

PREVALENCE OF HEPATITIS B AND HEPATITIS C MARKERS IN ALCOHOLICS WITH AND WITHOUT CLINICALLY EVIDENT HEPATIC CIRRHOSIS

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SUMMARY

We assessed the frequency of serological markers of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in 365 alcoholics by determining, by ELISA, the presence of HBsAg, anti-HBc, anti-HBs and anti-HCV. Fifty patients were cirrhotics and 315 had no evidence of hepatic cirrhosis; of the latter HBsAg was assessed in all, anti-HBc and anti-HBs in 130, and anti-HCV in 210. Among the alcoholics the frequencies of HBsAg (1.9%), anti-HBc (28.3%) and anti-HCV (3.8%) were higher ($p < 0.001$) than among the controls ($N=17,059$), 0.4%, 4.0% and 0.4% respectively. The frequency of positive HBsAg was higher ($p < 0.001$) in the cirrhotic patients (8.0%) than in alcoholics without cirrhosis (0.95%) and in controls (0.4%), and similar between the latter; of anti-HBc in alcoholics without cirrhosis (28.5%) was similar in cirrhotics patients (28.0%) and higher ($p < 0.001$) than in the controls (4.0%); of anti-HBs in alcoholics without cirrhosis (20.8%) was similar to that of the cirrhotic patients (10.0%), and the anti-HCV was similar between alcoholics with (6.0%) and without cirrhosis (3.3%) and higher ($p < 0.001$) than in controls (0.4%). We concluded that: a) alcoholics with or without cirrhosis have similar frequencies of infection with HBV and HCV between them, and higher than in nonalcoholics; b) alcoholics without cirrhosis had a frequency of HBV active infection (HBsAg+) which was similar to the controls, whereas among those who progressed to cirrhosis this frequency was significantly higher, what suggests that HBV may be implicated in the pathogenesis of cirrhosis in a few alcoholic individuals.

KEYWORDS: Hepatitis B virus; Hepatitis C virus; Alcoholism; Alcoholic liver disease; Alcoholic cirrhosis.

INTRODUCTION

From different geographical areas it has been reported that alcoholics may have higher prevalence of infections by hepatitis B virus (HBV)^{2,5,11,15,17,19-21} and hepatitis C virus (HCV)^{3,6,9,10,12,13,17,25,31} than nonalcoholics. However, the results of studies investigating the behavior of these infections in these patients are controversial: some have shown that alcoholics have an impaired clearance of HBV^{11,16,20}, probably due to an alcohol-related compromised immunologic system, whereas others show opposite results^{2,5,19,27}. Also controversial are the results of studies which assessed the likely participation of these viruses in the pathogenesis of the hepatic injury of alcoholics: positive correlation with HBV^{16,19,21,27,32} or HCV^{3,7, 9,13,23,25,28,34}, and negative correlation with HBV^{1,2,5,11,20,28} or HCV⁴ have all been described. The present study aims at assessing the frequency of HBV and HCV serological markers in alcoholics with and without clinically evident cirrhosis compared to each other and to a control group of healthy nonalcoholic individuals.

PATIENTS AND METHODS

We studied 315 (287 male and 28 female) alcoholics without clinical, laboratory or ultrasonographic evidence of hepatic cirrhosis, with mean age of 41 ± 10 years. They ingested a mean daily amount of 220 ± 80 g (minimum 80 g) of ethanol for a mean duration of 20 ± 10 years (minimum 5 years). In each of them we determined HBsAg, in 130 consecutive cases anti-HBc and anti-HBs, and in 210 consecutive cases, anti-HCV. We also assessed 50 alcoholics with hepatic cirrhosis, whose diagnosis was confirmed by liver biopsy, except for those whose altered coagulation tests prevented this intervention; in these individuals the diagnosis was made by clinical and laboratory findings, ultrasonography and/or computed axial tomographic scan. Out of these 50 individuals, 38 were males and 12 were females, with a mean age of 48 ± 10 years; they ingested a mean of 210 ± 70 g of ethanol per day for a mean duration of 22 ± 10 years. All of them were submitted to determination of serum HBsAg, anti-HBc, anti-HBs and anti-HCV. These two groups were compared to

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each other and to a control group of 17,059 blood donors from Uberlândia's Hemocentro Regional; each blood donor had a predonation medical interview where those with a history of chronic drinking were not accepted as donors. In the blood bank the donors were submitted to serological tests which included HBsAg, anti-HBc and anti-HCV, but not anti-HBs; all were first time donors.

