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Comparative Study of Hepatitis C Virus Antibody between Hemodialysis and Continuous Ambulatory Peritoneal Dialysis Patients

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We have done cross sectional and prospective studies to determine the prevalence and the clinical significance of antibodies to the hepatitis C virus (Anti-HCV) in 54 hemodialysis (HD) patients and 227 continuous ambulatory peritoneal dialysis (CAPD) patients. Fifteen patients(27.8%) were anti-HCV (+) among the HD group, and twelve patients(5.3%) were anti-HCV(+) among the CAPD group. In the HD group, the positivity of anti-HCV correlated with the duration of HD, but there was no significant correlation with the history of transfusion, the amount of transfusion and abnormal alanine aminotransferase(ALT). At the follow-up study in 164 cases (HD 50 cases, CAPD 114 cases) after 6 months, one of 14 anti-HCV (+) CAPD patients was converted to anti-HCV(−) and two of 35 anti-HCV (−) HD patients were converted to anti-HCV(+). In conclusion, the prevalence of anti-HCV was significantly higher in HD patients compared to CAPD patients, and the positivity for anti-HCV in HD patients correlated with the duration of HD. A regular follow-up of anti-HCV and isolation of anti-HCV(+) HD patients with a separate machine may be needed to prevent the transmission of the hepatitis C virus during hemodialysis.

Key Words: Hepatitis C virus antibody, hemodialysis, CAPD

Patients undergoing chronic dialysis therapy potentially have an increased risk of infection due to an impaired immune response and multiple transfusion requirements. Especially viral hepatitis is a major hazard for dialysis patients, and 1.9% of all deaths among hemodialysis (HD) patients are regarded as sequelae of viral hepatitis(Jakobs *et al.* 1977).

Hepatitis B infections have been reduced by immunization, periodic tests and improved disinfectant procedures. Despite these control measures, some patients on HD show an abnormal liver function test with an unclear etiology. Hepatitis by the hepatitis C virus (HCV) is thought to be a major cause in such cases(Alter *et al.* 1986; Zeldis *et al.* 1990).

With the successful cloning of the hepatitis C virus genome (Choo *et al.* 1989), a serological test to detect antibodies to HCV (anti-HCV) now permits the various investigation in this field, using radioimmunoassay (RIA) and enzyme-linked immunosorbant assay (ELISA)(Kuo *et al.* 1989).

The reported prevalence of anti-HCV in HD patients varied widely from 7.4% to 54.0% according to dialysis centers and countries (Esteban *et al.* 1989; Schripkoter *et al.* 1990; Geerlings *et al.* 1991; Jeffers *et al.* 1990; Yamaguchi *et al.* 1990; Oguchi *et al.* 1990; Lin *et al.* 1991; Huang *et al.* 1992), and there were many reports that showed the correlation between the prevalence of anti-HCV and duration of HD, transfusion and past history of

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renal transplantation (Hardy *et al.* 1992; Rafael *et al.* 1992; Dentico *et al.* 1992).

Patients on continuous ambulatory peritoneal dialysis (CAPD) require neither extracorporeal circulation nor manipulation of blood and fewer transfusions are required than for those on HD: therefore CAPD may reduce the potential for HCV infection. The reported prevalence of anti-HCV in CAPD has ranged from 5%-15.4% (Huang *et al.* 1992; Rafael *et al.* 1992). As the incidence of chronic sequelae of hepatitis C is the highest among all kinds of viral hepatitis and as there are no means of prophylaxis against infection, it may contribute to morbidity and mortality in HD patients (Geerlings *et al.* 1991).

We investigated the prevalence of anti-HCV in HD and CAPD patients and its relationship with clinical parameters such as duration of dialysis, amount of transfusion, markers of the hepatitis B virus and liver functions. After 6 months, we did a follow up study of anti-HCV and other parameters.

PATIENTS AND METHODS

This cross sectional study was performed in 54 patients (36 males and 18 females) on chronic hemodialysis and 227 CAPD patients (133 males and 94 females) at Severance Hospital, Yonsei University in July and August, 1992.

Hepatitis C virus antibodies were studied by the 2nd generation recombinant enzyme immunoassay method (Abbott Laboratories) based on the HCV C-100 antigen. Liver function test was measured by an SMA-12 autoanalyzer. The patients' records were reviewed to ascertain the duration of dialysis, amount of transfusion and history of hepatitis. An episode of hepatitis was defined when alanine aminotransferase (ALT) was above the upper normal limit (40 IU/L) for more than 2 consecutive months, with the peak level greater than twice the normal value.

