

Review Article

ANESTHESIA CONSIDERATIONS IN LIVER TRANSPLANTATION

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INTRODUCTION

Liver transplantation has emerged as an increasingly successful treatment for patients with end-stage liver disease (ESLD). It is now a routine procedure performed in numerous medical centers throughout the world. Currently, about 250 liver transplants are performed in the United States every month. One year survival rates >80-85% & five years survival rates 50-60%.

Orthotopic liver transplantation (OLT) is the replacement of a diseased liver with a healthy liver in the normal anatomic position. The operative procedure is extensive, complex, and technically challenging with multiple vascular transections and anastomoses. In addition, the liver is an extremely vascular organ and extensive bleeding can occur in patients with portal hypertension due to ESLD.

The main indications for orthotopic liver transplantation (OLT) in adults are *alcoholic cirrhosis, chronic cirrhosis due to non-A, non-B hepatitis and hepatitis C, primary biliary cirrhosis, cryptogenic cirrhosis, and primary sclerosing cholangitis*. Only a minority of recipients are transplanted for cirrhosis due to hepatitis B, fulminant hepatic failure, malignancy, autoimmune cirrhosis, and a variety of inborn errors of metabolism.¹ The most common indication for OLT in pediatric patients is biliary atresia, followed by metabolic disorders, fulminant hepatic failure, cryptogenic cirrhosis, neonatal hepatitis, and malignancy.

Factors contributing to the recent success in liver transplantation²

- 1). Use of immunosuppressant therapy with cyclosporin & tacrolimus (FK-506)
- 2). Greater understanding and experience with liver transplantation.

- 3). Introduction of rapid infusion devices that allow transfusion up to 2 L/min of warmed blood.
- 4). Safe use of venovenous bypass.

Problems complicating the anesthesia for liver transplantation

- 1). Multisystem nature of cirrhosis
- 2). Massive blood loss throughout the procedure.
- 3). Haemodynamic consequences of clamping and unclamping the IVC and portal vein.
- 4). Metabolic consequences of the anhepatic phase.
- 5). Risks of air embolism and hyperkalemia when circulation to the new liver is fully established.

Pre-anesthetic evaluation

Preoperative evaluation is performed in two stages. In the first-stage all liver transplant candidates are examined by anesthesiologist. The later, second-stage evaluation is performed immediately before surgery.

Organization of preparation phase

Use of resources is the prime consideration during preparation for transplant. One should plan for an operating room time of 8 to 20 hours³, with an average total time of 8.5 hours for anesthesia, 7 hours of which are devoted to surgery. The minimum anesthesia staff should be a 3:2 ratio of physician to certified registered nurse anesthetists or technicians to deal with simultaneous administration of anesthesia and operation of the rapid infusion system (RIS) device and the thromboelastograph (TEG). A courier, responsible solely for the transport of specimens and blood products, is indispensable.

Anesthetic Technique

Because of the possibility of delayed gastric emptying, a routine rapid sequence induction should be performed. Induction with thiopental or

ketamine with succinylcholine or vecuronium are techniques that work well. Maintenance of anesthesia with isoflurane in an air-oxygen mixture supplemented with sufentanil and vecuronium provides optimal conditions. Vecuronium is used so that the function of the new liver graft may be evaluated. The time for the return of a train-of-four (TOF) mode with a nerve stimulator correlates well with the function of the new graft⁴. Positioning and padding of the patient requires particular care be use the procedure may take many hours. The incidence of postoperative neuropathies is significant⁵.

Typical transfusion requirements consist of

1. 15-30 Units of FFP.
2. 15-25 Units of platelets.
3. 15-30 Units of red blood cells.
4. 10-20 Units of cryoprecipitates.

Blood salvaging techniques (cell saver) can be extremely useful in reducing donor red cell transfusion. Aprotinin or EACA infusion may significantly reduce blood loss.

Several lines required

- 1) Two arterial lines, one radial & one femoral.
- 2) One large bore peripheral intravenous catheter in the antecubital vein.
- 3) One large bore external or internal jugular catheter.
- 4) A Swan-Ganz catheter.

Monitoring

Liver transplantation requires the management of a) Severe coagulopathy b) Metabolic derangements c) Massive fluid shift & blood loss d) Temperature derangement e) Haemodynamic instability and Renal dysfunction.

Full invasive monitoring is mandatory with

Direct arterial pressure, Central venous pressure and Pulmonary artery pressure sensors. So that haemodynamic profiles can be calculated and appropriately managed. The presence of a 'stat lab' in the immediate operating suite area allows rapid analysis of haemostasis profiles, electrolytes, and glucose and blood gases.

Coagulation status monitored by prothrombin time, APTT, platelet count, fibrinogen level, D-dimer or TEG.