Serological markers of HBV were determined by the use of enzyme-linked immunosorbent assay (ELISA) and HCV by ELISA2.

Chi-square or Fisher's exact test were used for the comparison between frequencies of positivity for hepatitis markers between the groups, and the Mann-Whitney test was applied for comparisons of age, daily amount of ingested ethanol, and time of alcoholism between the groups of alcoholics with and without hepatic cirrhosis.

RESULTS

Among the alcoholics the frequencies of HBsAg (1.9%), anti-HBc (28.3%) and anti-HCV (3.8%) were higher ($p < 0.001$) than among the controls, 0.4%, 4.0% and 0.4% respectively. In the group of alcoholics without cirrhosis, out of 315 patients, three (0.95%) were HBsAg positive. This frequency was similar ($p > 0.05$) to that in the control group, where 65 (0.4%) out of 17,059 individuals tested positive; in each of these two groups this frequency was lower ($p < 0.001$) than in the individuals with cirrhosis (8.0%). Out of the 130 alcoholics without cirrhosis, 37 (28.5%) were anti-HBc positive; this frequency was similar ($p > 0.05$) to that in individuals with cirrhosis (28.0%), and in each of these groups this frequency was higher ($p < 0.001$) than in the control group (4.0%). The frequency of anti-HBs in the group of alcoholics without cirrhosis (20.8%), although twice as high as that of the group of individuals with cirrhosis (10.0%), was not statistically significant. As to the frequency of anti-HCV, it

was significantly higher ($p < 0.001$) among the alcoholics without cirrhosis (3.3%) and those with cirrhosis (6.0%) as compared to the controls (0.4%); there was no statistically significant difference between alcoholics with and without hepatic cirrhosis (Table 1).

The group of individuals with cirrhosis had a mean age significantly higher ($p < 0.01$) than the group of alcoholics without cirrhosis (48 ± 10 vs 41 ± 10 years); nevertheless, there was no significant difference between these two groups as to the daily ethanol ingestion (210 ± 70 vs 220 ± 80) as well as to duration of ingestion (23 ± 10 vs 20 ± 10 years). As to the age of the patient at the time of diagnosis of cirrhosis, we noticed that it was similar in those with and without HBV or HCV infection. At the time of the assessment we noticed that alcoholics with cirrhosis with and without HBV and HCV had similar AST and ALT levels and severity of liver disease.

DISCUSSION

Our results show that, like in other geographical areas, the frequency of markers of HBV and HCV infections in alcoholics in our community is higher than in nonalcoholics. As to the sources of infections, a study has showed a close relationship between increased prevalence of HBV infection and intravenous drug use²⁶, whereas in other studies no apparent cause has been identified^{11,19}. It has also been observed that HBV infection is more common in alcoholics whose parents are alcoholics, implying a possible familial role in viral spreading¹⁶. In our patients the only probable source of infection by HBV was sexual promiscuity.

