**Background and Purpose:** Many preventative strategies have been proposed to control hepatitis C virus (HCV) infection in the hemodialysis unit. The effectiveness of isolation as a preventive policy remains unclear. The aim of this study was to evaluate the effect of an isolation policy on the incidence of hepatitis C in our hemodialysis unit.

**Methods:** A total of 325 hemodialysis patients with a mean age of 62 ± 14 years and a mean duration of dialysis of 4.8 ± 4.4 years, who were treated from January 1993 to December 2000 were included in this retrospective study. Data were collected from medical records. HCV antibody was monitored at 6-month intervals. During the period before September 1997 all patients were dialyzed in a single room. Isolation started after September 1997, when an additional room became available. Patients positive for either hepatitis B or C were clustered in 1 area (Area 1). Anti-HCV-negative and hepatitis B surface antigen (HBsAg)-negative patients were assigned either to a segregated zone (Area 2) adjacent to Area 1 in the same room or to a separate independent room (Area 3). Dialyzers were not reused and hygienic precautions remained the same throughout the study period.

**Results:** Forty months after the implementation of the isolation policy, there was significant reduction in the total prevalence (49.7% vs 31.7%, p < 0.01) and incidence (9.1 vs 2.9 % patient-years, p < 0.01) of HCV infection. Seroconversion of anti-HCV was detected in 9 patients, 7 in Area 1, 2 in Area 2, with no new cases in Area 3. The incidence of seroconversion of anti-HCV was significantly different in the 3 areas. Regression analysis indicated that isolation was the most prominent independent factor in reducing seroconversion of anti-HCV.

**Conclusions:** These results support the use of an isolation policy to combat HCV infection among hemodialysis patients, particularly in high prevalence units.

**Key words:** Hepatitis C; Patient isolation; Infection control; Renal dialysis


In the past, blood transfusions have played a major role in the transmission of hepatitis C virus (HCV) in hemodialysis patients. With the introduction of erythropoietin and more sensitive screening tests for blood donors, the risk of post-transfusion hepatitis C has markedly reduced. Increasing years on dialysis has been the independent risk factor most consistently reported as being associated with a higher rate of HCV infection, even in patients who have not been transfused. Using contemporary molecular virological techniques, nosocomial transmission of HCV has been unequivocally documented.

Despite the success of preventive measures for preventing HCV infections among chronic hemodialysis patients, HCV transmission in this setting remains problematic. To block all the possible transmission routes, isolation of patients known to have HCV antibodies to separate machines and/or in a separate ward is still a controversial issue.

The prevalence of anti-HCV antibodies is about 50% in patients treated in our dialysis unit. Despite using standard hygienic measures and disposable dialyzers, the incidence of HCV infection remains high. The purpose of this study was to assess the effect of isolation of HCV-negative hemodialysis patients, either in a segregated area or in an independent room, on the reduction and prevention of HCV infection in our unit.

**Methods**

**Patients**

The retrospective study included a total of 325 unselected patients who were dialyzed for at least 1
year in our hemodialysis unit during the period from January 1, 1993 to December 31, 2000. There were 157 male and 168 female patients. The ages ranged from 34 to 83 years with a mean age of 62 ± 14 years. All patients were dialyzed 3 times a week. Time on dialysis ranged from 1 to 23 years with a mean of 4.8 ± 4.4 years. No patient was an intravenous drug user or had antibodies against the human immunodeficiency virus.

Isolation policy
From January 1993 through August 1997, isolation was not the policy in our unit. All patients were dialyzed in 1 room without isolation. In September 1997, we expanded our unit and an additional independent room became available, making isolation possible. Three different areas were assigned according to the serology of hepatitis. Patients (n = 112) positive for either positive hepatitis B or C (B+/C+, B+/C-, B-/C+) were clustered in Area 1. Anti-HCV-negative and hepatitis B surface antigen (HBsAg)-negative patients (B-/C-) were assigned either to a segregated zone (n = 66; Area 2) adjacent to Area 1 in the same room or to an independent room (n = 129; Area 3) [Fig. 1]. All patients were assigned to a single dialysis machine for all treatments. The disinfection procedure for the machine was performed according to the manufacturer’s instructions. Nurses assigned to the independent room (Area 3) were not allowed to provide patient care in Area 1 or Area 2.