After 6 months, a follow-up evaluation with anti-HCV and other clinical parameters was performed.

Student's t-test was used for comparing the differences between group means; whereas chi-square test was used for comparing the differences between the incidences (or positve rate) for each group.

RESULTS

Charateristics of patients

Fifty-four hemodialysis patients with a mean age of 48.4 years and 227 CAPD patients with a mean age of 46.6 years were investigated in our study.

The average duration of hemodialysis treatment was 68.5±39.2 months (range 2~173 months), and the average CAPD duration

Table 1. Characteristics of the patients

Parameters	HD	CAPD	p-value
No of patients	54	227	
Sex(M:F)	36:18	133:94	
Age(years)	48.4±14.0	46.6±36.7	NS
Duration of dialysis (months)	68.5±39.2	27.6±13.8	NS
Hx of hepatitis	12(22.2)	13(5.7)	NS
Hx of transfusion	47(87.0)	128(56.4)	<0.05
Amount of transfusion (pints/case)	13.5±21.0	3.0±6.5	NS
Anti-HCV(+)	15(27.8)	12(5.3)	<0.05
HBsAg(+)	6(11.1)	16(7.0)	NS

Values are mean±S.D.
( ): percent
NS: not significant

Table 2. Amount of transfusion in HD & CAPD patients

Pints of transfusion	HD	CAPD
0	7(13.0)	99(43.6)
1~5	24(44.4)	100(44.1)
6~10	7(13.0)	14(6.2)
11~15	5(9.3)	7(3.1)
16~20	3(5.6)	1(0.4)
21~	8(15.1)	6(2.6)
Total	54	227

( ): Percent

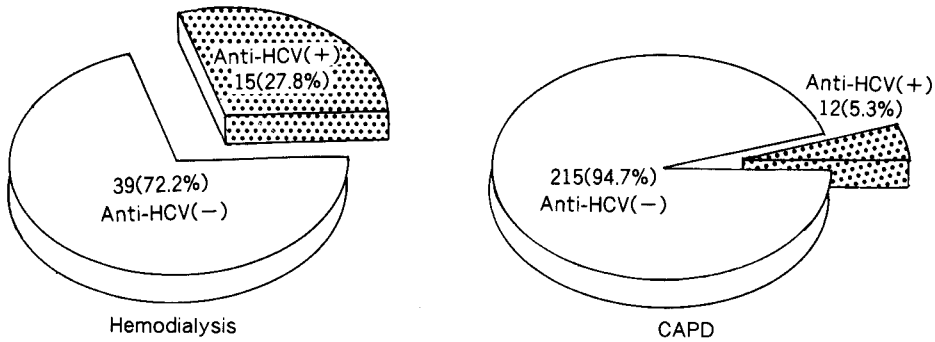

Fig. 1. *Prevalence of anti-HCV in hemodialysis and CAPD patients.*

Table 3. Comparison between anti-HCV(+) & anti-HCV(−) in HD patients

	Anti-HCV(+)	Anti-HCV(−)	p-value
Number	15	39	
Age	53.4±13.2	46.4±14.0	NS
Sex(M:F)	9 : 6	27 :12	
Duration of HD(months)	83.8±22.3	62.3±25.2	<0.05
Hx of transfusion(+)	12 (80.0)	35 (89.7)	NS
Total transfusion(pints/case)	11.5±10.3	16.3±25.2	NS
Previous Hx of Hepatitis	8 (53.3)	4 (10.3)	<0.05
AST(IU/L)	28.5±31.3	13.2± 7.6	NS
ALT(IU/L)	38.0±53.5	15.0±14.3	NS
HBV marker*	14 (93.3)	33 (84.6)	NS
HBsAg(+)	0	6 (15.4)	NS
AntiHBs(+)	13 (86.7)	18 (46.2)	<0.05
AntiHBc(+)	11 (73.3)	24 (61.5)	NS

Values are mean±S.D.
*: At least one HBV marker was positive.
NS: not significant
( ): percent

was 27.6±13.8 months (range 1~108 months) without a significant difference of duration of dialysis between HD and CAPD patients (Table 1).

Forty-seven (87%) HD patients had a past history of transfusion, which showed a significant difference with those of CAPD patients (128 patients, 56.4%). However, the average amount of transfusion of HD and CAPD patients were 13.5±21.0 pints and 3.0±6.5 pints respectively. Although HD patients received a greater amount of blood transfusion than CAPD patients, the difference was not statistically significant. Table 2 showing the amount of transfusion in HD and CAPD patients revealed that there was no significant difference between the two groups.

