Transplant Roundup

Extracorporeal Liver Support in Patients with Acute Liver Failure

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Dr. Sussman was a founder of Hepatix Inc., which was acquired by VitaGen and then by Vital Therapies. He has no ownership interest in either VitaGen or Vital Therapies.

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Treatment options for patients with acute liver failure (ALF) are limited to supportive care and liver transplantation. The shortage of donor grafts poses a severe challenge in treating the number of patients who would benefit from transplantation, and those who do receive a transplant face lifelong immunosuppression to prevent rejection. Nonbiological alternatives for support, including plasma exchange and sorbent perfusion systems, have not shown benefit in clinical trials.

Effective liver support measures must be designed to treat the causes of ALF, and these factors vary widely. For example, in the United States, acetaminophen overdose caused 46% of reported cases in adults (1998–2007); in Asia and Africa, viral hepatitis is the chief reason.[1] Acute-on-chronic liver failure involves severe deterioration in the presence of cirrhosis, such as in alcoholism. In all these conditions, the goal is to achieve functional stability until recovery or transplantation,[2-4] and thus the great interest in developing extracorporeal liver support systems.

Types of Liver Support Systems

Liver support systems are divided broadly into 2 categories: biological and mechanical. Biological systems combine the functional benefit of transplantation with that of hemodialysis, enabling noninvasive, continuous treatment for patients who have ALF; despite their safety and cost-effectiveness, they do not improve portal hypertension or portosystemic shunting, which occurs in patients with hepatitis C.

Mechanical liver support includes artificial and bioartificial systems. Two artificial systems, the molecular adsorbents recirculating system and the single-pass albumin dialysis, clear selected toxins; however, they provide no synthetic support, nor did they improve outcomes in a randomized clinical trial.[5]

Bioartificial liver systems may ultimately prove to be the most effective therapy for patients who have ALF in whom correcting metabolic derangements is crucial, such as when the patient loses a critical volume of hepatocytes. This is the most severe of liver emergencies, and it is reversible when hepatocytes can regenerate. Bioartificial liver systems contain living hepatocytes, as well as synthetic and biochemical production capabilities designed to restore metabolic stability. The combination of functional liver replacement and extracorporeal membrane perfusion may eventually serve as bridges to transplantation or promote recovery.

The extracorporeal liver assist device developed at Baylor College of Medicine contains the C3A human hepatoblastoma cultured cell line.[6,7] The system's initial design enabled perfusion with whole blood. A subsequent delivery circuit involved plasma perfusion via 4 cartridges and in-line oxygenation (each cartridge contained 200 g of cells). This newer circuit failed in the most recent clinical trial,[8] leading us to presume that hypoxia developed at the cellular level. The manufacturer plans additional study.

Future Goals

Beyond extracorporeal systems, the development of implantable liver technology is emerging. Hepatocytes can be grown on substrates that mimic the lobular structure of the liver.[9] Expanding the organoids into a full liver with complete vascular and biliary connections will be challenging. Experiments with decellularized animal livers are under way.

Although bioartificial livers have not yet shown clinical effectiveness, their refinement continues amid sound proofs of concept. Ongoing efforts to develop extracor-

poreal and implantable liver technologies hold promise in treating patients who have ALF.

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