Future Approaches and Therapeutic Modalities for Acute Liver Failure

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KEYWORDS

• Liver assist device • Hepatocyte transplant • Stem cell transplant • ELAD
• HepatAssist • MARS • Organogenesis • Acute liver failure

KEY POINTS

- Currently available hepatic assist devices have limited studies in acute liver failure.
- Hepatocyte transplantation for acute liver failure is a promising new approach for the treatment of acute liver failure.
- The translation of mouse model stem cell transplant to humans for acute liver failure is promising but needs further research.

INTRODUCTION

Patients with acute liver failure (ALF) are usually given high priority on transplantation waiting lists. Nevertheless, because of organ shortages and the duration of the disease, many of these patients die while waiting for a transplant. Additional factors, such as psychosocial barriers and comorbid conditions, preclude these patients from transplant.

Therefore, other treatment modalities that may reduce morbidity and mortality and perhaps serve as a bridge to transplantation might be an additional option. One particular avenue that has been investigated are the hepatic assist devices. Such devices aim to temporarily assume metabolic and excretory functions of the liver and thereby allow stabilization of patients who await transplant. These devices may be categorized as biological, artificial, or bioartificial systems.[1–4]

Biological systems use whole organ perfusion (human or animal) or hepatocyte bioreactors. These devices aim to assist prominent hepatic functions. On the other hand,

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artificial systems aim to detoxify via dialysis-based techniques. Bioartificial or hybrid devices combine both biological and nonbiological techniques.[2–5]

An artificial device for ALF that has been studied is the Molecular Adsorbent Recirculating System (MARS) assist device. Two bioartificial devices that use hepatocytes contained within a matrix of hollow fiber membranes include the Extracorporeal Liver Assist Device (ELAD; Vital Therapies Inc, San Diego, CA) and the HepatAssist system (Alliqua Inc, Langhorne, PA).[6]

MOLECULAR ADSORBENT RECIRCULATING SYSTEM

MARS is based on the concept of albumin dialysis and allows the removal of protein-bound as well as water-soluble toxins.[7] Albumin-bound substances can be dialyzed through a regular dialysis membrane if the dialysate contains clean albumin as a molecular acceptor. MARS was first developed in Germany in 1993 and was first commercialized and available for clinical use in 1998.[8]

Molecular Adsorbent Recirculating System Components

It comprises a modified hemodialysis with a high flux membrane permitting passage of hydrophobic, albumin-bound target substances, and an albumin-enriched dialysate. This albumin-dialysate is online regenerated by passage through a second dialyzer and 2 adsorber columns.[7] This process can be seen in **Fig. 1**.

MARS has been studied in ALF, acute on chronic liver failure, hepatic encephalopathy grade greater than II, increased intracranial pressure, acute hypoxic

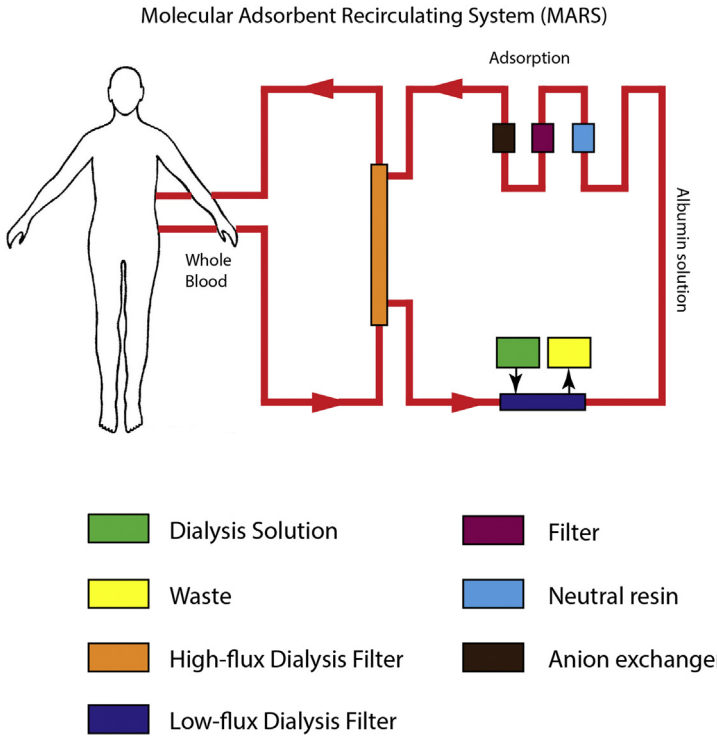

Fig. 1. MARS diagram.