Improving outcomes for patients with ACLF

Dr J Wendon

Since 1975, the mortality rate for ACLF has fallen in Europe. Conversely, the mortality rate has increased in England and Wales, with a notable increase in Scotland. Dr Wendon discussed ways in which this UK trend might be reversed. She showed that in patients with cirrhosis and an episode of HE, a high protein diet made no difference to HE when compared with a low protein diet, but that protein turnover and breakdown increased with a low protein diet. Glucose and metabolic control improved mortality rate and improved hepatic mitochondrial ultrastructure in postoperative surgical patients. Increased intra-abdominal pressure was improved by drainage, and by administration of albumin and the vasoconstrictor terlipressin. Patients are at risk of infection after variceal bleeding and terlipressin is also used effectively in its treatment.

SIRS is often associated with HE in patients with chronic liver disease. Dr Wendon indicated that patients with HE should be given a standard protein, high-calorie diet with a vegetable based fibre content, lactulose and enemas, and non-absorbable antibiotics. She suggested that in these patients, therapies, such as L-ornithine-L-aspartate and benzoate, should be considered to decrease ammonia levels. Sedation for patients with ACLF may be necessary, but should only be undertaken in a critical care environment and significant numbers of such patients may require formal ventilation to protect their airway.

Use of temporary liver support

Professor R Williams CBE

Early clinical applications of temporary liver support began with haemodialysis and exchange transfusion in 1958. More recently bioartificial livers have been introduced but have not improved survival over standard care for FHF. The entirely artificial system, MARS®, based on albumin dialysis, has proved effective for survival over standard care for FHF. The entirely artificial system, MARS®, based on albumin dialysis, has proved effective for survival over standard care for FHF. The entirely artificial system, MARS®, based on albumin dialysis, has proved effective for survival over standard care for FHF. More recently bioartificial livers have been introduced but have not improved haemodialysis and exchange transfusion in 1958. More recently bioartificial livers have been introduced but have not improved haemodialysis and exchange transfusion in 1958. More recently bioartificial livers have been introduced but have not improved haemodialysis and exchange transfusion in 1958.

A number of devices exist to remove circulating toxins following liver failure and renal blood flow, and HE can be corrected. It is unclear whether these interventions improve patient survival without a transplant. Liver support needs to be used much earlier with early intensive care support, but it is not yet known whether this will reverse deterioration in the underlying liver disease.

Key points

- The UK should aim to improve treatment of ACLF as has been done in other European countries.
- In Sweden, treatment of oesophageal varices improved markedly between 1969 and 2002, resulting in shorter hospital stays (5.6 versus 10.1 days, P<0.001), lower patient costs (US $6000 versus $19 000, P<0.001), and a lower 30-day readmission rate (13 versus 29%, P=0.01), without an increase in resource use.

Is acute-on-chronic liver failure a distinct entity?

Dr R Jalan

Acute-on-chronic liver failure (ACLF) is the result of an acute insult superimposed on chronic decompensated liver disease. The pathophysiological basis of ACLF is due to precipitating events, such as sepsis, hepatic inflammation, drugs or bleeding, which induce an inflammatory response of the liver with resultant end-organ failure of the circulatory system, brain, liver and kidney.

Dr Jalan highlighted that there is great heterogeneity between groups of patients with ACLF, but that the aetiology of the disease and the causes of the acute insult are often indistinguishable from each other. A comparative study of patients admitted to hospital between 2000 and 2005 showed that on average, patients without organ failure were admitted 27 days after the appearance of symptoms, had an 8% ‘in-hospital’ mortality rate, and were discharged after 11 days. Patients with organ failure had a hospital mortality rate of 53% and a time from organ failure to death of 10 days. The latter group could then be further subdivided into those with recent decompensation (mortality rate, 78%) and those without decompensation (mortality rate, 34%).

