancer Lett 2009; **286:** 9–14.
17. Boffetta P, Hashibe M. Alcohol and cancer. Lancet Oncol 2006; **7:** 149–56.
18. Suh B, Yun JM, Park S, Shin DW, Lee TH, Yang HK et al. Prediction of future hepatocellular carcinoma incidence in moderate to heavy alcohol drinkers with the FIB-4 liver fibrosis index. Cancer 2015; **121:** 3818–25.
19. Mori M, Hara M, Wada L, Hara T, Yamamoto K, Honda M et al. Prospective study of hepatitis B and C virus infections, cigarette smoking, alcohol consumption, and other factors associated with hepatocellular carcinoma risk in Japan. Am J Epidemiol 2000; **151:** 131–9.