The prevalence of anti-HCV; Risk factors

Hepatitis C antibodies were found in 15 of 54 HD patients (27.8%) and in 12 of 227 CAPD patients (5.3%) with a significant difference ($p<0.05$), (Table 1, Figure 1). Although there was no difference in sex and age dis-

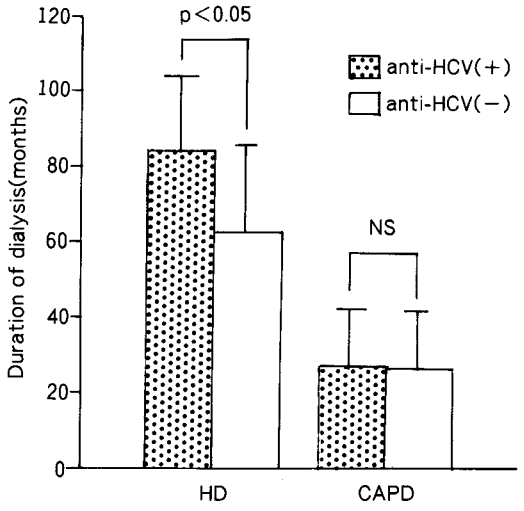

Fig. 2. *Duration of dialysis according to anti-HCV in HD & CAPD patients.*

tribution between anti-HCV positive and negative HD patients, the duration of HD was significantly longer in anti-HCV positive patients (83.8±22.3 months) than in anti-HCV negative patients (62.3±25.2 months) (Table 3, Figure 2). Figure 3 illustrates the correlation between the duration of HD and the prevalence of anti-HCV, which shows the tendency of an increasing anti-HCV prevalence with an increasing duration of HD. There was no correlation between the presence of anti-HCV and the amount of transfusion. Anti-HCV positive HD patients received an average of 11.5±10.3 pints of blood, compared to 16.3±25.2 pints for anti-HCV negative patients(Table 3). Figure 4 illustrates the correlation between the prevalence of anti-HCV and the amount of transfusion. The duration of CAPD in anti-HCV positive and negative patients were 26.3±21.0 months, 27.1±21.4 months respectively, but the difference was

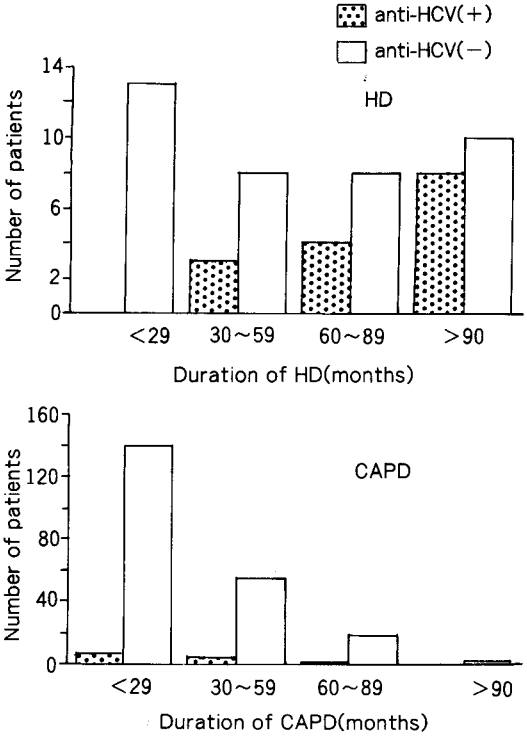

Fig. 3. *Prevalence of anti-HCV according to the duration of dialysis in HD and CAPD patients.*

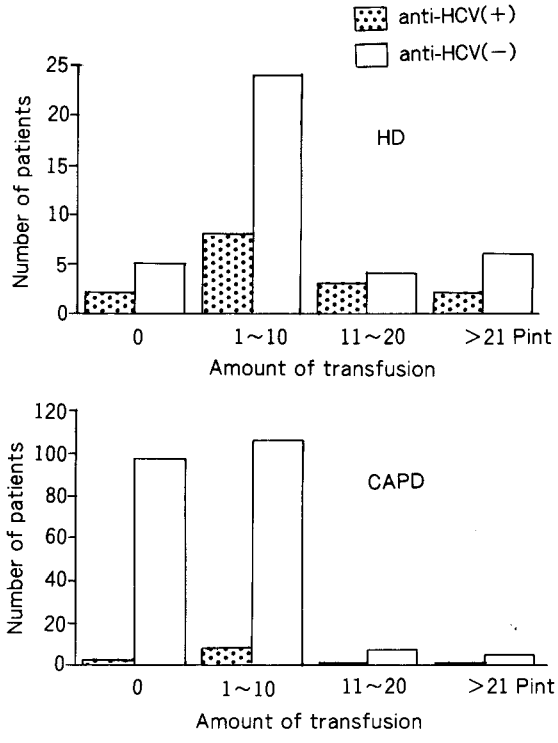

Fig. 4. *Prevalence of anti-HCV according to the amount of transfusion in HD & CAPD patients.*