Using four different scoring systems, it was apparent that patients with previous decompensation were likely to die with apparently less severe insults than those without previous decompensation. It was also concluded that the sepsis-related organ failure assessment (SOFA) score had greater prognostic power than other scoring systems, and had been validated for use with sequential data.

Key points

- ACLF may be defined as acute deterioration of chronic liver disease leading to at least one organ failure within 4–6 weeks, despite intervention to treat a defined precipitating factor.
- There are two types of ACLF:
  - type 1 occurs in patients admitted for decompensated liver failure in the previous 6 months, with a SOFA score of eight that does not improve from baseline.
  - type 2 occurs in patients without decompensation in the previous 6 months, with a SOFA score of nine that does not improve from baseline.
**Prognostic features**

*Professor PS Kamath*

In response to an acute insult in a patient with chronic liver disease cytokines may be released, leading to pre-ACLF, which may be reversible. However, Professor Kamath suggested that an acute insult resulting in ACLF and associated multiple organ dysfunction syndrome is unlikely to be reversible.

The prognosis for ACLF depends upon the severity of both the underlying liver disease and the insult. Two types of ACLF were defined – compensated cirrhosis (type 1), usually precipitated by major insults such as acute hepatits and surgery or infections; and decompensated cirrhosis (type 2), precipitated by infection or bleeding. Type 1 ACLF is potentially reversible but there is an initial rapid deterioration, sometimes linked to cerebral oedema, and patients benefit from liver support. In type 2 ACLF initial deterioration is slow, but both the potential for reversal and the benefit from liver support are low. The 3-month mortality rate for type 1 ACLF is 50% compared with 80% for type 2 ACLF.

Scoring systems for the prognosis of ACLF need to be diagnostic at the early stages to allow beneficial intervention. Retrospective studies have shown that the Mayo end-stage liver disease (MELD) score is a strong predictor of survival in ACLF, but is not as predictive for patients awaiting a liver transplant. Furthermore, use of the molecular adsorbent recirculating system (MARS®) for liver support was not a strong predictor of survival in ACLF, but is not as predictive for patients awaiting a liver transplant.

**Predictors of early post-operative mortality in cirrhotic patients undergoing surgery**

*W Sanchez, JA Talawalkar, PS Kamath*

This retrospective review of 379 patients with cirrhosis, who underwent surgery between 1988 and 2004, aimed to identify the clinical variables that may predict early death.

**Key points**

- None of the preoperative clinical variables studied, e.g. sodium, bilirubin or creatinine levels, or ASA patient class, were found to be associated with early mortality following surgery.
- Emergency surgery, longer operative times, and the need for aggressive medical support were more common in patients with early mortality compared to long-term survivors.
- Scores based on multi-organ dysfunction, such as the SOFA score, need further study.
- There may be unidentified intra-operative factors that trigger a systemic inflammatory response leading to ACLF.

**Is ACLF mediated by the systemic inflammatory response?**

*Dr R Stauber*

Bacterial infections in cirrhosis are common and are associated with spontaneous bacterial peritonitis (SBP), pneumonia, urinary tract infections, and an elevated C-reactive protein (CRP) level, which is a good indicator of sepsis and an independent predictor of death.

About one third of ACLF patients have bacterial infections, and the systemic inflammatory syndrome (SIRS) mediates several complications of cirrhosis including circulatory dysfunction and subsequent hepatorenal syndrome (HRS). SIRS also modulates hepatic encephalopathy (HE), and may have a role in hepatopulmonary syndrome and portopulmonary hypertension. In patients with acute liver failure mortality (%) is directly related to the number of SIRS components observed, e.g. zero components, 17%; one component, 28%; two components, 41%; three components, 65%. Furthermore, bacterial translocation from the gut leads to endotoxaemia and induction of nitric oxide synthase (iNOS), which causes a hypodynamic systemic circulation. In addition, oxidative stress, associated with enhanced plasma F2 isoprostane levels, leads to renal vasoconstriction (and HRS).

