34 Anesthetic Issues in the Management of Pediatric Liver Transplantation

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34.1 Introduction

Liver transplantation remains the only treatment of choice in a patient with end-stage liver disease. Pediatric liver transplant has become a common treatment of choice encouraged by an increasingly successful outcome in end-stage liver disease.

The perioperative management of this population poses unique challenges.

- Different indications according to the age; neonate, infants, and child with their particular characteristics.
- Different comorbidities present in this population.
- Difference in the physiology and size.
- Difference in the surgical techniques.

Through this chapter, we intend to provide an overview of anesthetic management in pediatric patients undergoing living related or cadaveric transplant and an overview also into acute liver failure pediatric patients.

34.2 Indications

The most common etiology for PLT (pediatric liver transplant) is cholestatic disorders like extrahepatic biliary atresia (EHBA) (43%), metabolic disease (13%), and acute hepatic necrosis (11%) [1, 2]. The etiology in 75% of acute liver failure is unknown. The etiologies are given in Table 34.1.

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V. Vohra et al. (eds.), *Peri-operative Anesthetic Management in Liver Transplantation*,
https://doi.org/10.1007/978-981-19-6045-1_34

Table 34.1 Indications for Pediatric Liver Transplantation

Chronic Liver Disease	Metabolic Disorders	Acute Liver Failure	Malignancy	Others
Biliary Atresia	Alpha 1 antitrypsin deficiency	Poisoning	Hepatoblastoma	Budd-Chiari Syndrome
Cryptogenic Cirrhosis	Criggler-Najjar Syndrome	Drug Induced	HCC	Carolis disease
Primary Sclerosing Cholangitis	Cystic Fibrosis	Viral Hepatitis	Sarcoma	Neonatal hemochromatosis
Familial Cholestasis Progressive	Galactossemia		Haemangio-Endothelioma	
Familial Intrahepatic Cholestasis	Gauchers disease			
Autoimmune Hepatitis	Glycogen Storage disorders			
Viral Hepatitis	Wilsons Disease			
	Niemann-Pick disease			
	Tyrosinemia			

Red - Common in neonates
Violet - Common in infants
Black - Common in older children

34.3 Basis for Allocation

Earlier waiting list for transplantation was greatly influenced by the disease severity and the duration on the waiting list. The pediatric end-stage liver disease score (PELD) in 2002, predicted the mortality within the next 3 months without transplant. It is valid for children younger than 12 years of age, above which the MELD score is used which incorporates serum bilirubin, INR and serum creatinine. Parameters used in PELD are growth failure, albumin, bilirubin, international normalized ratio (INR), age < 1 year.

$$\text{PELD} = 4.80\left[\text{Ln serum bilirubin}\left(\text{mg}/\text{dL}\right)\right] + 18.57\left[\text{Ln INR}\right] - 6.87\left[\text{Ln albumin}\left(\text{g}/\text{dL}\right)\right] + 4.36\left(<1\,\text{year old}\right) + 6.67\left(\text{growth failure}\right).$$

PELD exceptions are acute liver failure, hepatopulmonary syndrome, hepatic neoplasms, hepatorenal syndrome, and pulmonary hypertension.

34.4 Timing of Transplantation

This depends on the severity calculated by the PELD score and duration on the waiting list. Age and nutritional status play an important role [3].

In recent times due to better surgical, perioperative management (anesthesia and intensive care), nutritional support, immunosuppressants and elective early living donor liver transplant in this age group has shown improved survival rates similar to older children [4]. The timing of transplantation has been expedited and depends on donor availability, even before the child becomes very sick.

34.5 Pathophysiological Changes, Pre-operative Concerns, and Anesthetic Implications

The complexity of ESLD is enhanced by the multisystem involvement, comorbidities, and social situations. The time period required for work up ranges 1–5 weeks requiring a multidisciplinary team approach. This time period is crucial as it gives a window to assess the severity, presence of congenital anomalies, plan, counsel and make strategies for the specific transplant child. The pathophysiological changes affect all major organ systems.

34.5.1 Pulmonary

- Hypoxemia.
- Hepatopulmonary syndrome (HPS).
- Porto-pulmonary hypertension (POPH).
- Chest infections.