Table 4. Comparison between anti-HCV(+) & anti-HCV(−) in CAPD patients

	Anti-HCV(+)	Anti-HCV(−)	p-value
Number	12	215	
Age	52.5±15.1	46.3±13.7	NS
Sex(M:F)	8 : 4	125 : 90	
Duration of CAPD(months)	26.3±21.0	27.1±21.4	NS
Previous HD(+)	7 (58.3)	79 (36.7)	NS
Duration of HD	3.0±9.9	1.9±8.6	NS
Transfusion Hx	6 (50.0)	122 (48.7)	NS
Total Transfusion(pints/case)	2.7±3.6	3.9±7.4	NS
Previous Hepatitis	2 (16.7)	11 (5.2)	NS
AST(IU/L)	25.3±19.6	14.9± 7.5	NS
ALT(IU/L)	32.9±42.0	15.5±19.9	NS
HBV marker*	11 (91.7)	182 (84.7)	NS
HBsAg(+)	0	16 (7.4)	NS
AntiHBs(+)	9 (75.0)	124 (57.7)	NS
AntiHBc(+)	10 (83.0)	137 (63.7)	NS

Values are mean±S.D.
*: At least one HBV marker was positive.
NS: not significant
( ): percent

Table 5. Prevalence of anti-HCV after 6 months in HD & CAPD patient

	Initial		After 6 months	
	HD	CAPD	HD	CAPD
Number of patients	54	227	50	114
Anti-HCV(+)	15(27.8)	12(5.3)	17(34.0)	11(9.65)

( ): percent

not statistically significant (Table 4, Figure 2). In terms of age, history of transfusion, previous HD, duration of HD and history of hepatitis, no significant differences were observed between each parameter and anti-HCV positive rate (Table 4, Figure 3, Figure 4).

Anti-HCV positive HD patients showed a significantly higher incidence of documented episodes of hepatitis (53.3%) than did anti-HCV negative patients (10.3%, $p<0.05$). Three of eight HD patients who showed an increased ALT more than 2 months persistently showed abnormal ALT level up to 15 months as of the day of this evaluation (Table 6). Abdominal ultrasound was performed in 6 cases which showed a diffuse parenchymal liver disease pattern. Three of 4 cases, on whom a liver biopsy was performed, showed chronic persistent hepatitis and the other one showed chronic active hepatitis.

Only 2 patients (16.7%) among anti-HCV positive CAPD patients showed a previous history of hepatitis (Table 7).

The prevalence of anti-HCV and hepatitis B virus markers

Forteen patients (93.3%) of 15 anti-HCV positive HD patients were positive for any one of the hepatitis B virus markers.

No patient was positive for anti-HCV and HBsAg concurrently in our study.

The prevalence of anti-HBs was significantly higher in anti-HCV positive HD patients (86.7%) compared to negative patients (46.2%). There was no significant difference of the prevalence of anti-HBc between anti-HCV positive and negative patients (Table 3, 4).

Table 6. Clinical and laboratory characteristics of anti-HCV(+) HD patients

No.	Sex/Age	Duration of HD(month)	HBsAg	AntiHBc	Hx of Hepatits with duration	Current LFT (AST/ALT)	Abdominal U/S	Liver Bx.
1	M/44	98	−	+	377/1018*(7 m)	17/11	DLD	CPH
2	F/64	56	−	+	285/535 (3 m)	20/24	DLD	ND
3	M/59	97	−	+	−	6/17	ND	ND
4	F/50	92	−	+	328/460 (2 m)	17/ 8	ND	ND
5	F/62	104	−	+	−	33/20	ND	ND
6	M/37	110	−	+	−	14/24	ND	ND
7	M/53	116	−	−	101/248 (8 m)	50/52	DLD	CAH
8	M/66	84	−	+	−	11/21	ND	ND
9	M/53	80	−	+	−	17/29	ND	ND
10	M/32	90	−	+	175/540 (10 m)	26/65	DLD	CPH
11	F/42	73	−	−	80/89 (3 m)	30/30	ND	ND
12	F/76	58	−	−	65/87 (4 m)	21/11	DLD	CPH
13	M/48	60	−	+	−	3/ 5	ND	ND
14	M/40	60	−	−	−	13/ 7	ND	ND
15	F/73	40	−	+	76/118 (15 m)	60/60	DLD	ND

