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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 HBcab-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

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360 Park Avenue South, New York, NY 10010-1710

0041-1345/05/$–see front matter
doi:10.1016/j.transproceed.2005.07.049

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.

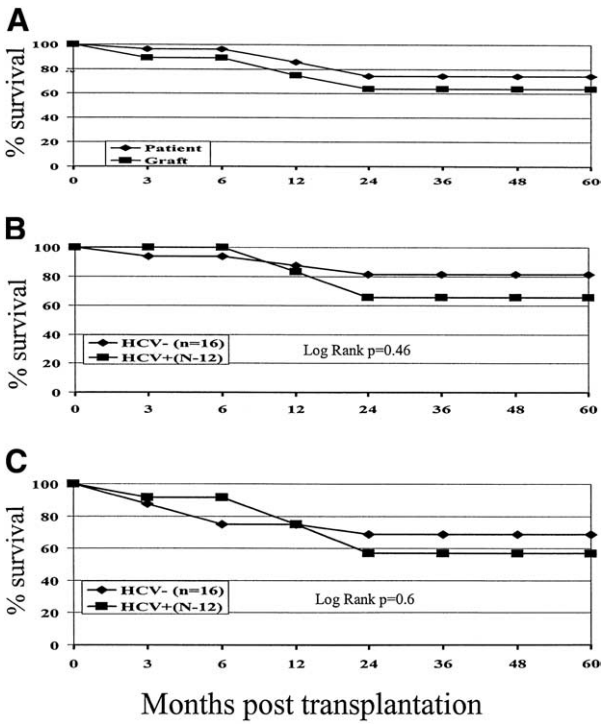

Fig 1. Recipient patient and graft survival statistics for HBcAb(+) donor transplants. **(A)** Overall patient and graft survival. **(B)** Patient survival for the HCV(+) and HCV(−) recipient groups. **(C)** Graft survival for the HCV(+) and HCV(−) recipient groups.

Results for the HCV(+) and HCV(−) Recipients

As noted, 12 patients were HCV(+) and 16 were HCV(−). The primary reasons HBcAb(+) grafts were used in the 12 HCV(+) cases were as follows: critically ill patient (n = 2), presence of HCC (n = 2), or HBcAb(+) (n = 8).

Four (33.3%) of the HCV(+) patients died at 7.5, 7.7, 19.1, and 23.2 months posttransplantation. The causes of death were cardiac arrest after recurrent HCV (n = 1), recurrent HCC (n = 1), cardiac arrest (n = 1), and sepsis due to recurrent cholangitis secondary to intrahepatic bile duct stricture (n = 1), respectively. The 6-year actuarial patient survivals for HCV(+) and HCV(−) groups were 66.6% and 81.3%, respectively (P = .46; Fig 1B).

One of the HCV(+) recipients had to be retransplanted after he developed hepatic artery thrombosis after 9 postoperative days. The 6-year actuarial graft survivals for HCV(+) and HCV(−) recipients were 57.8% and 68.8%, respectively (P = .06; Fig 1C).

None of the HCV(+) recipients developed HBV infection during the study period; all three recipients who developed HBV infection were HCV(−).

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

80%. The problem may even be greater in regions where the prevalence of HBV is very high.[5] Lamivudine therapy with or without HBIg has been suggested as prophylaxis in such cases.[1,6] However, the duration of treatment required has not been evaluated.[3,7] A recent survey showed inconsistency among the prophylactic regimens in use by different centers.[8] 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.

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