Hypoxemia is multifactorial, most common reason being mechanical restriction due to ascites, hepatosplenomegaly, and pleural effusion. Ascites and pleural effusion can be drained, if massive. Other strategies that can be employed are fluid restriction, diuretics, and albumin infusions.

HPS in acute or chronic liver dysfunction is a syndrome of arterial hypoxemia and right to left shunting due to vasodilation of pulmonary vasculature causing V/Q mismatch and new vessel formation [5]. HPS can be more severe than liver disease and is reversed following transplantation. A fall in arterial oxygen levels on standing from supine, clubbing, and dyspnea with the exclusion of any other cause of hypoxemia is diagnostic. Confirmation is done with Contrast Echocardiography and Technetium 99 labeled micro-aggregated albumin scans.

POPH is rare in pediatric ESLD. Mean PAP (pulmonary artery pressure) >25 mmHg, PCWP (pulmonary capillary wedge pressure) <15 mmHg, PVR (pulmonary vascular resistance) >3 wood units in the presence of portal hypertension. Very little is known about the disease process in pediatric patients. The therapy of POPH in children is challenging and outcomes are dismal.

Chest infections are common due to malnutrition, poor gastric emptying, encephalopathy, mechanical ventilation, recurrent hospitalizations and certain conditions like cystic fibrosis and alpha1 antitrypsin deficiency.

34.5.2 Cardiovascular

- Increased cardiac output (CO).
- Low systemic vascular resistance (SVR).
- Congenital cardiac anomalies (CHD).
- Pulmonary hypertension (PH).
- Cirrhotic cardiomyopathy (CMP).

High CO and low SVR are a result of reduced clearance of vasoactive compounds, e.g., nitric oxide (NO) and also fluid retention due to portal hypertension (PH).

CHD such as atrial septal defect and situs inversus are seen in EHBA children.

PH and pulmonary stenosis have been seen in Alagille syndrome (an autosomal dominant disease characterized by bile duct paucity, cholestasis, and cardiac, musculoskeletal, facial and developmental anomalies).

CMP in pediatrics is an entity evaluated lately especially in biliary atresia (BA). Criteria to diagnose CMP are LVMI (left ventricular mass index) > 95 g/m^2 and relative wall thickness of LV > 0.42 mm. CMP is believed to be more frequent in children especially with BA and is also a predictor of morbidity and mortality [6].

ECG, CXR, ECHO, and cardiac catheterization are required to evaluate.

34.5.3 Central Nervous System

Hepatic encephalopathy is a dangerous complication and is multifactorial. Alterations in cerebral metabolism, accumulation of ammoni and neuroactive peptides have been implicated in the pathophysiology of HE. Precipitating factors are sepsis, nitrogen load

from GI bleeding, electrolyte abnormalities, and constipation.

Seizures, airway protection, ventilation, and sedation for procedures would need careful and judicious evaluations.

Non-invasive monitoring of ICP by means of optic nerve sheath diameter and transcranial Doppler are promising monitoring strategies [7].

34.5.4 Renal

- Hepato-renal syndrome (HRS).
- Pre-renal Azotemia.
- Renal failure.

HRS is rare in children and is characterized by impaired RBF, low GFR, elevated serum creatinine, oliguria with low urinary sodium (<20 mmol/L), and high urine/serum creatinine ratio.

Pre-renal azotemia may develop due to fluid restriction and diuretic therapy.

Renal failure due to hyperoxaluria and metabolic disorders are seen.

34.5.5 Gastrointestinal

Gastric emptying is delayed. Intra-abdominal pressure increases due to ascites and organomegaly. Portal hypertension leads to the development of varices. This can present as upper and lower gastrointestinal bleeding. Recurrent hemorrhage with the poor nutritional state can further contribute to anemia.

Impairment of synthetic and metabolic hepatic function leads to impaired drug clearance, glucose hemostasis, and coagulopathy. Glycogen stores are decreased and impaired gluconeogenesis making them prone to hypoglycemia.

Impaired protein synthesis leading to low serum oncotic pressure and high levels of protein-bound drugs. Concentrations of clotting factors due to impaired synthesis or decreased absorption of vitamin K leads to the deficiency of factors II, VII, IX, X, and also antithrombin III, protein C, and protein S.

Splenomegaly also results in the sequestration of platelets and erythrocytes.