No fixed nurse-patient scheme was employed in Areas 1 and 2 (in the same room) throughout the study period. Dialyzers were not reused and preventive measures were not changed during the whole study period. All medical staff were HCV negative.

Data collection
Information on each patient’s age, gender, HCV serologic tests, and history of dialysis including the date of starting, dropout and ending of renal replacement therapy was obtained from medical records. Data on the cumulative number of units of blood transfusion were also collected from blood bank records, and the transfused blood volume was also evaluated. Assessment of HBV and HCV antibodies was performed in all patients every 6 months from 1993 to 2000. Patients who had less than 2 HCV serologic tests or who had missing data were excluded. Time on hemodialysis was defined as the duration from the date of the first hemodialysis to the date of inclusion in this study.

Serological tests
HCV antibodies were screened by first-generation enzyme-linked immunosorbent assay (ELISA I) [Abbott Laboratories, North Chicago, Ill] through August 1993, by second-generation ELISA (ELISA II) [United Biomedical, Inc., Hauppauge, NY] from September 1993 through July 1997, and by more sensitive third-generation ELISA (ELISA III) [Abbot Laboratories, Abbott Park, Ill] after 1997. Anti-HCV reactivity was interpreted as described in the manufacturer’s instructions. Patients with HCV antibodies at their first sero-examination were defined as HCV positive. Those without HCV antibodies were defined as HCV-negative subjects. The latent period of HCV seroconversion was assumed to be 6 months in our study. Seroconversion was defined as transition to anti-HCV antibody positive status and remaining positive thereafter in a patient who was previously anti-HCV negative.

The annual prevalence of HCV infection was calculated based on the number of cases versus the total number of patients at the end of each year. To evaluate the effect of duration of dialysis on HCV infection, the incidence of HCV infection was calculated using the number of incident cases versus the person-years at risk. The period of dialysis in each patient was calculated according to the starting date and the ending date (change to peritoneal dialysis and transplantation, transfer to another hemodialysis center, death, or end of this study) of dialysis.

Statistics
Data were expressed as mean ± standard deviation and the differences among the 3 areas were assessed.
by analysis of variance (ANOVA) on continuous variables. Calculation and testing of prevalence and incidence before and after isolation, and among the patients of the 3 areas after isolation measures were carried out. The 95% confidence intervals (CIs) on each rate, the rate difference, and a Normal (Z) test and $p$ value determination were performed in accordance with the descriptions of Rothman. The effects of seroconversion of anti-HCV with covariances such as isolation policy were obtained by logistic regression analysis. Age, gender, pack number of blood transfusion, time on hemodialysis, and policy of separated area were included in multiple logistic regression. “Disease” as an dependent variable ($y = 1$) was identified as those subjects with seroconversion of anti-HCV after introduction of the isolation policy. Odds ratio (OR) and 95% CI of the effects were calculated.

**Results**

A total of 325 long-term hemodialysis patients were included in this study. When isolation became the policy after September 1997, there were 307 patients in the study group. Their demographic features are shown in Table 1. Before September 1997, the prevalence (%) and incidence (% patient-years) of HCV infection were constantly high (53.0 and 7.6, 51.0 and 4.3, and 59.6 and 14.0, in 1994, 1995, and 1996, respectively), and steadily decreased after the adoption of the isolation policy (Fig. 2). The total prevalence and incidence were significantly decreased after the adoption of isolation policy (49.7 vs 31.7%, $p = 0.005$, and 9.1 vs 2.9 % patient-years, $p = 0.003$, respectively) [Table 2]. There was an outbreak in May 1997.

