ACUTE LIVER FAILURE

Incidence: < 10/1,000,000/yr		**Procedure**	**Recommendation**	**Category**
		TPE	Grade 2B	III
		TPE-HV	Grade 1A	I
No. of reported patients: > 300	**RCT**	**CT**	**CS**	**CR**
TPE	1(120)	1(158)	40(878)	54(73)
TPE-HV	1(182)	NA	NA	NA

TPE-HV: TPE-High Volume, not available in US.

Description of the disease

Acute liver failure (ALF) can develop in a normal liver (known as fulminant hepatic failure [FHF]) or in the setting of chronic liver disease. The most common causes are acetaminophen toxicity and viral hepatitis. Other known causes include ingestion of hepatotoxins/drugs, autoimmune hepatitis, critical illness, neoplastic infiltration, acute Budd–Chiari syndrome, and heat stroke. The mortality rate in FHF is 50–90% due to acute metabolic disturbances, hepatic encephalopathy, and severe coagulopathy; however, following liver transplantation, survival rates improve. Spontaneous recovery from FHF depends on the cause: high recovery rates are observed in fatty liver of pregnancy, acetaminophen ingestion, and hepatitis A; hepatitis B has intermediate prognosis; other drugs and unknown etiologies have a recovery rate < 20%.

Current management/treatment

For ALF with low likelihood of spontaneous recovery, the standard treatment is supportive care as a bridge to liver transplantation. If liver transplantation is not available, other liver support systems have been used. Liver support systems include cell-based and non cell-based therapies. Many of the cell-based liver support systems are considered experimental (Bioartificial liver, Extracorporeal Whole Liver Perfusion, Extracorporeal Liver Assist Device, and Modular Extracorporeal Liver Support). Non-cell-based therapies include: TPE, albumin dialysis, MARS (Molecular Adsorbents Recirculation System: i*n the US, the MARS system is cleared for use in the treatment of drug overdose and poisonings only)*, fractionated plasma separation and adsorption, Single Pass Albumin Dialysis, and Selective Plasma-Exchange Therapy. Other newer promising approaches include hepatocyte transplantation and tissue engineering.

Rationale for therapeutic apheresis

In FHF, TPE can remove albumin bound toxins as well as unbound toxins, including aromatic amino acids, ammonia, endotoxin, indols, mercaptans, phenols, and other factors which may be responsible for hepatic coma, hyperkinetic syndrome, and decreased systemic vascular resistance and cerebral blood flow. Recent studies indicate that the removal of inflammatory mediators appears to play a role and inflammatory mediators are removed by some apheresis techniques. Several studies show improved cerebral blood flow, mean arterial pressure (MAP), cerebral perfusion pressure, cerebral metabolic rate, increased hepatic blood flow, and improvements in other laboratory parameters such as cholinesterase activity or galactose elimination capacity. Despite these seemingly positive changes in physiological parameters, its impact on clinical improvement is still unclear. One study found that TPE does not reduce vasopressor requirement, despite positive changes in MAPs. TPE may also restore hemostasis by providing coagulation factors and removing activated clotting factors, tissue plasminogen activator, fibrin and fibrinogen degradation products. In some patients, the liver may recover during the period of TPE treatment and in other patients, failure may persist necessitating liver transplantation. Aggressive TPE has been used as a bridge to liver transplantation. When it is indicated, TPE is often performed emergently in this setting.

A recent randomized control trial in ALF patients with hepatic encephalopathy showed that both MARS and TPE + MARS therapy are equivalent with regard to clinical outcome (30-day mortality). However, TPE + MARS therapy reduced serum total bilirubin level more effectively. Similarly, Li (2014) reported that the combined use of TPE, hemoperfusion (HP), and conventional continuous veno-venous hemofiltration removed toxic metabolites, especially bilirubin more efficiently than other combination without TPE. A controlled trial by Yue-Meng (2016) showed significant survival benefit in patients who received TPE versus those who did not for patients with entecavir-treated hepatitis B and hepatic de-compensation or acute-on-chronic liver failure. The cumulative survival rates were 37% (TPE) and 18% (non TPE) at week 4 and 29% (TPE) and 14% (non TPE) at week 12 ($P < 0.001$). In Denmark, TPE-high volume (TPE-HV, often performed with PrismaFlex-TPE filter system, Gambro) has been used to treat ALF. A recent RCT (Larsen, 2016) performed in 183 patients demonstrate statistically significant overall survival benefit: 58.7% TPE-HV + standard care versus 47.8% standard care ($P < 0.001$) when three daily procedures were targeted.

Technical notes

Since plasma has citrate as an anticoagulant and there is hepatic dysfunction, whole blood: ACD-A ratio may need to be adjusted accordingly to prevent severe hypocalcemia. Alternatively simultaneous calcium infusion can be used. Calcium supplementation should be strongly considered. Patient should also be monitored for development of metabolic alkalosis. Some groups have performed simultaneous hemodialysis to mitigate this side effect. There is a preference for plasma as a replacement fluid due to moderate to severe coagulopathy; however, use of albumin is acceptable.

Volume treated: TPE: 1–1.5 TPV; TPE-HV: target 15% of ideal body weight **Frequency**: Daily
Replacement fluid: Plasma, albumin

Duration and discontinuation/number of procedures

In ALF, daily TPE is performed until transplantation or self-regeneration occurs. The biochemical response to TPE should be evaluated in laboratory values drawn the following day (≥12 h or more after TPE). Samples drawn immediately after completion of TPE would be expected to appear better compared to pre-TPE levels. The TPE-HV was performed on three consecutive days.

References

As of February 7, 2016, using PubMed and the MeSH search terms acute hepatic/liver failure, fulminant liver/hepatic failure, and plasmapheresis/plasma exchange for articles published in the English language. References of the identified articles were searched for additional cases and trials.

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