HEPATITIS C VIRUS INFECTION IN PATIENTS WITH CHRONIC RENAL FAILURE AND RENAL TRANSPLANTATION RECIPIENTS

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Abstract — The presence and significance of hepatitis C virus infection among patients with chronic renal failure (CRF) on hemodialysis and renal transplant recipient were evaluated a period of 30 months. A total of 125 patients, comprising 25 recieving chronic hemodialysis, 47 renal transplant candidates and 53 renal transplant recipients, were studied with a second generation immunoassay (ELISA II). We detected HCV antibody in 13% of hemodialysis patients which is 40 folds higher than the prevalence of HCV antibody in general population of Iran (0.3%), as expected. Fortynine (39.2%) of our patients were HCV antibody positive, 28 of them were transplanted and 21 were renal transplant candidates. We compared HCV antibody positive (group 1) and HCV antibody negative (group 2) patients. The results of this study showed a positive correlation between HCV seroconversion, CRF, duration on hemodialysis and elevated liver enzyme levels. Duration of follow-up were 29.62 ± 15.62 months and 31.25 ± 17.50 months in group 1 and 2 respectively (P = NS). Duration of preoperative hemodialysis were 54.14 ± 41.18 months and 16.00 ± 10.25 months in group 1 and 2 respectively (P = 0.0001). During follow-up, elevated ALT levels were present in 43.3% and 9.26% of patients in group 1 and 2 respectively (P=0.0001). Immunosuppressive drug toxicity, Postopeative complications including hyperacute rejection and acute tubular necrosis were more common in group 1.
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Key words: Hepatitis C virus; renal transplantation; chronic renal failure

INTRODUCTION

The success of renal transplantation as a therapy for end-stage renal disease has focused attention on factors affecting long-term patient and graft survival.

Liver disease is a common cause of morbidity and mortality in renal transplant recipients and in some series (1) represents one of the leading cause of death in long-functioning renal transplants (2).

Many factors including drug toxicity and viral infection, have been implicated in the etiology of post-transplantation liver disease. Hepatitis C virus (HCV) infection is the most common cause of chronic liver disease after renal transplantation (2).

The most striking clinical feature is that, 60% or more of anti HCV positive patients have or will develop chronic liver disease (3). The rate of progression and histopathological pathways to cirrhosis have not been clearly delineated, in part because of the short periods of follow-up in prior studies, variations in studies and between study populations and the relatively recent (since 1989) availability of serological methods to document HCV infection.

The aims of the current study were to:

1. Determine the preoperative seroprevalence of HCV antibody in renal allograft recipients using second generation immunoassay.

2. Assess the impact of HCV infection on short-term outcome of patients.

MATERIALS AND METHODS

Patients

From 1994 to 1996, 125 patients and 9 hemodialysis staff members were screened for HCV antibody and followed over a period of 30 months, comprising 25 receiving chronic hemodialysis, 47 renal transplant candidates and 53 renal transplant recipients.

Screening For HCV Antibody

Serum specimens were refrigerated at 4°C for a maximum of 5 days until tested. Antibodies to HCV were detected using a second generation immunoassay (ELISA II). Liver enzyme levels were recorded every 3 months.

Liver biopsies were studied by two pathologists and scoring was performed according to knodel's scoring system. The prevalence of HCV infection in CRF patients on hemodialysis, renal transplant recipients and hemodialysis staff members were determined. The association between CRF, duration of pre-transplant hemodialysis, number of blood transfusions, and acquisition of HCV was investigated by Chi-square and T-test, with significant level set at 0.05. Data are expressed as mean ± SD.

HCV antibody positive renal transplant candidates underwent liver biopsy. Patients with biopsy score of < 4 were transplanted and those with biopsy score of > 4 received interferon -2b (3 million units, 3 times a week

for 24 weeks). After cessation of treatment, another liver biopsy was performed and patients with biopsy score of < 4 underwent renal transplantation.

We compared liver enzyme levels, postoperative complications, drug dosage and toxicity between HCV antibody positive (group 1) and HCV antibody negative (group 2) patients.

RESULTS

HCV antibody was detected in 13% of hemodialysis patients in our center. All hemodialysis staff members were HCV antibody negative. Out of 125 patients, 49 (39.2%) were HCV antibody positive, 28 of them were transplanted and 21 were renal transplant candidates.

Eighteen patients received interferon -2b, 4 of them are transplanted and 14 are waiting for transplantation.

Patient characteristics according to preoperative anti HCV serostatus are as follows (Table 1).

Table 1.

