

Critical Care of the Liver Transplant ICU Patients: A Pittsburgh “Point of View”

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Abstract

The purpose of this review is to summarize the advances in critical care management of the liver transplant ICU patients (patients with end stage liver disease, before and after orthotopic liver transplant). The review is based on search of Medline literature, with a focus on liver failure patients and critical care issues around liver transplantation.

Starzl Transplantation Institute at the University of Pittsburgh Medical Center is one of the global leaders in the treatment of end stage liver disease (ESLD). This review is in part based on our work in the 28-bed liver transplant ICU at Montefiore Hospital, University of Pittsburgh Medical Center, in Pittsburgh, PA.

Over the past few years, our understanding of the several important pathophysiologic markers

Patients with end stage liver disease (ESLD) before and after orthotopic liver transplant (OLT) are complex clinical population with specific critical care requirements.

Intensive care units play important role in the care of liver failure patients. These patients are usually as challenging as patients with advanced sepsis, with several important similarities: “redistributional” hemodynamic instability, marginal respiratory status, frequent adrenal insufficiency, common renal failure, etc.

The patients with ESLD may present with progressive deterioration in hemodynamic, metabolic, endocrine, pulmonary, and nutritional status. Post

of end stage liver disease has been significantly improved. For example, we do now much better understand hyperdynamic circulation of liver failure, hepatorenal syndrome and its consequences, the role of TIPSS (transjugular intrahepatic portosystemic shunt) and adrenal insufficiency in liver failure patients. The management and prophylaxis of variceal bleeding and subacute bacterial peritonitis (SBP), has been successfully standardized.

These and other advances in understanding of ESLD pathophysiology and its clinical results, have certainly contributed to more promising outcomes in the ICU management of these complex patients.

transplant many of these complex derangements may initially continue, and certainly this is an additional challenging task for the critical care team.

Cardiovascular Response in ESLD (“Hyperdynamic” Circulation in Patients with Liver Failure)

It is traditionally believed that liver failure is associated with hyperdynamic circulation. However, hemodynamic measurements show that, while splanchnic vascular bed is markedly vasodilated and blood flow is increased, there is actually a significant reduction in blood flow and vasoconstriction in the upper and lower limbs and extrasplanchnic viscera including brain and kidneys. This “splanchnic steal” phenomenon [1] appears to be the fundamental cardiovascular consequence of liver failure.

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Interestingly, TIPSS – transjugular intrahepatic porto-systemic shunt, frequently inserted in patients with end stage liver disease (ESLD), to reduce the risk of life threatening variceal bleeding or to decrease ascites production by controlling portal hypertension through increased collateral shunting, although created to “unload” splanchnic circulation in the direction of systemic - may actually exacerbate hemodynamic derangements in cirrhosis leading to increase in cardiac output and progression of peripheral vasoconstriction.

A long acting analogue of vasopressin - terlipressin causes selective splanchnic vasoconstriction and thus improves blood pressure and renal function by reducing the splanchnic steal of blood and by diverting blood to the systemic circulation [2]. By the same token, because of its significant splanchnic vasoconstrictive effect, continuous intravenous “low dose” infusion of vasopressin may be a logical choice for hemodynamic resuscitation in ESLD patients. (Terlipressin is not U.S. Food and Drug Administration approved, and is unavailable for clinical use in the U.S.).

Another splanchnic vasoconstrictor, a somatostatin analogue octreotide can help correct the hemodynamic disturbances in cirrhosis and increase in systemic blood flow, although this is not universally accepted. In our institution, we “routinely” use octreotide i.v. drip perioperatively for all living donor liver transplant recipients, because of proposed interdependence between decrease in portal blood flow and increase in critical hepatic arterial blood flow. There is a little role, if any, for the use of low-dose dopamine (up to 5 µg/kg/min) for the unstable ESLD and liver transplant patients. Although this pressor may be preferred by some transplant surgeons, because of its lack of alpha-agonism at this dosing level, there is no benefit in producing splanchnic vasodilatation with “renal dose dopamine” in these patients, with already pathologically dilated splanchnic vascular bed.

The adrenoceptor agonist, norepinephrine (noradrenaline), appears to be as effective as terlipressin in liver failure patients, and especially patients with hepato-renal syndrome (HRS). It seems that norepinephrine should be given in combination with intravenous albumin [3]. Cardiovascular effects (ventricular arrhythmias), although rare, have been reported.