*: Peak value of AST/ALT
DLD: Diffuse liver disease pattern
CPH: Chronic persistent hepatitis
CAH: Chronic active hepatitis
ND: Not done

Table 7. Clinical and laboratory characteristics of anti-HCV(+) CAPD patients

No.	Sex/Age	Duration of HD(month)	HBsAg	AntiHBc	Hx of Hepatits with duration	Current LFT (AST/ALT)	Abdominal U/S	Liver Bx.
1	M/38	53	−	+	150/300*(46 m)	78/100	DLD	ND
2	M/23	32	−	+	151/371 (40 m)	60/ 68	DLD	ND
3	M/59	55	−	+	−	19/ 12	ND	ND
4	M/73	63	−	+	−	23/ 19	ND	ND
5	M/67	2	−	+	−	3/ 15	ND	ND
6	M/50	16	−	+	−	11/ 12	ND	ND
7	F/47	41	−	+	−	6/ 27	ND	ND
8	F/38	19	−	+	−	13/ 14	ND	ND
9	F/65	7	−	−	−	12/ 9	ND	ND
10	M/58	4	−	−	−	22/ 17	ND	ND
11	F/44	12	−	+	−	31/ 12	ND	ND
12	M/68	10	−	+	−	11/ 12	ND	ND

*: Peak value of AST/ALT
DLD: Diffuse liver disease
ND: Not done

Follow-up study

Follow-up studies of the clinical parameters were done in 164 patients (HD 50 patients, CAPD 114 patients) after 6 months to investigate the changes of these parameters during this short period. The patients with positive anti-HCV in this group consisted of 17 HD and 14 CAPD cases. By the follow-up

after 6 months, 2 HD patients had positive seroconversion from negative anti-HCV and one CAPD patient had negative seroconversion from positive anti-HCV at the initial study.

DISCUSSIONS

Renal failure patients potentially have an increased risk of infection due to an impaired immune response and blood transfusions. Infections are therefore one of the major causes of morbidity and mortality in patients with end stage renal failure accounting for 20% of deaths (Keane & Raij 1983; Ruiz *et al.* 1990; Tolkoff & Rubin. 1990; Degast *et al.* 1976). Viral hepatitis is a major hazard for dialysis patients, and 1.9% of all deaths among HD patients are regarded as sequelae of viral hepatitis (Jakobs *et al.* 1977). It is well known that the prevalence of anti-HCV in patients with maintenance dialysis is higher than that of an healthy blood donor and that HCV is a major cause of non-A non-B hepatitis (Schlipkoter *et al.* 1990; Dienstag & Alter. 1986; Marchesi *et al.* 1988). Acute hepatitis by HCV shows a relatively mild clinical course with a mean incubation period of 7~8 weeks, but about 80% of acute hepatitis progresses to chronic hepatitis (Alter *et al.* 1989; Sibrowski *et al.* 1989; Parfey *et al.* 1989).

The reported prevalences of anti-HCV were variable according to dialysis centers and countries with 7.4%~54% in HD patients and 5.0%~12.4% in CAPD.

In our study, the prevalence of anti-HCV in HD and CAPD were 27.8%, 5.3%, respectively, comparable to other reports (Hardi *et al.* 1992; Rafael *et al.* 1992; Dentico *et al.* 1992).

A remarkably lower incidence of anti-HCV in CAPD patients than that in HD patients remains to be explained, but the lack of risk of extracorporeal circulation-related blood contamination, lower requirements of transfusion and higher immunity compared to HD patients could be responsible.

The fact that anti-HCV positivity was directly proportional to the duration of HD indicates that the risk of HCV infection is directly related with the dialysis process itself through such factors as extracorporeal circulation, repetitive transfusion, common equipments without isolation of positive HCV patients (Schlipkoter *et al.* 1990; Yamaguchi *et al.* 1990; Dentico *et al.* 1992; Mondelli *et al.* 1990). Poel *et al.* (1990) reported that blood transfusion is an important risk factor in transmission of HCV, and 9 of 26 patients(35 %) who were initially anti-HCV negative demonstrated either anti-HCV seroconversion or clinical evidence of posttransfusional non-A non-B hepatitis after an anti-HCV positive blood transfusion (Poel *et al.* 1990). However, we did not find any significant correlation with the amount of transfusion in our study. Jeffers *et al.* (1990) reported that the prevalence of anti-HCV was not related with the transfusion, and Hardy *et al.* (1992) observed the high prevalence of anti-HCV in HD patients with the duration of dialysis for more than 2 years and suggested the possibility that the HD procedure had a risk of exposure to HCV.