**Evaluation of four prognostic scores in patients with ACLF**

*RE Stauber, V Stadlbauer, G Struber, P Kaufman*

The aim of this study was to evaluate four prognostic scores commonly used in hepatology and intensive care medicine as predictors of in-hospital mortality in 71 patients with ACLF, admitted between 1995 and 2005, and analysed retrospectively.

**Key points**

- Management of ACLF in relation to SIRS requires:
  - Control of precipitants, with an aggressive search for infection and appropriately targeted antibiotic treatment, alcohol abstinence, and control of gastrointestinal bleeding.
  - Treatment of the inflammatory response by nitric oxide inhibition, antioxidants and anti-cytokine therapies.
  - Support of end organs with terlipressin/albumin for HRS and L-ornithine-L-aspartate for HE.
  - Consider extracorporeal liver support, if ACLF is unresponsive to standard medical treatment.

**The overall mortality of patients with ACLF in the 10 years studied was 66%.**

In patients with ACLF, global prognostic scores (Acute Physiology And Chronic Health Evaluation, SOFA) were superior to specific scores for liver dysfunction (CPS, MELD). Therefore, short-term survival in patients with ACLF is determined by end-organ failure rather than liver dysfunction.

CRP on admission was found to be an independent predictor of mortality implying an important role of infection for prognosis of ACLF.
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Consequences of acute bleeding
Professor AK Burroughs

Since 1960, the risk of mortality from variceal bleeding has declined from approximately 70 to 35%. Professor Burroughs showed that patients with cirrhosis have an impaired peripheral vasoconstrictor response arising from autonomic neuropathy. It is believed that bacterial infection and endotoxaemia may be major precipitants of bleeding because they increase portal pressure, impair liver function and impair blood coagulation. Patients with cirrhosis are particularly prone to endotoxaemia due to bacterial overgrowth, intestinal dysmotility and increased intestinal permeability.

Endotoxaemia is associated with priming of monocytes and an increase in levels of nitric oxide (NO) and tumour necrosis factor-alpha (TNF-α). Endotoxaemia increases the degree of bacterial translocation, further increasing NO and TNF-α levels and leads to systemic vasodilation, reduced vasoconstriction and an increased risk of bacterial infections. Bacterial infections are associated with variceal bleeding, renal failure, hepatocellular injury, encephalopathy and mortality.

The hepatic venous pressure gradient rises with the severity of SBP.

Antibiotics improve systemic haemodynamics and prevent early variceal rebleeding.

In future variceal bleeding is likely to be prevented by additional antibiotics, probiotics and prokinetics. Prokinetics will also aid in prevention of SBP.

Key points

Sepsis in ACLF
Dr D Patch

Patients with cirrhosis are prone to sepsis due to poor immune responses, often termed immune paralysis. Dr Patch reported that a prospective study revealed that bacterial infection occurs in 34% of patients with cirrhosis, and that 95% of these infections were community acquired and 41% were hospital acquired. Regardless of the source of infection, in-hospital mortality of patients with cirrhosis is 15% for infected patients versus 7% for uninfected patients.

Bacterial infections worsen liver dysfunction. In 33% of patients with cirrhosis there is bacterial overgrowth and altered small bowel motility, which causes delayed intestinal transit, and impairment of intestinal permeability due to portal hypertension. Bacterial translocation and endotoxaemia also occurs in many patients. In patients with cirrhosis, cisapride and antibiotics improve small bowel dysmotility. Propanolol prevents SBP and increases motility by reducing post-surgical infections.

Key points

Treatment of sepsis and cirrhosis should be performed by administration of appropriate antibiotics, pressor support using glypressin, modifying nutrition and regularly changing intravenous catheters. Albumin should be used for fluid management in SBP.

Future dangers of infection for patients with cirrhosis are likely to stem from methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus, multiresistant Klebsiella and multiresistant Acinetobacter.

The SOFA score may reflect mortality in the immediate postoperative period.

A scoring system using MELD, age, and ASA class may be used to make decisions on management of patients.