Clotting tests and viscoelastic tests show the actual status of the hemostatic condition.

34.6 Pre-operative Workup

Concerns of the systems discussed above should be evaluated in details by a battery of investigations.

Blood tests for complete blood count (Hb, TLC, DLC, platelet count).
Clotting profile with PT, PTT fibrinogen, and FDP.
KFT along with serum electrolytes (Ca, Mg, Na, K) levels. Serum ammonia level when required.
LFT with the bilirubin levels, liver enzymes, albumin, and A/G ratio.
Blood sugar.
Blood grouping and cross-matching.
Serum lactate levels and pH for acidosis.
Baseline cytomegalovirus (CMV) and Epstein–Barr virus (EBV) status.
Blood and urine culture.
Chest X-ray, CT chest.
ECHO or cardiac catheterization (when indicated).

Detailed discussion and history taking with parents/guardian is mandatory. Previous surgeries, hospitalizations (for infections, bleeding, banding, sclerotherapy, dialysis, cardiovascular problems), medications, allergies, vaccination history should be documented.

It is recommended that the vaccination status of the child should be recorded, and the child should be referred for appropriate vaccinations at the time of listing. Many transplant centers will do routine pretransplant serology for vaccine-preventable diseases such as Hepatitis B, Varicella, measles, mumps, and rubella to guide individual vaccine recommendations. Table 34.2 contains recommendations for vaccinations in pediatric patients.

Table 34.2 Immunization s prior to transplantation

Vaccine	Inactivated/live attenuated (I/LA)	Recommended before transplant
Influenza	I	Yes
Hepatitis B	I	Yes
Hepatitis A	I	Yes
Pertussis	I	Yes
Diphtheria	I	Yes
Tetanus	I	Yes
Inactivated polio vaccine	I	Yes
H. influenzae	I	Yes
S. pneumoniae (conjugate vaccine)	I	Yes
S. pneumonia (polysaccharide vaccine)	I	Yes
N. meningitidis	I	Yes
Human papillomavirus	I	Yes
Rabies	I	Yes
Varicella (live-attenuated)	LA	Yes
Rotavirus	LA	Yes
Measles	LA	Yes
Mumps	LA	Yes
Rubella	LA	Yes
BCG	LA	Yes
Smallpox	LA	No
Anthrax	I	No

Explanation of the course of care from pre-surgical period to the post-surgical and following discharge and long-term care should be done.

Perioperative morbidity, mortality, blood transfusion requirements, ICU stay, mechanical ventilation should be discussed along with consent.

Crucial to the success of the program is an efficient blood bank and a hematology laboratory.

34.7 Pre-operative Medication and Theater Preparation

Antiseptic scrub and bath.

Intravenous dextrose for maintenance fluids.

Antibiotics as per institutional protocol (Usually a board spectrum antibiotic coverage with antifungal. At author's current institute, we use piperacillin—tazobactam, teicoplanin, and fluconazole).

The operating room should be warm prior to induction with the air conditioning preferably turned off. This is especially important as the child will be kept exposed for a while to facilitate placement of intravenous catheters.

Equipment required range from the usual pediatric airway trolley (laryngoscopes, endotracheal tubes, airways, bougies, etc.).

Anesthesia machine capable of delivering low tidal volumes and weaning modes of ventilation.

Suction machine and catheters.

Anesthetic drugs and antibiotics are prepared as per the institutional protocol.

Inotropic drugs as per the table (Table 34.3).

Intravenous lines—2 large bore 22/20/18G as per the age group and venous access available, preferably on either upper limb.

Central venous access in the IJV with a triple lumen 4.5/5.5Fr 8 cm length. Antibiotic impregnated one can be kept for longer especially in children with difficult veins or sick ones.

Sterile lines, water proof, and transparent dressings are mandatory to observe for signs of inflammation at insertion sites.

Arterial lines 24/22/20G for both radial and femoral. Radial line is preferred due to the reliability during the cross-clamping phase. Some anesthesiologists prefer femoral access as in sick children and on high inotropic support, it gives better reliability, as it is more central and larger [8]. Generally, two invasive arterial lines are preferred as one can be used for sampling.

Warming devices for intravenous fluids and blood and blood products.

Bodywarmers such as the temperature control machine (TCM) with water blanket, convection warmers with appropriate blankets.

