Commentary

The Molecular Adsorbent Recirculating System (MARS®) in the intensive care unit: a rescue therapy for patients with hepatic failure

Faouzi Saliba

AP-HP, Hôpital Paul Brousse, Service d'hépato-gastroentérologie, Villejuif, 94804, France

Corresponding author: Faouzi Saliba, faouzi.saliba@pbr.aphp.fr

Published: 8 February 2006
This article is online at http://ccforum.com/content/10/1/118
© 2006 BioMed Central Ltd

Critical Care 2006, **10:**118 (doi:10.1186/cc4825)

Abstract

Treatment in the intensive care unit of patients with end-stage liver disease has been limited. Liver transplantation has been a major improvement in this and has become standard in the management of these patients. However, many patients die awaiting liver transplantation, mainly due to the scarcity of organ donors. Conventional hemodialysis techniques have little or no effect on liver detoxification and do not improve the prognosis of these patients. In patients with acute hepatic failure, the majority of endogenous toxins leading to organ failure and accumulating in the blood are bound to albumin; therefore, the concept of albumin dialysis is of major interest. To date, the most widely developed system has been the Molecular Adsorbent Recirculating System (MARS®), which is based on the selective removal of albumin-bound toxins from the blood. MARS® enables simultaneous liver and kidney detoxification, improving the patient's clinical condition. It is a major improvement in the management of patients with hepatic failure that could permit, when appropriately indicated, recovery from an acute episode and enhance the chances of survival while waiting for an available organ donor.

Introduction

During the past decades, few therapeutic measures have been developed for the treatment of patients with end-stage liver disease. Despite a great improvement in the field of transplantation, the mortality in patients developing hepatic failure remains very high and many patients die while awaiting liver transplantation. In recent years, a major interest has been the replacement of the liver by extracorporeal systems that may provide a lifeline until a spontaneous recovery of the liver or until an appropriate donor is available. Many non-biological liver support therapies based on detoxification of the patient's blood have been developed. These include standard or high-flux hemodialysis, continuous veno-venous hemofiltration or hemodiafiltration, charcoal perfusion, hemadsorption with non-biological adsorbents and plasma or blood exchange [1-4]. To date, the most widely developed system has been the Molecular Adsorbent Recirculating System (MARS®), which uses albumin dialysis to mainly replace the detoxification function of the liver. Two other systems using a similar approach have been developed recently, the Prometheus® and the Single-Pass Albumin Dialysis (SPAD®) systems; few patients have been treated with these systems to date, but their results could be promising [5,6].

Molecular Adsorbent Recirculating System

MARS® is a liver support system that uses an albumin-enriched dialysate to facilitate the removal of albumin-bound toxins. The system has three different fluid compartments: a blood circuit, a circuit containing 600 ml of 20% human albumin with a charcoal column and an anion exchange resin column and a dialysate circuit [7]. MARS® requires a standard dialysis machine or a continuous veno-venous hemodiafiltration device (CCVVHD) to control the blood and dialysate circuits.

MARS® has been used in the intensive care unit in most clinical situations of hepatic failure [8,9]. The main indications of treatment with MARS® are now better established but they need further validation; they are summarized in Table 1.

Efficacy results

In patients suffering from acute decompensation on chronic liver disease

MARS® has already been the object of three prospective randomized studies to evaluate its short-term benefits in patients suffering from acute decompensation on chronic liver disease. Mitzner and colleagues [10] randomized 13 patients with hepato-renal syndrome, 8 in the MARS® group and 5 in a control group. Mortality was 100% in the control group and 75% in the MARS® treated group ($p < 0.01$). Effectiveness was also demonstrated by the increase in

CCVVHD = continuous veno-venous hemodiafiltration device; MARS = Molecular Adsorbent Recirculating System.