Before an operation, it may not always be possible to determine which patient will require liver support postoperatively.

Key points

Effects of extracorporeal liver support systems on serum cytokine levels
V Stadlbauer, P Krisper, R Aigner, B Haditsch, A Jung, C Lackner, RE Stauber

Cytokines are believed to play an important part in ACLF. The effects of two currently available extracorporeal liver support systems on cytokine levels were compared (ACLF: MARS® and the Prometheus FIBROspectSM II machine) in eight patients.

Neither MARS® nor Prometheus caused any changes in cytokine levels, although some cytokines were effectively cleared from plasma.

This lack of effect on serum cytokine levels may be due to a high rate of cytokine production in ACLF.

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The effects of precipitating events in ACLF

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Precipitating events: ACLF and surgery
Professor PS Kamath

Professor Kamath demonstrated that patients with cirrhosis had significantly reduced survival in the first 90 days following major surgery compared with outpatient controls and patients undergoing minor surgery (P=0.03). Beyond 90 days and up to 3 years, however, there was no change in survival in all three patient groups. Patient factors determining prognosis included the MELD score, age, and American Society of Anesthesiologists (ASA) patient classification. Older patients with high MELD scores and high ASA classifications were less likely to survive. Postoperative mortality was independent of the type of surgical procedure once these factors were taken into consideration, but depends on intra-operative factors, such as portal hypertension.

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Key points
Acute alcoholic hepatitis
Dr R Mookerjee

Dr Mookerjee discussed the effects of inflammation in alcoholic hepatitis (AH) on circulatory dysfunction and organ failure. Acute deterioration of liver function often occurs in active drinkers and is accompanied by histological inflammation, evidenced by SIRS, and increases in white blood cell count and CRP level. Anti-TNF-α treatment (e.g. pentoxifylline) reduces the portal pressure gradients, improves short-term survival in patients with AH, and reduces the risk of HRS. Inflammation and oxidative stress appear to reduce hepatic endothelial NOS (eNOS) activity which generates NO to maintain vascular tone. A decline in the level of NO leads in an increase in intrathoracic resistance. Inflammation also promotes a state of immune dysfunction by impairing neutrophil phagocytosis and decreasing monocyte-derived TNF-α and expression of human leukocyte antigens (HLA-DR), which participate in generation of the respiratory burst to kill bacteria.

Key points
- Improved characterisation of the pathophysiology of AH may identify better predictors of poor outcome and novel interventions to reverse ACLF progress.

Cardiovascular disturbance in ACLF
Professor P Hayes

In patients with cirrhosis there are severe disturbances of the cardiovascular system – the circulation becomes hyperdynamic, cardiac output increases, both blood pressure and systemic vascular resistance decrease, and there is an increase in plasma volume due to ascites and HRS. Professor Hayes showed that these disturbances are correlated with changes in albumin and bilirubin levels, alterations to the partial prothrombin time and with bleeding of the gastrointestinal tract. In patients with cirrhosis, peripheral vasodistension occurs accompanied by splanchnic vasoconstriction, with the exception of the liver circulation, which is bypassed. In fulminant hepatic failure (FHF) splanchnic and systemic arteriolar vasodilation are accompanied by low arterial-venous oxygen differential with consequent tissue ischaemia. More humoral factors are involved in FHF than in cirrhosis and these include NO, cytokines and toxins.

Key points
- A number of haemodynamic changes are associated with sepsis including:
  - Vasodilation of resistance arteries.
  - Myocardial dysfunction (due to circulating factors such as TNF-α and interleukin-1β).
  - Loss of autoregulation of cerebral blood flow.

The pathophysiology of renal failure in ACLF
Dr R Marley

Renal failure is a common and frequently terminal consequence of acute on chronic liver failure. There are several causes of deterioration in renal function which should be considered in addition to the hepatorenal syndrome (HRS). HRS is a consequence of intense renal vasoconstriction, the pathophysiology of which is multifactorial. Contributing factors include activation of the sympathetic nervous system, an imbalance between vasoconstrictors and vasodilators, and possibly activation of a hepatic reflex.

