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<https://doi.org/10.15017/7318883>

出版情報：福岡醫學雑誌. 87 (11), pp.237-241, 1996-11-25. 福岡医学会
バージョン：
権利関係：



原 著

Alcohol Consumption and Seroconversion from Hepatitis B e Antigen in the Okinawa Japanese

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Key words: alcohol, ethyl; hepatitis B e antigen; seroconversion

Abstract A total of 1,113 hepatitis B surface antigen (HBsAg) carriers of Yaeyama District in Okinawa, Japan, were investigated in attempts to elucidate effects of alcohol consumption on seroconversion from hepatitis B e antigen (HBeAg). All of HBsAg carriers were tested for HBeAg. The subjects over 20 years of age were asked about their habitual intake of alcohol and were ranked into three categories: nondrinkers, light drinkers (1-59g/day), and heavy drinkers (≥ 60 g/day). The prevalence of HBeAg decreased with advancing age and did not differ between the sexes. Logistic regression analyses of the data revealed prevalence curves of HBeAg, depending on the age of subjects. The prevalence curves tended to be higher and decrease more slowly in heavy drinkers than in the nondrinkers. Thus, the possibility that heavy alcohol drinking prolongs seroconversion from HBeAg seems worthy of further consideration.

Introduction

Dane particles, infectious hepatitis B virus (HBV) particles, have been observed in serum samples of hepatitis B e antigen (HBeAg) positive carriers¹²⁾. The presence of circulating HBeAg is closely related to deoxyribonucleic acid (DNA) polymerase activity and HBeAg is linked to HBV activity¹⁰⁾. Therefore, HBeAg is apparently a factor related to deterioration of the liver.

Heavy alcohol consumption often leads to liver disease such as fatty liver, hepatitis, and liver cirrhosis, and alcohol consumption intensifies development of liver diseases caused by HBV⁹⁾.

As there are few reports on the relation between alcohol and the HBeAg status, we examined the effects of alcohol consumption on

seroconversion from HBeAg. Particular attention was given to the agespecific prevalence of HBeAg among HBV carriers, according to alcohol consumptions.

Subjects and Methods

Residents of the Yaeyama District in the subtropical area of Okinawa, Japan were surveyed in 1982-1985. A total of 19,108 persons in the Yaeyama District were investigated to search for the presence of HBV markers. We selected 1,113 persons (5.8 per cent) who were hepatitis B surface antigen (HBsAg) positive for at least six months and we termed this group HBsAg carriers. We tested all HBsAg carriers for HBeAg, and divided all HBsAg carriers into two groups, HBeAg-positive and HBeAg-negative carriers.

Blood samples were collected from subjects assembled at public halls. Included were children from high, junior high, and nursery schools.

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We asked all HBsAg carriers over age 20 years their history of alcohol consumption. As alcohol drinking by persons under age 19 years is prohibited by law in Japan, almost all drinkers begin to consume alcoholic beverages at age 20. Questions asked included age when they started drinking, duration, the frequency and amount of alcoholic beverages currently being consumed. Those who did not imbibe alcoholic drinks were grouped into the nondrinkers and all other were classed as drinkers. Duration of alcohol intake in all drinkers over age 25 years was more than five years. We asked drinkers how many days a week they consumed alcoholic beverages and how much beer, liquor, rice wine, and Awamori (liquor made from rice) they drank in one day. Based on data obtained at these interviews, we estimated the total grams of ethanol consumed in an average day, using information from the United States Department of Agriculture Handbook 456¹⁾: beer, 22.3g/633ml; liquor, 15.1g/43ml; sake, 23.8g/180ml; and Awamori, 54.0g/180ml. We divided drinkers into two groups, light drinkers (1-59g/day) and heavy drinkers (≥ 60 g/day).

Reversed passive hemagglutination (Reverscell, Meguroken, Osaka, Japan) was used to test for HBsAg. HBeAg was determined by radioimmunoassay (Abbott-HBe, Abbott Laboratories, North Chicago, IL).

