Biologic-DT system in the treatment of advanced hepatic encephalopathy, a technology whose time has come

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Abstract

Management of severe acute liver failure remains a major clinical challenge (Lee, 1993). Although substantial advances have been made in general supportive therapy and critical care, mortality in some forms of acute liver failure, specifically fulminant hepatic (FHF), remains unacceptably high (Lee, 1993). This primarily because of incomplete understanding of the pathophysiology of the disease in general and FHF in particular. It is still unclear why patients with acute exacerbation of underlying chronic liver disease do not, as a rule, have cerebral edema, whereas patients without chronic liver disease often experience rapid onset of intracranial hypertension (Demetriou, 1994; Frederick, et al., 1997). Despite incomplete understanding of the pathophysiology of the disease, clinicians have attempted to develop rational, new therapeutic methods (Demetriou, 1994). Most attempts focused on plasma detoxification, based on the assumption that "toxins" accumulate in the plasma as a result of failure of the diseased liver to perform key metabolic functions (Silk, et al., 1997; Gimson, et al., 1982; Bihari, et al., 1983). Such treatments include plasma separation with plasma perfusion over charcoal or liver cells (Razga, et al., 1992), and dialysis with albumin impregnated membranes (Stange, et al., 1993). Plasma exchange has been shown to cause improvement in mild hepatic encephalopathy "grade 2 or less", but no improvement in higher grades, and overall patient survival ranges between 12 and 35% (Zieve, 1975; Matsubara, et al., 1986, 1987; Yamazaki, et al., 1987; Usami, et al., 1989; Omokawa, et al., 1991; Riviello, et al., 1991). Hemoperfusion over coated activated charcoal is another approach designed to remove protein bound substances. The benefits of this procedure, however, are offset by deleterious effects, and the results equal good intensive care management, at best (Omokawa, et al., 1991; Hughes, et al., 1992). Whole liver perfusion has been used successfully to treat patients with FHF and other more chronic forms of liver failure (Fox, et al., 1993). The major limitation in the case of perfusion with whole human liver remains the shortage of organs; additionally it can be argued that if a liver suitable for perfusion, it should be suitable for transplantation. Xenogenic whole liver perfusion has been shown to be effective (Fox, et al., 1993; Chari, et al., 1994). The major challenges that need to be resolved with this approach are immunologic and logistic. Liver transplantation is now widely accepted as treatment for a variety of irreversible acute and chronic liver diseases for which no alternative therapy is available (Kroff, 1995). Prior to 1980, one year survival following liver transplantation was 30% (Kroff, 1995), but the continued refinement in surgical techniques, introduction of better immunosuppressive agents, and improved comprehensive care of transplant recipients led to current one-year survival rates of 85-90% at many centers (Health Resources and Services Administration, Bureau of Health Resources Development, 1995). A major current problem in the performance of liver transplantation is severe organ donor shortage (UNOS data 1997). Also, there are medical and psychological contraindications in many patients (Arkadopoulou et al., 1998) and the non feasibility of OLT in many countries. The Biologic-DT is an extracorporeal blood detoxifier that combines features of haemodialysis with chemical absorption (hemodiabsorption). A cellulosic plate dialyser actively pumps blood through a single lumen access, and a suspension of finely powdered charcoal and cation exchanger in the dialysate selectively removes certain organic chemicals with a MW of 100 to 5000 for many hours without saturation (Shihab-Eldien et al., 1987; Ash et al., 1992 (a,b,c); Ash et al., 1993).

Keywords

Color coded Doppler, umbilical artery, uterine artery, induced hypertension, pregnancy,