Hepatitis Virus Infection and Hepatic Disease in Hospitalized Dental Patients

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Introduction

Viral hepatitis is an important disease in dental practice, in light of infections from patient-to-patient or patient-to-doctor, as well as bleeding tendencies during treatment¹⁻³⁾. Although the transmission of hepatitis virus B (HBV) and C (HCV) is mainly via blood and blood products²⁾, saliva may also be one source of infection with HBV⁴⁾ and HCV^{5,6)}. Needle-stick injury during dental treatment may be responsible for infection, among dental personnel. In our dental hospital⁷⁾, needle-stick injuries have occurred 35 times during the past 3 years, in which 8 patients were HCV-seropositive and 1 was positive for HB surface (HBs) antigen. Dentists have a higher prevalence of seropositivity for HBs and HCV than controls, indicating high occupational risk for HBV^{8,9)} and HCV infection^{10,11)}. In particular, the prevalence was high among oral surgeons^{8,9,12)}. To protect dentists from these viruses, it is essential to have a precise knowledge of the prevalence of hepatitis virus carriers in dental patients. Recently, Shopper et al (1995)¹³⁾ have reported the prevalence of exposure to HCV in a sample of dental school outpatients, demonstrating that more than 5 % were positive for anti-HCV. This rate of HCV seropositivity was apparently higher than in the general population.

In this study, we screened a large population of hospitalized dental patients to elucidate the prevalence of hepatitis viruses B and C carriers correlated with a clinical history of liver disease. The serum chemistries and bleeding tendencies associated with HBV and HCV also were evaluated.

Patients and Methods

Subjects included 1239 consecutive dental patients who were hospitalized from January 1994 to December 1995 at the First and Second Divisions of Oral Surgery, Kyushu Dental College Hospital, Kitakyushu, Japan. It may be important that we emphasize the fact that these were

Table 1 Clinical characteristics of study patients

Sex :	M	n = 664 (53.6),	F	n = 575
Age :	41.1±0.6 (0 to 97 years old)			
Dental diagnosis :				
	Inflammation	n = 407 (32.8)	Cysts	n = 166 (13.4)
	Trauma	n = 161 (13.0)	Cancer	n = 160 (12.9)
	Impacted teeth	n = 119 (9.6)	Anomaly	n = 79 (6.4)
	Benign tumors	n = 78 (6.3)	Sialolithiasis	n = 17 (1.4)
	Others	n = 52 (4.2)		
HBs antigen :				
	Positive	n = 16 (1.6)	Negative	n = 982
HCV antibody :				
	Positive	n = 60 (6.1)	Negative	n = 918
History of liver disease :				
	Positive	n = 97 (7.8)	Negative	n = 1142

() : %

in-patients receiving oral and dental care. This study was approved by the Human Investigations Committees of Kyushu Dental College. The clinical characteristics of the patients are shown in Table 1. Inflammation comprised one third of all dental diseases, followed by cysts, trauma, and cancer. The diagnosis classified as the inflammation was 179 periostitis, 122 phlegmone, 39 sinusitis, 14 osteomyelitis, 11 abscess, 10 lymphadenitis, 10 paradentitis, 7 stomatitis, 6 salivary gland inflammation, and 9 the others. Any clinical history of liver disease was asked of each patient by a physician in charge. The main medical diseases other than dental or liver disease were 132 hypertension, 61 ischemic heart disease, 57 diabetes mellitus, 42 drug allergy, 23 gastro-duodenal ulcer, 23 arrhythmia. Blood samples were taken for the measurement of blood chemistry, which included: aspartate transaminase (AST), alanine transaminase (ALT), fasting plasma glucose (FPG), red cell, white cell, and platelet counts, hematocrit, and hemoglobin. Bleeding times and coagulation times also were examined. Bleeding time was done by a small cut in ear lobe. Serum HBs antigen and HCV antibody (using a second generation serologic enzyme immunoassay) were determined. This enzyme immunoassay for HCV antibody detects human antibody to recombinant HCV antigen proteins c200, c22-3, HC-34, and HC-31. All data are presented as the mean $\pm$ SEM. Differences were examined with the unpaired Student's T test where appropriate, and categorical variables were compared using the chi square test. Results were considered to be significant when the p value was less than 0.05.

