



Impact of Hepatitis B and C Virus Infections on Kidney Transplantation: A Single Center Experience

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ABSTRACT

Objective. The impacts of hepatitis C virus (HCV) and hepatitis B virus (HBV) infections on patient and renal graft survivals are controversial. This study sought to evaluate the effects of pretransplantation HCV and HBV infections on renal transplant patients and their grafts at our center.

Patients and Methods. We retrospectively examined 1224 renal transplantations performed between 1992 and 2006, including 28 HBsAg positive; 64, anti-HCV; 9, anti-HCV plus HBsAg positive; and 1123, negative for anti-HCV and HBsAg. The mean posttransplantation follow-up was 5.6 ± 4.1 years.

Results. The prevalences of HBV infection were 6.2% in 1994 and 2.3% in 2006 and those of HCV infection were 6.8% in 1998 and 5.2% in 2006. The rejection rate was higher among HBV+ (46.4%) and HCV+ (40.6%) groups than the negative groups (31.5%), but it was not significant. There were no significant differences in patient and graft survivals among the groups. The major cause of patient death was liver failure among patients with concomitant HBV+ and HCV+ infections and cardiovascular disease among HCV+ and negative patients.

Conclusions. There has been a decrease in the prevalence of recipients with hepatitis virus infections over the last 15 years. Patient and graft survivals were not affected by HCV or HBV infection.

CONTROVERSY PERSISTS regarding the impact of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in renal transplant recipients. Some studies have reported an increased risk of death among patients who test positive for HCV antibody and HBsAg prior to kidney transplantation,^{1,2} whereas others have reported no effect on patient or graft survivals.^{3,4} The aim of this study was to evaluate the impact of HCV and HBV infections on renal transplant patients and their grafts, at a single center. This study also sought to analyze the evolution of prevalence of these infections over the last years in Portugal.

PATIENTS AND METHODS

This retrospective study examined the results of 1224 renal transplantations performed between January 1992 and December 2006 at a single center, including 28 HBsAg-positive patients (HBV+); 64, HCV antibody (HCV+ group); 9, HCV antibody plus HBsAg positive (concomitant HBV+ and HCV+); and 1123 patients with no HCV antibody and negative HBsAg (negative cohort) at time of transplantation. According to their viral state the groups were compared for the incidence of acute rejection episodes and patient

and graft survivals. The mean follow-up time was 5.6 ± 4.1 years. Acute rejection was defined by biopsy or clinically by a positive response to anti-rejection therapy. Graft failure was considered if the recipient returned to dialysis or when the recipient died with a functioning graft.

Statistical Analysis

Categorical differences between groups were calculated using chi-square and continuous variables by Student *t* test. All results were expressed as mean values (SD). Graft and patient survivals were estimated using Kaplan-Meier analyses with comparisons by log-rank tests.

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RESULTS

The prevalences of HBV infection were 6.2% in 1994, 4.1% in 1998, 3.2% in 2002, and 2.3% in 2006; comparable results for HCV infection were 2.8% in 1994, 6.8% in 1998, 6.2% in 2002, and 5.2% in 2006. The prevalences of concomitant HBV plus HCV infection were 0.4% in 1998 and 0.7% in 2002 and 2006. Forty-six negative patients and 1 HCV+ patient received their grafts from living donors. Univariate analysis of data showed no significant difference with regard to recipient age, recipient gender, HLA mismatch, donor age, donor gender, cold ischemia time, on delayed graft function when comparing HBV+, HCV+, or concomitant HBV+ plus HCV+ groups with the negative group.

Hepatitis B

HBV+ patients had been significantly longer on dialysis than negative patients (67.4 ± 54.9 vs 35.3 ± 32.9 months; $P < .001$). The acute rejection rate seemed to be higher among HBV+ (48.1%) than negative patients (32.9%); however, the difference was not significant. Posttransplantation graft survivals were 85.7% at 1 year and 75% at 5 and 8 years in the HBV+ group vs 90.4%, 78.7%, and 70.4% at similar times among the negative group ($P = \text{NS}$). The major cause of graft failure in HBV+ (71.4%) and negative groups (42.2%) was chronic allograft nephropathy. Posttransplantation patient survivals were 100% at 1, 5, and 8 years in the HBV+ group, and 94.8%, 88.4%, and 84.4% at 1, 5, and 8 years in the negative group ($P = \text{NS}$).

