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Estrogen and Androgen Receptors in the Liver after Orthotopic Liver Transplantation

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ESTROGEN and androgen receptors are known to be present in the liver but their precise function has not been determined.^{1,2,3} Nonetheless, certain functions of mammalian liver are known to display a sexual dimorphism.⁴

Donors for clinical liver transplantation are selected with regard only to their ABO blood group and size compatibility with the recipients. The sex of the donor is not taken into consideration. In this study we determined the effect of orthotopic liver transplantation on the estrogen and androgen receptor content of the liver.

MATERIALS AND METHODS

Twenty-four adult inbred male Lewis rats were subjected to orthotopic liver transplantation using livers from male donors. Transplantation of the liver was performed using the cuff technique for the portal vein, suprahepatic vena cava and infrahepatic vena cava. At various times up to eight weeks postoperatively groups of animals were anesthetized with ether, their livers were removed and used to determine the level of the estrogen and androgen receptor activity in the transplanted liver.

The activity of the cytosolic estrogen receptors within the liver was determined by measuring the specific binding of a saturating concentration of ³H-estradiol, as described by Eagon et al.⁵ The cytosolic androgen receptor activity was determined by measuring the specific binding of a saturating concentration of tritiated R1881, a synthetic androgen, as described by Francavilla et al.⁶

RESULTS

The changes in the cytosolic estrogen receptor activity in the liver after orthotopic transplantation of a liver from a male donor to a male recipient are shown in Table 1. The estrogen receptor activity in the hepatic cytosol remained stable up to 20 days after the transplant. A small but significant reduction in the level of the estrogen receptor activity was observed at 30 days postoperatively ($p < 0.05$). Thereafter the level of estrogen receptor activity increased steadily and returned to preoperative basal male levels by 50 days after transplantation.

The effect of orthotopic liver transplantation, from a male donor to a male recipient, on the cytosolic androgen receptor activity of the liver is shown in Table I. The normal baseline androgen receptor activity level in the hepatic cytosol was

3.45 ± 0.45 fmoles/mg protein. The level of androgen receptor activity in the hepatic cytosol at 10 days after the transplant was significantly lower than preoperative baseline levels ($p > 0.01$). The reduction in the androgen receptor activity persisted for at least 40 days. At 40 days the androgen receptor activity in the male allograft was still significantly lower ($p < 0.05$) than it was preoperatively.

DISCUSSION

In this study, orthotopic transplantation of a liver from a male donor into a male recipient, except for a slight decrease seen at 30 days post transplantation, did not alter the estrogen receptor activity present in the hepatic cytosol. In contrast, a significant reduction in the level of the cytosolic androgen receptor activity in the liver was observed at 10 days after transplantation. Thereafter, however, the androgen receptor activity increased with time in the new host but was still reduced, compared to preoperative or intact male levels, at 40 days after the transplant procedure.

The findings reported herein may have important long-term implications. Since the liver is known to display a sexual dimorphism with regard to several important functions, these changes in the estrogen and androgen receptor content of the liver after transplantation described above, may be important both for the initial success of the transplant procedure and possibly the long-term performance of the liver in the recipient.

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Table 1. Changes in Estrogen Receptor Activity (fMoles/MG Protein) and Androgen Receptor Activity (fMoles/MG Protein) in the Hepatic Cytosol After Orthotopic Liver Transplantation From a Male Donor Into Male Recipient

	0	1.0	2.0	3.0	4.0	5.0
Estrogen Receptor Activity (fmoles/mg prot)	13.82 ± 1.23	12.94 ± 2.19	12.28 ± 0.86	8.97 ± 0.77	10.76 ± 2.14	12.14 ± 1.12
Androgen Receptor Activity (fmoles/mg prot)	3.45 ± 0.47	1.21 ± 0.07	1.46 ± 0.12	1.58 ± 0.2	2.29 ± 0.39	1.50 ± 0.16

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