Results

Sixteen of 998 inpatients, for whom a blood sample was available, had HBs antigen in their

Fig. 1 Prevalence of the frequency of Hepatitis B surface antigen (HBV) and HCV antibody (HCV) in patients with or without a history of hepatic disease.

***: $p < 0.001$ in comparison with subjects with and without hepatic disease

Fig. 2 Serum aspartate transaminase (AST; IU), alanine transaminase (ALT; IU), fasting plasma glucose (FPG; mg/dl), and platelet counts (Platelet; $\times 10^4/\text{mm}^3$) in patients with or without a history of hepatic disease.

***: $p < 0.001$ in comparison with subjects with and without hepatic disease

serum (1.6 %), while 60 of 978 were HCV seropositive (6.1 %) (Table 1). The occurrence of a positive reaction was higher for HCV antibody than HBs antigen ($p < 0.001$). Ninety-seven patients had a present or past history of liver disease, and the other 1142 had no history of liver disease (Table 1). The prevalence of HBs antigen was much higher in the former than in the latter (11.6 % vs. 0.66 %; $p < 0.001$) (Fig. 1). Similarly, dental patients with a history of hepatic disease were positive more frequently for HCV antibody than those without (51.2 % vs. 1.79 %, $p < 0.001$).

Dental patients with a history of hepatic disease had increased serum levels of AST ($p < 0.001$), ALT ($p < 0.001$), and FPG ($p < 0.001$) as compared to those without hepatic disease (Fig. 2). Blood platelet counts in subjects with hepatic disease were significantly lower than in those without ($p < 0.001$), but bleeding tendencies examined by both bleeding time and coagulation time, did not differ between the two groups. The red blood cell counts, white blood cell counts, hemoglobins, and hematocrits were similar in the groups. The subjects with liver disease were older than those without (54.4 ± 1.5 vs. 40.1 ± 0.6 , $p < 0.001$).

Figure 3 shows a comparison of serum chemistries, platelet counts and ages between subjects with and without hepatitis virus B or C infection. HB virus (HBV) carriers had slightly decreased blood platelet cell counts than non-carriers, but FPG, AST, and ALT levels did not differ between the groups. On the other hand, among HCV-antibody positive reactors, FPG, AST, and ALT were significantly higher and platelet counts were lower than

Fig. 3 Age, platelet counts (Plat), FPG, AST, ALT with or without serum HBs antigen (Upper panel) and with or without serum HCV antibody (Lower panel).

*: $p < 0.05$, ***: $p < 0.001$ in comparison with subjects with and without HBs antigen (upper) or HCV antibody (lower)

in the HCV-negative group. HCV-positive group was older than HCV-negative group, while age did not differ between the subjects of HBs antigen-positive and -negative.

Further analysis of the occurrence of serum HBs antigen, HCV antibody, and liver disease history by age-stratification (Fig. 4) shows that the highest prevalence of HCV and a history of liver disease was detected in 60 to 69 year old patients, but HBs antigen was most frequently noted in 30 to 39 year old subjects. The prevalence in 10-year age-groups of HBs

antigen ranged from 0 to 3.5 %, and that of HCV antibody from 0 to 10.3 %. The occurrence of HBs antigen was similar in patients with different dental diseases, such as inflammation (1.7 %), cysts (2.0 %), trauma (0.7 %), cancer (0 %), impacted teeth (1.9 %), anomalies (0 %), and benign tumors (2.8 %). HCV-antibody also was detected similarly in patients with various dental diseases (inflammation 7.7 %, cysts 3.4 %, trauma 3.7 %, cancer 8.0 %, impacted teeth 5.8 %, anomalies 5.6 %, benign tumors 5.8 %). Although the prevalence of HBs antigen in benign tumors, and that of HCV-antibody in cancer seems be greater than the others, no significant differences were noted either in the case of HBs antigen or HCV antibody, probably due to small number of patients for each group.