During the 40-month follow-up after the isolation policy, a total of 9 patients had seroconversion of anti-HCV, including 7 in Area 1, 2 in Area 2, and no cases in Area 3 who were dialyzed in a separate room. Furthermore, the incidence was significantly different between each area (Table 3). The incidence was significantly lower in patients dialyzed in the segregated zone (Area 2) compared with those in Area 1 without isolation ($p = 0.036$), but higher in Area 2 than in Area 3 ($p = 0.026$). All patients with HCV seroconversion remained in a seropositive state throughout the remainder of the study period.

Among the 9 new cases of HCV infection that occurred during the study period, seroconversion to

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<th>Table 1. Characteristics of patients in the 3 areas after implementation of isolation.*,†</th>
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* Standard deviation of age and hemodialysis duration was determined by 1-way analysis of variance.
† Gender distribution was determined using Chi squared test.

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Fig. 2. Prevalence and incidence of anti-hepatitis C-positive patients in the dialysis unit.
anti-HCV was not related to age (OR, 0.88; 95% CI, 0.98 to 1.10), gender (OR, 1.33; 95% CI, 0.79 to 2.24), blood volume transfused (OR, 1.04; 95% CI, 0.98 to 1.10), but was related to the time on hemodialysis and the isolation policy. After adjusting for the duration of dialysis, isolation was the most prominent independent factor reducing HCV infection in the multivariate logistic regression analysis (Table 4).

**Discussion**

The prevalence of anti-HCV antibodies among patients on dialysis is consistently higher than in healthy populations, suggesting that dialysis patients are at higher risk of acquiring HCV infection. Recent, more sensitive screening tests and prescription of erythropoietin have reduced the risk of post-transfusion hepatitis C. However, the incidence of HCV infection remains high in our hemodialysis unit. Molecular virological studies have clearly shown nosocomial transmission of HCV to hemodialysis patients. Reuse of dialyzers, internal contamination of hemodialysis monitors, and patient-to-patient spread either indirectly or directly through contaminated surfaces are possible mechanisms of transmission. However, the main transmission route remains unclear.

In the past, we were diligent in the use of standard hygienic precautions. Nevertheless, up to the middle of 1997, the results were disappointing and the incidence of HCV acquisition remained high. In May 1997, there was an outbreak of HCV infection in our hemodialysis unit, which was noted after sharp increases in alanine aminotransferase (ALT) and positive HCV antibody status was found in 4 patients. Genotyping and identification of HCV strains by sequence analysis were done. Type 2a of HCV strain was identified in 3 of the 4 patients. The genotype of HCV among those who seroconverted was the same as the genotype of HCV infected patients reported in a previous study of patients in our dialysis unit. These findings corroborate the hypothesis of nosocomial transmission of HCV, and suggest the need for adopting an isolation policy as part of a rational strategy to block all possible transmission routes in the prevention of HCV infection. In September 1997, we set up an independent room in our hemodialysis unit making isolation of HCV infected patients possible. To the best of our knowledge, this is the first long-term follow-up study to simultaneously compare the incidence of HCV infection among a segregated zone, independent room, and an area without isolation in a hemodialysis unit of a single medical center.

At the start of the time of introduction of isolation measures, the prevalence of HCV infection was significantly decreased due to the increase of new patients as we expanded our unit. However, the incidence decreased further after the adoption of isolation measures. This observation is even more impressive considering that the more sensitive test of ELISA III was employed during the post-isolation period. Over a 40-month follow-up, the incidence was significantly less in patients dialyzed in a segregated
zone (Area 2) than in Area 1 without isolation. No case of seroconversion of anti-HCV was found in Area 3, where patients were dialyzed in an independent room. The duration of hemodialysis and volume of blood transfusion were associated with higher HCV infection (data not shown), which is consistent with the findings of our previous study. However, in the 9 new cases of HCV infection in the post-isolation period, seroconversion was not related to the blood volume transfused, but was related to the duration on hemodialysis. After adjusting for blood volume transfused and duration of dialysis, it appears that isolation was the most significant independent factor in reducing seroconversion of anti-HCV in the regression analysis. Our results suggest that nosocomial infection is the principal mode of HCV transmission, that transmission of HCV might be enhanced by physical proximity and that the isolation policy is effective in reducing the risk of acquiring HCV infection.