Nasogastric tube and urinary catheter.

Cotton roll, sponge or head ring to support the head.

Neutral positioning and placement of the child to prevent any pressure sore or positioning-related injury like foot drop and pressure alopecia.

Table 34.3 Dilutions and dosages of commonly used vasoactive drugs

Drug	Dilution	Dosage
Noradrenaline	(0.3 × weight in kg) mg + 50 mL NS 1 mL/h = 0.1 mcg/kg/min	0.05–0.1 mcg/kg/min to a maximum of 1 mcg/kg/min
Adrenaline	(0.3 × weight in kg) mg + 50 mL NS 1 mL/h = 0.1 mcg/kg/min	0.1–1.0 mcg/kg/min
Dopamine	(15 × weight in kg) mg + 50 mL NS 1 mL/h = 5 mcg/kg/min	5–20 mcg/kg/min
Vasopressin	(0.3 × weight in kg) units +50 mL NS 1 mL/h = 0.0001 units/kg/min	0.0003–0.002 units/kg/min
Dobutamine	(15 × weight in kg) mg + 50 mL NS 1 mL/h = 5 mcg/kg/min	5–20 mcg/kg/min

34.8 Intraoperative Management

34.8.1 Induction

Anesthetic induction should be individualized based on the multiple factors evaluated in the preoperative workup. These could be massive ascites, gastrointestinal bleeding, cardiac conditions, pulmonary conditions, and hemodynamic instability.

Since most children would be already having an intravenous (IV) access, IV induction is usually preferred. Pre oxygenation is extremely important as many a times these patients desaturate during laryngoscopy. Moreover visualization of larynx might be difficult in certain cases. Its wise to have a smaller size endotracheal tube than the one appropriate for the age of the child. Rapid sequence induction in children with massive ascites is safer.

The choice of induction agent depends on the anesthetic protocol of the institution, usually, they are fentanyl and propofol though ketamine and etomidate can also be used. Succinylcholine and rocuronium are used when rapid sequence induction (RSI) is needed. In most centers atracurium or cisatracurium followed by its infusion is used as muscle relaxants. Higher doses of nondepolarizing muscle relaxants might be required owing to an increased volume of distribution and binding to acute phase reactants. Vecuronium and rocuronium are metabolized in the liver and excreted in bile thus prolonging their action in advanced liver disease. Plasma Pseudocholinesterase level is reduced in liver disease.

Endotracheal intubation is preferably done with a low pressure cuffed endotracheal tube as the variability of pulmonary compliance is an issue due to disease and surgical retraction and manipulation. The cuff pressure should be measured following inflation and just an adequate amount to prevent major leaks is recommended. Newer endotracheal tubes made of polyurethane instead of polyvinyl chloride may help in achieving tracheal sealing at lower pressures. Fixation of the ETT is of utmost importance as it is very common to encounter upper lobe collapse and endobronchial tube migration due to surgical manipulation and retractor application. PEEP of up to 5cmH_2O is useful to prevent atelectasis and improve oxygenation.

34.8.2 Intravenous (IV) and Intraarterial (IA) Access

uring of IV and IA access is done after induction of anesthesia. This might take a substantial amount of time and resources depending on the health of the child. Infants and children are particularly prone to inadvertent hypothermia due to their malnourished state, increased cardiac output and peripheral vasodilatation. The OT air conditioning needs to be switched off during securing of lines and placing the child on a warming blanket is very helpful to maintain normothermia. Both active and passive maneuvers should be applied such as conduction warming blanket, convective warming systems such as Bair Hugger, mechanical ventilation with heat and moisture exchanger, and high flow fluid warming devices.

Upper extremities are preferred as IVC cross-clamping is done during the grafting phase. Peripheral IV access with two large bore cannulas in both the upper limbs is ideal. A triple lumen central venous catheter is secured for vasoactive drugs, monitoring the CVP (central venous pressure) and rapid infusion/transfusion during the reperfusion phase or hypovolemic phase. CVP catheter is usually placed using a real-time ultrasound machine to prevent potentially dangerous complications in the already sick, coagulopathic child.