To evaluate the relationship between the prevalence of HBeAg and age of three groups of nondrinkers, light drinkers, and heavy drinkers, we applied logistic regression to data obtained for each group. And the regression equation of prevalence of HBeAg on age for each group of alcohol consumption was estimated as

$$P = \exp(a + bx_n) / 1 + \exp(a + bx_n),$$

Where P is the estimated prevalence of HBeAg, x_n is age (years), a is constant term, and b is coefficient for age. We then estimated the prevalence curves of HBeAg on age in the three groups and evaluated the significance of all the relationships. A level of 0.05 was considered to have a statistical significance.

Results

The age- and sex-specific prevalence of HBeAg is shown in Table 1. The overall prevalence of HBeAg was 14.4 per cent. Prevalences of HBeAg were 15.4 per cent for males and 12.5 per cent for females. Prevalence of HBeAg in both sexes decreased with advancing age. All HBsAg carriers over 50 years of age were HBeAg-negative. There was no difference in prevalence between males and females, in each age group.

Prevalence of HBeAg by age and alcohol consumption is shown in Table 2. Prevalence of HBeAg was higher in both light and heavy

Table 1 Age and sex specific prevalence of HBeAg among HBsAg carriers in the Yaeyama District, Okinawa, Japan.

Age (years)	Males		Females		Total	
	No. patients	No. HBeAg positive (%)	No. patients	No. HBeAg positive (%)	No. patients	No. HBeAg positive (%)
0-19	120	74 (61.7)	65	36 (55.4)	185	110 (59.5)
20-29	166	20 (12.1)	97	9 (9.3)	263	29 (11.0)
30-39	143	11 (7.7)	74	5 (6.8)	217	16 (7.4)
40-49	101	4 (4.0)	53	1 (1.9)	154	5 (3.2)
50+	176	0 (0.0)	118	0 (0.0)	294	0 (0.0)
Total	706	109 (15.4)	407	51 (12.5)	1,113	160 (14.4)

HBeAg: hepatitis B e antigen

(%): prevalence of HBeAg

Table 2 Prevalence of HBeAg by age and alcohol consumption among HBsAg carriers over age 20 years in the Yaeyama District, Okinawa, Japan.

Age (years)	Nondrinkers		Light drinkers		Heavy drinkers	
	No. patients	No. HBeAg positive (%)	No. patients	No. HBeAg positive (%)	No. patients	No. HBeAg positive (%)
20-19	139	16 (11.5)*	76	7 (9.2)	48	6 (12.5)
30-39	98	6 (6.1)	65	6 (9.2)	54	4 (7.4)
40-49	72	1 (1.4)*	48	1 (2.1)	34	3 (8.8)
50+	166	0 (0.0)	85	0 (0.0)	43	0 (0.0)
Total	475	23 (4.8)	274	14 (12.5)	179	13 (7.3)

HBeAg: hepatitis B e antigen

(%): prevalence of HBeAg

Table 3 Result of the logistic regression analysis of prevalence of HBeAg on age for three groups of alcohol consumption in the Yaeyama District, Okinawa, Japan.

Alcohol consumption	Constant term	Coefficient	Odds ratio*	95 % confidence
Nondrinkers	0.586	-0.102	0.4	0.3-0.4
Light drinkers	-0.046	-0.080	0.4	0.3-0.7
Heavy drinkers	-0.298	-0.062	0.5	0.3-1.0

* Odds ratio associated with a difference of ten years

drinkers than in nondrinkers in the age groups 30-39 and 40-49 years. And prevalence of HBeAg was significantly lower in the age groups 40-49 than in the age groups 20-29 only in nondrinkers ($p < 0.05$). The prevalence curve of HBeAg tended to be higher and decrease more slowly in heavy drinkers than in nondrinkers over age 20 years.