The frequency of HBV infection was similar among alcoholics with and without cirrhosis, but in each of them it was higher ($p < 0.001$) than in the controls. However, active infection (HBsAg positive) was higher in the individuals with cirrhosis than in those without cirrhosis

TABLE 1

Frequency of positivity (in percentage) of HBV and HCV markers, determined by ELISA, in alcoholics (N=365), with (N=50) and without (N=315) hepatic cirrhosis, and nonalcoholic controls (N=17,059). Statistical analysis by chi-square or Fisher' exact test

groups	markers			
	HBsAg	anti-HBc	anti-HBs	anti-HCV
Alcoholics	1.9*	28.3*	17.8	3.8*
	(7 in 365)	(51 in 180)	(32 in 180)	(10 in 260)
without cirrhosis	0.95	28.5*	20.8	3.3*
	(3 in 315)	(37 in 130)	(27 in 130)	(7 in 210)
with cirrhosis	8.0**	28.0*	10.0	6.0*
Controls	0.4	4.0	—	0.4

* $p < 0.001$ alcoholics or alcoholics with or without cirrhosis vs controls; ** $p < 0.001$ alcoholics with cirrhosis vs alcoholics without cirrhosis or controls

or controls. The frequency of HBsAg positive in our control group (0.4%) was similar to those of other 10 towns and cities of southeastern Brazil, which ranged from 0.3 to 3.22%⁸.

Abuse in alcohol consumption may favor the development of HBV chronic infection because alcohol can compromise the immune system^{16,27}. Some authors have found evidences of a role of HBV in the pathogenesis of liver injury in alcoholics^{16,19,21} and that the prevalence of this infection is higher in those alcoholics whose liver disease is more severe^{15,19}; this participation should occur mainly in those who are HBsAg positive^{27,32}. To such individuals complete alcohol abstinence has been suggested³². However, these findings have not been confirmed by other authors, neither in relation to the role of HBV in the pathogenesis of hepatic injury in alcoholics^{1,2,5,11,20} nor its relationship with disease severity^{1,11,18}. In our patients it was not possible to establish whether HBsAg positive cirrhotics had more severe disease than those HBsAg negative: the mean age of the patients at the time of diagnosis was similar in both, and as these patients alternate periods of hepatic compensation and decompensation it was not possible to establish a parallelism between them.

In the group of cirrhotics the frequency of HBsAg positive was higher ($p < 0.001$) than in the group of alcoholics without cirrhosis and in the controls, what leads us to hypothesize a possible etiopathogenetic role of HBV in the cirrhosis of the alcoholic. Although our alcoholic patients with cirrhosis were older than the alcoholic patients without cirrhosis ($p < 0.01$), there was no significant difference between the two groups as to the mean daily ingestion of ethanol or to the mean time of alcoholism. However, other factors (nutritional, immunologic, genetic, comorbidity, etc) can be synergetic to alcohol in injuring the liver of alcoholics¹.

It was also of note a higher frequency of anti-HBc when compared to anti-HBs, both in alcoholics with cirrhosis and those without cirrhosis; four possible explanations for this fact have been proposed: chronic carriers with undetectable HBsAg serum levels, "window period" observed in acute infections, healed HBV infection with loss of anti-HBs, or false positive tests²⁶.

Among alcoholics the transmission of HCV is mostly parenteral^{3,10,31}, but often no risk factor is detected^{6,26}; this infection apparently has no relationship with amount or duration of alcoholism nor with tattooing³¹. Among our alcoholic patients who were anti-HCV positive only one had history of intravenous drug use. In these individuals we noticed that the frequency of anti-HCV was higher ($p < 0.001$) among the alcoholics with cirrhosis (6%) and in those without cirrhosis (3.3%) than in the controls (0.4%) and, although not significant, it was proportionally higher in those with cirrhosis than in those without it.

It has been demonstrated that alcoholics during periods of heavy ingestion have increased viremia due to increased viral replication, probably related to altered cell immunity^{14,24,30}. Moreover, some authors have found that the prevalence of HCV infection increases in

parallel with the severity of liver disease in alcoholics^{1,3,9,12,23,25,30}, and that HCV infection is positively correlated with clinical severity of the disease and with the presence of histologic findings which imply chronic viral infection¹⁸. Liver biopsy in alcoholics with HCV infection can show purely alcohol-related injuries or injuries with a mixed pattern^{9,10,22}. These findings have led some authors to suggest that HCV would participate in the pathogenesis of the liver disease of the alcoholics^{3,7,9,13,23,25,28,34} and of the hepatocarcinoma that these individuals are more likely to develop^{29,30,33}. On the other hand, it has been reported a group of patients with alcoholic liver disease without HCV infection⁴, and alcoholics with and without HCV infection with similar AST and ALT levels¹³ and similar severity and duration of clinical disease⁷. As to our cirrhotic patients with and without HCV infection, it was not possible to differentiate them as to the severity of disease, possibly due to the small number of HCV positive patients.

