Acta virol. **37**: 199-201, 1993

LONG-TERM TREND OF DECREASING FREQUENCY OF HEPATITIS B VIRUS INFECTION

M. SENBA, T. NAKAMURA, M. I. SENBA, M. WATANABE, X. ZHONG, H. ITAKURA

Department of Pathology, Institute of Tropical Medicine, Nagasaki Unviersity, Nagasaki 852, Japan

Received August 14, 1992

Summary. - Statistical and histopathological analysis was carried out to determine whether hepatitis B surface antigen (HBsAg) with the autopsy diagnosis of hepatitis, cirrhosis, and hepatocellular carcinoma declined during 1964-1991. In this study, the liver specimens from 673 autopsy cases at Nagasaki University Hospital were used, and these materials were stained for HBsAg with immunoperoxidase method. For statistical calculation, we used Cochran's chi-square test with one degree of freedom for linear trend for proportions. We investigated HBsAg positive rates for the four time periods, 1964-1970, 1971-1977, 1978-1984, and 1985-1991, and for the diagnosis of hepatitis, cirrhosis, and hepatocellular carcinoma. The decreasing linear trend of HBsAg positivity with time was significant for hepatocellular carcinoma and cirrhosis.

Key words: hepatitis B surface antigen; hepatitis; cirrhosis; hepatocellular carcinoma; immunoperoxidase method

Introduction

Hepatocellular carcinoma becomes clinically manifest after cirrhosis has been well formed, and the major factor predisposing hepatocellular carcinoma in a population appears to be the presence of cirrhosis caused by chronic hepatitis B virus (HBV) infection in that population. The oncogenic potential of HBV in the development of hepatocellular carcinoma is well known (Sherlock *et al.*, 1970; Vogel *et al.*, 1970). The authors reported the decreasing trend of HBsAg positivity with time for hepatocellular carcinoma in the liver specimens collected at Nagasaki University Hospital between 1964-1984 (Senba *et al.*, 1988). We also observed a decreasing trend of HBsAg positive rate among hepatocellular carcinoma patients examination by the reports of the Liver Cancer Study Group of Japan during 1968-1981 (Okuda, 1980; The Liver Cancer Study Group of Japan, 1980, 1984, 1987). The authors were, thus, concerned with the recent trend of HBsAg positivity rates in hepatitis, cirrhosis, and hepatocellular carcinoma since 1985.

Materials and Methods

The liver specimens collected at Nagasaki University Hospital from 673 autopsy cases of various liver diseases (hepatitis 75, cirrhosis 228, hepatocellular carcinoma 370) were fixed in formalin and embedded in paraffin for immunohistochemical study. Sections were cut at 4 μm, and stained with haematoxylin-eosin, Mallory's method for collagen fibers, and silver impregnation method for reticulum fibers. For immunohistochemical study, these specimens were stained for HBsAg (Dako PAP kit) by the immunoperoxidase method. Statistical calculation was performed using the BMDP (Dixon *et al.*, 1981) on the IBM 4341 system in the Data Center of A-bomb Disaster in Nagasaki University. The statistical method for this study is the Cochran's chi-square test with one degree of freedom for trend of proportions.

Results and Discussion

The Table 1 shows HBsAg positive rates for the four time periods, 1964–1970, 1971–1977, 1978–1984, and 1985–1991, and for diagnosis of hepatitis, cirrhosis, and hepatocellular carcinoma. Cochran's chi-square test for the linear trend of HBsAg positive rate in hepatitis during the periods resulted in $p > 0.4$ in hepatitis, $p < 0.05$ in cirrhosis, $p < 0.001$ in hepatocellular carcinoma, and $p < 0.001$ in total of these diseases. The decreasing linear trend of HBsAg positive rates in hepatocellular carcinoma during 1964–1991 was highly significant, marginally significant in cirrhosis, and highly significant in total. Therefore, in this study, proportions of HBsAg carrier in cirrhosis and hepatocellular carcinoma in the last 28 years were found to have been decreasing.

The major impact of the HBV carrier state is on both the individual and the public health. Owing to the frequency of chronic liver disease in HBV carriers and the risk of HBV carriers developing hepatocellular carcinoma, prevention of HBV infection of infants and children is of particular importance. A high frequency of transmission from the carrier mother to her infant has been well documented. On a global basis, the carrier mother may be the most important

Table 1. Frequency of HBsAg positivity in hepatitis, cirrhosis, and hepatocellular carcinoma in 1964–1991

Diseases	1964–1970	1971–1977	1978–1984	1985–1991	p*
Hepatitis	3/18(17 %)	2/16(13 %)	2/18(11 %)	2/23 (9 %)	>0.4
Cirrhosis	23/67(34 %)	15/53(28 %)	12/57(21 %)	9/51(18 %)	<0.05
Hepatocellular carcinoma	56/87(64 %)	57/102(56 %)	37/82(45 %)	16/99(16 %)	<0.001
Total	82/172(48 %)	74/171(43 %)	51/157(32 %)	27/173(16 %)	<0.001

* for trend

source of HBV transmission. The likelihood of transmitting HBV to susceptible contacts is related to many factors including personal and environmental hygiene, public education, and the safety of blood transfusion. We believe that intervention with hepatitis B vaccine and health education may lead to an eradication of HBV infection. This strategy will lead to a reduced incidence of hepatitis, cirrhosis, and hepatocellular carcinoma caused by HBV infection.

References

Dixon, W. J., Brown, E. L., Frane, J. W., Hill, M. A., Jennrich, R. I., and Toporek, J. D. (1981): BMDP statistical software. University of California Press, Berkeley.

Okuda, K., and The Liver Cancer Study Group of Japan (1980): Primary liver cancers in Japan. *Cancer* **45**, 2663–2669.

Senba, M., Nakamura, T., Toda, T., and Matsumura, H. (1988): Decreasing frequency, with time, of hepatitis B surface antigen positive liver biopsy in hepatitis, cirrhosis, and hepatocellular carcinoma. *Lancet* **i**, 588–589.

Sherlock, S., Fox, R. A., Niazi, S. P., and Scheuer, P. J. (1970): Chronic liver diseases and primary liver-cell cancer with hepatitis-associated (Australia) antigen in serum. *Lancet* **i**, 1243–1247.

The Liver Cancer Study Group of Japan (1984): Primary liver cancer in Japan. *Cancer* **54**, 1747–1755.

The Liver Cancer Study Group of Japan (1987): Primary liver cancer in Japan. *Cancer* **60**, 1400–1411.

Vogel, C. L., Anthony, P. P., Mody, N., and Barker, L. F. (1970): Hepatitis-associated antigen in Ugandan patients with hepatocellular carcinoma. *Lancet* **ii**, 621–624.