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HLA-DR Matching Effect in Orthotopic Liver Transplantation Under FK 506

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UNLIKE in kidney transplantation, graft survival was not influenced by the degree of HLA matching in human liver transplantation. In fact, our preliminary results revealed that 0 DR-matched liver transplant patients had inferior graft survival rates compared with those of 1 or 2 DR-mismatched transplants.[1]

FK 506 is a new, powerful immunosuppressant, and it is effective for both liver and kidney transplantation.[2] To study the effect of DR matching further in liver transplantation, we analyzed the DR matching effect for patients under FK 506.

MATERIALS AND METHODS

This study consisted of a total of 772 patients who received orthotopic liver transplantation (OLTx) at the Presbyterian University Hospital (Pittsburgh, Pa) and the Pittsburgh Children Hospital from March 1989 to December 1991. All patients had first OLTxs with a negative T-lymphocyte crossmatch. The only patients precluded from the study were those who had simultaneous pancreas, kidney, or small intestine transplantation. In addition, 335 patients who had a first-cadaver kidney transplant during the same period were studied. Initial immunosuppressive drug therapy for both liver and kidney-transplanted patients consisted of either cyclosporine A (CyA) or FK 506 in combination with prednisone. Acute cellular rejection was treated with bolus methylprednisolone and/or OKT3.

HLA typing was performed according to the standard National Institutes of Health method[3] using an HLA typing tray obtained commercially (Gen Trak, Inc, Plymouth Meeting, Pa and One Lambda, Inc, Cannoga Park, Calif).

Both patient death and allograft removal, regardless of reasons, were considered graft failure. Graft survival rates were computed by life table methods and generalized Wilcoxon test was used for the statistics.

RESULTS

The HLA-DR matching effect was clearly shown in cadaver kidney transplant patients whose initial immunosuppressant was CyA (Fig 1). Patients with a 0 DR-matched transplant had an 85% 1-year graft survival rate, whereas patients with a 1 and 2 DR-mismatched transplant had 80% and 76% 1-year survival rates, respectively. Although the best graft survival rate was still observed in patients with a 0 DR-mismatched transplant, the DR matching effect became smaller when FK 506 was given as an initial immunosuppressant. One-year graft survival rates for 0, 1, and 2 DR-mismatched kidney transplant patients were 84%, 85%, and 78%, respectively.

In OLTx, 0 DR-matched transplant patients had the lowest survival rates regardless of their initial immunosuppressive drug (Fig 2). Interestingly, the best survival rate

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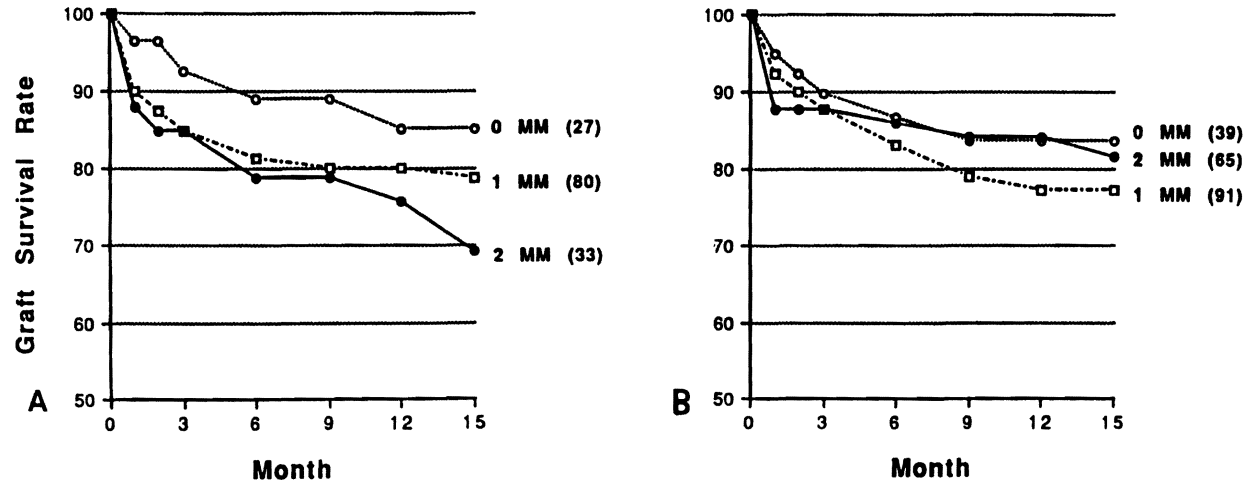

Fig 1. Actuarial first-kidney graft survival rates according to the number of HLA DR-mismatched antigens under CyA or FK 506. **(A)** CyA; **(B)** FK 506.