Being alcoholic individuals of high risk for HCV infection they can represent an important source for this viral infection in the community¹⁷, and due to the risk of these individuals to develop chronic liver disease and hepatocarcinoma, complete alcohol abstinence has been proposed^{7,30}.

In the present study we observed that out of the 50 alcoholic patients with cirrhosis, 43 (86%) were not HBsAg positive or anti-HCV positive, showing that in these patients alcohol seems to be the only cause of cirrhosis. The fact that some alcoholics developed liver disease and others did not seems to be also related to factors like genetic predisposition, nutrition, environmental and immunologic factors, or comorbidity¹.

Our findings allow us to conclude that: a) alcoholics with and without cirrhosis have frequencies of HBV and HCV infections similar to each other, and higher than in nonalcoholics; b) alcoholics without cirrhosis had a frequency of HBV active infection (HBsAg+) which was similar to the controls, whereas among those who progressed to cirrhosis it was significantly higher, what suggests that HBV may be implicated in the pathogenesis of cirrhosis in a few alcoholic individuals; c) the frequency of HCV infection was statistically similar between alcoholics with and without cirrhosis, but tended to be higher in the former; d) 86% of the alcoholic with cirrhosis were HBsAg and anti-HCV negative, what confirms alcoholism by itself as an important cause of cirrhosis.

RESUMO

Prevalência de marcadores de hepatite B e hepatite C em alcoólicos com e sem cirrose hepática clinicamente evidente

Nós avaliamos a frequência de marcadores sorológicos das hepatites B e C em 365 alcoolistas, determinando pelo método ELISA, a presença de HBsAg, anti-HBc, anti-HBs e anti-HCV. Cinquenta deles eram cirróticos e 315 não tinham evidências de cirrose hepática; nestes últimos determinamos HBsAg em todos, anti-HBc e anti-

HBs em 130, e anti-HCV em 210. Entre os alcoolistas as freqüências de HBsAg (1,9%), anti-HBc (28,3%) e anti-HCV (3,8%) foram maiores ($p<0,001$) do que entre os controles ($N=17.059$), 0,4%, 4,0% e 0,4% respectivamente. A freqüência de HBsAg+ no grupo de alcoolistas sem cirrose (0,95%) foi semelhante a do grupo controle (0,4%) e menores ($p<0,001$) do que no grupo cirrótico (8,0%); a de anti-HBc+ nos alcoolistas sem cirrose (28,5%) foi semelhante a dos cirróticos (28,0%) e maiores ($p<0,001$) do que nos controles (4,0%); a de anti-HBs+ em alcoolistas não cirróticos (20,8%) foi semelhante a dos cirróticos (10,0%). A de anti-HCV+ nos alcoolistas não cirróticos (3,3%) foi semelhante a dos cirróticos (6,0%) e maiores ($p<0,001$) do que no grupo controle (0,4%). Concluímos que: a) alcoolistas não cirróticos e cirróticos têm freqüências de infecção pelos vírus B e C da hepatite semelhantes entre si, e maiores do que não alcoolistas; b) alcoolistas sem cirrose tiveram freqüência de infecção ativa pelo vírus B (HBsAg+) semelhantes aos controles, enquanto entre aqueles que evoluíram para cirrose esta freqüência foi significativamente maior, o que sugere que o VHB possa estar implicado na patogênese da cirrose de alguns indivíduos alcoólicos.

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