In addition to habitual intravenous drug use, sexual exposure and household contact have been suggested as risk factors for HCV transmission (Hess *et al.* 1989; Perez *et al.* 1990; Thaler *et al.* 1991). However, the infectivity of an anti-HCV carrier is known to be less than that of the hepatitis B virus and the vertical and intrafamilial transmissions are actually low (Kiyosawa *et al.* 1991).

Gilli *et al.* (1990) identified that a possible route of contamination is the common use of multi-dose vials for heparin in HD units with high anti-HCV prevalence.

Despite these suspicious risk factors, the exact transmission route of HCV is not fully clarified yet (Alter *et al.* 1989).

Oguchi *et al.* (1992) reported in their study with patients in eleven dialysis units that patients with positive anti-C-100-3 had an high incidence of chronic liver disease. The incidence of chronic liver disease with elevated serum ALT more than 6 months was 39% in patients with positive anti-C-100-3 while 9% in negative patients but there was no significant difference in the history of chronic liver disease between the patients with a positive and negative HBV marker (21% vs. 11%, $p > 0.05$). Those results are in accordance with the study of Furuta *et al.* suggesting that

HCV infection is a very important cause of chronic liver disease in patients with maintenance HD.

According to the report of Furuta *et al.* (1991), 81% of anti-C-100-3 positive acute NANBH progresses to chronic hepatitis, in contrast to the significantly lower incidence of chronicity (24%) in anti-C-100-3 negative NANBH. In our study, 53.3% of the anti-HCV positive HD patients revealed liver dysfunction more than 2 months, but most of them had no clinical symptoms with intermittent episodes of mildly increased ALT levels. The mean ALT level in anti-HCV positive HD and CAPD patients was within the normal limit at the time of the study, and 80% of the anti-HCV positive HD patients and 83.3% of the anti-HCV positive CAPD patients revealed normal ALT. The clinical significance of positive anti-HCV in patients with a normal liver function test is still controversial. One study with a liver biopsy in patients with HBsAg positive renal failure showed that 56% of patients with a normal liver function test revealed chronic liver disease including liver cirrhosis (Park *et al.* 1993). Based on the above results, the decision to perform a renal transplantation has to be made sincerely and a liver biopsy may be necessary to rule out active liver disease before renal allografts in patients with positive anti-HCV even though they show normal liver functions. This is our policy in renal recipient studies.

A significant association between anti-HBc status in blood donor and NANBH in recipients was noted by Stevens *et al.* (1984). Some reports suggested that anti-HBc could be used as a paradoxical (surrogate) marker for non-A non-B hepatitis agents in donated blood (Oguchi *et al.* 1992; Koziol *et al.* 1986; Aach *et al.* 1981). However, there was no relation between anti-HCV and anti-HBc in our study and the prevalence of anti-HBc was higher (HD 64.8%, CAPD 64.7%) than that other studies.

A recent study about anti-HCV in the home and hospital HD patients reported that the anti-HCV positive rate was higher in the hospital HD group compared to the home HD group with 29% of 68 hospital patients and 5 % of 20 home patients, respectively (Julio *et al.* 1993). This strikingly higher prevalence of anti-HCV in in-hospital HD patients than in home HD patients, even though there was no significant difference in sex, age, duration of HD and transfusion amount, suggested that HCV infection somehow occurs during the procedure of hemodialysis by contamination; therfore, isolation of those HCV positive patients during HD is recommended as with those patients with positive HBsAg.

Because the presence of anti-HCV does not discriminate the ongoing infection from past infections nor infectivity from immunity, and because there is some controversy concerning the interpretation of anti-HCV in the same manner as in an healthy individual, a prospective longterm study with new patients just entering HD and CAPD programs, to follow the evolution of their anti-HCV status, is needed.

In summary, we have shown that the prevalence of anti-HCV was significantly higher in HD patients compared to CAPD patients and that this difference was related to the duration of HD in HD patients. There was no significant correlation between anti-HCV and the amount of transfusion. Considering these observations, we recommend the isolation and use of a separate machine for anti-HCV positive HD patients.

