Use of Hepatitis B Core Antibody–Positive Liver Allograft in Hepatitis C Virus–Positive and –Negative Recipients With Use of Short Course of Hepatitis B Immunoglobulin and Lamivudine

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ABSTRACT

Introduction. With the shortage of donor organs, increasing number of hepatitis B core antibody (HBcAb–positive [HBcAb(+)]) liver allografts are being used for liver transplantation (LTx) in patients who are HBsAb-negative [HBsAb(−)]. This study was aimed at assessing outcomes for hepatitis C virus (HCV)-positive [HCV(+)] and HCV-negative [HCV(−)] patients who received HBcAb(+) liver grafts from deceased donors and also received a short course of hepatitis B immunoglobulin (HBIg) with long-term lamivudine therapy after LTx.

Materials and methods. From February 1995 through February 2003, 28 patients (mean age 53.8 ± 10.2 years, 19 men and nine women, 16 HCV−; 12 HCV+) received HBcAb(+) liver allografts. All recipients received a short course of HBIg prophylaxis (10,000 units/day for 4 days) and long-term lamivudine 100 mg/d after LTx in addition to a tacrolimus-based immunosuppressive regimen.

Results. Seven (25%) of the 28 recipients died during follow-up and three recipients required retransplantation. Three recipients (10.7%) developed HBV infection during follow-up, one of whom died 36 months after LTx and the other two had YMDD mutant HBV. The overall 6-year actuarial patient survival after transplantation was 74.4% and those for HCV− and HCV+ recipients were 81.3% and 66.6%, respectively (P = .46). The overall 6-year actuarial graft survival was 63.9% and those for HCV(+) and HCV(−) recipients were 68.8% and 57.1%, respectively (P = .6).

Conclusion. We conclude that HBcAb(+) liver grafts can be used for both HCV(+) patients and HCV(−) patients who are critically ill, have early hepatocellular carcinoma, or have been exposed to HBV in the past. A short course of HBIg-lamivudine combination therapy provides effective prophylaxis against HBV infection in 89% of recipients of HBcAb(+) grafts.

Liver grafts from donors who are positive for hepatitis B core antibody (HBcAb) are mainly used in patients who have been vaccinated against hepatitis B virus (HBV) and have developed hepatitis B surface antibodies (HBsAb) and in patients who are HBV carriers HBsAg(+) The HBV carriers who undergo a liver transplant receive a long course of anti-HBV immunoglobulin (HBIg) after transplant.

With the shortage of deceased donor organs, increasing numbers of HBcAb(+) liver allografts are being used for liver transplantation (LTx) in patients who are HBsAb(−). The risk of transmitting HBV infection in these cases is well documented.1–3 However, this risk is considered acceptable for patients who are critically ill or have stage I/II hepatocellular carcinoma (HCC). The numbers of patients with hepatitis C virus (HCV) infection receiving liver transplants is increasing in the United States. To date, no study has...
examined outcomes for recipients of HBcAb(+) livers from deceased donors who complete a short course of HBIG and take long-term lamivudine after LTx.

Our aim in this study was to assess outcome for HCV(+) and HCV(−) patients who received HBcAb(+) liver grafts from deceased donors and also received a short course of HBIG with long-term lamivudine therapy after LTx.

PATIENTS AND METHODS
From February 1995 through February 2003, 28 patients at our institution received liver allografts from HBcAb(+) deceased donors. The recipients were 19 men and nine women of mean age 53.8 ± 10.2 years. The primary reason for use of HBcAb(+) donor grafts were as follows: critically ill recipient (n = 11), HCC stage I/II (n = 6), and HBcAb(+) recipient (n = 11). Some of these patients had more than one of these conditions. Polymerase chain reaction identified 16 of the patients as HCV-RNA(−) and 12 as HCV-RNA(+). All recipients were followed until November 2004 (mean follow-up period 36.4 ± 19.0 months). All donors in the United States are routinely screened for HBV infection using hepatitis B surface antigen (HBsAg), HBsAb, and HBcAb. The present study focused on liver transplants with a HBcAb(+) liver allograft alone at our center during the study period. These donors were further screened for HBcAb immunoglobulin (Ig) and HBcAb IgM and all grafts that were HBsAg(+) or HBcAb IgM(+) were excluded from transplantation. All serology was done using one-step enzyme immunoassay. The mean donor age for the study group was 53.6 ± 15.8 years.

Each of the 28 patients received a short course of intravenous HBIG prophylaxis (10,000 units daily for 4 days) and long-term lamivudine 100 mg/day after LTx. After transplantation, all patients were placed on an immunosuppression protocol of tacrolimus, mycophenolate mofetil, and steroid, as previously described.4

Data are presented as mean ± standard deviation. Actuarial survival was calculated using the Kaplan-Meier formula, and differences in survival for the HCV(+) and HCV(−) groups were compared using the log-rank formula. The software package SPSS for Windows version 11.5 was used for all calculations.

RESULTS
Overall Patient and Graft Survival
Seven (25%) of the 28 recipients died during follow-up. The causes of death were sepsis (n = 3), cardiac failure (n = 2), recurrent HBV infection (n = 1), and recurrent metastatic HCC (n = 1). The actuarial patient survival at 6 years after transplantation was 74.4% (Fig 1A). Three patients lost their grafts due to hepatic artery thrombosis and had to be retransplanted. The actuarial graft survival at 6 years was 63.9% (Fig 1A).

Overall Incidence of HBV Infection
Three patients (10.7%) became HBV-DNA-positive during follow-up. One of these recipients died of liver failure from HBV infection 36 months after LTx. HBV-DNA results from the other two patients revealed YMDD mutation. Both these recipients are currently being treated with adefovir.

DISCUSSION
The risk of transmitting HBV or developing it after LTx involving an HBcAb(+) donor is well documented. Without prophylaxis, the reported infection rates are higher than...
The problem may even be greater in regions where the prevalence of HBV is very high. Lamivudine therapy with or without HBIG has been suggested as prophylaxis in such cases. However, the duration of treatment required has not been evaluated. A recent survey showed inconsistency among the prophylactic regimens in use by different centers. We felt that our protocol of using a short course of HBIG with long-term lamivudine may provide a satisfactory balanced approach to this problem.

We observed lower patient and graft survivals with use of HBCAb(+) in HCV(+) recipients compared to HCV(-), but the differences were not statistically significant and these results were due to patient characteristics rather than donor characteristics, since none of the HCV(-) individuals developed HBsAg positivity.

Our results indicate that a short course of HBIG-lamivudine combination therapy provides effective prophylaxis against HBV infection in 89% of recipients of HBCAb(+) grafts. Nonetheless, routine periodic HBV screening of HBCAb(+) graft recipients is mandatory for early detection of HBV infection and identify known viral mutations.

In conclusion, we conclude that HBCAb(+) liver grafts can be used for both HCV(+) patients and HCV(-) patients who are critically ill, have early HCC, or have been exposed to HBV in the past. A short course of HBIG-lamivudine combination therapy provides effective prophylaxis against HBV infection in 89% of recipients of HBCAb(+) grafts.

REFERENCES