Table 1

Main Indication groups for MARS® therapy

1	Acute liver failure
2	Acute decompensation on chronic liver disease
	Complicated by progressive jaundice
	Complicated by hepatic encephalopathy
	Complicated by renal dysfunction
3	Intractable pruritus in cholestasis
4	Acute intoxication or overdose with substances potentially bound to albumin
5	Other indications
	Acute hepatic failure after major hepatectomy
	After liver transplantation
	Primary non-function or primary dysfunction of the graft
	Acute decompensation of the graft (disease recurrence…)
	Secondary liver failure or multi-organ failure

arterial pressure and the urinary volume, and the decrease in creatininemia and bilirubinemia. In a second clinical trial, Heemann and colleagues [11] randomized 24 patients with severe cholestasis (bilirubin >20 mg/dl) not improving after 3 to 5 days of standard medical therapy (SMT) in two groups, SMT versus SMT plus MARS®. The determining factors for acute decompensation were infection, drug intoxication, hemorrhage and alcohol abuse. The results showed a significant difference ($p < 0.05$) in the 30-day survival rate in favor of the MARS® group: 6 deaths in the SMT group (survival = 50%) against only one in the MARS® group (survival = 91%). Effectiveness was also shown by improvements in hepatic-encephalopathy and arterial pressure, and a decrease in bilirubinemia, biliary acids, and creatininemia. Recently, the results of a prospective randomized multicenter study including 70 patients with grade 3 and 4 hepatic encephalopathy have been presented with the primary objective of decreasing by two stages the degree of encephalopathy after five days of therapy [12]. The study showed a significant improvement in the degree of encephalopathy in 64% of the patients treated with MARS® and 38% of the control group ($p = 0.04$). In particular, ammonia levels were significantly reduced in patients treated with MARS®.

Other uncontrolled studies have shown a beneficial effect of MARS® in severe cholestatic liver disease [13], acute alcoholic hepatitis [14], hypoxic liver [15], and graft dysfunction after liver transplantation [16].

In patients with acute fulminant liver failure

Several uncontrolled studies have been performed using MARS® in patients with acute fulminant liver failure, showing improvements in encephalopathy, a decrease in intracranial pressure, and an increase in cerebral perfusion pressure, mean arterial blood pressure, systemic vascular resistances and cardiac index [17,18]. Currently we are undertaking a prospective controlled, randomized, multicenter study in patients suffering from fulminant hepatitis to evaluate the beneficial effect of MARS® on survival with or without transplantation.

Safety

As MARS® treatment uses the same blood-contacting tubes and membranes that are used extensively in 24 h hemodiafiltration treatment in intensive care unit patients and the dialysate solution is supplemented with approved human albumin that has no ability to cross the hemofilter membrane and to enter the patients blood, the risks of the treatment are limited to all known risks of conventional hemodialysis. These risks may be related to catheter problems or inadequate anticoagulation. In patients with end-stage liver disease, however, coagulopathy disorders are frequent and the risk of bleeding is increased. Faybik and colleagues [19] observed that although MARS® can lead to a further decrease in platelet count and fibrinogen concentration, platelet function, measured by thromboclastography, remains stable and, in particular, MARS® did not enhance fibrinolysis.

Conclusion

The concept of albumin dialysis in patients with end-stage liver disease is a novel approach. Albumin dialysis with MARS® has demonstrated interesting results in controlled and uncontrolled trials in improving hepatic encephalopathy and short-term survival. It has a good safety profile similar to the CVVHD techniques. Technical improvements and randomized controlled trials focusing on specific indications are still needed to evaluate the impact of these therapies in medical practice.

Competing interests

The author(s) declare that they have no competing interests.

References

1. O'Grady JG, Gimson AE, O'Brien CJ, Pucknell A, Hughes RD, Williams R: **Controlled trials of charcoal hemoperfusion and prognostic factors in fulminant hepatic failure.** *Gastroenterology* 1998, **94:**1186-1192.
2. Wilkinson AH, Ash SR, Nissenson AR: **Hemodiabsorption in treatment of hepatic failure.** *J Transpl Coord* 1998, **8:**43-50.
3. Iwai H, Nagaki M, Naito T, Ishiki Y, Murakami N, Sugihara J, Muto Y, Moriwaki H: **Removal of endotoxin and cytokines by plasma exchange in patients with acute hepatic failure.** *Crit Care Med* 1998, **26:**873-876.
4. Wang YJ, Wang ZW, Luo BW, Liu HL, Wen HW: **Assessment of resin perfusion in hepatic failure in vitro and in vivo.** *World J Gastroenterol* 2004, **10:**837-840.
5. Rifai K, Er T, Kretschmer U, Bahr MJ, Schneider A, Hafer C, Haller H, Manns MP, Fliser D: **Prometheus a new extracorporeal system for the treatment of liver failure.** *J Hepatol* 2003, **39:**984-990.
6. Sauer IM, Goetz M, Steffen I, Walter G, Kehr DC, Schwartlander R, Hwang YJ, Pascher A, Gerlach JC, Neuhaus P: **In vitro comparison of the Molecular Adsorbent Recirculation System (MARS) and Single-pass Albumin Dialysis (SPAD®).** *Hepatology* 2004, **39:**1408-1414.

