Editorial

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The challenges and excitement of liver transplantation

Liver transplantation is life-saving for patients with end-stage liver disease, as there is no established alternative to provide support such as dialysis and artificial ventilation available for kidney and respiratory failure, respectively.

Thomas Starzl at the University of Colorado performed the first liver transplant in 1963, but it was not until the 1980s that liver transplantation became an acceptable procedure. During the past 10 years, the expertise with transplant surgery and the perioperative care has evolved to an extent that it is now accepted as a viable option in Indian scenario as well. Liver transplantation has been static at 6200–6400/year in US for the last 5–7 years whereas in India, the numbers have jumped from 200 to 1000/year, a five-fold increase during the same period.[1]

Organ for transplantation is obtained from the deceased donor after declaration of brain death or from a living related donor whereby a part of the liver is removed.

The timing of transplant is important; a patient needs to be sick enough to derive benefit from transplantation, but well enough to survive complex surgical procedure. The severity of liver disease and hence, the need for liver transplantation is assessed on the basis of Child Turcotte Pugh score which takes into account ascites, encephalopathy, serum bilirubin, serum albumin and prothrombin time (PT). Another score which is used to assess the severity of chronic liver disease is the model for end-stage liver disease (MELD). A MELD score of >15 represents survival benefit of transplantation to a patient with end-stage liver disease.[2]

The patients with end-stage liver disease who require liver transplantation will need pre-operative optimisation, post-operative intensive care as well as advanced monitoring intra-operatively. Therefore, there is need to have specialised intensive care units which can handle patients with multi-system involvement. Acute liver failure patients may require ventilatory management along with dialysis or even albumin dialysis in the perioperative period.

Liver failure is associated with micro-circulatory changes resulting in arterio-venous shunting, thereby leading to increased cardiac output. Patient may have left-ventricular hypertrophy, cardiomyopathy (cirrhotic), autonomic neuropathy and even coronary artery disease. The progression of liver disease can lead to decompensation in the form of ascites and possible spontaneous bacterial peritonitis, hepato-renal syndrome, hepato-pulmonary syndrome, porto-pulmonary hypertension and coagulation abnormalities. There is truly multi-system involvement with disease progression and may require support for various organ systems. Typically, liver failure patients are vasodilated, which is more marked in the splanchnic circulation than the systemic circulation. It makes a logical sense to move the blood from splanchnic to the systemic circulation. In this issue of the journal, an article by Ibrahim *et al*. from Egypt has been published where they have used terlipressin intra-operatively and have assessed its effect on haemodynamics and renal parameters.[3] Terlipressin mobilizes blood from splanchnic circulation to the systemic circulation thereby improving systemic haemodynamics including the blood flow to the kidneys. Terlipressin does not have much effect on systemic circulation and the haemodynamic changes

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produced are primarily due to the mobilisation of blood from the splanchnic circulation.

Cirrhotic cardiomyopathy is a chronic cardiac dysfunction that is evident under stressful conditions in patients with end-stage liver disease. The clinical presentation can be a baseline high cardiac output status with diastolic dysfunction, prolonged QT interval and impaired systolic response to stress. This can lead to cardiac failure and pulmonary oedema during reperfusion or even in the post-operative period. There is no single test to identify this entity pre-operatively. Patients, who survive intra-operative and early post-operative period, have a complete reversal of both systolic and diastolic dysfunction. Contrary to the earlier belief, coronary artery disease is a known risk factor in patients undergoing liver transplantation. The morbidity and mortality related to coronary artery disease in liver transplant patients can be 50% and 80%, respectively.[4] All patients for transplantation should undergo screening for coronary artery disease. The risk factors for coronary artery disease in this population are age >50 years, obesity, diabetes, male gender and hypertension. Patients with non-alcoholic steato-hepatitis (NASH) have independently increased risk of coronary artery disease. Targher and Arcaro reported an incidence of 23% in patients with NASH.[5] Liver transplantation can produce three-fold change in cardiac output and thereby, produce a stressful condition, which can result in precipitating cirrhotic cardiomyopathy or ischaemic heart disease. As a part of pre-operative assessment, all patients undergo dobutamine stress echocardiography, but it has shown a poor sensitivity but a negative predictive value of 75% for obstructive coronary artery disease.[6]

Direct and continuous monitoring of intra-vascular pressures is essential and radial or femoral vessels are preferred. Pulmonary artery catheters (PACs) are used routinely by some centres whereas other centres use it very selectively. There is need to monitor cardiac output and systemic vascular resistance along with intra-vascular pressures due to rapidly changing cardiac output and vascular tone. Vascular tone is affected by vasodilatory substances like nitric oxide, carbon monoxide etc., present in patients with portal hypertension as well as due to endotoxin release during translocation of bacteria at the time of portal vein clamping. Minimally invasive monitoring in the form of pulse contour analysis (FLOTRAC®, LIDCO®) of the arterial waveform has been successfully used to derive cardiac output, systemic vascular resistance and stroke volume variation. This method gives a good estimate of trends of the parameters, but the values are not comparable to those derived from PAC using thermo-dilution.[7]

Renal function is altered in up to 40% patients who undergo a liver transplant. Liver disease progression leads to activation of renin-angiotensin aldosterone system, besides development of hepato-renal syndrome.[8] Hepatitis C is also an important cause of chronic liver failure and is known to be associated with higher incidence of diabetes and renal dysfunction.

Management of coagulopathy in the peri-operative period is another challenge during transplantation as liver is the key organ in the haemostatic pathway. Both coagulation factors and their inhibitors are reduced due to liver failure. The patients are at risk of severe bleeding as well as thrombosis. The aim of coagulation management is to prevent severe coagulopathic bleeding as well as avoiding thrombo-embolic complications. Besides the traditional laboratory parameters – PT, activated partial thromboplastin time, platelet count, fibrinogen levels, it is desirable to do whole blood clotting test preferably as point of care testing. Various methods available for point of care whole blood testing are-thromboelastography (TEG®), rotational thromboelastometry (ROTEM®) and Sonoclot®. The conventional coagulation tests do not provide information on the kinetics of clot formation which is seen with point of care coagulation monitors like TEG. The lack of coagulation factors, platelet function, fibrinolysis as well as hypercoagulable states are best identified in a very short time by the point of care testing devices.[9]

In India, we are presently performing more living donor liver transplants than the deceased donor liver transplants (DDLT) due various reasons – lack of education and religious beliefs being important reasons but there is an apparent shift in this aspect, and there is a significant increase in deceased organ donations. Living donor liver transplantation is reported to have higher complication rates but lower mortality as compared to DDLT. The higher complications rate is due to much more intricate surgical dissection in donor and anastomosis in the recipient vessels and biliary track.[10] These issues may lead to longer hospitalisation but are resolved with the help of interventional radiology, allowing for complete recovery.

Liver transplantation has well-described indications in the form of chronic liver failure as well as acute liver failure. In the western countries, paracetamol poisoning is a leading cause of acute liver failure whereas this is rarely seen in Indian population. In this issue, Pandey *et al*.[11] have reviewed another cause of acute liver failure, which is pregnancy induced. This is a very sensitive issue whereby a choice is to be made whether to allow the pregnancy to continue or not, along with liver transplant procedure.

In India, we are at a stage when the liver transplant is now recognised as a viable modality to treat end-stage liver disease with 1-year survival post-liver transplant of over 80%, which is as good as in any other established programme in the world. We are therefore right in the midst of exciting times that will lead to a rapid increase in liver transplants all over the country as we have all the ingredients for success, that is, the patients, technical expertise and the evidence of good reproducible results of the procedure.

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