The exact contribution of endogenous vasoconstrictors, such as endothelin and prostaglandins, and endogenous vasodilators, such as nitric oxide, remains to be fully clarified. Such systems provide potential targets for pharmacological therapies. A potential area of interest is the involvement of adenosine and adenosine receptors in mediating a neural reflex altering renal blood flow as a consequence of changes in portal blood flow.

Key points
- Renal failure in acute on chronic liver failure has several causes, including development of HRS.
- Intense renal vasoconstriction is the hallmark of HRS.
- The exact pathogenesis of the HRS has not been elucidated.

The pathophysiologic basis of hepatic encephalopathy in ACLF: central role for ammonia and inflammation
Dr D Shawcross

Patients with liver dysfunction have impaired urea synthesis, which results in hyperammonaemia, and the brain acts as an alternative detoxification pathway. Astrocytes convert ammonia to glutamine causing them to swell, resulting in cerebral oedema and increased intracranial pressure (ICP). Dr Shawcross suggested in cirrhosis, there may be low-grade cerebral oedema associated with Alzheimer type II astrocytosis and neuropsychological dysfunction.

Sepsis is a frequent precipitant of HE and recent studies suggest that inflammation and its cytokine mediators (TNF-α and the interleukins-6 and -8), which may be generated by astrocytes, could be important in modulating the cerebral effect of ammonia in liver disease. NO has also been implicated in HE pathogenesis and may form peroxynitrite due to the interaction of increased astroglial NO with superoxide.

Key points
- Astrocytes are the cells most commonly involved in the pathogenesis of HE.
- Inflammation is critical in modulating the manifestation of HE.
- The production of reactive oxygen species and increased protein tyrosine nitration may alter astrocyte function and contribute to or precipitate episodes of HE.

Goal directed therapy
Dr N Murphy

Goal directed therapy (GDT) attempts to predefine resuscitation endpoints because clinical signs are subjective and can be misleading. In patients with shock and subsequent end-organ dysfunction it is important to restore adequate perfusion pressure and flow as rapidly as possible to improve oxygen delivery (DO2) to the organs. In some high risk surgical patients increasing global DO2 above normal may be beneficial, but in patients with sepsis and/or septic shock, additional care is needed to reduce organ failure and mortality. ACLF management includes prevention of sepsis with antibiotics, early adequate resuscitation and diagnosis, counteraction of circulatory changes using vasoconstrictors such as norepinephrine or noradrenaline, and volume expansion with albumin or starch. Using a “care bundle” approach provides a framework on which to base and audit care for a patient group, and may be a way to improve the management of patients with ACLF.

Key points
- Adequate endpoints for resuscitation are difficult to define and recognise clinically.
- Early GDT, and resuscitation before organ failure to defined endpoints, improves mortality in patients with sepsis and in high-risk surgery.
- Late GDT, once organ failure has occurred, is not associated with improved outcome.
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Scoring prognosis in ACLF

Dr E Forrest
The desirable features of a clinical score are that it should be calculable at the bedside, reproducible, valuable both as a ‘one-off’ and as an ‘over-time’ measurement, act as an aid to directing clinical decisions, and be applicable in most clinical settings with readily available data. Although the Childs-Turcotte-Pugh (CTP) score is easy to calculate and clinically based, it has limited discriminatory ability. There is subjectivity of assessment of ascites and encephalopathy, and laboratory variation in measurement of plasma prothrombin time (PT). In comparison, the MELD score is objective, statistically calculated, and assesses renal function, but is difficult to calculate, and relies on variable measurements of creatinine and international normalised ratio (INR) for clotting. Both scores give very similar assessments of patient mortality, but only the MELD score gives an assessment of the probability of renal failure. Disease-specific scores may also be used in ACLF, e.g. the Glasgow Alcoholic Hepatitis Score (GAHS) where there is clinically relevant alcoholic hepatitis.

