

Correlation between Hepatitis delta virus infection and hepatitis B virus serum markers

Chun-Hua Song, Min-Yu Wu, Xiang-Lin Wang, Qun Dong, Rong-Hua Tang, Xiao-Lin Fan

Chun-Hua Song, Min-Yu Wu, Xiang-Lin Wang, Qun Dong, Department of Microbiology and Immunology, Wannan Medical College, Wuhu 241001, Anhui Province, China

Rong-Hua Tang, Xiao-Lin Fan, Department of Infectious Disease, Yijishan Hospital, Wannan Medical College

Chun-Hua Song, Assistant Professor, having 10 papers published.

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Correspondence to: Dr. Chun-Hua Song, Assistant Professor, Department of Microbiology and Immunology, Wannan Medical College, Wuhu 241001, Anhui Province, China
Telephone: +86-553-3832468-270

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Abstract

AIM: To analyse the correlation between HDV infection and HBV serum markers.

METHODS: Patients who were positive for HBV serum markers were selected and HDV infection was examined in them. Blood donors were used as a control group. Both HDV infection and HBV serum markers were tested by enzyme-linked immunosorbent assay.

RESULTS: HDV infection was detected in 40 of 289 patients who were positive for HBV serum markers. The overall positive rate of HDV infection was 13.8%. The positive rates of HDV infection in HBsAg(+) group, HBcAb(+) group and HBeAb(+) group were 17.6%, 18.8% and 25.2%, respectively, which were higher than that in HBeAg(+) group (10.9%), and none was detected in HBsAb(+) group. HDV infection appeared in HBsAg(+)HBcAb(+)HBeAb(+) patients with a positive rate of 26.2%, which was much higher than that in HBsAg(+)HBcAb(+)HBeAg(+) patients (10.9%).

CONCLUSION: HDV coinfection is more frequent in HBsAg(+) HBcAb(+)HBeAb(+) patients than in HBsAg(+)HBcAb(+)HBeAg(+) patients. HDV infection is not completely related with the speed and amount of HBV replication.

Key words: Hepatitis delta virus infection; Hepatitis B; Enzyme linked immunosorbent assay

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INTRODUCTION

Hepatitis delta virus (HDV) is a defective RNA virus which is related to viroids and requires HBsAg synthesis for its assembly and infectivity. HDV occurs either in a coinfection form with hepatitis B virus (HBV) resulting in acute or fulminant hepatitis, or in a superinfection form in a chronic HBV carrier resulting in severe chronic hepatitis B and liver cirrhosis^[1]. There is a high rate of HBV infection in China and many reports have reported HDV infection. However, these reports concentrated much on the observation of symptoms of hepatitis D, and on epidemiological study of HDV infection in the patients with acute or chronic hepatitis B^[2]. In China, the serological diagnosis of HBV infection plays an important role in the diagnosis of hepatitis B, and HBV serum markers can to some extent reflect the HBV replication state, HBV infectivity and progress of the patients. In order to draw some hints about the relation between HDV infection and active state of HBV replication, we observed the positive rate of HDV infection in 289 patients with HBV who were positive for serum markers and analysed the correlation between HDV infection and HBV serum markers.

MATERIALS AND METHODS

Patients

From June 1995 to December 1995, a total of 289 serum samples from HBV carriers visiting our hospital were examined. There were 195 males and 94 females, ranging in age from 5-62 years (mean, 32.6 years). The selected patients were positive for at least 1 of 5 HBV serum markers (HBsAg, HBsAb, HBcAb, HBeAg, and HBeAb), including 60 patients with only HBsAb(+) who refused to be vaccinated (group A), 21 patients with only HBsAg(+) (group B), 107 patients with HBsAg(+)HBcAb(+)HBeAb(+) (group C) and 101 patients with HBsAg(+)HBcAb(+)HBeAg(+) (group D).

