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CASE REPORT | LIVER

Molecular Adsorbent Recirculating System in Acute Liver Failure

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ABSTRACT

Acetaminophen (APAP) overdose is the most common cause of acute liver failure (ALF) in the United States. Liver transplantation (LT) is potentially lifesaving for patients with ALF, but its feasibility in clinical practice is limited. Liver assist devices, such as the Molecular Adsorbent Recirculating System (MARS), are used in some centers as a "bridge" to liver transplantation or as a means of liver recovery, but their role in the treatment of ALF is not well-defined. We present the case of a 44-year-old man with APAP-associated ALF who experienced hepatic recovery after treatment with MARS.

KEYWORDS: acute liver failure; artificial liver support; liver failure; MARS

INTRODUCTION

Acute liver failure (ALF) is a distinct orphan syndrome characterized by abnormal liver biochemistries, coagulopathy, and encephalopathy in a patient without pre-existing liver disease.[1] Acetaminophen (APAP)-associated ALF (APAP-ALF) is often characterized by marked elevations in serum aminotransferases in the absence of profound jaundice. It is commonly accompanied by metabolic acidosis, acute kidney injury, and hypoglycemia. Patients with APAP-ALF should be treated with N-acetylcysteine (NAC), which serves as a glutathione store to detoxify the toxic metabolite N-acetyl-p-benzoquinone; glutathione supplementation has also shown to act as a free-radical scavenger and improve both hepatic and global perfusion in fulminant hepatotoxicity.[3,4]

Historically, ALF-associated mortality approached 80%, but overall survival rates in patients with APAP-ALF have improved drastically,[2] owed in part to NAC and LT. A recent review indicated that survival for APAP-ALF patients who were not transplanted was 16.7% compared to 78.8% for transplanted patients; approximately half of those who did not undergo LT were too sick to be considered as potential transplant candidates. Unfortunately, the use of LT in APAP-ALF is not just limited by severity of illness, but also by diagnostic dilemmas at the time of presentation and psychosocial concerns,[2] especially in the setting of intentional APAP overdoses.[5]

Given the limitations of current treatments and potential barriers to LT, additional therapeutic options for management are required. Liver assist devices, such as MARS, a so-called "liver dialysis" that uses albumin dialysate to remove protein-bound toxins and mimics the detoxification function of the liver, are evolving as a therapeutic option for patients with APAP-ALF.

CASE REPORT

A 44-year-old man with a history of alcohol use disorder and schizophrenia presented to the hospital with altered mental status. The patient's partner reported that the patient took 40 tablets of APAP over the past 1–2 days. On arrival, the patient was normotensive, tachycardic, and agitated, requiring restraints. He also appeared jaundiced.

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Table 1. Pertinent laboratory testing results

Pertinent laboratory testing results	Before initiation of MARS	After first session of MARS	After fifth sessions of MARS
TB (mg/dL)	10.6	9.2	6.0
ALP (U/L)	195	130	126
AST (U/L)	5,605	1,590	131
ALT (U/L)	7,000	3,644	510
Albumin (g/L)	2.6	3.1	2.2
INR	3.9	2.9	1.3
Sodium (mmol/L)	130	140	142
BUN (mg/dL)	39	38	17
Creatinine (mg/dL)	7.78	6.41	1.84
Lactate (mmol/L)	11.9	3.3	1.4
Ammonia (mmol/L)	215	188	83
APAP (ug/mL)	75	53	<5

ALP, alkaline phosphatase; ALT, alanine aminotransferase; APAP, acetaminophen; AST, aspartate aminotransferase; BUN, blood urea nitrogen; INR, international normalized ratio; MARS, Molecular Adsorbent Recirculating System; TB, total bilirubin.

Initial laboratory tests were significant for elevated serum aminotransferases and total bilirubin (TB), elevated arterial ammonia, and a positive APAP level; pertinent laboratory test results are included in Table 1. Abdominal imaging was unremarkable. A complete evaluation for etiologies of ALF was completed, and a final diagnosis of APAP-ALF was made.

The patient was promptly admitted to the medical intensive liver unit, and NAC was given as 12.5 mg/kg/h on day 1 and continued for 5 days. He was rapidly evaluated and subsequently declined for LT, given psychosocial concerns and polysubstance use. Initial cross-sectional imaging of the brain was normal, although mental status deteriorated within the first 24 hours. He was ultimately intubated, and interval imaging demonstrated poor gray-white matter differentiation. Hypertonic saline was administered, given a concern for elevated intracranial pressure (ICP). An intraparenchymal ICP monitor was placed on day 2; ICP was 12–13 mm Hg. He became progressively oliguric requiring continuous renal replacement therapy (CRRT).

After multidisciplinary discussion, MARS therapy was initiated as a potential bridge to recovery on day 1 of admission and planned for 6 hours daily for 5 days. He was monitored with serial complete metabolic panels and coagulation studies every 8 hours. Laboratory parameters rapidly improved while on MARS. On day 6 of admission, after completing MARS therapy, his liver biochemistries were TB 6.0 mg/dL, ALP 160 U/L, AST 131 U/L, ALT 510 U/L, and INR 1.3. The intraparenchymal ICP monitor was removed after ICPs normalized; the patient stabilized, mental status returned to baseline, liver function continued to improve, and he was ultimately discharged. He continues to receive care in the ambulatory setting.