Fluid Resuscitation

Fluids high in sodium are generally avoided in patients with end stage liver disease because of the activated renin-angiotensin-aldosterone axis, which results in ardent sodium and total body water retention. 0.45% sodium chloride solution, with addition of 5% Dextrose is used as a crystalloid solution of choice in liver failure patients, at our institution. The use of 25% human concentrated “salt poor” albumin solution (SPA) in fluid maintenance and resuscitation has theoretical advantages, given the potential to restore oncotic pressure and encourage intravascular mobilization of fluid in hypoalbuminemic patients. The albumin molecule has anti-oxidant, anti-inflammatory and drug and hormone-binding properties. They are all potentially beneficial in liver failure patients.

The clinical complexity of human albumin solution (HAS) has led to analysis of outcomes in the general intensive care unit population, most recently in the large Saline versus Albumin Fluid Evaluation trial [4] and in meta-analyses [5]. No survival benefit in those resuscitated with HAS have been seen in the large randomized controlled trials. However, the evidence for a specific benefit in liver failure patients is stronger.

A recent, unfortunately not controlled, study by a group from Barcelona [6], has added more weight to this claim. They monitored hemodynamic parameters in 12 patients with cirrhosis during treatment with HAS, and detected an increase in left ventricular stroke work index (76–97 g*m per m²) and systemic vascular resistance (635–770 dyne*s per cm⁵). Although a rise in preload as a result of fluid repletion was supported by increases in right atrial pressure, pulmonary capillary wedge pressure, and deactivation of the renin-angiotensin system, the authors hypothesized that the ability of HAS to bind cardio depressant cytokines, TNF-alpha and nitric oxide, may have also contributed to the improvement in cardiac function in these patients.

Respiratory Compromise

Patients with end stage liver disease have minimal respiratory reserve and do not tolerate respiratory compromise well. Endotracheal intubation

and ICU readmission in these patients, already “immunocompromised” because of ESLD, Kupffer cells and neutrophil dysfunction, promote infection and increase mortality. Levy *et al* reviewed the reasons for ICU readmission following liver transplantation and concluded that the most common cause for ICU readmission was cardiac and respiratory failure, which emphasizes the importance of fluid balance and optimal fluid therapy at all the times [7].

Certainly, fluid overload and heart failure are not the only cause of pulmonary edema in the ESLD patients, especially when transplanted. A brief but well designed study by Yost *et al* collected the endotracheal fluid within 15 minutes of the development of acute pulmonary edema in OLT patients - perioperatively. No patient had hemodynamic parameters consistent with a hydrostatic pulmonary edema and cardiac dysfunction. Six of the seven patients whose edema fluid was analyzed had edema fluid/plasma protein ratios ≥ 0.75 , characteristic of increased permeability pulmonary edema [8]. The authors speculated that the most likely cause of the reaction is transfusion-related acute lung injury (TRALI), although it is clear that other elements, such as reperfusion of the newly implanted liver, or the effect of immune “preconditioning” agents administered during transplant procedure (alemtuzumab frequently used in our transplant program), could not be ruled out as the contributing factor.

Reperfusion of the donor liver during the orthotopic liver transplantation, especially when combined with transfusion of blood products, historically is known to be sometimes associated with, potentially severe form of acute lung injury, although certainly rare today, as a result of improvements in organ preservation solutions and organ transfer techniques.

A clinical hypothesis was postulated connecting frequently unexpected development of pulmonary edema with liver allograft failure and reestablishment of hyperdynamic circulation, adding nonhydrostatic pulmonary edema to the list of clinical signs that may herald acute rejection of the transplanted liver [9].

Although ***endotracheal intubation with mechanical ventilation remains the “therapy of choice” in critically ill patients with ESLD,***

noninvasive ventilation (NIV) is an attractive option for respiratory compromised liver failure patients, and may allow ESLD patients to remain “safely nonintubated” with satisfactory oxygenation, while “fluid imbalance” is dealt with. To date, 2 randomized controlled studies have been performed to test this hypothesis. In a prospective, randomized trial, Antonelli *et al* [10] showed the advantage of NIV in significantly improving the outcome of patients undergoing solid organ transplantation who developed acute respiratory failure. In this randomized, prospective study from Italy 40 solid organ transplant recipients (with liver, renal or lung transplant) and with acute respiratory failure (respiratory rate $>35/\text{min}$, $\text{PaO}_2/\text{FiO}_2 <200$, or presence of clinical respiratory distress and use of accessory muscles), received either supplemental oxygen therapy or noninvasive (face mask) positive pressure ventilation. All patients were treated with chest physiotherapy and incentive spirometry. The early administered noninvasive ventilation group had fewer intubation (4 of 20 vs 10 of 20), a shorter ICU stay (5.5 vs 9 days), and decreased hospital mortality (7 of 20 vs 11 of 20).

