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Liver transplantation in children younger than 1 year—the Cincinnati experience

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Abstract

Background/Purpose: The success of pediatric orthotopic liver transplantation (OLTxp) has improved greatly since its widespread application in the 1980s. No group has benefited more from this than infants younger than 1 year. The authors reviewed their experience in the management and outcome of children who underwent OLTxp when they were younger than 1 year.

Methods: A retrospective review of the medical records of patients who at the time of OLTxp were younger than 1 year was performed. Patients were stratified according to the period when transplanted.

Results: Eighty-one infants younger than 1 year underwent OLTxp. End-stage liver disease secondary to biliary atresia was the most common indication for transplantation. The overall survival was 77%. One-year patient and graft survival improved from 58% and 50% in the period 1986-1989, respectively, to 88% and 81% in the period 2000-2003, respectively. Technical complications such as hepatic artery thrombosis (n = 5) and portal vein thrombosis (n = 8) occurred, and although 4 patients required retransplantation, all but one survived. Complications associated with immunosuppression, sepsis/multisystem organ failure (MSOF) (n = 11), and posttransplant lymphoproliferative disease (PTLD) (n = 1) were the most common cause of poor outcome.

Conclusions: Successful OLTxp in infants is possible with improved posttransplant survival during the study period. Technical complications (hepatic artery thrombosis/portal vein thrombosis) may require retransplantation but were uncommon causes of patient loss. Multisystem organ failure was the most significant adverse complication. The consequences of immunosuppression (MSOF/PTLD) were the most common cause of patient loss. Further improvement in overall survival will require better immunosuppressive strategies.

Over the last 25 years, orthotopic liver transplantation has evolved from an experimental measure to become the standard of care in the salvage of a child with end-stage liver disease [1]. The technical developments of reduced-size and living related allografts [2], improvements in critical care, and new immunosuppressive agents have markedly altered the management scheme of children who require liver transplantation [3]. As a result, the outcome of these children, especially the young infant, has improved significantly [4-7].

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The purpose of the present study was to report our experience in the management of children who underwent liver transplantation at an age younger than 1 year. We compared the outcome of infants who were transplanted at different periods during the evolution of our transplant program and found that patient and graft survival initially showed improvement but has now reached a plateau. Sepsis/multisystem organ failure (MSOF) and posttransplant lymphoproliferative disease (PTLD), complications of immunosuppression, have been the most common causes of a poor outcome. Further improvements in patient survival will require better immunosuppressive strategies that minimize the unintended consequences of immunosuppression.

1. Methods

A search of the liver transplant database at Cincinnati Children's Hospital Medical Center was performed to identify all recipients who were younger than 1 year at the time of their liver transplant. The study was approved by the hospital's Institutional Review Board before the initiation of the study. Health Insurance Portability and Accountability Act guidelines were followed to ensure patient privacy.

1.1. Data collection

Among the 267 patients who have undergone liver transplantation at Cincinnati Children's Hospital, 81 patients were younger than 1 year at the time of transplantation. The medical records of these 81 patients were reviewed and the following specific information was recorded: primary cause of liver failure, age at the time of transplant, weight at the time of transplant, United Network for Organ sharing (UNOS) status at the time of transplant, recipient blood type, donor age, donor blood type, donor weight, type of graft used, occurrence of hepatic artery or portal vein thrombosis (PVT), infectious complications, immunosuppression protocol, recurrence of disease, occurrence of PTLD, duration of graft, and patient survival. Patients were stratified according to the following periods: 1986-1989, 1990-1994, 1995-1999, and 2000-2003.

1.2. Patient care protocol

All patients were managed by a multidisciplinary team of pediatric hepatologists, transplant surgeons, and transplant coordinators. In the preoperative period, nutritional supplementation was used when necessary. Deceased donor (DD) whole grafts and surgically reduced left lobe (LL) and left lateral segment (LLS) grafts were used in all the periods. The use of living donor LLS grafts began in 1995. Postoperative hepatic artery and portal vein flow was documented by ultrasound immediately after transplantation and daily for the next 5 days. Anticoagulation therapy with aspirin was begun once the recipient's coagulation profiles corrected to a prothrombin time of less than 14 or an international normalized ratio less than 2. Perioperative antibiotics were maintained for a minimum of 48 hours after surgery or longer if an active bacterial infection was present at the time of transplantation. Recipients were maintained on antifungal, antiviral, and antipneumocystis prophylaxis for 6 months, 3 months, and 1 year, respectively, after transplantation. Two immunosuppression protocols were used during the study period. From the years 1986 to March 1996, the immunosuppression protocol consisted of OKT-3 antibody induction followed by corticosteroids, azathioprine, and cyclosporine. In 1996, the immunosuppression protocol was changed to tacrolimus and corticosteroids. Several patients also received anti–interleukin 2 receptor monoclonal antibody (Basiliximal) induction therapy in addition to tacrolimus and steroids. Initially, surveillance for Epstein-Barr virus (EBV) infection by serial measurement of serum EBV IgG antibody titers was performed. In 2000, monitoring was converted to serial screening of the blood for EBV DNA by polymerase chain reaction.

1.3. Statistics

Kaplan-Meier survival curves were generated using the program GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego, Calif).

2. Results

Eighty-one patients were identified to have undergone liver transplantation at an age of less than 1 year. The mean age at the time of transplantation was 0.63 years (range, 0.08-0.99 years). The mean weight at the time of transplantation was 6.4 kg (range, 2.4-12.7 kg). Table 1 lists the primary cause of liver failure among the 81 patients. Biliary atresia was the most common cause of end-stage liver disease. The UNOS status of the patients at the time of

Table 1 Indications for primary liver transplantation—infants younger than 1 year

	N	%
Cholestatic liver disease	54	66.6
Biliary atresia	52	
TPN cholestasis	2	
Fulminant hepatic failure	6	7.4
Metabolic disease	11	13.6
$Alpha_1$-antitrypsin deficiency	2	
Urea cycle abnormality	3	
Tyrosinemia	3	
Neonatal iron storage disease	2	
Glycogen storage disease	1	
Hepatitis/cirrhosis	6	7.4
Neonatal hepatitis	3	
Cryptogenic cirrhosis	3	
Other	4	5
Hepatoblastoma	2	
Hemangioendothelioma	1	
Budd-Chiari syndrome	1	