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Liver Transplantation Indications in Children

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THE WIDE SPECTRUM of liver transplantation (LT) indications can be summarized in general terms as follows[1]: (1) progressive primary liver disease with the expected outcome of hepatic failure, (2) stable liver disease with remarkable morbidity or a known mortality, (3) hepatic-based metabolic disease, (4) fulminant hepatic failure of known or unknown cause, (5) liver diseases secondary to systemic illness, (6) hepatic malignancies, (7) miscellaneous. The criteria (common clinical features) of end-stage liver disease that indicate LT are as follows[1,2]: (1) hepatic encephalopathy, (2) hepatosplenomegaly, (3) portal hypertension (variceal bleeding, hypersplenism, ascites; all refractory to medical treatment), (4) growth failure, (5) fat soluble vitamin deficiency, (6) indirect bilirubin >6 mg/dL, (7) intractable pruritis, (8) recurrent cholangitis, (9) poor synthetic function, (10) partial thromboplastin time > 20 seconds, (11) cholesterol < 2.6 mmol/L, (12) spontaneous bacterial peritonitis. Biliary atresia is the major indication for LT during childhood. Hepatic portoenterostomy prior to LT is recommended by many LT centers.[2]

Metabolic diseases comprise the second largest group of hepatic disorders indicating LT. Therefore LT, to correct the metabolic defect should be considered before the specific disease potentially affects other organ systems or results in complications that would prove to be contraindications for transplantation. Although results of LT are excellent in this subgroup, current research efforts in the areas of auxiliary transplantation, orthotopic partial hepatic replacement, hepatocyte transplantation, and ultimately gene therapy may be a better option in the future.[1,3] For example, the recent discovery of a chemical 2-nitro-4-trifluoro-methylbenzoyl (NTBC), which prevents the formation of toxic metabolites and reverses the clinical and biochemical manifestations of Tyrosinemia type I may alter not only the natural history but the indication for LT.[3] LT should be performed in patients with Wilson's disease who present with acute liver failure and those in whom penicillamine treatment is ineffective. Reduction hepatectomy and improvements in technical expertise resulted in successful outcome in neonates with hemochromatosis who were considered to be too young and sick for LT. Adequate medical treatment should prevent the need for LT in galactosemia or glycogen storage disease, although the development of cirrhosis in glycogen storage disease type IV may be an indication.[4] LT should be performed before the development of mental retardation and poor quality life in children with Crigler-Najjar type I, urea cycle defects, and propionic acidemia.[3,4] Although plasmapheresis or medical treatment may control cholestrol concentrations in heterozygotes with familial hypercholesterolemia, it is unlikely that this therapy will prevent the development of coronary artery disease in homozygous patients that necessitate LT.[5] Emerging technological breakthroughs suggest the potential that in the future single-enzyme defects such as Crigler-Najjar type I and phenylketonuria may be amenable to gene therapy or hepatocyte transplantation.[1–3]

Patients with fulminat hepatic failure without recognized antecedent liver disease present diagnostic and prognostic difficulties. It is important to establish the etiology of hepatic failure because the potential for recovery will influence the need for emergency transplantation. Because there is such a shortage of pediatric donor organs, a need for supporting the failing liver until it recovers or a donor becomes available is necessary to improve survival. Acute fulminant hepatitis carries greater than a 70% mortality rate without LT. Survival rates with LT range from 40 to 80% depending on the severity of liver failure. In general, the most significant difficulty in dealing with these patients has been the late consideration of LT. Poor results of previous reports were related to waiting too long, most often until after the onset of deep hepatic coma. However, a new concept emphasizing the importance of aggressive management of cerebral edema in these patients improved the results both in adults and children. Early use of intracranial extradural pressure monitoring has allowed early recognition and directed treatment of increased intracranial pressure. Failure to maintain a cerebral perfusion pressure (mean blood pressure—intracranial pressure) of more than 50 mm Hg has been associated with very poor neurologic recovery, and transplantation should be questioned.[6] LT for primary hepatic malignancy is uncommon in children; thus experience is limited. LT is indicated only for children whose neoplasm is confined to the liver and is

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unresectable by conventional means associated with chemotherapy and radiotherapy.[7]

Appropriate candidate selection and organ allocation were complicated by the lack of a test to quantitate the amount of functional hepatic reserve. But the introduction of monoethylglycinexylidide (MEG-X) helped the medical team with the quantitative assessment of hepatic reserve. The formation of MEG-X, a first-pass metabolite of lidocaine in the liver, is decreased in proportion to the severity of the liver disease. The objective of quantitatively stratifying the severity of liver disease is to allow earlier referral of the potential recipient for transplantation with possible improved outcome.[1,5–7]

Improvements in immunosuppression, patient selection, donor selection and preservation, operative techniques, and postoperative management all have led to excellent survival rates in LT. The spectrum of LT in the near future will be altered by ultrastructural treatment modes (gene therapy, hepatocyte transplantation).

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