Hilbert *et al* [11] also demonstrated in a prospective randomized controlled study conducted in immunosuppressed patients with pneumonitis and hypoxemic acute respiratory failure, that early application of NIV was effective in avoiding endotracheal intubation in comparison with standard oxygen supplementation. Patients randomized to NIV had significantly lower rates of endotracheal intubation, major or fatal complications, and intensive care unit and hospital mortality. Even though further studies are needed, avoiding intubation should be an important objective in the management of respiratory failure in immunocompromised patients, and NIV may help achieve that goal.

Porto pulmonary hypertension (PPHTN), affecting 5-10% patients with end stage liver disease is defined by both portal hypertension in combination with mean pulmonary arterial pressure >25 mmHg, with no evidence of left heart failure ($\text{P}_{\text{cwp}} <15$ mmHg). The pathogenesis of this condition involves both vasoconstriction and microthrombosis, and when severe (mean Pa pressure >45 mmHg), carries prohibitive high mortality, when OLT performed [12]. The role of liver transplantation in PPHTN

is not clear because of the increased intraoperative and postoperative mortality, and actually reports of worsening pulmonary hypertension after OLT. In our transplant center, patients with established diagnosis of PPHTN are not transplanted: these unfortunate patients are “inactivated” on the transplant list, pending treatment for pulmonary hypertension.

On the contrary, *hepatopulmonary syndrome (HPS)* is characterized with pulmonary vasodilatation, clinically presenting as hypoxemia with right-to-left shunting, increased alveolar-arterial oxygen gradient, and absence of intrinsic cardiopulmonary pathology. Intrapulmonary vascular dilatations are the major cause of hypoxemia in HPS. The exact cause of the pulmonary vascular dilatations and impaired vasoconstriction remains poorly understood. Platypnea and orthodeoxia are common in patients with HPS because the intrapulmonary vascular dilatations that underlie these two manifestations are predominantly found in the lower lung fields. Liver transplantation remains the only curative option, with resolution of the syndrome described to occur within days of transplant and up to 15 months after transplantation [13].

Renal Dysfunction, Ascites and Hepatic Hydrothorax

Hepatorenal syndrome (HRS) could be understood as an adverse manifestation of renal response to portal hypertension and liver disease. Hepatorenal syndrome is present in 7-15 % of liver failure patients, and may present as: *type I*, rapidly progressive, usually triggered by a discrete event and associated with high mortality, and *type II* is characterized with slow, but stable decrease in glomerular filtration rate (GFR) [14]. The understanding of central role of portal hypertension and ascites has important implications for the treatment of renal dysfunction in cirrhotic patients.

Previously considered fatal without liver transplantation, treatment with vasoconstrictors and albumin has been demonstrated to improve renal function in patients with type I HRS. The best treatment is prevention, with aggressive treatment of any derangement exacerbating pre-renal pathophysiology of hepatorenal syndrome. For example, in patients with spontaneous bacterial peritonitis, a dose of intravenous

albumin on diagnosis and 2 days later decreased the development of hepatorenal syndrome and renal failure from 33% to 10% in a prospective randomized trial [15]. Treatment of portal hypertension with insertion of a transjugular portosystemic shunt (TIPSS) also improves renal function and decreases mortality [16].

A small study treated 12 patients with hepatorenal syndrome with 1 week of intravenous long acting vasopressin analogue terlipressin, in addition to intravenous albumin. Renal function improved, with creatinine decreasing by half and median urinary sodium increasing almost fivefold [17]. However, the beneficial effects on renal function were temporary, and the only survival benefit was provided by performing OLT.

Liver transplantation is considered the best definitive treatment for HRS. A review of the literature would suggest that renal function improves in most patients with HRS after the orthotopic liver transplantation. However, in recently published study from University of Pittsburgh Medical Center Drs. Marik, Wood and Starzl have shown that type I HRS resolved in only 58% of patients post-transplantation. They reviewed the hospital course of 28 patients who met the International Ascites Club criteria for type I HRS and who underwent orthotopic liver transplant [18].