7. Mitzner SR, Stange J, Klammt S, Peszynski P, Schmidt R and Nôldge-Schomburg G: **Extracorporeal detoxification using the molecular adsorbent recirculating system for critically ill patients with liver failure.** *J Am Soc Nephrol* 2001, **12:**S75-S82.
8. Novelli G, Rossi M, Pretagostini M, Pugliese F, Ruberto F, Novelli L, Nudo F, Bussotti A, Corradini S, Martelli S, Berloco PB: **One hundred sixteen cases of acute liver failure treated with Mars.** *Transplant Proc* 2005, **37:**2557-2559.
9. Saliba F, Ichaï P, Gonzales M, Azoulay D, Adam R, Castaing D, Samuel D: **Extracorporeal liver support using the MARS® Albumin dialysis system: a rescue therapy in patients with end-stage liver disease and renal failure.** *Liver Transpl* 2005, **11:**Abs 41 C-11.
10. Mitzner SR, Stange J, Klammt S, Risler T, Erley CM, Bader BD, Berger ED, Lauchart W, Peszynski P, Freytag J, *et al.*: **Improvement of hepatorenal syndrome with extracorporeal albumin dialysis MARS: results of a prospective, randomized, controlled clinical trial.** *Liver Transpl* 2000, **6:**277-286.
11. Heemann U, Treichel U, Loock J, Philipp T, Gerken G, Malago M, Klammt S, Loehr M, Liebe S, Mitzner S, *et al.*: **Albumin dialysis in cirrhosis with superimposed acute liver injury: a prospective, controlled study.** *Hepatology* 2002, **36:**949-958.
12. Hassanein T, Tofteng F, Brown R, McGuire B, Lynch P, Mehta R, Larsen F, Gornbein J, Stange J, Blei A: **Efficacy of albumin dialysis (MARS) in patients with cirrhosis and advanced grades of hepatic encephlopathy: a prospective, controlled, randomized multicenter trial.** *Hepatology* 2004, **38:**LB04: 726A.
13. Campli C, Gaspari R, Mignani V, Stifano G, Santoliquido A, Verme LZ, Proietti R, Pola P, Silveri NG, Gasbarrini G, Gasbarrini A: **Successful Mars treatment in severe cholestatic patients with acute on chronic liver failure.** *Artif Organs* 2003, **27:**565-569.
14. Jalan R, Sen S, Steiner C, Kapoor D, Alisa A, Williams R: **Extracorporeal liver support with molecular adsorbents recirculating system in patients with severe acute alcoholic hepatitis.** *J Hepatol* 2003, **38:**24-31.
15. Banayosy A, Kizner L, Schueler V, Bergmeier S, Cobaugh D, Koerfer R: **First use of the Molecular Adsorbent Recirculating System technique on patients with hypoxic liver failure after cardiogenic shock.** *ASAIO J* 2004, **50:**332-337.
16. Kellersmann R, Gassel H-J, Buehler C, Thiede A, Timmermann W: **Application of Molecular Adsorbent Recirculating System in patients with severe liver failure after hepatic resection or transplantation: initial single-centre experiences.** *Liver* 2002, **22(Suppl 2):**56-58.
17. Ben Abraham R, Szold O, Merhav H, Biderman P, Kidron A, Nakache R, Oren R, Sorkine P: **Rapid resolution of brain oedema and improved cerebral perfusion pressure following the molecular adsorbent recycling system in acute liver failure patients.** *Transplant Proc* 2001, **33:**2897-2899.
18. Schmidt LE, Wang LP, Hansen BAH, Larsen FS: **Systemic hemodynamic effects of treatment with the molecular adsorbents recirculating system in patients with hyperacute liver failure: a prospective controlled trial.** *Liver Transplant* 2003, **9:** 290-297.
19. Faybik P, Bacher A, Kozek-Langenecker SA, Steltzer H, Krenn CG, Unger S, Hetz H: **Molecular adsorbent recirculating system and hemostasis in patients at high risk of bleeding: an observational study.** *Crit Care* 2006, **10:**R24.