As conflicting opinions exist, the US Center for Disease Control does not recommend dedicated machines, patient isolation or a ban on reuse of dialyzers in HCV-positive patients. The rationale for isolation of HCV-infected patients was based on the success of the segregation of HBV-positive patients in the control of HBV infection as a promising model. Few studies have found that the use of dedicated machines and isolation of anti-HCV-positive patients either in a segregated zone or in a separate room may reduce the incidence of HCV infection. In fact, to isolate hemodialysis patients according to HCV serology would necessitate 4 wards (B+/C+, B+/C−, B−/C+, B−/C−). Several investigators regard such a strategy as unwarranted due to increased cost and logistical problems. In addition, there is evidence that strict adherence to universal precautions seems to be adequate to prevent HCV infection, by blocking direct patient-to-patient or healthcare worker-to-patient transmission. Gilli et al observed no cases of seroconversion within their unit when allowing HCV-positive and -negative patients to share dialysis machines while employing strict universal precautions. In line with their findings, a 54-month follow-up in a Belgian multicenter study by Jadoul et al also demonstrated that during three consecutive 18-month periods, the yearly incidence of seroconversion of anti-HCV dropped from 1.41% to 0.56% and 0% when universal precautions were reinforced. In contrast to the low prevalence (13.5%) of HCV infection at the outset of their study, our unit, despite hygienic precautions, had a relatively high prevalence of HCV infection (59.5 to 51%) before isolation measures.

Phylogenetic analysis of HCV isolated from infected patients within the same unit has clearly shown that patient-to-patient transmission is the main mechanism of contagion in the dialysis unit. It has also been shown that the incidence of new cases in dialysis units is directly related to the prevalence in these units. Thus, the low rate of seroconversion of anti-HCV found in western countries can be achieved without isolation. Strict implementation of universal preventive measures is probably sufficient to eliminate nosocomial infection in units with a low HCV prevalence. However, it has been reported that in actual practice, the application of universal hygiene precautions is frequently suboptimal.

Throughout the Asian region, as in our unit, the much higher prevalence rates of anti-HCV antibodies continues to be a serious public health problem among hemodialysis patients. Additional preventive strategies are crucial in order to combat HCV infection, in addition to universal hygiene precautions. The results of this study suggest that isolation of HCV-negative patients in a segregated zone or in an independent room can reduce or eliminate HCV infection. Similar to our findings, Arenas Jiménez et al in Spain also demonstrated decreased HCV infection in their high prevalence unit (about 30%) when HCV-positive patients were isolated in a separated zone.

Of note, at the time of follow up, neither abrupt increases of ALT level nor positive anti-HCV antibodies were detected in patients of Area 3. This finding suggests that separation of patients on the basis of HCV antibody detected by more sensitive third-generation assays is justified. Considering the serological window phase, HCV RNA assay is more accurate than enzyme immunoassay. However, detection of HCV RNA is impractical in view of the high cost and technical difficulties of the method.

In conclusion, with regard to infection control in dialysis units, our data suggest that besides strict adherence to the universal precautions, the implementation of isolation policy can further reduce the risk of infection and the likelihood of occasional lapses of preventive hygiene precautions or unpredictable accidents taking place in dialysis units. Further large-scale prospective studies are needed to substantiate these data supporting isolation of hemodialysis patients with hepatitis C infection, particularly in endemic areas.

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