Methods

Five HBV serum markers were measured by enzyme-linked immunosorbent assay (ELISA) using a commercially available kit (Kohua, Shanghai). HDAG, total anti-HD and anti-HD IgM were also measured in the 289 serum samples by ELISA (Yelikan Biological Company Ltd., Yangzhou, China). The patients whose sera were positive for one or more than one of the 3 HDV serum markers were considered as having HDV infection. Positive results were verified by a repeat test. A control group consisted of normal sera from blood

Table 1 Positive rate of HDV infection in each HBV serum marker (+) group *n*(%)

	HBsAg (<i>n</i> = 227)	HBsAb (<i>n</i> = 64)	HBcAb (<i>n</i> = 208)	HBeAg (<i>n</i> = 101)	HBeAb (<i>n</i> = 111)
HDAg	17	0	17	8	9
Total anti-HD	5	0	5	0	5
anti-HD IgM	19	0	18	3	15
Total	40 (17.6)	0	39 (18.8)	11 (10.9)	28 (25.2)

Table 2 Positive rate of HDV in common HBV serology pattern groups *n*(%)

	Group A (<i>n</i> = 60)	Group B (<i>n</i> = 21)	Group C (<i>n</i> = 107)	Group D (<i>n</i> = 101)
HDAg	0	0	9 (8.4)	8 (8.0)
Total anti-HD	0	0	5 (4.7)	0
anti-HD IgM	0	1 (4.8)	15 (14.0)	3 (3.0)
Total	0	1 (4.8)	28 (26.2)	11 (10.9)

donors.

Statistical analysis

U-test of rates between two groups was used for statistical analysis. *P* < 0.05 was considered significant.

RESULTS

Positive rate of HDV infection in patients positive for HBV serum markers

HDV infection was detected in 40 of 289 patients with HBV serum markers(+). All had only one positivity of HDV serum indicator except that one had both total anti-HD and anti-HD IgM. The overall positive rate of HDV infection was 13.8%, HDAg positive rate was 5.9%, total-anti-HD was 1.7% and anti-HD IgM 6.6%.

Positive rate of HDV infection in each serum marker group

HDV infection was detected in 28 (25.2%) of 111 sera from patients with HBeAb(+), 39 (8.8%) of 208 sera with HBcAb(+), 40 (17.6%) with HBsAg(+) and 11 (10.9%) with HBeAg(+). However, none of the 64 patients with HBsAb(+) was found positive. The statistical analysis was carried out between every two groups, and a significant difference (*P* < 0.01) between all of them except between HBsAg(+) group and HBcAb(+) group was seen (Table 1).

Positive rate of HDV infection in common HBV serology pattern

HDV infection was found in 28 (26.2%) of 107 patients in group C, 11 (10.9%) of 101 patients in group D, and 1 (4.8%) in group B. The differences of positive rates between every two groups were significant (*P* < 0.01) (Table 2).

DISCUSSION

Clinical recognition of HDV infection is complex because of its diverse manifestations and variable outcomes. The detection of HDV serum indicators is a helpful measure, though the problems of the test sensitivity and sampling time could lead to false negative results. HDAg appears transiently during the earliest phase of HDV infection prior to the onset of symptoms. IgM or anti-HD IgG may also appear either transiently or late in the course of the disease^[3]. Smedile found that anti-HD IgM appeared in both acute and chronic hepatitis D, and the patients with total anti-HD used to be grouped into chronic hepatitis D^[4]. Now it has been proven that the presence of either IgM or anti-HD IgG is in accord with active HDV replication, so the patients positive for one of HDV serum markers can be

considered as having HDV infection^[3]. Our results showed that the positive rates of HDAg and anti-HD IgM were higher than that of total anti-HD (mainly IgG type), possibly because most of the patients tested were with acute hepatitis D or in the early phase of HDV infection, or because the sensitivity of total anti-HD detection was lower than that of the others.

HDV requires the help of HBV for its replication. HBsAg in HBV infected cells is used by HDV, and it is important for the carrying of chronic HDV^[1]. These facts can explain why all the 40 cases of HDV infection in our study appeared in the HBsAg(+) patients, but none in the infected patients positive for only HBsAb. Interestingly, the positive rate of HDV infection varied significantly in different HBV serum marker groups (Table 1) and in common HBV serology pattern groups (Table 2). It could be easily understood that no HDV infection was detected in patients positive for only HBsAb because there was no HBV replication, and that much lower positive rate of HDV infection in patients positive for only HBsAg (group B) was because of less HBV replication. These results suggest that HDV infection has relations with HBV replication. However, the positive rate in HBsAg(+)HBcAb(+)HBeAb(+) patients (group C) was higher than that in HBsAg(+)HBcAb(+)HBeAg(+) patients (group D), in whom HBV replicates more rapidly and has a greater quantity. This reveals that HDV infection is not completely related with the amount and speed of HBV replication. Until now, the mechanism of this phenomenon is unclear, and it is possibly because there exists a co-interference between HDV and HBV replication. It has been found that HDV replication not only depends on HBV replication, but also can suppress the expression of HBsAg and HBcAg in hepatocytes^[5].

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