Immediate improvement of renal function following transplantation was observed in only two patients in this study. The mean time to resolution of HRS was 21 ± 27 days, with a range of 4–110 days. Alcoholic liver disease, as a cause of ESLD independently predicted the failure of HRS to resolve after transplantation. But, the authors were unable to accurately define that group of patients with HRS who required long-term dialysis and could theoretically benefit from combined liver–kidney transplantation. When *portal hypertensive ascites* is present, the best option is to direct the treatment to the cause of ascites. A serum-to-ascites albumin gradient (SAAG) greater than 1.1 suggests it is portal hypertension due to liver cirrhosis causing ascites. Common cirrhotic ascites is managed with diuretics and sodium restriction [19]. Usually, both anti-aldosterone agents (spironolactone) and loop-diuretics (furosemide) are used. Rapid diuresis can precipitate hepatorenal syndrome, and should be

avoided if possible. Unfortunately, ascites usually with progression of liver cirrhosis, becomes less treatable conservatively. If patients no longer respond to 400 mg of spironolactone and 160 mg of furosemide daily, they are understood to have “refractory ascites”

Large-volume paracentesis (greater than 5 lit.) was shown to be safe and effective. When performing large-volume paracentesis in patients with end stage liver disease, an infusion of 12.5 g (50 ml of 25% solution) of albumin i.v., for each liter of ascites removed, prevents the development of hemodynamic instability, often associated with large fluid shifts. The treatment of portal hypertension with insertion of transjugular portal systemic shunt (TIPSS) was shown to improve renal function in cirrhotic, and to decrease mortality.

When a patient presents with a large unilateral, frequently symptomatic, pleural effusion (hepatic hydrothorax), available data strongly argue against placing a chest tube. This procedure is prone to complications, and is largely ineffective. Simple, repeated aspiration or “pigtail” percutaneous catheter drainage are apparently safer and recommended [20]. Also, when maximal medical treatment fails, transjugular intrahepatic portosystemic shunting (TIPSS) is the procedure of choice (or temporizing measure of choice) for symptomatic hepatic hydrothorax. Since hepatic hydrothorax usually means advanced liver failure, OLT is the only real treatment, with long lasting benefit for the patient.

Post-transplant Kidney Injury and Hypertension

Calcineurin inhibitors (CNI) cyclosporine - A and tacrolimus are almost mandatory part of modern immunosuppressive regimen following orthotopic liver transplant. Nephrotoxicity is a serious side effect of CNI therapy and it has been attributed primarily to renal hemodynamic alterations, caused by afferent arteriolar vasoconstriction. The *calcium channel blockers* (CCB) have the capacity to counteract the direct vasoconstrictive effect on renal afferent arteriole of cyclosporine and tacrolimus. Also, the effect of other vasoconstrictors, such as endothelin or thromboxane, stimulated by CNI therapy is reversed by calcium antagonists [21].

Progressive decline in renal function is the most severe in the first 3–12 months after transplant. Other predictors of chronic renal failure include older recipient, pre-transplant renal failure, female sex, cyclosporine (compared to tacrolimus), hepatitis C pre-transplant, and pre-transplant diabetes [22]. Late toxicity associated with CNIs is frequently seen with typical, although nonspecific renal histologic lesions (isometric tubular vacuolization).

Hypertension is the most common cardiovascular complication after liver transplantation. Systemic vasoconstriction underlies transplant hypertension, but the mechanisms contributing to this remain incompletely understood [23]. Elevation in plasma endothelin - ET-1 and an increase in arterial stiffness are potential important mechanisms underlying the development of hypertension after liver transplant. During the first 6 months, the renin-aldosterone system does not play a significant role in post transplant hypertension in liver transplant recipients. In contrast to being the main causes of death following kidney transplantation, cardiovascular diseases are of lower importance following OLT [24]. This may be due to the fact that diabetes mellitus, one of the main cardiovascular risk factors, is very often the contributing factor of kidney failure in renal transplant recipients. In addition, advanced cardiovascular illness is an exclusion criterion for OLT in most centers. It seems logical to recommend the routine use of calcium channel blockers for treatment of post transplant hypertension in OLT patients. It should be remembered that some calcium antagonists such as verapamil, diltiazem and nicardipine may increase serum level of cyclosporine or tacrolimus, so that daily dosing of these medications should be appropriately adjusted to achieve the wanted level.