REFERENCES

Aach RD, Szmuness W, Mosley JW: Serum alanine aminotransferase of donors in relation to the risk of non-A non-B hepatitis in recipients. *New Eng J Med, 304: 989, 1981*

Alter MJ, Favero MS, Maynard JE, Bonino F, Colombo M, Lee WS, Kuo C, Berg K, Shuster JR, Overby LR, Bradley DW, Houghton M: Impact of infection control strategies on the incidence of dialysis-associated hepatitis in the United States. *J Infect Dis 153: 153, 1986*

Alter MJ, Sampliner RE, Hepatitis C: and miles to go before we sleep (editorial). *New Eng J Med, 321: 1538, 1989*

Alter MJ, Purcell RH, Shin JW, Melpolder JC, Houghton M, Choo QL, Kuo G: Detection of antibody to hepatitis C virus in prospectively followed transfusion recipient with acute and chronic non-A non-B hepatitis. *New Eng J Med 30: 1494, 1989*

Huang CC, Wu MS, Lin DY, Law YF: The preva-

lence of hepatitis C virus antibodies in patients treated with continuous ambulatory peritoneal dialysis. *Peritoneal Dial Int 12: 31, 1992*

Choo QL, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M: Isolation of a cDNA clone derived from a blood-borne non-A non-B viral hepatitis genome. *Science 244: 359, 1989*

Degast G, Howen B, Van der Hem K: T-lymphocyte number and function and the course of hepatitis B in hemodialysis patients. *Inf Immun 14: 1138, 1976*

Dentico P, Buongiorno R, Volpe A, Carlone A, Carbone M, Manno C, Proscia E, Schraldi O: Prevalence and incidence of hepatitis C virus (HCV) in hemodialysis patients: Study of risk factors. *Clin Nephrol 38: 49, 1992*

Dienstag JL, Alter MJ: Non-A Non-B hepatitis: Evolving epidermiologic and clinical perspective. *Semin Liver Dis 6: 67, 1986*

Esteban JI, Esteban R, Viradomiu L, Lopez-Talavera JC, Gonzalez A, Hernandez JM, Roget M, Vargas V, Buti M, Guardia: Hepatitis C virus antibodies among risk group in Spain. *Lancet 2: 294, 1989*

Furuka S, Tanaka E, Kiyosawa K, Suzuki H, Nishioka K, Oda T: Viral hepatitis C, D and E, Experta Medica, Amsterdam *1: 79, 1991*

Geerlings W, Tufveson G, Brunner FP: 21st combined report on regular dialysis and transplantation in Europe. *Nephrol Dial Transplant 6 (suppl 4): 1, 1991*

Gilli P, Moretti M, Shoffritti S, Marchi N, Malacarne F, Bedani PL, Flocchi O, Menini C: Non-A non-B hepatitis and anti-HCV antibodies in dialysis patients. *Int J Artif Organ 13: 737, 1990*

Hardy NM, Sandroni S, Danielson S, Wilson WJ: Antibody to hepatitis C virus increase with time on hemodialysis. *Clin Nephrol 38: 44, 1992*

Hess G, Massing A, Rossel S: Hepatitis C virus and sexual transmission. *Lancet 2: 987, 1989*

Jakobs C, Brunner C, Hantler C: *Dialysis, Transplantation, Nephrology.* Proc 14th Congr Eur. Dial Transplant Assoc, *1977*

Jeffers LJ, Perez GO, De Medina MD, Ortiz-Interian CJ, Schiff ER, Reddy KR, Jimenerz M, Bourgoignie JJ, Vaamonde CA, Duncan R, Houghton M, Choo QL, Kuo G: Hepatitis C infection in two urban hemodialysis units. *Kidney Int 38: 320, 1990*

Julio P, Teruel JL, Liano F, Ortuno J: Home hemodialysis protect against hepatitis C virus transmission. *Nephron 64: 314, 1993*

Keane WF, Raij LR: *Replacement of renal function by dialysis*, ed 2, Boston, Nijhoff, *1983*

Kiyosowa K, Sodeyama T, Tanaka E: Intrafamilial transmission of hepatitis C virus in Japan. *J Med Virol 33: 114, 1991*

Koziol DE, Holland PV, Alling DW: Antibody to hepatitis B core antigen as a paradoxical marker for non-A non-B hepatitis agents in donated blood. *Ann Intern Med 104: 488, 1986*

Kuo G, Choo QL, Alter MJ, Gitnick GL, Redeker AG, Purcell RH, Miyamura T, Dienstag JL, Alter MJ, Stevens CE, Tegtmeier GE, Bonino F, Colombo M, Lee WS, Kuo C, Berger K, Shuster JR, Overby LR, Bradley DW, Houghton M: An assay for circulating antibodies to a major etiologic virus of human non-A non-B hepatitis. *Science 244: 362, 1989*