Thromboelastography (TEG)

TEG has proved extremely valuable for relatively fast interpretation and understanding of the dynamic and complex coagulopathy pattern inherent in this procedure, thus guiding effective clinical therapy. Clinically useful information available within 30 minutes.

Transplant surgery can be divided into 3 phases:-

1. *Preanhepatic phase.* Through a wide subcostal incision, the liver is dissected so that it remains attached only by the inferior vena cava, portal vein, hepatic artery and common bile duct.
2. *Anhepatic phase:* This stage includes the hepatectomy and ends when vascular anastomosis of the IVC and portal vein is complete; the intrahepatic IVC anastomosis is prepared but not completed until late in this stage.
3. *Neohepatic phase* (Reperfusion and biliary reconstruction).the donor liver is incorporated into the recipient circulatory system by releasing, in sequence, clumps from the portal vein, the infrahepatic IVC and suprahepatic IVC. The portal artery anastomosis is then performed and after adequate hemostasis the bile duct is reconstructed.

Each phase requires careful consideration by the anaesthesiologist.

Preanhepatic phase

At the beginning of surgery high filling pressure due to fluid overload, ascites, plural effusion, pulmonary hypertension, hyperdynamic circulation. Major fluid shift occurs due to drainage of liters of ascitic fluid, transection of large varices, surgical manipulation of liver & major vessels. These lead to decreased venous return & hypotension. Aggressive correction of coagulopathy is not necessary unless bleeding is excessive.

Packed red cells, FFP, platelets & cryoprecipitates are given according to coagulation status.

Anhepatic phase

Total hepatectomy is performed. Significant changes in haemodynamic indices with decreased venous return & fall of cardiac output, increased splanchnic & lower caval pressure, decreased renal perfusion pressure, decreased systemic arterial pressure

Venovenous bypass (VVB)

Technique is used in patients identified at increased risk with venacava clamping. This technique involves cannulating the IVC and portal vein and diverting their blood flow (1-3 L/min) away from the liver and back to the heart, usually via an axillary vein. VVP is suggested for venous decompression, improve hemodynamic stability, and decreased intraoperative blood loss⁶.

Neohepatic phase

This phase of surgery is marked by the release of portal blood flow through the graft. Severe haemodynamic instability known as the postperfusion syndrome may follow within a few minutes with severe hypotension, decreased heart rate, decreased SVR, increased pulmonary arterial pressure.

Hypotension is treated by strong vasopressors like, dopamine, epinephrine, phenylephrine & norepinephrine⁷.

Coagulopathies should be corrected during this stage to obtain excellent haemostasis. Fibrinolysis if detected by TEG, reversed with aminocaproic acid & tranexemic acid

Hyperkalaemia & systemic acidosis may occur due to sudden influx of a cold, acidic, hyperkalemic fluid into the circulation. It is corrected by NaHCO₃ (50mEq) just before unclamping & CaCl₂ (500mg) exactly simultaneous with portal unclamping.

Fluid & metabolic consideration

Maintenance with IV fluid that does not contain lactate is a prudent choice. Infusion of crystalloid guided by renal function & haemodynamic parameter. Urine output is optimized by fluid challenge, osmotic & loop diuretics, dopamine infusion⁸. Ionised calcium levels should be monitored closely.

Postoperative management

If the new liver is functioning well, the patient can be extubated within two hours and transferred out of the intensive care unit within 24 hours. Marginal grafts may respond to continued infusions of PGE₁ and careful management of fluid, electrolyte, and coagulation status. Postoperative bleeding requires early surgical intervention. Postoperative pain can be well controlled with the use of a patient-controlled analgesia pump.

New immunosuppressive drugs - Cyclosporin is the most commonly used maintenance immunosuppressive drug. Steroids are almost invariably added⁹. Azathioprine may be used as a third agent to reduce the dose of cyclosporine and, in some cases, may replace cyclosporine altogether when the latter is contraindicated or can no longer be used because of adverse side effects.

Anti-lymphocyte globulin preparations, including the mono-clonal antibody OKT-3¹⁰, have been given prophylactically and for specific indications to prevent rejection. OKT-3 reacts against all mature T lymphocytes.

Other new drugs have been developed and tested in multicenter trials in the last decade. The most prominent is tacrolimus (FK506), which became an established immuno-suppressant agent for primary and rescue therapy in patients with liver, kidney and pancreas transplants.

Summary

Liver transplantation is no longer experimental and has become an acceptable therapy for chronic liver failure. Good anesthetic support is an essential element of a liver transplantation service. Anesthesia consideration for liver transplantation include the management of severely deranged physiology, pharmacology and biochemistry as all organ systems may be affected adversely by the failing liver. A close working relationship between all members of the operating team is necessary for the success of the program. The development of such teams in major transplant centers has resulted in a marked reduction in the morbidity and mortality of this procedure and a concomitant reduction in the cost.

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