Results of liver transplantation in fulminant hepatic failure

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Liver transplantation has dramatically changed the management of patients with fulminant hepatic failure and subacute hepatic failure. A wide range of survival rates (55% to 90%) reported from different centers performing liver transplantation for fulminant hepatic failure reflects variations in patient selection and the centers' experience. Results of transplantation appear to be improving, with survival rates approaching 80% at 1 year in some series. The improved results are attributed to vigorous perioperative management, using intracranial pressure monitoring and continuous arteriovenous hemofiltration when required, early listing of patients with organ-sharing network, and exclusion of patients who are unlikely to recover neurologically after successful transplantation. Use of piggyback hepatectomy to minimize hemodynamic alterations during surgery has also contributed to better results in critically ill patients. Patients with acetaminophen toxicity have a more favorable outcome than those with viral hepatitis or non-acetaminophen drug hepatotoxicity. Because of limited availability of cadaveric organs, emergency living-related liver transplantation, use of ABO incompatible and marginal livers need consideration. Auxiliary liver transplantation is desirable for those who have a chance of spontaneous recovery, thus obviating life-long immunosuppression after recovery of the native liver. [Indian J Gastroenterol 2003;22(Suppl 2):S75-S77]

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The first reference in scientific literature to hepatic replacement was by Welch1 in 1955 in dogs. Starzl2 first reported prolonged survival after hepatectomy and orthotopic liver transplantation (OLTx) in humans in July 1967. However, it took almost two decades till the introduction of more effective immunosuppressive agents for liver transplantation to be accepted as a beneficial procedure.

The term fulminant hepatic failure (FHF) was first introduced 30 years ago by Trey and colleagues.3 Since then, a number of definitions4-7 have been proposed to describe rapid damage to an otherwise healthy liver. Acetaminophen poisoning is the most common cause of FHF in the UK, whereas viral hepatitis8 is responsible for most cases in the US. In India, viral hepatitis is responsible for over 90% of patients with FHF, followed by drug-induced liver injury in 7.4%.9

Timing of transplantation

Liver transplantation (LT) has dramatically changed the management of patients with FHF and subacute liver failure (SALF).10 An important responsibility of clinicians involved in care of these patients is making an early decision regarding chances of recovery of the native liver and considering referral to a transplant center. Timely referral to an LT unit and availability of suitable donor liver are important for a successful outcome. A number of prognostic models have been developed to identify the most appropriate patients for LT; of these, the King's College Hospital11 and Clichy12 criteria are most popular.

Timing of LT poses a difficult dilemma for the clinician. If one waits for progression to pre-terminal stages, an allograft may not become available in time and results of LT may be significantly inferior. However, LT in all patients with FHF early in the course of disease will result in unnecessary transplantation in those 20%-40% of patients who would have spontaneously recovered.13 Thus, it is preferable to list the patient for LT as soon as prognostic signs suggest a poor outcome; a final decision can then be made when a liver becomes available.

Results of orthotopic LT

FHF is responsible for 9% of cases of liver failure in adults referred to the Australian National Liver Transplantation Unit.14 In the US, of the nearly 2500 adults who receive liver allograft each year, 6% are transplanted for FHF; in the pediatric age group, FHF is responsible for 11% of liver transplants.15 LT is able to rescue critically ill patients, more than 80% of whom would not have survived with medical management.11,16,17,18 One-year actuarial survival rate of 50%-60% is reported by most centers during the early period. These results are inferior to those reported in patients with chronic liver disease. The wide range of survival rates (55% to 90%) reported from different centers performing LT reflects variations in patient selection criteria and in these centers' experience.19,20,21

However, the results of LT appear to be improving, with one-year survival rates of patients with successful LT of more than 80% in some series.22,23,24 Castelli et al13 reported a survival rate of 79% in patients who underwent LT for acute liver failure as compared to 6% in those who could not be transplanted. The improved
results were partly attributed to vigorous perioperative management, using intracranial pressure monitoring and continuous arterio-venous hemofiltration when required, early listing of patients with organ-sharing network, and exclusion of patients who are unlikely to recover neurologically after successful LT.22

OLTx is the treatment of choice for FHF in children also. Of 38 patients who underwent OLTx, 30 (79%) survived, whereas of the 29 who did not undergo OLTx, only 36% survived.10 Bonatti et al23 reported their experience of 17 LT procedures for acute liver failure in 15 recipients younger than 1 year of age. All grafts were retrieved from pediatric or young adult donors (mean age 10 years, range 0.5-21; mean weight 30 Kg, range 6.9-60) and only reduced size grafts were used.

Fulminant viral hepatitis

Fulminant viral hepatitis is the most common cause of FHF treated by LT. Mortality rate of patients with FHF due to hepatitis A virus (HAV) or hepatitis B virus (HBV) without LT is about 50%-80%.5,11 OLTx was successful with a 1-year survival rate of 66% in adults.25 Use of LT in HBV-positive patients has been controversial. There is a high frequency of persistent viremia in the post-transplant period and a rapidly progressive form of cholestasis fibrosis in some allografts.26,27 However, patients with HGF due to viral hepatitis have a low likelihood of post-transplantation re-infection because the vigorous immune response that destroys the hepatocytes also clears the virus. Moreover, the results have further improved recently with the routine use of HBV immunoglobulin infusion28,29 and nucleoside analogues;30,31 however, viral mutations leading to drug resistance remains a significant problem.32 The risk of HBV recurrence was 17% in fulminant hepatitis B as compared to 67% in HBV-related cirrhosis.59

Re-transplantation for a failing allograft secondary to recurrent hepatitis B is associated with a high mortality and is usually avoided; but it may be acceptable if combined with aggressive immunosuppression.33 Other therapies that have been tried to control recurrent HBV infection following LT include prostaglandin E1,34 ganciclovir,35 famciclovir36 and interferon alpha.37

Auxiliary liver transplantation

OLTx is the preferred approach in patients without potential for recovery. However, the success of hemodialysis for kidney failure and the fact that 20%-30% of patients may recover spontaneously has inspired investigations into alternative approaches to tide over the crisis. Auxiliary LT, hepatocyte transplantation, xenotransplantation, bioartificial liver-assist devices, and extracorporeal liver perfusion have been attempted and are under investigation.

Auxiliary liver needs adequate portal venous flow. Native portal vein banding to preferentially divert blood to allograft and incomplete abdominal closure to avoid raised intra-abdominal pressure have been used successfully.38,39,40 Some surgeons preemptively transect the portal vein to the native liver, in order to obtain optimal graft portal blood flow, with minimal damage to the native liver.41

We conclude that FHF is a rare cause of liver failure, but its rapid progression and high mortality necessitate immediate intervention. The availability of LT has provided means to rescue such patients from near certain death. Results of OLTx in FHF are as good as those for LT in chronic liver.

References


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