Key points
Improved characterisation of the pathophysiology of AH may identify better predictors of poor outcome and novel interventions to reverse ACLF progress.

Key points
In compensated chronic liver disease the CTP and MELD scores are equally useful.

In decompensated chronic liver disease the MELD score has more utility.

For disease-specific exacerbation of chronic liver disease, disease-specific scores, e.g. the GAHS, are of greater value than either the CTP or MELD scores.

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Astrocytes are the cells most commonly involved in the pathogenesis of HE.

Inflammation is critical in modulating the manifestation of HE.

The production of reactive oxygen species and increased protein tyrosine nitration may alter astrocyte function and contribute to or precipitate episodes of HE.

Cardiovascular disturbance in ACLF

Professor P Hayes
In patients with cirrhosis there are severe disturbances of the cardiovascular system – the circulation becomes hyperdynamic, cardiac output increases, both blood pressure and systemic vascular resistance decrease, and there is an increase in plasma volume due to ascites and HRS. Professor Hayes showed that these disturbances are correlated with changes in albumin and bilirubin levels, alterations to the partial prothrombin time and with bleeding of the gastrointestinal tract. In patients with cirrhosis, peripheral vasoconstriction occurs accompanied by splanchnic vasoconstriction, with the exception of the liver circulation, which is bypassed. In fulminant hepatic failure (FHF) splanchnic and systemic arterial vasodilation are accompanied by low arterio-venous oxygen differential with consequent tissue ischaemia. More humoral factors are involved in FHF than in cirrhosis and these include NO, cytokines and toxins.

Key points
A number of haemodynamic changes are associated with sepsis including:

- Vasodilation of resistance arteries.
- Myocardial dysfunction (due to circulating factors such as TNF-α and interleukin-1β).
- Loss of autoregulation of cerebral blood flow.

Goal directed therapy

Dr N Murphy
Goal directed therapy (GDT) attempts to predefine resuscitation endpoints because clinical signs are subjective and can be misleading. In patients with shock and subsequent end-organ dysfunction it is important to restore adequate perfusion pressure and flow as rapidly as possible to improve oxygen delivery (DO2) to the organs. In some high risk surgical patients increasing global DO2 above normal may be beneficial, but in patients with sepsis and/or septic shock, additional care is needed to reduce organ failure and mortality. ACLF management includes prevention of sepsis with antibiotics, early adequate resuscitation and diagnosis, counteraction of circulatory changes using vasocomstutors such as teflafen and noradrenaline, and volume expansion with albumin or starch. Using a “care bundle” approach provides a framework on which to base and audit care for a patient group, and may be a way to improve the management of patients with ACLF.

Key points
Adequate endpoints for resuscitation are difficult to define and recognise clinically.

Early GDT, and resuscitation before organ failure to defined endpoints, improves mortality in patients with sepsis and in high-risk surgery.

Late GDT, once organ failure has occurred, is not associated with improved outcome.

The pathophysiology of renal failure in ACLF

Dr R Marley
Renal failure is a common and frequently terminal consequence of acute on chronic liver failure. There are several causes of deterioration in renal function which should be considered in addition to the hepatorenal syndrome (HRS). HRS is a consequence of intense renal vasoconstriction, the pathophysiology of which is multifactorial. Contributing factors include activation of the sympathetic nervous system, an imbalance between vasoconstrictors and vasodilators, and possibly activation of a hepatorenal reflex.