Fig. 4 Prevalence of subjects with a positive reaction to HBs antigen (HBV), HCV antibody (HCV) and those with hepatic disease, being divided according to age-stratification.

Discussion

In this large population study of dental college hospital inpatients, the prevalence of HBs antigen was 1.6 %, and that of HCV antibody 6.1 %, which are apparently higher than in the general populations of recent Japan (0.41 % for HBs antigen and 1.39 % for HCV antibody in 1993)¹⁴⁾, the United States, and Western Europe¹⁵⁾. There are areas such as Italy, Spain perhaps Japan and Egypt where HCV is endemic. Although hepatitis viruses infections might be endemic diseases in our local area, the prevalence of anti-HCV was 286 (2.0 %) of 14,341 subjects among the general population of Fukuoka¹⁶⁾, Japan where our study has been performed. Similarly, the other study showed the prevalence of anti-HCV was 3.3 % in the general population in Fukuoka¹⁷⁾, Japan. On the other hand, the frequency of subjects with HBs antigen was 18 (1.1 %) of 1638 for health care personnel in Fukuoka¹⁸⁾, Japan. Therefore, these observations with the present results further suggest that dental college hospital inpatients are infected with hepatitis viruses B and C more frequently than subjects in a general population. Since the prevalence of HBs antigen or HCV antibody was similar in patients with different dental diseases in our study, differences in dental disease do not explain the high prevalence. In a dental school outpatient (n=500) population, Shopper et al.¹³⁾ have reported a similar high occurrence (5.5 %) of serum HCV-antibody, similar to our observation, indicating that dental school hospital patients are infected frequently with both HBV and HCV. The reason why the dental patients have hepatic disease or be carriers of HCV or HBV was not answered by this study. Although social class may be related with

hepatitis viruses infection, each patient was not asked question about his social histories, since those such as annual income, educational background, type of job, official position, birthplace should not be taken in Japan in case of usual hospitalization to protect a individual patient right.

This high prevalence of HBV- and HCV-infected dental patients may lead to an increase in the occurrence of HBV and HCV infections in dental staff through accidents such as needle-stick injury. Therefore, dentists should pay careful attention to avoid infection with hepatitis viruses during dental practice. Immunization against HBV may decrease the occurrence of HBV infection^{3,19)}.

The reason for the discrepancy with the findings by Nagao et al. (1995)²⁰⁾, who have demonstrated high prevalence of hepatitis C virus antibody and RNA in oral cancer patients, remains unknown. They analyzed 100 oral cancer patients who had been admitted from 1989 to 1993. On the other hand, we in this paper examined 160 hospitalized cancer patients admitted from 1994 to 1995. We have 4 times more oral cancer patients annually than them. This may simply reflect differences in patients population between their hospital and ours.

A comparison of HBs-antigen with HCV-antibody seems somewhat peculiar. However, the measurement of HCV-RNA, which indicates the carrier state for HCV, in all 998 inpatients serum is considerably hard and expensive. Therefore, instead of HCV-RNA, we measured HCV-antibody. After this study completion, serum HCV-RNA was examined only in subjects with HCV-antibody. In patients with anti-HCV antibody, 53.2 % were positive for HCV-RNA²¹⁾.

