ALBUMIN DIALYSIS FOR EXTRACORPOREAL LIVER SUPPORT: BASICS AND CLINICAL RESULTS

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Extracorporeal liver support carries the prospect of removing liver failure toxins and thus permitting autoregeneration of the liver. The fact that most of the potential liver toxins, such as hydrophobic bile acids, bilirubin or plasmatic nitric oxide use albumin as their transport protein has lead to the development of albumin dialysis. In short, it comprises of a modified hemodialysis with a non-albumin-permeable, high flux membrane permitting passage of hydrophobic target substances (albumin-bound toxins, ABT) and an albumin-enriched dialysate. In the case of the Molecular Adsorbent Recirculating System (MARS) this albumin-dialysate is on-line regenerated by passage through a second dialyzer and two adsorber columns (charcoal and anion-exchanger). The aim is to remove both ABT and water-soluble toxins without loosing valuable plasma compounds (see Fig). MARS was developed at Rostock University, Germany in the early nineties. To date, it represents the most frequently used liver support method in Europe. Results were reported in more than 250 PUBMED-listed experimental and clinical papers. During ten years of clinical experience with MARS a stable spectrum of indications has evolved. According to the International MARS Registry, acute decompenation of chronic liver disease (acute on chronic liver failure, AoCLF) and acute liver failure (ALF) account for more than three quarters of all treatments (50% and 25%, resp.). The following complications of liver failure improved during MARS: Hepatic encephalopathy, Hepatorenal Syndrome, systemic and regional hemodynamics, liver synthesis, hepatic pruritus (for review see Mitzner S. Curr Opin Nephrol Hypertens 2007; 16:589-95).

In ALF precipitating events were acute infection (hepatitis B/ C or other), drug overdose and intoxication (chemicals, poisonous mushroom), idiosyncratic drug reaction, Wilsons disease or unknown. A downscaled version of MARS with a smaller extracorporeal blood volume was successfully used in pediatric ALF.

The primary aim of the MARS treatment in ALF and other transplant waiting list patients is to safely bridge the patient to liver transplantation. Not only was the treatment reported to be safe but patient’s condition improved markedly in a substantial number to such an extent that sustained liver regeneration was achieved. In rare cases, anhepatic patients were bridged. Koivusalo et al. report 56 patients with ALF (29 toxic, 22 unknown, 5 other). All fullfilled liver transplantation criteria or had ingested a lethal dose of a known toxic agent (e.g. paracetamol, Amanita phalloides). Mean number of 3 MARS treatments were performed per patient, target treatment duration was 22h/session. The 1 year survival was 84%. Recovery of native liver function occurred in 30 pats (1y survival: 79%). In the transplanted group 1 y survival was 94%. In the subgroup of toxic ALF the recovery rate was 76% and 23% in the ALF of unknown origin (Transplant Proc. 2005;37:3315-7). Camus et al. found similar results in their liver transplantation-candidates. They treated two times/pat. for 8 hours/session and found a transplantation-free survival of 29% (Intensive Care Med. 2006;32:1817-25). A number of other groups reported safe and successful bridging to liver transplantation or even recovery of native liver function in their patients, among others in children (Novelli G et al. Transplant Proc. 2005;37:2557-9; Doria C et al. Dig Dis Sci. 2006;51:47-53; Yuan JZ et al. World J Gastroenterol. 2006;12:5055-9; Nadalin S et al. Transpl Int. 2007;20:519-27). Randomized controlled trials with MARS in ALF showed significant improvement of hemodynamics (Schmidt LE et al. Liver Transpl. 2003;9:290-7) and, in an animal trial, significant decrease of ICP (Sen S et al. Crit Care Med. 2006;34:158-64). MARS as bridging to liver transplantation in ALF is currently studied in a multicenter randomized clinical trial in France.
In summary, MARS represents the most frequently used liver support method in Europe at present time. It allows the safe and effective removal of albumin-bound as well as water-soluble substances. Data from clinical trials indicate that albumin dialysis can be used to safely bridge patients to liver transplantation. An encouraging number of ALF-patients recovered native liver function. The currently running large randomized clinical trials will add greatly to our knowledge. The use of a non-albumin permeable synthetic membrane seems to be a key feature of the clinical success. It facilitates good hemocompatibility and selectivity of the detoxification procedure.