The results of logistic regression analysis are shown in Table 3. Constant terms were smaller in the order of heavy, light and nondrinkers. Odds ratios of prevalence of HBeAg associated with a difference of ten years were significantly smaller than 1.0, except for heavy drinkers. Estimates of the regression coefficients for age were all negative, and they were smaller in order of nondrinkers, light and heavy drinkers. This would suggest that the prevalence of HBeAg is greater in heavy drinkers of an advanced age.

Discussion

The objective of our study was to determine whether alcohol drinking influences the seroconversion from HBsAg. To our knowledge, this paper represents the first epidemiological evidence of effects of alcohol consumption on the seroconversion of HBeAg.

In the Yaeyama District in Okinawa, the prevalence of HBsAg was found to be higher than that in other districts in Japan⁶. As the mean daily alcohol consumption in the Yaeyama District (20.2g/day) was larger than that in the main islands of Japan (12.4g/day), excluding the islands of Okinawa⁴, we studied the relation between alcohol and seroconversion of HBeAg in this district.

In agreement with data in the literature², our study showed that the prevalence of HBsAg was higher in males. There are data on differences between sexes regarding seroconversion from HBeAg to antibody to HBeAg (anti-HBe).

Sakaki et al. showed that females carriers cleared HBeAg more rapidly than males¹¹⁾ and Chu et al. reported that seroconversion from HBeAg to anti-HBe occurred at an earlier age for males than for females³⁾. Male carriers apparently have a higher annual HBeAg clearance rate than do the females⁸⁾. In the subjects we examined, we found no difference between the sexes with regard to the prevalence of HBeAg, in each age group.

In agreement with our previous findings⁷⁾, the prevalence of HBeAg decreased with age. In the present study, the greater the alcohol consumption, the more slowly did the prevalence curve of HBeAg decrease with age. Thus, our finding suggests that in heavy drinkers, the clearance rate of HBeAg seems to be low and that heavy alcohol consumption tends to prolong the interval between seroconversion from HBeAg to anti-HBe.

We also found that in this area the prevalence of HBeAg decreased with age more rapidly in asymptomatic carriers than in carriers with liver abnormalities⁵⁾. Therefore, the prolongation of seroconversion of HBeAg in heavy drinkers may be due to liver injury induced by alcohol. In ongoing studies, we are attempting to determine if the cause of this may be alcohol induced liver injury or the direct effect of alcohol.

In general, alcohol and hepatitis B virus, particularly HBeAg or HBV DNA are thought to be factors linked to liver damage. Villa et al. reported that asymptomatic HBsAg carriers seemed to be at risk for hepatic biochemical abnormalities when drinking an amount of ethanol which appeared harmless for HBsAg negative persons¹³⁾. We also reported that alcohol consumption intensifies the development of liver disease caused by HBV, and that the prevalence of liver abnormalities in HBeAg positive heavy drinkers is the highest among other HBsAg carriers⁹⁾.

In light of these observations, we advise HBsAg carriers, particularly HBeAg positive

carriers to cease consuming large amounts of alcohol, especially in a habitual pattern.

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(Received for publication September 3, 1996)

(和文抄録)

沖縄住民における飲酒と HBe 抗原の seroconversion について

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沖縄県八重山地区の 1113 名の B 型肝炎キャリアーについて、HBe 抗原の seroconversion におよぼす飲酒の影響について検討をおこなった。対象者全例の HBe 抗原を測定した。20 歳以上の対象者については、飲酒習慣について問診を行い、3 グループに分けた。非飲酒者・少量飲酒者（1 日の飲酒量：1-59 g）・大量

飲酒者（1 日の飲酒量：60 g 以上）。HBe 抗原の陽性率は、加齢とともに低下し、性別にて差はみられなかった。多変量解析によると、HBe 抗原の年齢による予測曲線の低下率は、大量飲酒者が非飲酒者に比べ緩やかであり、大量飲酒は、HBe 抗原の seroconversion を遅らせているように考えられた。