New studies help establish potential of artificial liver support devices

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Results from two studies presented today at the International Liver Congress 2010 have shown that treatment with extracorporeal devices may not confer a survival advantage for severe liver failure patients, despite positive dialysis effects. However, results among a small sub-group of patients show promise.

Extracorporeal liver support therapy is in its infancy but is valued as a detoxification treatment option for patients with cirrhosis who have rapid worsening of their liver function. The objectives of these two studies were to better understand the potential of two new devices (Molecular Adsorbent Recirculating System - MARS - and Prometheus®) in terms of survival benefits for patients who suffer from cirrhosis.

Commenting on the studies, Professor Burroughs from the Royal Free Hospital NHS Trust, London UK, said: "The accepted prognosis for these patients is generally poor and current treatment strategies involve supportive therapy, with the hope that liver function will recover if sufficient time is allowed. Extracorporeal support systems such as the two included in these studies are very useful bridges, but the overall data on survival is disappointing. The positive data for severely ill patients with hepatorenal syndrome I or a MELD score over 30, though, does offer some encouragement".

About the studies

In the first study , 145 patients with cirrhosis and rapid deterioration of their liver function were recruited across seven European countries. This study is the first large prospective randomized controlled trial on the survival of patients with the condition (HELIOS study). Prometheus® is a new extracorporeal liver support system allowing the removal of protein bound and water soluble toxins by fractionated plasma separation and absorption (FPSA). Patients were randomized to standard medical therapy or standard medical therapy plus FPSA and the primary endpoints of the study were survival at 28 and 90 days regardless of liver transplantation.

The results show that difference in the overall survival was not statistically different overall (66% vs. 63% p=0.7 at day 28 and 47% vs. 38% p=0.35 at day 90). Only in pre-defined patient sub-groups with hepatorenal syndrome type I* and MELD** score >30 was a significant survival benefit with treatment with FPSA observed (p=0.04 and p=0.02 respectively).

*Hepatorenal syndrome type I is a common type of rapidly progressive kidney failure that affects individuals with liver cirrhosis, with a doubling of serum creatinine to a level greater than 2.5 mg/dL or a halving of the creatinine clearance to less than 20 mL/min over a period of less than two weeks.

**The Model for End-Stage Liver Disease, or MELD, is a scoring system for assessing the severity of chronic liver disease. MELD uses the patient's values for serum bilirubin, serum creatinine, and the international normalized ratio for prothrombin time (INR) to predict survival.

In the second study , 189 patients with acute-on-chronic liver failure across six European countries were randomized either to treatment with the Molecular Adsorbent Recirculating System (MARS) or to standard

therapy. Treatment with MARS was scheduled at low dose (up to ten sessions of 6-8 hours during 21 days) and the main endpoint was survival at 28 days.

Results showed a significant decrease in serum creatinine (20.0 ±33.1% vs. 6.4 ±33.5% p=0.02) and bilirubin (26.4 ±26.1% vs. 8.9 ±22.3% p=0.001) as well as higher improvement in the hepatic encephalopathy (estimated by the percentage of evaluations in which HE decreased from II-IV at inclusion to 0-I during therapy, 56% vs. 39% p=0.06) in the MARS group. The primary endpoint was not met however, with the proportion of patients dying within 28 days almost identical in both groups (40.8% vs 40.0%). Findings show that MARS at low dosage is a safe procedure which has significant dialysis effect and improves severe hepatic encephalopathy in patients with cirrhosis and rapid deterioration of their liver function; however a significant beneficial effect on survival could not be demonstrated.

More information:

References:

Rifai et al. Extracorporeal liver support by fractionated plasma separation and absorption (Prometheus®) in patients with acute-on-chronic liver failure (HELIOS study): a prospective randomized controlled multicenter study. Presented at the International Liver Congress 2010.

Bañares et al. Extracorporeal liver support with the molecular adsorbent recirculating system (MARS) in patients with acute-on-chronic liver failure. The RELIEF trial.

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