Arterial catheter single or two in number is placed in the radial artery in both the upper limbs. One could be used for sampling or used if the other one gets damped or misplaced. Femoral arterial monitoring is used in certain centers especially in very sick children on high inotropic support or very hemodynamically unstable as they are more central and give a more reliable reading. This could be debatable though as it will be damped during aortic cross-clamping if and when an arterial conduit from the aorta is constructed.

34.8.3 Maintenance of Anesthesia

A mixture of isoflurane/sevoflurane with air and oxygen along with fentanyl and atracurium infusions. Fentanyl does tend to accumulate with repeated boluses or infusion. Remifentanil, which is metabolized by red cell esterases, has a very short half-life and is easily eliminated. Remifentanil is not available in India and we have no experience using it. More important than the technique of anesthesia used are the goals of maintaining hemodynamic stability, temperature, metabolic, and coagulation abnormalities.

34.8.4 Temperature Management

Hypothermia is very common due to numerous reasons like. Exposure of abdomen to room air, infusion of cold fluids, blood and blood products, cold irrigating fluids form the graft and long duration of surgery. The child should be draped in such a way that ascites and blood should drain away not pool on their bodies. Special drapes are available for the same. Convective warmers and warming mattress should be used. Warm fluids should be used and this can be achieved by using fluid warmers during transfusions or fluid infusions.

34.8.5 Metabolic Management

Hypoglycaemia is common, hence it would be wise to run an infusion of 0.45% normal saline as maintenance during surgical procedure along with monitoring of the blood sugar at regular intervals.

Hypokalemia due to chronic administration of diuretics is common, routine correction is not done unless it is associated with rhythm disturbances and if lower than 3 meq/L. Potassium level usually tends to rise on its own during the course of the operation due to the acidosis, administration of blood products, and reperfusion.

Normal serum ionized calcium levels are very important for preserving myocardial contractility and also for the coagulation pathway. Citrate in the blood products tends to decrease ionized calcium levels, especially during the anhepatic phase. Calcium levels are maintained by administering calcium chloride or calcium gluconate infusions.

34.8.6 Hemodynamic Management

Maintaining hemodynamics is the main focus of anesthetic management in liver transplantation. The reasons for hemodynamics instability are multifactorial. Decreased preload, low systemic vascular resistance, vascular clamping, ongoing fluid, and blood losses are some of the reasons for hypotension.

CVP monitoring is technically unreliable due to changes in intra-abdominal pressures. Massive ascites, when present, can lead to a false elevation of CVP which is followed by a drastic fall on the drainage of ascitic fluid. Maneuvers like

retraction of the diaphragm, external compression and pulling of IVC and manipulation of the large-sized liver can lead to erratic reading of CVP. The monitoring of the trend of CVP along with close communication with the surgeon gives an idea of the preload.

Flow trac even though extensively used in adults is not validated for use in children. Most centers do not prefer using pulmonary arterial catheters in children owing to the complications associated with insertion. Minimally invasive cardiac output monitors like PICCO and LIDCO are used in some centers.

TEE is a definitive monitor of the intravascular volume. Small biplanar probes are available for pediatric patients. It provides an excellent assessment of ventricular filling and function along with diagnosing structural abnormalities. However, interpretation of TEE requires significant skill, training and also carries the risk of rupturing esophageal varices.

In addition, constant communication with the surgical team, direct visualization of the IVC and the turgidity of the liver graft is of paramount importance and provides very useful information.

34.8.7 Hematological Management

The degree of coagulopathy present will depend on the severity of liver disease. Blood loss can be significant during the dissection phase especially if the patient has undergone a Kasai procedure. In the past or has had spontaneous bacterial peritonitis. Coagulopathy worsens during the anhepatic phase due to absent synthesis of hepatic clotting factors. Frequent monitoring of coagulation parameters like PT, aPTT, INR, platelets, fibrinogen should be done. Thromboelastogram (Viscoelastic study) will give an idea of the global hemostasis. Observing the surgical field and communication with the surgeon perhaps is the best real-time way to assess coagulation and administer blood products.

In pediatric liver transplant all over the world full correction of the coagulation parameters is not carried out. This is in order to avoid causing vascular thrombosis and early graft occlusion. Correction is done in the presence of an obvious coagulopathic bleed and an abnormal TEG. Depending on the coagulation parameters, decision of the blood product to be used is taken. Preferably cryoprecipitate and platelet transfusion are withheld unless deemed necessary.

