Incidence of Antibodies to Hepatitis C Virus in Patients Undergoing Chronic Dialysis and CAPD

FUMIYUKI NAKASHIMA, MICHIO SATA*, SHIGERU TOKESHI*, HITOSHI NAKANO*, MIEKO NAKASHIMA, NOBUYUKI NAKASHIMA, KENICHI MOTOMURA**, SEIJI MOTOMURA**, MICHIO IDE** AND KYUICHI TANIKAWA*

Namazuda Clinic, Fukuoka, *Department of Medicine, Kurume University School of Medicine, Kurume, 830 and **Division of Internal Medicine, St. Maria Hospital, Kurume, 830 Japan

Received for publication October 25, 1993

Summary: We measured antibodies to hepatitis C virus (anti-HCV) in patients who were receiving hemodialysis or continuous ambulatory peritoneal dialysis (CAPD). Sixty seven patients (28%) were anti-HCV positive. The anti-HCV positive frequency increased with the time of treatment with dialysis, the frequency being 50% with a dialysis period ≥10 years. The frequency of anti-HCV positivity was similar in patients with a history of blood transfusion (48/152, 32%) and in those without this history (19/89, 21%, p>0.05). Therefore, in addition to blood transfusion, there may be other routes of HCV infection associated with long-term dialysis. Chronic liver disease was observed in 31% (21/67) of the patients positive for anti-HCV but in only 6% (11/174) of the negative patients (p<0.01). HCV seems to be important as a cause of chronic liver disease in dialysis patients.

Key words: dialysis patients—hepatitis C virus (HCV)—C100-3 antibody—liver function impairment—post-transfusion hepatitis

Introduction

Dialysis patients are susceptible to hepatitis virus infection due to frequent blood transfusions. A high incidence of hepatitis B virus (HBV) infection has been reported (Szmuness et al. 1974), but this infection can now be prevented using hepatitis B vaccine. However, non-A non-B hepatitis viruses exist, and removal of these viruses from blood for transfusion is impossible. Hepatitis C virus (HCV) accounts for more than 90% of the non-A non-B hepatitis viruses in Japan. A detection method for HCV was developed in 1989 by Chiron Co., Ltd. in the US (Choo et al. 1989) and has allowed clinical measurement of this virus. Many findings about the incidence of hepatitis C virus have been reported. In November, 1989, screening for HCV antibody in donated blood was initiated, decreasing the incidence of post-transfusion hepatitis. However, since dialysis patients have already received frequent blood transfusions or blood preparations, the incidence of HCV in these patients is likely to be high. Therefore, we measured anti-HCV (C100-3 antibody) in dialysis patients to evaluate the state of HCV contamination.
Subjects and Methods

The subjects were 241 patients (154 males and 87 females) who were receiving hemodialysis or CAPD in April, 1991 at the Namazuda Clinic or the Kidney Center of St. Maria Hospital. Their mean age was 53.7 years, and the mean dialysis period was 7.0 years. Blood was collected before the initiation of dialysis, and the serum was stored at −20°C until assayed for HCV antibodies. The history of blood transfusion was examined using clinical records. In patients who were referred to these hospitals, information was obtained by interview of the patients. Chronic liver disease was considered to be present when the serum GPT level was 36 KU or higher at least 2 times during the 6-month period before and after the collection of the serum samples for the measurement of anti-HCV. Anti-HCV was measured by RIA (Otsuka Assay Institute HCV Ab RIA test kit). The cut-off value was 0.15, and higher values were regarded as positive. Differences were analyzed by Student’s t test and chi-square test.

Results

History of blood transfusion and of chronic liver disease according to age. As shown in Table 1, the percentage of patients with a history of blood transfusion did not differ among the age groups. Of the 241 patients, 149 (61.8%) had a history of blood transfusion. Chronic liver disease was frequently observed in the 3rd decade (20%) and the 6th decade (20%) but was not associated with age.

History of blood transfusion and chronic liver disease according to duration of dialysis treatment. As shown in Fig. 1, a history of blood transfusions was observed in 58 of 111 (52%) patients with a duration of dialysis treatment 5 years, in 49 of 71 (69%) with a duration of 5-10 years, in 32 of 43 (74%) with a duration of 10-15 years, and in 13 of 16 (87%) with a duration ≥15 years. The number

Fig. 1. Correlation between duration of hemodialysis treatment and history of transfusion and liver injury.