DISCUSSION

ALF can be therapeutically challenging, given its variable etiologies, associated multiorgan failures, and often unpredictable prognostic models. Despite improvements in critical care medicine and opportunities to pursue LT, morbidity and mortality in ALF remain high. Extracorporeal liver support (ECLS) devices offer options for provider teams to stabilize liver function while allowing for native hepatic recovery or bridging

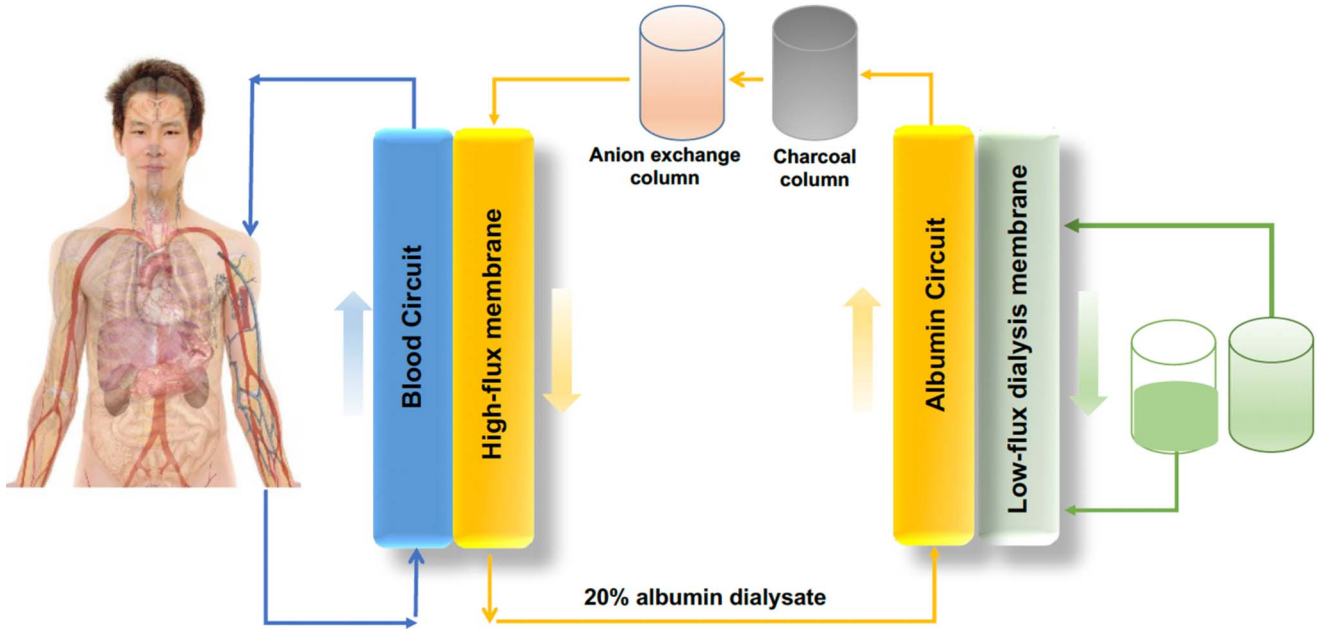

Figure 1. Schematic of Molecular Adsorbent Recirculating System.

to LT.[6] ECLS devices are intended to remove proinflammatory cytokines and vasoactive toxins that lead to oxidative stress, immune dysregulation, and cellular damage in patients with ALF.[5] ECLS devices are classified as either artificial ECLS or bioartificial ECLS.

MARS is one of three currently available artificial ECLS devices; it can remove both protein-bound and water-soluble toxins that have been implicated in the pathogenesis of ALF.[7] The device transmits a patient's blood through a circuit consisting of an albumin-impregnated membrane with adsorbent columns and a 20% human albumin dialysate to remove albumin-bound toxins that are >50 kDa. MARS is coupled with a standard RRT circuit to remove water-soluble toxins. The MARS circuit is depicted in Figure 1. Compared with other ECLS devices, MARS treatment has been associated with improvement in both mean arterial pressure and systemic vascular resistance.[6]

The use of MARS for ALF is controversial. Only one study, conducted in 16 French LT centers, was controlled and randomized (although not blinded). There was no mortality benefit in nontransplanted patients receiving MARS treatment for APAP-ALF, although there was a trend toward improved survival compared with those receiving standard-of-care therapy.[8] In addition, there have been case reports in APAP-ALF demonstrating enhanced APAP clearance while on MARS[9]; this is particularly important because additional data have indicated reduced NAC levels while on MARS, suggesting that further APAP clearance is larger driven by the MARS circuit itself and not the high-dose NAC administration.[10] Despite the lack of mortality benefit, the use of MARS was associated with consistent improvements in hepatic encephalopathy, a trend that has been noted in numerous other studies,[11–13] including a single-center observational study from Norway. Findings from this study suggested that MARS may be beneficial in objectively sicker patients awaiting LT as either a bridge to LT or native hepatic recovery,[14] the latter of which was seen in our patient.

Despite the potential of ECLS devices such as MARS, the current focus of ALF treatment continues to be the appropriate and timely administration of critical care medicine. This includes fluid management and CRRT, both of which are associated with reductions in serum bilirubin and ammonia levels.[1] The benefit of ECLS devices in ALF is difficult to determine, given the direct effects of the treatment on many of our current markers of prognostication, such as improvement in TB levels. Furthermore, the real-world clinical utility of MARS is limited by availability, high cost and nursing needs, risks of thrombocytopenia and catheter-related complications, as well as difficulty with drug-dosing in the setting of dialysis.[7] Well-conceived randomized trials of ECLS devices in defined patient cohorts, such as those specifically with APAP-ALF, are necessary for future study to better understand the role of these devices in patients with ALF.

DISCLOSURES

Author contributions: All authors have made substantial contributions to all of the following: the conception and design of the study, or acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be submitted. Khaled Alsabbagh Alchirazi is the article guarantor.

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