The Molecular Adsorbent Recirculating System (MARS®)

A therapy for the treatment of liver failure; review and case study

Nigel Fealy • RN
Clinical Educator, Department of Intensive Care, Austin Health, Heidelberg, VIC

Ian Baldwin • RN
Course Coordinator, Department of Intensive Care, Austin Health, Heidelberg, VIC
Adjunct Professor of Nursing, RMIT University, Bundoora, VIC

Martin Boyle • RN
Clinical Nurse Consultant – Intensive Care
Department of Intensive Care, The Prince of Wales Hospital, Randwick, NSW

Abstract

The consequences of liver failure include hepatic encephalopathy, haemodynamic instability, cerebral oedema, renal failure, susceptibility to infection, coagulapathy and metabolic derangement. Liver transplantation is the only established treatment for patients who do not respond to medical management. However, the supply of organs for transplant is limited. Artificial liver support therapies are available to support patients in acute liver failure to allow time for liver recovery or to provide a bridge to transplantation.

A young woman presenting with hyperacute liver failure resulting from paracetamol overdose was treated with an extracorporeal liver support therapy using albumin as a dialysis medium, referred to and marketed as the Molecular Adsorbents Recirculating System (MARS®). MARS® setup, priming and initiation of therapy was undertaken by intensive care nursing staff and required new and advanced skills. On admission, her INR was 8.2, alanine transferase 10157 u/L and paracetamol level 218 µmol/L. After three treatments for 19, 19 and 20 hours, respectively, using the MARS® technique, this patient began to recover. On day 6, all life support therapies were ceased and she made a full recovery and was discharged from hospital 17 days after hospital admission to Intensive Care.

If MARS® gains increased acceptance, Australian critical care nurses are well placed to manage this new therapy using their past Continuous Renal Replacement Therapy (CRRT) experience as a foundation for learning a new extracorporeal organ support technique.

Key Words: *paracetamol overdose, liver failure, artificial liver support, albumin dialysis, MARS®*

INTRODUCTION

The consequences of liver failure include hepatic encephalopathy, haemodynamic instability, cerebral oedema, renal failure, susceptibility to infection, coagulapathy, and metabolic derangement [1, 2]. Acute liver failure (ALF), without pre-existing liver disease, can result from hepatotoxic drugs, toxins, viral infection and the effect of inflammatory mediators [1]. Despite improvements in supportive medical care that have had a substantial impact on survival, the mortality rates for ALF remain high [1].

Whilst in some patients with ALF, there is potential for recovery of liver function, in those where there is no likelihood of liver recovery, transplantation is the only viable therapeutic option [1]. Unfortunately, as a result of a shortage in organs available for transplant, many potential organ recipients experience lengthened waiting times. Thus, patients can become critically ill before a transplant is possible [3].

Liver failure can also occur as an acute decompensation of chronic liver disease (acute-on-chronic liver failure: AoCLF) or as an endstage decompensation of chronic liver failure. AoCLF can be precipitated by bacterial or viral infection, bleeding or intoxication and results in the same clinical syndrome as seen in ALF [1]. End stage decompensation of chronic liver failure (CLF) represents irreversible deterioration with inadequate residual function to maintain homeostasis and transplantation is the only viable treatment [1]. However in AoCLF, function of the residual liver cell mass is adequate to maintain homeostasis if the acute precipitating event can be treated and the patient supported during the period of acute failure [1].

The development of artificial liver support therapies arises from experience that demonstrates that recovery may occur in some patients with ALF. There is also the need to support life until a transplant organ is procured and when recovery appears likely during an acute exacerbation in AoCLF [4].

Biological and non-biological systems are available for liver support. The biological systems utilise pig hepatocytes or hepatoma cells to achieve removal of toxins [1]. These systems require complex technical support restricting use only in specialist centres [1]. Non-biological systems, on the other hand, are very similar to renal replacement circuits and use albumin as a dialysis medium or dialysis against an activated charcoal medium as a mechanism for toxin removal and liver support [1].

An extracorporeal liver support therapy, using albumin as a dialysis medium, has been available for clinical use since 1998 and has been used in the treatment of over 3,300 patients (more than 16,000 single treatments) mainly in Europe and China [5]. This system

became available for clinical use in Australia in 2002 and is named and marketed as the Molecular Adsorbents Recirculating System (MARS®).

THE ROLE OF ALBUMIN

In order to understand the utility of MARS® therapy, it is important to understand the role albumin has in the context of liver failure and toxin transport during MARS®.

The albumin molecule contains reversible binding sites for substances such as fatty acids, hormones, enzymes, dyes, trace metals and drugs [4, 6-8]. Albumin plays a vital role in the clearance from the body of substances that are toxic in the unbound state by reversible binding and transport to the liver where they are metabolised and excreted into the biliary system or in a water soluble form via the kidneys [4].

Albumin binds substances that accumulate in liver failure and are implicated in the development of the hepato-renal syndrome, hepatic encephalopathy, haemodynamic instability, ongoing liver injury and inhibition of liver cell regeneration. It has been proposed that, in liver failure, the decreased hepatic clearance of albumin bound toxin leads to a saturation of the available albumin binding sites and an accumulation of toxic substances causing secondary organ dysfunction [4].