The exact contribution of endogenous vasoconstrictors, such as endothelin and prostaglandins, and endogenous vasodilators, such as nitric oxide, remains to be fully clarified. Such systems provide potential targets for pharmacological therapies. A potential area of interest is the involvement of adenosine and adenosine receptors in mediating a neuronal reflex altering renal blood flow as a consequence of changes in portal blood flow.
Improving outcomes for patients with ACLF
Dr J Wendon

Since 1975, the mortality rate for ACLF has fallen in Europe. Conversely, the mortality rate has increased in England and Wales, with a notable increase in Scotland. Dr Wendon discussed ways in which this UK trend might be reversed. She showed that in patients with cirrhosis and an episode of HE, a high protein diet made no difference to HE when compared with a low protein diet, but that protein turnover and breakdown increased with the high protein diet. Glucose and metabolic control improved mortality rate and improved hepatic mitochondrial ultrastructure in postoperative surgical patients. Increased intra-abdominal pressure was improved by drainage, and by administration of albumin and the vasoconstrictor terlipressin. Patients are at risk of infection after variceal bleeding and terlipressin is also used effectively in its treatment.

SIRS is often associated with HE in patients with chronic liver disease. Dr Wendon indicated that patients with HE should be given a standard protein, high-calorie diet with a vegetable based fibre content, lactulose and enemas, and non-absorbable antibiotics. She suggested that in these patients, therapies, such as L-ornithine-L-aspartate and benzoate, should be considered to decrease ammonia levels. Sedation for patients with ACLF may be necessary, but should only be undertaken in a critical care environment and significant numbers of such patients may require formal ventilation to protect their airway.

Use of temporary liver support
Professor R Williams CBE

Early clinical applications of temporary liver support began with haemodialysis and exchange transfusion in 1958. More recently bioartificial livers have been introduced but have not improved survival over standard care for FHF. The entirely artificial system, MARS®, based on albumin dialysis, has proved effective for removal of albumin bound toxins including free fatty acids, bile acids, tryptophan, bilirubin, phenol, ammonia, drugs with high protein bound ratios up to 50 kDa and aromatic amino acids. When using MARS®, renal blood flow and cerebral perfusion are improved, portal pressure is decreased, and there is little effect on mean arterial pressure. Furthermore, daily albumin dialysis with MARS® results in rapid improvement of HE in comparison with standard treatment. Similar results may be obtained with the recently introduced Prometheus device based on fractionated plasma separation.

Key points

SIRS is often associated with HE in patients with chronic liver disease.

Dr-j-wendon.jpg

Acute-on-Chronic Liver Failure
University College London, Friday 21 April 2006

Is acute-on-chronic liver failure a distinct entity?
Dr R Jalan

Acute-on-chronic liver failure (ACLF) is the result of an acute insult superimposed on chronic decompensated liver disease. The pathophysiological basis of ACLF is due to precipitating events, such as sepsis, hepatic inflammation, drugs or bleeding, which induce an inflammatory response of the liver with resultant end-organ failure of the circulatory system, brain, liver and kidney.

Dr Jalan highlighted that there is great heterogeneity between groups of patients with ACLF, but that the aetiology of the disease and the causes of the acute insult are often indistinguishable from each other.

A comparative study of patients admitted to hospital between 2000 and 2005 showed that on average, patients without organ failure were admitted 27 days after the appearance of symptoms, had an 8% ‘in-hospital’ mortality rate, and were discharged after 11 days. Patients with organ failure had a hospital mortality rate of 53% and a time from organ failure to death of 10 days.

The latter group could then be further subdivided into those with recent decompensation (mortality rate, 78%) and those without decompensation (mortality rate, 34%).

Using four different scoring systems, it was apparent that patients with previous decompensation were likely to die with apparently less severe insults than those without previous decompensation. It was also concluded that the sepsis-related organ failure assessment (SOFA) score had greater prognostic power than other scoring systems, and had been validated for use with sequential data.

Key points

- ACLF may be defined as acute deterioration of chronic liver disease leading to at least one organ failure within 4–6 weeks, despite intervention to treat a defined precipitating factor.

- There are two types of ACLF:
  - type 1 occurs in patients admitted for decompensated liver failure in the previous 6 months, with a SOFA score of eight that does not improve from baseline.
  - type 2 occurs in patients without decompensation in the previous 6 months, with a SOFA score of nine that does not improve from baseline.