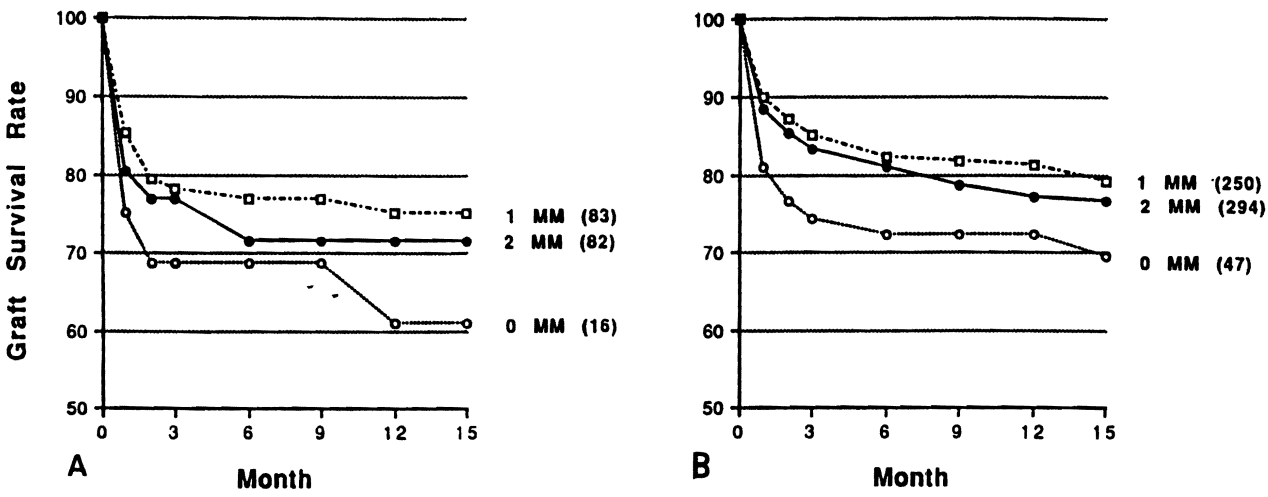

Fig 2. Actuarial first-liver graft survival rate according to the number of HLA-DR mismatched antigens under CyA or FK 506. **(A)** CyA; **(B)** FK 506.

was observed in patients with 1 DR-mismatched transplants.

DISCUSSION

From this study, HLA-DR matching was clearly shown when patients were treated with CyA in kidney transplant; however, its effect became smaller when FK 506 was used as an initial immunosuppressant. In OLTx patients, the DR matching effect was not obtained regardless of initial immunosuppressive drugs. The matching effect of histocompatibility antigens has been clearly demonstrated in experimental animal models; however, it should be noted that the most significant matching effect was observed in the transplant model without any immunosuppressant. The more the recipients are immunosuppressed, the less the effect of matching in histocompatibility antigens. In fact, the HLA matching effect was much clearer in the era of azathioprine compared with that observed in the era of CyA. Since FK 506 seems to be a more potent immunosuppressant than CyA, it is possible that the HLA matching effect might be veiled under FK 506 treatment. Thus, the data presented in this study might simply reflect the strength of initial immunosuppressant and potency of FK 506 in kidney transplantation.

We failed to obtain the DR matching effect in OLTx. It is believed that the HLA matching effect would appear in chronic stage after the transplantation. However, a majority of the graft failures of OLTx patients in this study in 0 DR-mismatched transplantation was seen within 3 post-transplant months. Thus, it is possible that the phenomenon which we observed in this study might not reflect the real HLA matching effect; the causes of failure in those patients must be further studied.

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