Potential role for artificial liver support devices

Results from a study presented at the International Liver Congress 2010 showed that treatment with an extracorporeal device 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 whose liver function is rapidly worsening. The study aimed to better understand the potential of a new device in terms of survival benefits for patients who suffer from cirrhosis. Prometheus is a new extracorporeal liver support system allowing the removal of protein bound and water soluble toxins by fractionated plasma separation and absorption.

In the study by Rafai et al (2010), 145 patients with cirrhosis and rapidly deteriorating liver function were recruited. Patients were randomized to standard medical therapy or standard medical therapy plus fractionated plasma separation and absorption and the primary end-points were survival at 28 and 90 days regardless of liver transplantation.

The difference in the overall survival was not statistically significant (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 Model for End-Stage Liver Disease (MELD) score >30 was a significant survival benefit seen with treatment with fractionated plasma separation and absorption (P=0.04 and P=0.02 respectively).

Professor Andrew Burroughs from the Royal Free Hospital NHS Trust, London, 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... 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.'

Rifai K, Kribben A, Gerken G et al (2010) 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. Abstract 141. International Liver Congress, Vienna, Austria: 14–18 April

Long-term prophylaxis of hepatitis B reinfection

The first subcutaneous hepatitis B immune globulin (Zutectra) is efficacious and well tolerated when used in long-term prophylaxis of hepatitis B re-infection after liver transplantation. These conclusions come from a phase III, open-label, prospective study presented during the Annual Meeting of the European Association for the Study of the Liver (Vienna, 14–18 April 2010).

The study included 23 patients who had undergone liver transplantation following hepatitis B-associated liver failure. Patients all had stable liver function at the start of the study and had received long-term prophylaxis with intravenous hepatitis B immune globulin (Hepatect) before switching to subcutaneous administration. During the 24 weeks of the study, hepatitis B surface antigen serum concentrations remained stable between 350 and 400 IU/litre, and no patient became re-infected with hepatitis B virus.

All except one of the patients were self-administering their subcutaneous treatment by the end of the study. The subcutaneous formulation was well tolerated, with no significant changes in laboratory parameters, vital signs or the patients' physical condition. Two patients developed injection site haematomas, which resolved within 1 and 4 days.

Commenting on the study Professor Giovan Di Constanzo, Naples, said: 'Subcutaneous hepatitis B immune globulin is a new step in improving prophylaxis and patient quality of life. Self-treatment is now a feasible option for patients.'

Hepatitis B prophylaxis with high-dose hepatitis B immune globulin and nucleoside/nucleotide analogues has lowered the hepatitis B virus re-infection rate to ≤4% after liver transplantation (Jiang et al, 2009). However, intravenous and intramuscular formulations cannot be self-administered and require regular hospital visits.

Subcutaneous hepatitis B immune globulin was approved in Europe at the end of 2009. It is administered once weekly, beginning at least 6 months after liver transplantation following initial prophylaxis with intravenous hepatitis B immune globulin.

Sue Lyon

Jiang L, Jiang LS, Cheng NS, Yan LN (2009) Current prophylactic strategies against hepatitis B virus recurrence after liver transplantation. *World J Gastroenterol* **15**(20): 2489–99

Pain severity and personal socioeconomic status linked

People suffering from severe pain are nine times more likely to be unable to work as a result of sickness compared to those who are not suffering from pain, according to data presented at the British Pain Society Annual Scientific Meeting in April.

The findings, looking at the pain status of 9419 adults, conclude that there is a significant association between pain and reduced mental health of an individual and socioeconomic disadvantage, having a considerable impact on society in terms of work production and costs to health services.

The study, funded by an unrestricted educational grant from Grunenthal, extracted data from the Health Survey for England 2005. The findings reinforce the link between severe pain and socioeconomic disadvantage: 51.8% of respondents in severe pain earned less than £15 600 per annum and 55.2% of this group were receiving non-pension-related benefits. These figures are more than halved in those who are not experiencing pain; 25.6% earned less than £15 000 and only 12.2% are receiving non-pension-related benefits.

Dr Joan Hester, Consultant in Pain Medicine at King's College Hospital, London, commented: 'The study highlights [the] limited awareness and understanding about the impact of persistent pain.'