| TABLE 1. The incidence of transfusion, liver injury and anti-HCV antibodies according to age in patients with hemodialysis and CAPD |
|---|---|---|---|
| Age (yrs) | No. of patients | Transfusion (+) | Liver injury (+) | Anti-HCV (+) |
| 20~29 | 10 | 50% (5/10) | 20% (2/10) | 10% (1/10) |
| 30~39 | 38 | 68% (26/38) | 13% (5/38) | 37% (14/38) |
| 40~49 | 59 | 56% (33/59) | 8% (5/59) | 19% (11/59) |
| 50~59 | 55 | 67% (37/55) | 20% (11/55) | 45% (25/55) |
| 60~69 | 50 | 58% (29/50) | 10% (5/50) | 16% (8/50) |
| 70~ | 29 | 72% (21/29) | 10% (3/29) | 28% (8/29) |
| Total | 241 | 61.8% (149/241) | 12.9% (31/241) | 27.8% (67/241) |
of patients with a history of blood transfusion increased with the duration of the dialysis treatment. There was a significant difference between the patients with a dialysis history <5 years and those with a dialysis history of 5-10 years or ≥10 years (p<0.05 and p<0.01, respectively). The relation with the number of units of blood transfusion could not be evaluated because some medical records were lost in the long-term dialysis patients, and medical records could not be investigated in patients who were referred to these hospitals. On the other hand, the percentage of patients with chronic liver disease was evaluated according to the duration of dialysis treatment. As shown in Fig. 1, chronic liver diseases were observed in 10-20% of the patients regardless of duration of the dialysis treatment.

The anti-HCV positive rate according to the age groups varied from 10 to 45% and was very high in the 4th decade (37%) and the 6th decade (45%) (Table 1). The mean age in anti-HCV positive patients was 53.5 years, and that in negative patients was 52.6 years (p<0.05). The antibody positivity was higher with a longer duration of dialysis treatment (Fig. 2). Positivity was more than 50% in both the patients with a treatment of 10-15 years and those with a treatment duration ≥15 years (p<0.05). The anti-HCV positive rate was 32% (48/152) in the patients with a history of blood transfusion and 21% (19/89) in those without the history (Fig. 3). Chronic liver disease was observed in 31% (21/67) of the antibody-positive patients but only in 6% (11/174) in the antibody-negative patients (Fig. 4).
Discussion

Of the 241 dialysis patients in this study, 149 (61.8%) had a history of blood transfusion. The number of patients with a history of blood transfusion increased with a longer dialysis period. On the other hand, chronic liver disease was observed in 10-20% of the patients in each dialysis period, suggesting no association between them. A study in general blood donors showed a higher anti-HCV positive rate with age. In the dialysis patients in this study, the anti-HCV positive rate was very high in each age group compared with the general population. The anti-HCV positive rate increased with a longer dialysis period. In particular, the positive rate in the patients with a dialysis period ≥10 years was more than 50%, being significantly higher than that in the patients with a dialysis period <10 years. On the other hand, the mean age was slightly lower in the patients with a longer dialysis period than in those with a shorter dialysis period. This finding rejects the speculation that a higher number of patients in longer dialysis period groups causes the high anti-HCV positive rate. The anti-HCV positive rate was high in the patients with a history of blood transfusion. However, anti-HCV was also detected in 21% of the patients without a history of blood transfusion. Since no significant difference was observed between the two groups, the HCV infection route may not be blood transfusion alone. Some studies have suggested blood transfusion as the HCV infection route in dialysis patients (Oguchi et al. 1990; Aach et al. 1991). On the other hand, another study reported the case of a patient who became anti-HCV positive after a dialysis treatment of more than 1 year without blood transfusion. One of our subjects also became positive about 1.5 years after the initiation of dialysis without blood transfusion. Measurement of C100-3 antibody by ELISA is known to sometimes yield false-positive reactions. The high positive rate in dialysis patients may be partly due to some false-positive cases. Our results obtained by RIA, which is considered to produce less false-positive reactions, were similar to previously reported positive rates obtained by ELISA. Compared with the anti-HCV positive rate in the general population (1-2%), the antibody positive rate in dialysis patients is very high in Japan (Esteban et al. 1989; Oguchi et al. 1990). In other countries, the anti-HCV positive rate in dialysis patients is also high (Evans et al. 1989), and dialysis patients are considered to be a high risk group for HCV infection. The anti-HCV positive rate in Japan was reported to be significantly higher than that in western countries, and its cause should be clarified. In this study, HCV infection due to blood transfusion alone could not explain the high antibody positive rate in dialysis patients. In long-term dialysis therapy, the possibility of HCV infection by routes other than blood transfusion should be also considered. As infection routes other than blood transfusion, various environmental factors have been suggested such as an acupuncture or tattooing. The background factors of the patient should be also evaluated in detail. Recent studies suggested the possibility of HCV infection also in patients with hemophilia treated with only heated blood preparations when the use was frequent (Simmonds et al. 1990). In dialysis patients, in whom albumin preparations are used, the possibility that these blood preparations cause HCV infection cannot be excluded. This route should be evaluated in detail. The anti-HCV positive rate was 65.6% (21/32) in the dialysis patients with chronic liver disease and 22.0% (46/203) in those without chronic liver disease. A significant correlation was observed between chronic liver disease and anti-HCV
(p<0.01). These results suggest that HCV infection is the cause of chronic liver disease in dialysis patients. This may also support the hypothesis that the C100-3 antibody, i.e., the antibody against the NS3, 4 region of the HCV gene, is involved in the development of chronic liver disease. Recently, antibody against the core region of HCV can be also measured. The state of HCV infection should be studied in more detail using this measurement system.

References