In addition to the above, normal calcium level, normothermia, and correction of metabolic acidosis also help in maintaining normal coagulation.

34.9 Stages of Liver Transplantation and the Specific Anesthetic Considerations

34.9.1 Dissection Phase- (Pre-hepatic Stage)

It extends from skin incision to occlusion of hepatic artery and portal vein.

This phase involves mobilization of liver from the inferior vena cava and various adhesions as well as dissection of the porta. There is a potential for significant bleeding from adhesions from previous abdominal surgeries such as Kasai procedure. The aim should be volume replacement to maintain hemodynamic stability, blood glucose levels, and correction of coagulopathy. Excessive ascitic fluid drainage can also lead to hypotension and acidosis and this can be managed by 5% albumin or colloid replacement. Vasopressors such as Nor Adrenaline, dopamine can be started to increase the systemic vascular resistance (SVR).

Application of retractors against the diaphragm reduces the lung compliance and there is an increase in the airway pressure. Ventilatory parameters may need to be readjusted and air entry to both lungs rechecked.

34.9.2 Anhepatic Phase

The characteristic feature is the decrease in venous return due to clamping of the IVC (partial or complete) leading to hypotension though the presence of collaterals may help in better tolerance. There is also compensatory tachycardia to maintain cardiac output.

In children with less developed collaterals especially ones having a relatively normal hepatic function and minimal portal hypertension; acidosis, aggravating hyperkalemia, interruption of gluconeogenesis, and hypoglycemia can be seen.

Care must be taken not to overhydrate the patient during this stage since it may lead to graft edema post-reperfusion.

Acidosis tends to worsen due to decreased clearance of acids and lactate by the liver. Routine administration of soda bicarbonate is not recommended unless the patient is hemodynamically unstable and acidotic.

The anhepatic phase ends with reperfusion of the portal vein. During reperfusion unclamping of the vascular anastomosis is done, the circulatory system of the recipient being exposed to cold fluids, potassium ion, ischemic factors that can lead to hypotension, malignant ventricular dysrhythmia, and unstable hemodynamic states. In anticipation of reperfusion syndrome, all metabolic abnormalities should be corrected prior to reperfusion. The hemoglobin levels are maintained at around 8 g/dL. pH, ionized calcium, and potassium are all kept within the normal range prior to reperfusion.

Temporary administration of 100% oxygen, reduction of volatile agents, stepping up inotropes, a small bolus of calcium chloride, sodium bicarbonate or phenylephrine can mitigate post-reperfusion syndrome. Preparation for necessary cardiopulmonary resuscitation or cardiac defibrillation on occurrence of life-threatening arrhythmias should be always kept in mind.

34.9.3 Neohepatic Phase

This phase is the completion of arterial and biliary anastomosis. Coagulopathy may continue along with oozing from the raw edges of the graft. Volume resuscitation and blood transfusion continues though it has to be judicious to prevent graft congestion and fluid overload. The hematocrit (Hct) is maintained below 30%, the INR and platelet count kept under corrected to decrease blood viscosity in order to decrease chance of arterial and venous thrombosis. As the neohepatic function improves correction of acid base, lactic acidosis, electrolyte abnormalities, and blood sugar levels stabilizes. The production of bile from the graft also gives an idea of the graft function.

On completion of all the anastomosis a Doppler ultrasound is done to confirm vascular patency. Biliary drainage is established by either duct to duct anastomosis or hepatico-jejunostomy.

The risk of hepatic artery thrombosis is higher in pediatric patients especially if there is greater arterial size discrepancy, lower patient weight, reoperation, and longer surgical times. Many institutions take strict initiative to maintain a HCT of <30%. PT, aPTT carefully monitored to prevent over correction. Acetylsalicylic acid, alprostadil (PGE1), and heparin infusions may be started in situations where vascular thrombosis is observed intraoperative. After heparin infusion a close watch on the TEG and aPTT is kept, with a target aPTT being >1.5 times control.

Drains are inserted and abdomen closed. It is important that the anesthesiologist pays attention to the closure of the abdomen to mitigate tight closure leading to respiratory compromise. It can also lead to abdomen compartment syndrome carrying a risk of graft hypoperfusion, and compression. In such cases staged closure of the abdomen is recommended and/or downsizing of the graft prior to anastomosis (Table 34.4).