Diagnosis and Treatment of Spontaneous Bacterial Peritonitis (SBP)

The prevalence of spontaneous bacterial peritonitis (SBP) among hospitalized patients has remained stable during the past 3 decades, ranging between 12% and 21%. However, mortality from SBP has declined from a 15% to 50% range, to an 8% to 17% range, as a result of improvement in diagnosis and treatment. Renal dysfunction is the most important

predictor of death in spontaneous bacterial peritonitis. Intravenous albumin prevents renal failure and improves survival in spontaneous bacterial peritonitis [25].

A randomized unblinded study performed in patients with spontaneous bacterial peritonitis showed that albumin (n = 10), but not hydroxyethyl starch (n = 10), increased arterial pressure and suppressed plasma renin activity significantly, indicating hemodynamic improvement [26]. Current practice guidelines for the management of ascites have included standardized methods for the paracentesis technique and for ascitic fluid analysis. Accepted definition of SBP that describe the broad clinical spectrum of SBP (laboratory confirmation of ascitic neutrophile $>250/\text{mm}^3$), now identify more individuals who are eligible for prophylaxis and therapy. Clinical trials demonstrating the safety and efficacy of nonnephrotoxic systemic antibiotics have been incorporated into clinical practice [27]. Observational studies have identified clinical risk factors for index and recurrent SBP with subsequent confirmation of beneficial effects from antibiotic prophylaxis. In one of the studies, the use of intravenous albumin with cefotaxime compared with antibiotic monotherapy was associated with significant improvements in renal impairment and survival among selected patients [28].

Management of Variceal Bleeding

Variceal bleeding is one of the most frequent causes of death in patients with cirrhosis and portal hypertension. Advances in treatment have been made in pharmacotherapy to reduce splanchnic blood flow and portal pressure and in the prevention of infection in this immunocompromised group of patients.

The uses of TIPSS in well-chosen patients and improvements in supportive care have further decreased the mortality. A large body of evidence supports the use of beta-blockers for the prophylaxis of esophageal variceal bleeding in patients with cirrhosis. Eleven RCTs (randomized controlled trials) have shown a 40% risk reduction with use of beta-blockers as primary prophylaxis against index esophageal variceal hemorrhage (change in incidence from 25% to 15% during 2 years). Propranolol (9 RCTs) and nadolol (2 RCTs) appeared equally effective. These agents are

also recommended for use in secondary prophylaxis of variceal bleeding. Patients with medium to large esophageal varices and no evidence of ascites benefited the most [29]. No overall survival benefit was seen in the first trial of recombinant factor VIIa in upper gastrointestinal bleeding (variceal and non-variceal) in 245 patients with cirrhosis [30].

Infection after a variceal bleed is very common, affecting up to 66% within 2 weeks of the event. This put these patients in risk of sepsis, affecting coagulation negatively and may contribute to ongoing elevations in portal pressure, with increased risk of re-bleeding. A randomized control trial in 120 patients tested antibacterial prophylaxis (ofloxacin) in clinically uninfected patients who bled versus antibiotics given only when infection was suspected or diagnosed. Those in the prophylactic arm had a reduced risk of re-bleeding in the first 7 days post-index bleed (7% versus 34%), and also required less transfused blood. Survival was not influenced [31].

Successful liver transplant and functional allograft almost completely remove the risk of the variceal (re)-bleeding. Upper gastrointestinal (UGI) bleeding happens in liver transplant recipient and it affects negatively the outcome and long term survival in these patients, as shown in an earlier study from UPMC [32]. But, as long as the liver allograft is performing well, UGI bleeding in liver transplant recipient is never the result of bleeding varices. (Good liver allograft and variceal bleeding cannot “co-exist”).

The Hepatoadrenal Syndrome: “A Common Yet Unrecognized Clinical Condition” [33]

The main finding of this recent study from University of Pittsburgh Medical Center was the surprisingly high incidence of adrenal failure in critically ill patients with liver disease, an entity for which the authors have coined the term “hepatoadrenal syndrome.” In this study, a random cortisol level was used to diagnose adrenal insufficiency in highly stressed, critically ill patients and also a low-dose (1- μg) cosyntropin test in less severely stressed ICU patients. Using this diagnostic approach, 72% of the patients studied had adrenal insufficiency. The authors found no correlation between the serum cortisol and serum-albumin levels, negating the postulate

that low cortisol levels may merely be a function of low levels of cortisol binding globulin with normal free cortisol levels. Furthermore, the hemodynamic response to hydrocortisone provides compelling evidence to support the conclusion that low cortisol levels are clinically relevant and that treatment with hydrocortisone may be beneficial.