Biomarkers may allow tailored rheumatoid arthritis therapy

Research presented at the British Society of Rheumatology annual conference reveals that rheumatoid arthritis patients who test positive to certain autoantibodies are more than twice as likely to achieve remission when taking rituximab (MabThera) plus methotrexate than those who test negative, effectively putting the painful and disabling disease into hibernation (remission: seropositive 13.2% *vs* seronegative 5.9% at 48 weeks).

Additionally, seropositive patients are three times more likely to experience a significant improvement in symptoms with rituximab than patients who are seronegative (ACR70: 20.9% *vs* 6.9% at 48 weeks). Approximately 80% of patients with rheumatoid arthritis (around 552 000 people in the UK) are seropositive for rheumatoid factor, one of the autoantibodies which was studied.

Professor John Isaacs, Professor of Clinical Rheumatology at Newcastle University and lead investigator, commented: 'This is an important breakthrough in the treatment of this chronic and debilitating condition, heralding the beginning of an exciting new era for patients, physicians and indeed the entire rheumatoid arthritis community.

Professor John Isaacs, Professor of Clinical Rheumatology, Newcastle University

He continued: 'Conventional practice is based on treating the patient population as a whole, leading to some patients cycling on ineffective treatments before achieving the optimum response. By identifying in advance which groups are most likely to respond to, or to have an enhanced response to, drugs like rituximab, we can ensure they are treated early enough to prevent irreversible joint damage and disability. Additionally this will reduce treatment costs by avoiding the use of ineffective drugs.'

Long-term lung deficits for very preterm babies

More than half of children who were born at 25 weeks or less have abnormal lung function and are twice as likely as their full-term peers to have a diagnosis of asthma, according to researchers from the Institute of Child Health in London, who followed a national cohort of extremely preterm infants to the age of 11 years (Fawke et al, 2010).

'Following extremely preterm birth, impaired lung function and increased respiratory morbidity persist into middle childhood, especially those with bronchopulmonary dysplasia,' said principal investigator, Janet Stocks, professor of respiratory physiology at the University College London, Institute of Child Health. 'Many of these children may not be receiving appropriate treatment.'

The researchers used data from the Medical Research Council-funded EPICure study, which tracked all babies born in the UK or Ireland at or below 25 completed weeks' gestation between March and December 1995. The children were assessed for lung function and respiratory health at 2.5, 6 and 11 years of age and compared to age-, gender- and race-matched peers at school who were randomly selected to serve as controls.

'For a variety of reasons, rates of preterm birth are increasing in developed countries,' explained Dr Stocks. 'Despite sophisticated medical interventions, we know that preterm birth is often associated with serious respiratory problems. We wanted to look at the longer-term implications of the complications as these children grow up.'

Of 307 children who survived to the age of 11 years, 182 completed satisfactory baseline spirometry at school, 129 (71%) of whom had had bronchopulmonary dysplasia. In addition to the finding that 56% of extremely preterm children had abnormal baseline spirometry, indicating impaired lung function and that one in four had a diagnosis of asthma, 27% had a positive bronchodilator response, indicating that their airway obstruction was at least partially reversible.

Furthermore, while nearly two-thirds (65%) had not had any respiratory symptoms for the past 12 months, nearly half (48%) of non-symptomatic extremely preterm children had abnormal spirometry results.

Fawke J, Lum S, Kirkby J et al (2010) Lung function and respiratory symptoms at 11 years in extremely preterm children: The EPICure Study. *Am J Respir Crit Care Med* 8 April (Epub ahead of print)

Sleep apnoea linked to increased risk of stroke

Obstructive sleep apnoea is associated with an increased risk of stroke in middle-aged and older adults, especially men, according to new research from the National Heart, Lung, and Blood Institute of the National Institutes of Health and published online in *American Journal of Respiratory and Critical Care Medicine*.

Shorter treatment for hepatitis C possible

24 weeks of treatment could be sufficient to cure between 93 and 100% of treatment-naïve chronic hepatitis C virus genotype 1 infected patients if they have a fast antiviral response to telaprevir with peginterferon and ribavirin, according to research presented at the International Liver Congress.

Extra burden of chemotherapy-induced neutropenia

Results from a new European study have shown that 33% of patients in the UK experienced an infection as a result of chemotherapy, of which 57% were associated with neutropenia or febrile neutropenia. This is despite the widespread availability of prophylactic treatments.