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HEPATIC DIALYSIS IN NEONATES WITH ACUTE LIVER FAILURE

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ABSTRACT

Hepatic dialysis is an artificial extracorporeal liver support device designed to filter out toxins accumulated in patients with acute liver failure. Although it is a rare entity encountered in neonates, acute liver failure is a highly fatal condition, with seventy percent resulting in mortality without liver transplantation. Scientific data on extracorporeal liver support concerning the pediatric population is scarce in literature. Artificial extracorporeal liver support devices in the form of bridge therapy have been designed to improve survival of patients with acute liver failure while awaiting transplantation.

Keywords: Liver transplantation, acute liver failure, neonate

INTRODUCTION

Hepatic dialysis is an artificial extracorporeal liver support device designed to filter out toxins accumulated in patients with acute liver failure (ALF). First developed in the 1950s, however scarcely employed, hepatic dialysis gained its reputation as an efficacious modality of liver bridging therapy (1).

In 1996, Bhaduri and Mieli-Vergani proposed the definition of ALF as "a rare multisystem disorder in which severe impairment of liver function, with or without encephalopathy, occurs in association with hepatocellular necrosis in a patient with or without recognized underlying chronic liver disease" (2).

Mortality Attributed to Acute Liver Failure in Neonates:

Although rarely encountered in neonates, it is a highly fatal condition, with a staggering mortality rate of 70% without liver transplantation. The main parameter used to establish the necessity of transplantation is an INR ≥4, since it is associated with mortality in more than 90% of cases (3). The causes of ALF are diverse ranging from perinatal infections and inborn errors of metabolism to septicemia and septic shock (4, 5). Due to its markedly high mortality rate, neonates suffering from ALF should be admitted to the Neonatal Intensive Care Units (NICU) and managed by a highly skilled, multidisciplinary team comprising neonatologists, hepatologists and transplant surgeons until hepatic transplantation or liver regeneration takes place (3).

Hepatic Dialysis as Bridge Therapy for Liver Transplantation:

As a result of the often detrimental clinical course and prognosis of ALF, liver support devices have been further implemented in order to function as bridge therapy until transplantation is available (3, 6). Bridging therapy is in even higher demand in cases where transplantation is contraindicated, such as in cases with uncontrolled sepsis. Liver support devices are promising in ALF due to their inherent capacity of removing accumulated metabolites that accumulate secondary to deficient hepatic clearance (6).

Types of Hepatic Dialysis:

Extracorporeal liver support (ELS) devices can be divided into bioartificial systems, which use human or animal hepatocytes, and artificial, cell-free systems, as hepatic dialysis. Currently, there are three types of artificial ELS devices available: Single Pass Albumin Dialysis (SPAD), Molecular Adsorbent Recirculating System (MARS) and the Fractionated Plasma Separation and Absorption (FPSA), called the "Prometheus System" (7).

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SPAD was the first ELS device to be adopted in clinical practice. This method is carried out using continuous veno-venous hemodialysis using a standard hemodialysis machine, but with a high-flux polysulfone membrane. Blood is dialyzed against a standard dialyzing solution, but enriched with a 20% human albumin solution, resulting in 5% albumin concentration, with a dialysate flow of 700 mL/h (8).

As SPAD, the MARS method also functions based on the principle of clearing protein-bound substances. However, instead of unidirectional high flux excretion of albumin-bound substances, here the semi permeable membrane is functional on both sides; with high flux on one side and slow flux on the other. The slow flux allows for albumin regeneration through two charcoal columns. The regenerated albumin is then used, again, for the detoxification process of each cycle (8, 9).

FPSA "Prometheus System" was introduced by Falkenhagen et al. in 1999 (10). In this system a special albumin-permeable polysulfone filter is used with a cut-off of 250 kD. The purpose of the 250 kD cut-off value is to allow the passage of large molecules such as fibrinogen into the secondary circuit, composed of an isotonic saline solution, where they are trapped. Next, the filtered plasma in the secondary circuit acts as a medium where the hepatic toxins are directly adsorbed and the purified plasma is then returned to the side of the filter adjacent to and in contact with the bloodstream (11).

Literature Regarding Hepatic Dialysis in the Pediatric Population:

Scientific data on ELS concerning the pediatric population is scarce in literature (12, 13). Although MARS dialysis is the most extensively studied type of ELS, it is limited to case reports and small case series, on as few as 20 patients (14).

DISCUSSION

Despite progress in critical care and highly specialized intensive care units, ALF is still a multisystem condition associated with high mortality (3, 15). Artificial extracorporeal liver support devices were designed to improve the survival of patients with ALF by carrying out the detoxification processes, in the form of bridge therapy, while awaiting transplantation (16).

Hepatic Dialysis as Bridging Therapy in Adults:

Acute liver failure in the adult population has been much more adequately studied compared to that of the pediatric population, primarily due to the larger prevalence of chronic hepatic diseases. Hepatic dialysis has been proven to be a safe and efficacious modality of bridging therapy in adults for treating liver failure complications such as hepatic encephalopathy (HE), hemodynamic instability and progressive hyperbilirubinemia (6).

Ten Years of Experience with the Molecular Adsorbent Recirculating System in the Pediatric Population:

Although scientific data regarding ELS in the pediatric population is scarce, we gained access to the largest study performed thus far, from a hospital with 10 years of experience with the MARS method. In the study performed by Lexmond et al. (14), MARS was the method of ELS employed in 20 pediatric patients suffering from ALF listed for high urgency liver transplantation. The decision to employ MARS was made by a multidisciplinary team consisting of pediatricians, hepatologists, nephrologists, neurologists and transplant surgeons. MARS was applied for 8 consecutive hours daily, up until transplantation. All patients were mechanically ventilated and were on vasopressor therapy. This technique of ELS was deemed successful in decreasing serum ammonia and bilirubin. The only encountered adverse effect from the therapy was thrombocytopenia with bleeding, requiring blood and platelet mass transfusions, in five children, with one case of mortality (14).

Total Parenteral Nutrition:

Parenteral nutrition-associated cholestasis (PNAC) is the most common complication of Total Parenteral Nutrition (TPN) in neonates and infants. In a study performed by Hsieh et al. (17) in 2009, consisting of 62 infants on TPN, 11 (17.7%) developed PNAC. The proposed beneficial effect of TPN on neonates with ALF is the avoidance of constant hepatic stimulation, subsequently attenuating the metabolic load on the liver. Furthermore, intermittent amino acid intake favors nutrient oxidation by hepatocytes, preventing hepatocellular damage (18).

Future Perspectives in the Treatment of Acute Liver Failure:

Shedding light on the current trend of regenerative medicine, hepatocyte transplantation is another modality of bridging therapy in ALF. In this procedure, hepatocytes from live donors are infused into the failing liver of a recipient in order to provide an additional mass of functioning hepatic tissue while the native liver regenerates. Although this method yielded promising results in animal models, it is still only experimental in humans (19).

CONCLUSION

Progressive liver failure, in any human being, regardless if an elderly individual, or a neonate, has the potential to result in death within a few days without liver transplantation (20, 21, 22). Since literature regarding hepatic dialysis in the pediatric and especially the neonatal population is scarce, large-scale prospective studies are urgently needed to determine the exact benefits and potential adverse effects as well as to assess survival rates after such a procedure. Furthermore, randomized control trials culminating in international guidelines would be beneficial in order to determine the most effective modality of hepatic dialysis for neonates.

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