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The Clinical Outcome of Anti-HCV(+) Renal Allograft Recipients

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=국문초록=

C형 간염 항체(anti-HCV) 양성인 말기 신부전증 환자에서 신이식 후의 임상 경과에 관한 연구

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신이식 환자에서 만성 간질환은 환자 및 이식신 생존율에 영향을 미치는 것으로 알려져 있다. 혈액투석 환자의 10~40%에서 anti-HCV가 양성인 점을 고려할 때, C형 간염이 신이식 환자의 장기적인 임상 경과에 미치는 영향을 규명하는 것이 중요함에도 불구하고 아직까지 확고한 정설은 확립되어 있지 않은 실정이다. 이에 저자 등은 anti-HCV 양성인 신수혜자에서 C형 간염 바이러스가 이식후의 임상 경과에 미치는 영향을 알아보고자, 1984년 2월부터 1994년 12월사이에 연세의료원에서 신이식 수술을 받고, cyclosporine A를 면역억제제로 사용한 1097예를 대상으로, 이식전 anti-HCV 검사 결과에 따라 anti-HCV 양성군과 음성군으로 나누어 각 군의 임상 경과를 비교하여 다음과 같은 결과를 얻었다.

1) 이식전 anti-HCV 양성군은 29예로 평균 연령은 39.1세이었고 남녀비는 1.1 : 1, 평균 추적기간은 32.1(3.64~67.1)개월이었다. 이식전 간조직 검사는 19예에서 시행하였으며, 10예에서는 만성 지속성 간염(chronic persistent hepatitis, 이하 CPH), 8예에서는 정상(normal histology, 이하 carrier), 그리고 1예에서는 만성 활동성 간염(chronic active hepatitis) 소견을 보였다.

2) Anti-HCV 양성군에서는 음성군에 비해 이식 후 만성 간염의 발생(20.7% vs. 1.1%, $p<0.05$)이 의미있게 많았으나, 급성 거부반응, 간외 감염, 그리고 간부전과 관련된 사망은 양군 사이에 의의있는 차이가 없었다.

3) 간조직 소견에 따른 임상 경과를 비교하여 보았을 때, CPH 군과 carrier군 모두 anti-HCV 음성군에 비해 만성 간염의 빈도가 높았으며(25.0%, 20.0% vs. 1.1%, $p<0.05$), carrier군에서는 급성 거부반응의 빈도도 anti-HCV 음성군에 비해 의미있게 많았다(75.0% vs. 34.1%, $p<0.05$).

4) Anti-HCV 양성군의 5년 이식신 생존율은 75.0%, 환자 생존율은 83.4%로 anti-HCV 음성군의 84.0%, 91.2%와 통계학적인 차이는 없었다. 또한 CPH군과 carrier 군으로 나누어 보았을 때에도 각군의 이식신 및 환자 생존율은 anti-HCV 음성군과 비교하여 의미있는 차이가 없었다.

5) 이식전 HCV-RNA 검사는 6예에서 시행하였으며, 이중 2예는 HCV-RNA 양성이었다. HCV-RNA 양성인 2예 모두 이식 후 안정된 간기능 소견을 보였으며, HCV-RNA 음성 환자 4예 중 1 예에서 혈청 ALT의 상승과 함께 HCV-RNA 양성으로 전이되었다.

이상의 결과로 단기간 추적 검사상 이식전 anti-HCV 양성이 이식신 및 환자 생존율에 큰 영향을 미치지는 않은 것으로 보이나, 이식 후 만성 간염의 빈도가 많음을 고려할 때, 간기능의 주기적인 검사를 포함한 장기간의 추적 관찰이 필요할 것으로 사료된다.

Key Words: Anti-HCV(+), Clinical outcome, Renal allograft

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Chronic liver disease has an influence on long-term patient and graft survival[1]. Several studies[2,3] confirmed hepatitis C virus(HCV) as the leading cause of non-A, non-B hepatitis among renal allograft recipients. Considering that 10~40% of hemodialysis patients are anti-HCV positive, the contribution of HCV infection to long-term patient outcome is important issues but is still controversial. The aim of this study was to investigate the impact of hepatitis C virus infection on the clinical outcome of renal allograft recipients, including the liver histology.

PATIENT AND METHOD

We analyzed the records of 1097 living donor kidney transplantation between February 1984 to December 1994. Pre-transplant anti-HCV(+) patients were 29 with mean age of 39.1 years. Male to female ratio was 15 : 14, and a follow-up period was 3.6 to 67.1 months(mean: 32.1 months).

Anti-HCV was determined with Abott HCV kit(first and second generation enzyme immunoassay method). HCV-RNA was detected with reverse transcriptase polymerase chain reaction method. Pre-transplant liver biopsy was performed in 19 anti-HCV(+) patients and the histologic features were chronic persistent hepatitis(CPH) in 10, normal histology(carrier status) in 8, and chronic active hepatitis(CAH) in 1, in order. Chronic hepatitis was defined as persistent serum alanine aminotransferase elevation(twice above the upper normal limit) of greater than 6 months. Acute rejection was defined as the initiation of antirejection treatment, and extra-hepatic infection was regarded as the one requiring admission more than 2 weeks. Graft or patient survival were estimated with Kaplan-Meier analysis.