DESCRIPTION OF MARS® THERAPY

The MARS® treatment is achieved by the combined use of blood and fluid pumps, albumin pump and monitor unit (MARS® I TC monitor, Teraklin AG, Rostock, Germany) and the MARS® treatment kit (Teraklin AG, Rostock, Germany) (refer to Figures 1 and 2).

The treatment kit consists of an albumin haemodialyser, a standard haemodialyser, an activated carbon adsorber and an anion exchanger. The circuit is filled with 600mL of 20% human albumin solution. The albumin acts as a dialysate and is pumped through a hollow-fibre membrane haemodialyser (MARS® Flux dialyser) countercurrent to blood. Water-soluble substances diffuse into the albumin solution whilst albumin bound toxins move by physicochemical interactions between the plasma, albumin molecules bound to the dialysis side of the membrane and the circulating albumin solution. The albumin is then passed through another dialyser counter-current to a standard buffered dialysis solution where diffusive clearance of water-soluble substances occurs [9]. A concentration gradient is maintained by circulation of the albumin solution and disposal of the albumin bound toxins by passage through activated charcoal and anion exchange columns [4, 7].

MARS® therapy has been shown to result in a significant removal of albumin bound toxins such as fatty acids, bile acids, tryptophan and bilirubin. Physiologically important proteins and hormones are not significantly removed [7]. MARS® treatment has consistently resulted in reduced plasma levels of bilirubin and bile acids [4, 5-7]. The removal rates of bilirubin and bile acids, for a single treatment, are approximately 28% and 55% respectively [10, 11].

MARS® THERAPY – THE EVIDENCE

Use of MARS® in AoCLF

MARS® treatment significantly reduces plasma levels of the markers of albumin bound toxins, bilirubin and bile acids. Ammonia, a water-soluble molecule, is also significantly cleared with MARS® therapy, as are the markers of uraemia control (urea and creatinine)

Figure 1: The MARS treatment circuit.

The MARS® albumin pump and monitor unit (A) was placed in series with a standard CRRT CVVHD circuit (B). The CRRT machine serves as a blood pump and dialysate controller.

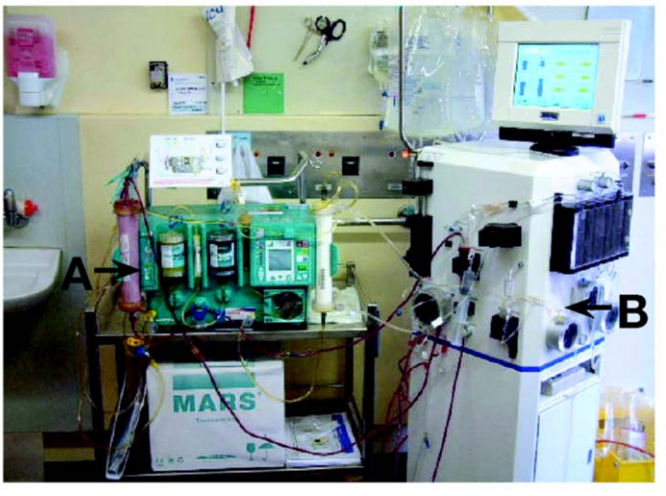
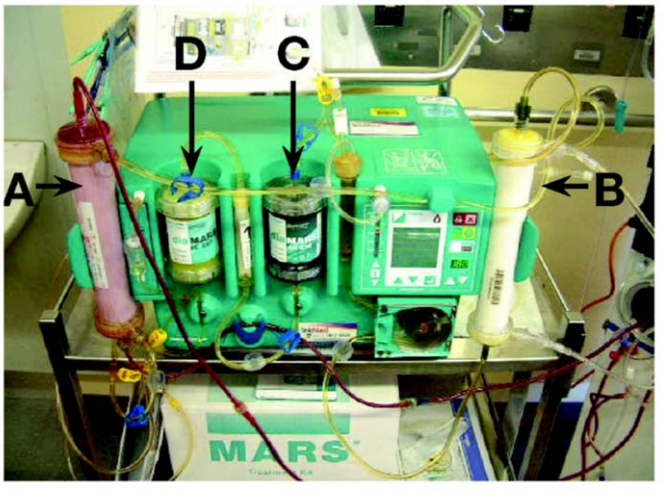


Figure 2: The MARS monitor and treatment kit.

The albumin acts as a dialysate and is pumped through a hollow-fibre membrane haemodialyser counter-current to blood (A). Protein bound toxins and water-soluble substances diffuse into the albumin solution. The albumin is then passed through another dialyser counter-current to a standard buffered dialysis solution where diffusive clearance of water-soluble substances occurs (B). The albumin solution is then cleaned of its albumin bound toxins by passage through an activated carbon adsorber (C) and an anion exchanger (D).



[4, 12-15]. MARS® has also been shown to effectively clear nitric oxide possibly increasing arterial blood pressure (NO) [16].

Improvements in haemodynamic stability indicated by improved mean arterial pressure and reduction in vasopressor dose have been reported, as have improvements in neurological state measured by reduction in encephalopathic symptoms or grading and intracranial pressure [13, 17-19]. MARS® has been reported to be used with some success in the treatment of intractable pruritus resulting from intrahepatic cholestasis [20].

Small, randomised, controlled trials have assessed outcomes of MARS® therapy compared to standard medical therapy. A study published by Mitzner *et al.* [12] concluded the MARS® group had a significant decrease in bilirubin and an improved prothrombin activity. The 30-day mortality was 75% and 100% for MARS®