Subjects with hepatic disease were reactive much more frequently to HCV-antibody and HBs-antigen than those without liver disease. The liver disease patients or hepatitis virus carriers had not only increased levels of AST and ALT, but decreased platelet counts, which might be associated with bleeding tendencies during dental procedures. In addition, FPG values were higher in these subjects, which might cause infection after dental surgery. These observations suggest that taking a history of liver disease is useful for estimating whether the patient is a hepatitis virus carrier, and dentists should treat patients with a history carefully to avoid infection. Additionally, since in these patients hemorrhagic accidents or infection might be induced by dental procedures, sufficient hemostasis and bleeding prevention, as well as high dosages of antibiotics should be used. The prevalence (7.8 %) of hepatic disease based on history in our study was similar to that from patient self-completed health questionnaires reported by Fenlon and McCartan (1991)²²⁾, who found hepatitis in 7.9 % of subjects attending a primary health care dental practice. Although most hepatitis virus carriers had a history of hepatic disease, 6 of 912 and 16 of 892 subjects without a history were carriers of HBV and HCV, respectively. This means that history taking cannot completely eliminate the risk that the patient is a carrier of these viruses. Careful dental technique for all patients is needed to prevent transmission of hepatitis viruses.

In conclusion, the prevalence of HBV and HCV carriers is higher in dental college hospital inpatients than in the general population. A clinical history of liver disease is useful in

determining whether the patient is a carrier of a hepatitis virus or impaired liver function.

Summary

We determined the prevalence of hepatitis virus carriers in a large population of hospitalized dental patients. The serum chemistries and bleeding tendencies associated with hepatitis B virus (HBV) and hepatitis C virus (HCV) also were evaluated. Twelve hundred thirty-nine consecutive hospitalized patients in a dental ward were questioned regarding a medical history of liver disease. Blood samples were taken for blood chemistry and platelet count. Serum HBs antigen and HCV antibody also were measured. Sixteen of 998 inpatients had serum HBs antigen (1.6 %), while 60 of 918 were HCV seropositive (6.1 %). Ninety-seven patients had a present or past history of liver disease (7.8 %), and the other 1142 had no history of liver disease. The prevalence of both HBs antigen and HCV antibody was much higher in the former than in the latter. This group had increased serum levels of aspartate transaminase, alanine transaminase, and fasting plasma glucose. Blood platelet counts in hepatic disease subjects were decreased. We determined that in a large population of dental college hospital inpatients, the occurrence of HBs antigen was 1.6 %, and that of HCV antibody 6.1 %, which is greater than in the general population. In patients with a history of liver disease dentists should take care to avoid exposure to viruses.

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歯科入院患者における 肝炎ウイルス感染と肝臓病

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歯科入院患者を対象に、肝炎ウイルス感染者の頻度及び、肝臓病の病歴とウイルス感染・血液生化学値との関連を検討した。1994年1月から1995年12月までに九州歯科大学口腔外科に入院した1239名から肝臓病の病歴聴取、血液生化学・血小板数・HBs抗原・HCV抗体の測定を行った。HBs抗原陽性率は1.6%、HCV抗体陽性率は6.1%であった。7.8%の患者が肝臓病の病歴を持っていた。肝疾患の病歴を有する者は病歴がない者に比し、明らかにHBs抗原（11.6%対0.66%）とHCV抗体（51.2%対1.79%）の陽性率が高かった。また、肝臓病病歴陽性者は病歴陰性者に比べ有意に血清GOT、

GPT、血糖が高値で、逆に血小板数は少なかった。また、HBs抗原陽性者は陰性者よりも血小板数が少なかった。HCV抗体陽性者は陰性者に比し、血清GOT、GPT、血糖が高値で血小板数は低値であった。歯科疾患別ではHBs抗原が良性腫瘍患者に、HCV抗体が悪性腫瘍患者に高頻度に陽性である傾向にあったが双方とも有意ではなかった。以上の結果から、歯科入院患者は一般住民よりもHBs抗原とHCV抗体の陽性率が高い可能性が示唆された。肝臓病の病歴を有している患者の歯科治療時には肝炎ウイルス院内感染予防のための十分な対策が必要と考えられた。