Albumin Apheresis as a Novel Approach to Artificial Liver Support

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ABSTRACT

Currently, there is no direct therapy for liver failure. Extracorporeal devices utilizing adsorption processes are commonly employed for the removal of albumin bound toxins such as bilirubin and tryptophan. In large-scale controlled trials MARS® (albumin dialysis) and Prometheus® (plasma fractionation with adsorption) demonstrated improvements in clinical variables and blood chemistry, but failed to show survival benefit. Conventional blood/plasma filtration techniques do not provide survival advantage in liver failure patients either, because they have only limited ability to remove pro-inflammatory cytokines, toxins covalently bound to albumin, defective forms of circulating albumin, and endotoxins. We have previously described selective plasma exchange therapy (SEPET) using a hemofilter permeable to substances that have an effective molecular weight of up 100 kDa. The proof-of-concept studies were followed by a single-arm Phase I study in patients with decompensated cirrhosis. Hemofiltration using albumin-leaking membrane was found to be safe and effective in removing target molecules, alleviating severe encephalopathy and improving blood chemistry. This study describes a novel large-pore hemodiafilter that has the capacity to effectively remove a wide spectrum of pathogenic factors implicated in the pathophysiology of hepatic failure, including protein bound toxins, defective forms of circulating albumin and pro-inflammatory cytokines. We labeled it ALEX to underscore the ability of the device to provide Albumin EXchange (apheresis). In liver failure, albumin binding capacity is reduced and significant amounts of endogenous albumin may be permanently damaged. Albumin apheresis may therefore enhance detoxification by restoring functional capacity of albumin. In bench testing, ALEX filter showed aqueous clearance values comparable to commercially available dialyzers with an active membrane surface of 1.9 m² or higher. High-performance online DF using ALEX was
found to be significantly more effective compared to albumin DF, conventional low-flow DF and ultrafiltration. Data from this study provide rationale for clinical evaluation of the ALEX hemodiafilter for blood detoxification and albumin apheresis. Albumin apheresis can become a novel, readily available and low-cost therapy for liver failure.