Hepatitis C

The duration of dialysis was significantly longer among HCV+ patients (68.9 ± 40.4 months; $P < .001$) than negative patients. HCV+ recipients displayed a greater incidence of acute rejection episodes (43.3%), but the difference was not significant. Posttransplantation graft survivals were 92%, 81.6%, and 56.7% at 1, 5, and 8 years in the HCV+ group ($P = \text{NS}$). The major cause of graft failure was chronic allograft nephropathy in the HCV+ group (57.1%). Posttransplantation patient survivals were 95%, 91.3%, and 83.9% at 1, 5, and 8 years in the HCV+ group ($P = \text{NS}$). The major cause of death in the HCV+ (60%) vs negative group (43.2%) was cardiovascular disease.

Concomitant HCV Plus HBV

This group had been significantly longer on dialysis (100 ± 77.8 months; $P < .001$) than negative patients. There were no significant differences between the groups with respect to the frequency of acute rejection episodes. Posttransplantation graft survivals were 100%, 85.7%, and 85.7% at 1, 5, and 8 years ($P = \text{NS}$), and posttransplantation patient survivals were 100%, 85.7%, and 85.7%, respectively, among the concomitant HCV+ plus HBV+ group ($P = \text{NS}$). The major cause of death in this group was liver failure (100%) and the major cause of graft failure was patient death (100%).

DISCUSSION

Our study, as well as previous reports,⁵ have shown a marked decline in the prevalence of HBV and HCV infections over the last 15 years. There are many factors that may have contributed to the reduction in hepatitis prevalence, such as active hepatitis B vaccination, screening of blood donors, and the use of erythropoietin. Although the prevalence of chronic hepatitis has declined among patients awaiting renal transplantation, it remains a relevant clinical problem, mainly for patients with a long history of dialysis who may have been infected many years ago. The effect of hepatitis on patient survival after renal transplantation has been a subject of discussion. Several authors observed a negative influence of HCV and HBV infections on patient survival.⁶⁻⁸ Our data, as well as those of some other studies, have shown no difference in patient survival.^{9,10} Any differences appear to be a consequence of the time of follow-up. The prognosis of HBV+ patients has probably improved given the increased efficacy of antiviral therapy¹¹; thus defining the natural history of chronic hepatitis in renal transplantation remains difficult. Furthermore, HCV+ candidates who remain on the waiting list show a greater risk of mortality than those who are transplanted.^{12,13}

Some authors have observed that liver-related mortality is an important cause of death after renal transplantation in patients with chronic hepatitis.¹⁴ However, we noted in our HCV+ group that patient mortality was primarily related to cardiovascular disease; in the HBV+ group, no patients died during follow-up. Mortality of the concomitant HBV plus HCV-infected patients was associated with liver failure. It is known that coinfecting patients show enhanced HBV replication and an increased risk for cirrhosis and fulminant hepatic failure.^{15,16} Graft survival of our patients was not influenced by infection with either HCV or HBV. Increased incidences of acute rejection episodes after renal transplantation in patients with HCV+ have been reported by some authors.^{9,17} The rejection rate among our patients seemed to be higher for HBV+ plus HCV+ patients; however, there were no significant differences. Chronic allograft dysfunction was the most common cause of graft failure among HBV+, HCV+, and negative patients. The results of this retrospective analysis may have been influenced by the use of various immunosuppressive regimens over the 15 years. Also activity and severity of liver disease were not recorded.

In conclusion, graft and patient survivals were not influenced by HBV or HCV infection during the follow-up period. Our experience suggested that these patients, after a good screening and with clinical surveillance, remain acceptable candidates for kidney transplantation.

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