	Group 1 N = 49	Group 2 N = 25	
Variable			P value
Age (years)	34.51±12.29	31.60±9.33	NS
Gender (M/F)	36/13	16/9	NS
Follow-up (months)	29.62±15.62	31.25±17.50	NS
Preop. hemodialysis (months)	54.14±41.18	16.60±10.25	0.0001
Blood transfusion (units)	10.00±13.01	6.72±7.14	NS

Table 2. Biochemical Characteristics of Patients

		Group 1 N = 49	Group 2 N = 25	
Variable	N.L range			P value
AST	7-34	36.00±24.00	21.75±13.72	0.0001
ALT	7.40	58.88±85.69	31.61±36.21	0.0001
ALK-P	up to 190	252.74±195.96	122.33±65.45	0.0001
Creatinine (mg/dl)		1.03±1.83	1.06±2.70	NS

Table 3. Histological characteristics of group 1 (N=49) are as follows

Score	N	%
0-3	22/49	44.89%
4-8	23/49	46.93%
9-12	2/49	4.08%
13-18	1/49	2.04%
19-22	1/49	2.04%
Fibrosis	N	%
0	18/49	36.73%
1	9/49	18.36%
2	11/49	22.44%
3	11/49	22.44%

Table 4. Immunosuppressive drug dosage and toxicity in renal transplant recipients are as follows

	Group 1 N = 28	Group 2 N = 25	
Variable			P value
CyA dosage (mg/day)	118.88±127.63	222.00±50.66	<0.001
CyA level (ng/ml)	354.25±292.85	175.00±72.18	0.001
CyA toxicity (>300 ng/ml)	14/28 (50%)	2/25 (8%)	0.001
Pred. dosage (mg/day)	7.67±11.30	11.98±4.81	0.03
Aza dosage (mg/day)	28.88±41.37	70.00±67.08	<0.001
Double therapy (CyA+Pred)	10/28 (35.71%)	7/25 (28%)	NS

Table 5. Postoperative complications according to anti HCV serostatus

	Group 1 N = 28	Group 2 N = 25	
Variable			P value
Hyperacute rejection	2/28 (7.14%)	0/25 (0%)	NS
Acute rejection	6/28 (21.42%)	7/25 (28%)	NS
Chronic rejection	1/28 (3.57%)	5/25 (20%)	0.001
Acute tubular necrosis	6/28 (21.42%)	2/25 (8%)	0.001

DISCUSSION

Using a second generation anti HCV assay 13% of our hemodialysis patients were HCV antibody positive, which is 40 folds higher than prevalence of HCV antibody in the Iranian general population (0.3%).

The prevalence of anti HCV positive hemodialysis patients varies considerably among nations. Ten to fourty of hemodialysis patients in the United States are anti HCV positive (3) and in the majority of Mediterranean countries the prevalence ranges between 20% and 30%. European countries have lower prevalences (UK, 2%, Sweden, 8%, Germany, 7.5% and Austria, 10%) (4).

Prevalence of HCV infection in hemodialysis staff members was 0% which is consistent with other centers experience (5). These findings may be due to low level of viremia in HCV infected hemodialysis patients.

The only definite risk factor for transmission of HCV is duration of pretransplant hemodialysis (P=0.0001). The association between duration of dialysis and increased prevalence of anti HCV has been confirmed in numerous studies (6-12).

Although several studies have shown a highly significant association between the number of blood transfusions and prevalence of anti HCV among hemodialysis patients (4), our study failed to establish such a relationship.

During follow-up, group 1, had higher levels of liver enzymes (P = 0.0001). In group 1 elevated ALT and AST levels were detected in 43.3% and 48.5% respectively and in group 2 ALT and AST levels were

normal in 90.74% and 96.29% respectively. Biochemical evidence of liver disease has been reported in 20% to 70% of ELISA-2 positive renal transplant recipients (4). Furthermore, in the study by Roth et al, 51% of HCV RNA positive renal transplant patients maintained normal liver biochemistry throughout the post-transplantion follow up (68.7 + 28.8 months).

Liver biopsies in group 1 revealed chronic active hepatitis in 57.14% and chronic persistant hepatitis in 42.86% of patients. Out of 49 liver biopsies, 44.86% score > 8. Grade of inflammatory changes was mild in 91.4% and sever in 7.69% of patients. Fibrosis was mild in 55.09% and moderate to severe in 44.88% of liver biopsies. Based on above data, there is a direct correlation between liver enzyme levels and grade of inflammatory changes, but there is no correlation between enzyme level and portal inflammation and liver fibrosis. About 8% of patients had moderate to severe inflammatory lesions while about 45% had severe fibrosis. This may be due to propensity of CRF patients to develop more fibrosis with HCV infection or due to hemodialysis per se. Since there is a strong correlation between liver fibrosis and duration of hemodialysis ($r = 0.64$, $P < 0.05$), the latter is more likely. Immuno-suppressive drug dosage were lower in group 1 and drug toxicity was more common in this group.

Retrospective study of our renal transplant recipient admitted in nephrology ward revealed that group 1 need more admission than group 2. Acute tubular necrosis was more common in group 1.

In contrast to other studies (5) acute and chronic rejection were less common in group 1, which may be due to higher serum levels of immunosuppressive drugs in that group.

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