Lin HH, Huang CC, Sheen IS: Prevalence of antibodies to hepatitis C virus in hemodialysis unit. *Am J Nephrol 11: 192, 1991*

Marchesi D, Arici C, Poletti E, Mingaedi E, Minola E, Mecca G: Outbreak of non-A non-B hepatitis in center hemodialysis patients: A retrospective analysis. *Nephrol Dial Transplant 3: 795, 1988*

Mondelli MU, Cristina G, Filice G, Rondanelli EG, Piazza V, Barbieri C: Anti-HCV positive patient in dialysis units? (Letter) *Lancet 336; 244, 1990*

Oguchi H, Miyasaka M, Tokunaka S, Hora K, Ichikawa S, Ochi T, Yamada K, Nagasawa M, Kanno Y, Aizawa T, Watanabe H, Yoshizawa S, Sato K, Terashima M, Yoshie T, Oguchi S, Tanaka E, Kiyosawa K, Furuta S: Hepatitis virus infection (HBV and HCV) in eleven Japanese hemodialysis unit. *Clin Nephrol 38: 36, 1992*

Oguchi H, Terashima M, Tokunaga S: Prevalence of anti-HCV in patients on long-term hemodialysis. *Nippon Jinzo Gukkai Shi 32: 313, 1990*

Park CS, Kim KY, Kim HS, Choi KH, Han GH, Chun JY, Lee HY, Han DS: Liver disease in Korean HBsAg carriers with end stage renal disease. *Korean J of Nephrology 12: 136, 1993*

Parfey PS, Farge D, Forbes RDC, Dandavino R, Kenick S, Guttman RD: Chronic hepatitis in end stage renal disease: Comparison of HBsAg positive and HBsAg negative patients. *Kidney Int 28: 959, 1985*

Perez RM, Sanchez QA, Lissen E: Transmission of hepatitis C virus. *Ann Intern Med 113: 411, 1990*

Poel CL, Cuypers HTM, Reesink HW, Weine AJ, Quan S, Nello R, Boven JJP, Winkel I, Mulder FD, Exel OPJ, Wchaasberg W, Leentuaan KA, Polito A, Houghton M, Lelia PN: Confirmation of hepatitis C virus infection by new four-an-

tigen recombinant immunoblot assay. *Lancet 337: 317, 1991*

Poel CL, Reesink HW, Schaasberg W, Leentuaan KA, Lelia PN: Infectivity of blood seropositive for hepatitis C virus antibodies. *Lancet 335: 558, 1990*

Rafael S, Rosa MZ, Jose RR, Jesus M, Carmen R, Blanca M, Jose LM: Prevalence of hepatitis C antibodies (HCV) in a dialysis population at one center. *Peritoneal Dial Int 12: 28, 1992*

Ruiz P, Gomez F, Schreibner A: Impaired function of macrophage FcY receptors in end stage renal disease. *N Eng J Med 322: 717, 1990*

Schlipkoter U, Roggendorf M, Ernst G, Rasshoper R, Deinhardt F, Weise A, Gladziwa U, Luz N: Hepatitis C virus antibodies in hemodialysis patients. *Lancet 335: 1409, 1990*

Sibrowski W, Kuhnl P, Knodler B, Loliger C, Seidl S: *Hepatitis C virus antibody prevalence in German patients on hemodialysis.* 1st Int Meet Hepatitis C Virus, Rome, *1989*

Stevens CE, Aach RD, Hollinger FB: Hepatitis B virus antibody in blood donors and the occurrence of non-A non-B hepatitis in transfusion recipients. Analysis of transfusion-transmitted viruses study. *Ann Intern Med 101: 733, 1984*

Thaler MM, Choong KP, Landers DV: Vertical transmission of hepatitis C virus. *Lancet 338: 17, 1991*

Tolkoff RN, Rubin R: Uremia and host defense. *N Eng J Med 322: 770, 1990*

Yamaguchi K, Nishimura M, Fukuoka N, Machida J, Ueda S, Kusumoto Y, Futami G, Ishii T, Takatsuki K: Hepatitis C virus antibodies in hemodialysis patients. *Lancet 335: 1409, 1990*

Zeldis JB, Depner TA, Kuramoto IK, Gish RG, Holand PV: The prevalence of hepatitis C virus antibodies among hemodialysis patients. *Ann Int Med 112: 958, 1990*