In patients with adrenal insufficiency, the mortality rate was lower in those patients treated with glucocorticoids. Although this was a nonrandomized study, these data support the contention that treatment of critically ill patients with adrenal insufficiency (low baseline cortisol level) may improve outcome.

The association between low serum HDL levels and adrenal insufficiency that was observed in this study further supports the notion that liver disease may lead to impaired cortisol synthesis. The adrenal gland does not store cortisol; increased secretion arises due to increased synthesis under the control of adrenocorticotropin. Cholesterol is the principal precursor for steroid biosynthesis in steroidogenic tissue.

Fulminant Hepatic Failure (FHF)

Patients with FHF are always admitted to ICU, close to the liver transplant center. Hepatic encephalopathy can rapidly progress from mild confusion to deep coma, and this may be heralded by worsening coagulopathy. Etiology of FHF is important, as certain conditions demand prompt specific treatment (N-acetylcysteine for acetaminophen poisoning, for example). The National Institute of Health Acute Liver Failure Study reported in 308 patients acetaminophen poisoning as the cause in 39% of patients, idiosyncratic drug reaction in 13%, hepatitis B, or hepatitis A in 6% of patients each. When this syndrome develops, without liver transplant overall mortality is very high (90-97%) [34].

ICU management is largely supportive, including nutrition, electrolyte balance, avoidance of hypoglycemia, aspiration precautions, and maintenance of hemodynamic stability. Cerebral edema is commonly encountered complication with high mortality. Cerebral perfusion pressure should be kept above 60 mmHg, and this goal has to be addressed often by increasing

mean arterial pressure and/or decreasing intracranial pressure (ICP).

In patients with preserved renal function, mannitol is treatment of choice for increased ICP, but barbiturates may be used first in the setting of renal dysfunction. The patient's head should be elevated (15-20%), and ICU procedures or techniques that may raise ICP (tracheal suctioning, high level of PEEP, hypoventilation) should be avoided. We have completely abandoned direct intracranial pressure monitoring as recommended by some authors for patients with suspected cerebral edema. Transcranial Doppler imaging and/or repeated neurologic evaluation is probably safer and equally clinically useful alternative.

Two theories prevail in the understanding of the pathophysiology of intracranial hypertension (IH) during FHF [35]. Ammonia and glutamine may cause cytotoxic cerebral injury: excessive circulating ammonia in patients with FHF is detoxified in the brain to glutamine, which has osmotic effects in astrocytes that may account for the development of brain edema. Second, an increase in cerebral blood flow (CBF) is of critical importance for the development of brain edema, and the high ICP is the result of cerebral vasodilation caused by loss of autoregulation.

Several novel therapeutic maneuvers have been proposed in the treatment of brain edema in patients with FHF, some of which are clinically acceptable in this setting: induced hypothermia, hypertonic saline and propofol sedation, for example induced hypothermia (core temperature 32–33°C) reduces cerebral edema in patients with FHF. Several relatively small recent studies have shown that hypothermia produced sustained and significant reduction in arterial ammonia concentration and its brain metabolism, cerebral blood flow, brain cytokine production, and other markers of oxidative stress [36].

Similarly to “traditional” (osmotic) diuresis with mannitol, hypertonic saline acts as a dehydrating agent and effectively reduces brain water content in humans. Hypertonic saline has also been shown to improve regional cerebral perfusion by reducing endothelial swelling, improving microvascular blood flow [37].

Although routine use of sedation in patients with FHF is not recommended, propofol permits a faster return to wakefulness and may be a useful agent for neurological evaluation in patients with FHF. Liver failure does not influence propofol pharmacokinetics. Propofol decreases cerebral metabolic rate (CMR), causes a decrease in intra-cranial pressure (ICP), potentiates GABA mediated inhibition and inhibition of NMDA glutamate receptors, etc. Propofol decreases ICP in patients with either normal or increased ICP [38]. Propofol reduces CMR by approximately 40%; this effect is dose dependent. Cerebral metabolic autoregulation is maintained during burst suppression with propofol. In our institution propofol is the “ICU

sedative” of choice, as long as blood pressure is not significantly depressed.

Conclusion

Orthotopic liver transplant remains the only curative modality for patients with end stage liver disease. Increased use of liver transplantation has reduced mortality from liver failure. At this level of knowledge, the role of critical care medicine is probably to prevent serious complications, reverse life-threatening problems and give the patient better chance on the liver transplant list.

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