Table 34.4 Surgical stages and anesthetic considerations

Surgical stage	Anesthetic considerations
Dissection	• Blood loss • Fluid and blood resuscitation • Maintenance of normothermia
Anhepatic	• Fluid management • Correction of hypocalcemia, hyperkalemia, acidosis • Correction of coagulopathy • Prepare for reperfusion with adequate intravascular volume and correction of metabolic abnormalities
Reperfusion	• Management of hypotension • Management of hyperkalemia and hypocalcemia • Fluid and blood replacement • Air embolism
Neohepatic	• Maintain hematocrit around 25% • Preparation for extubation if suitable

34.9.4 Elective Ventilation Vs. on Table Extubation

Traditionally pediatric patients were electively ventilated post-transplantation due to various reasons. Vascular patency was a major problem in the post-operative period with children requiring frequent imaging which was difficult in a restless and agitated child. This coupled with the high rate of re-explorations in children, prolonged use of sedatives and tight abdominal closure meant most of the institutions used to electively ventilate these patients post operatively. However, recently encouraged by positive results of fast tracking in adults many pediatric centers perform on table extubation or early extubation in the ICU which has shown favorable results. At author's current institute, we extubate the patients on table whenever possible at the discretion of the treating anesthetist.

The patient has to fulfill certain criteria to attempt an on table extubation which includes (1) Absence of encephalopathy pre-operatively, (2) Hemodynamic stability, (3) Confirmation of vascular patency by doppler, (4) Absence of tight abdominal closure, (5) Stable blood gases, (6) Absence of massive blood transfusion.

34.9.5 Early Post-operative Course

As mentioned earlier most centers electively ventilate the patients after the transplantation. Opioid infusions are commonly used to sedate the children. An infusion of muscle relaxants can also be added if ventilation becomes difficult due to a diminished lung compliance. Fluid management should be given as per the maintenance requirements and also keeping in mind the loses through the drains which might be quite significant. We usually use a balanced salt solution with dextrose as maintenance and 5% albumin for drain replacement during the first 48 h. Hematocrit is maintained at not more than 25% to reduce the occurrence of vascular thrombosis.

Frequent blood gases are performed to optimize ventilation and also to have an idea about the graft function. It is a good idea to perform a chest X-ray as soon as the patient arrives in the ICU and look for potential problems like misplacement of endotracheal tube and central line, fluid overload, pleural effusions, and position of nasogastric tube. In general, most children undergoing an elective liver transplant and who are having a satisfactory graft function post-operatively can be considered for early extubation. Fast tracking is always preferred if the condition of child permits. This decision should be taken in consultation with the surgeon, hepatologist and the critical care physicians.

34.10 Pediatric Liver Transplantation: Special Circumstances

34.10.1 Acute Liver Failure

Pediatric acute liver failure (PALF) is one of the most challenging critical illnesses which rapidly progresses into a severe multisystem organ failure with unpredictable and potentially devastating complications. The etiology varies according to age. In the neonatal period, neonatal hemochromatosis is the most common cause, whereas in children viral hepatitis, metabolic conditions and drug toxicities are the commonest. The most

widely accepted consensus defines PALF as follows [9]:

Biochemical evidence of liver injury in a child without evidence of chronic liver disease.

Coagulopathy not corrected by vitamin K administration.

INR > 1.5 with encephalopathy or INR > 2 without encephalopathy.

There are many criteria which are used worldwide, but the most common criteria used is the Kings college criteria. The Kings college criteria was devised in 1989 to determine if there are any early indices of poor prognosis in patients with acute liver failure. It is important that physicians identify these patients who have less chances of spontaneous recovery and will require liver transplantation (Table 34.5).

34.10.1.1 Management of PAL

F is Management of PALF is complicated and needs a multidisciplinary team in a specialized center. The children should ideally be cared for in an intensive care unit. Intubation and ventilation are carried out pre-emptively if the child presents with encephalopathy in order to prevent aspiration and ensure oxygenation.

Once the airway has been secured the child should be nursed in a calm and quiet room. Propofol is an ideal agent for sedation if the patient is hemodynamically stable, otherwise, opioid-like fentanyl can also be used. Muscle relaxants like Atracurium can be used to ease ventilation along with high doses of intravenous sedatives.