RESULTS

Following renal allograft, the anti-HCV(+) recipients had a significantly greater number of chronic hepatitis

Table 1. Clinical outcome according to anti-HCV status

	Anti-HCV	
	Positive (N=29)	Negative (N=1068)
Acute rejection	13(44.8)	364(34.1)
Extra-hepatic infection	4(13.8)	97(9.1)
Chronic hepatitis	6(20.7)#	12(1.1)
Death from hepatic failure	0/4(0.0)	4/74(5.4)

Numbers in parenthesis are percentages, #p<0.05, vs. the anti-HCV(−) group

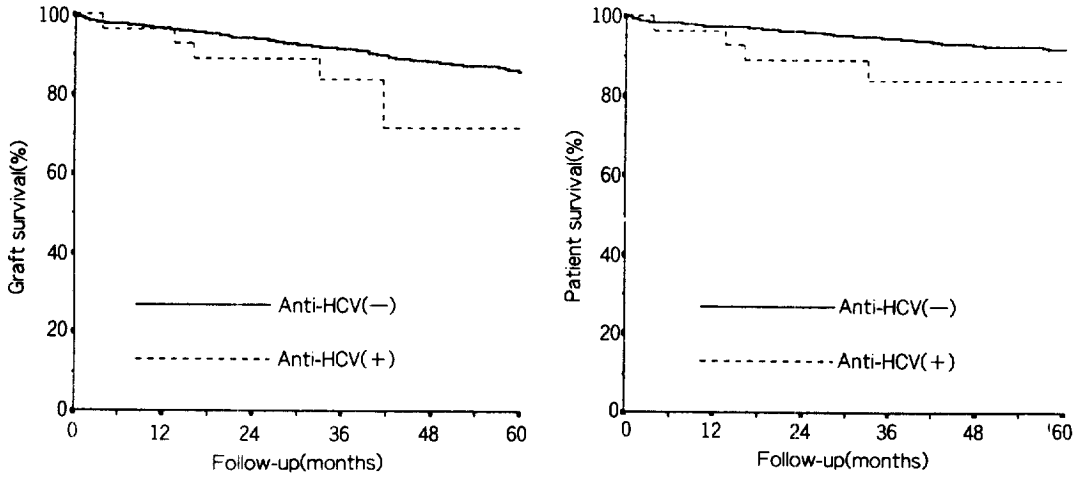

Fig. 1. Graft and patient survival according to anti-HCV status.

than the anti-HCV(−) recipients(20.7% vs. 1.1%, p<0.05). There were no differences in the numbers of acute rejection, extra-hepatic infection and hepatic failure-related death between the anti-HCV(+) and (−) recipients(Table 1). In comparison according to histologic features, the recipients with CPH or carrier status also had a higher incidence of chronic hepatitis than the anti-HCV(−) recipients. The patients with normal histology had a greater number of acute rejection than the anti-HCV(−) recipients. The graft and patient survival at 5 year in anti-HCV(+) recipients were not significantly different from the anti-HCV( ) recipients(75.0% vs. 84.0%, 83.4% vs. 91.2%, respectively) (Fig. 1). The graft survivals at 3 year in recipients with CPH or carrier status were 66.7% and 71.1%, and the patient survivals were 66.7% and 88.9%, respectively, which were not significantly different from anti-HCV( ) recipients.

Pre-transplant HCV-RNA tests were performed in 6 anti-HCV(+) cases, and 2 of them were positive. Two HCV-RNA(+) patients had relatively stable liver enzymes post-transplant. One HCV-RNA( ) patient had a higher elevation of ALT with conversion into HCV-RNA(+), following renal allograft.

DISCUSSION

This study showed that the anti-HCV(+) recipients had higher incidence of post-transplant hepatic dysfunction than the anti-HCV( ) recipients, which was consistent with previous reports[4,5]. There have been conflicting reports[4,5] on the rate of acute rejection, extra-hepatic infection, and mortality from hepatic failure in anti-HCV (+) recipients. In our study, there were no significant differences in these parameters between the anti-HCV(+) and (−) recipients. As the possible explanation for conflicting reports, the variability in HCV strain virulence, viral burden and different immunosuppressive regimen can be suggested[4]. The greater number of acute rejection was observed in the recipients with norml histology, but studies in a larger number of patients should be needed for confirmation. The graft and patient survival in anti-HCV(+) recipients were not significantly different from those in anti-HCV(−) recipients in short-term follow-up. There was also no difference in graft or patient survival between CPH and carrier status recipients. From these results, it seems that anti-HCV(+) is not a poor prognostic indicator[6]. Two HCV-RNA(+) recipients maintained relatively stable liver function, suggesting the low sensitivity of liver enzymes to detect active viral replications[4].

In conclusion, the graft and patient survival appear not to be influenced by anti-HCV status in short-term follow-up, but long-term follow-up with close monitoring should be required in view of the increased risk for post-transplant hepatic dysfunction.

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