Once the airway is secured central venous lines and arterial lines are placed to help with regular blood sampling and administration of inotropes. Use of ultrasound while placing these catheters are recommended because of the coagulopathy associated with PALF. As with all other patients with hemodynamic compromise, maintaining adequate intravascular volume status is the first step of management. Once an adequate intravascular volume is achieved and hypotension persists, vasoconstrictor medications should be initiated.

Since raised ICP is the main cause of mortality in ALF measures should be taken to maintain ICP < 20 mm Hg. The child's head should be in a neutral position with 10–15° head up to optimize jugular—venous drainage. Given the association between intracranial hypertension and ammonia, ammonia lowering strategies should be initiated in the form of lactulose, non-absorbable antibiotics, etc. The low molecular weight of ammonia makes it amenable to dialysis, so we employ CRRT in all patients with ammonia more than 100 mmol/L. Fever and shivering must be aggressively controlled as they can lead to surges in ICP. In addition to the above measures, hypertonic saline and mannitol are also administered as part of osmolar therapy to prevent intra cranial hypertension.

Invasive monitoring of intracranial pressures in patients with acute liver failure is controversial as it is associated with bleeding complications with no benefits in overall survival. Ultrasound derived optic nerve sheath diameter and transcranial doppler to measure the pulsatility index of the middle cerebral artery might be useful non-invasive ways to measure intracranial pressure. CT scan can reliably detect the presence of cerebral edema and brain herniation, however, it is associated with the inherent risks of having to transport a critically ill patient.

As it might be expected outcomes post-liver transplantation in acute liver failure is signifi-

Table 34.5 Criteria for Liver Transplantation in Acute Liver failure

Acetaminophen-induced ALF	Non-acetaminophen ALF
1. Arterial pH < 7.3 irrespective of grade of encephalopathy	1. INR > 6.5 (PT > 100 s), irrespective of grade of encephalopathy
OR	OR any 3 of the following:
1. PT > 100 s	1. INR > 3.5 (PT > 50 s)
2. Serum creatinine >3.4 mg/dL	2. Age < 10 or > 40 years
3. Stage 3 or 4 encephalopathy	3. Serum bilirubin >18 mg/dL
	4. Jaundice to encephalopathy interval > 7 days
	5. Non-A, non-B hepatitis, syncratic drug reaction

cantly lower than those with chronic disease. The decision not to proceed for liver transplantation must be made when there are features of irreversible neurological damage like fixed dilated pupils and cerebral herniation on neuroimaging. Patients with cardiovascular instability with escalating inotropes and those with high ventilatory requirements are also unlikely to have favorable outcomes post-liver transplantation.

Intraoperative management of these patients is essentially an extension of the pre-operative ICU management. Additional venous access might have to be secured anticipating the major fluid shifts associated with liver transplantation. If the patient was on CRRT pre-operatively, it should be continued intra operatively as well. Ultrafiltrate of CRRT can be adjusted according to the hemodynamics of the patient. Pupillary reaction and symmetry must be noted at frequent intervals. It is important to know that surges of icp can occur intraoperatively due to the rapid administration of fluid and electrolytes. Continuation of CRRT during the surgery as well as judicious use of fluids, blood, and products will help in tackling this problem.

These patients are sedated and electively ventilated. Neurological monitoring should continue in the early postoperative period. CRRT can be discontinued postoperatively once there is evidence of adequate graft function. Sedation is usually continued for 24–36 h and then subsequently the sedation weaned off. The decision to extubate will depend upon the neurological recovery and adequacy of graft function.

34.10.2 Primary Hyper Oxaluria

Primary hyperoxaluria is a rare autosomal recessive disorder arising from the deficiency of the enzyme alanine glyoxylate aminotransferase located in the liver [10]. This results in the deposition of calcium oxalate crystals in kidney, progressive renal failure, and systemic oxalosis. A combined liver and kidney transplantation is the only solution that results in improved graft and patient survival. These children have varying degrees of cardiac function abnormalities and oxalate osteopathy due to oxalate deposition in the bone marrow. Aggressive renal replacement therapy should be initiated pre-operatively to keep oxalate levels at 30–45 mmol/L. Due to the massive systemic oxalate burden and slow resolubalization of oxalate, it is recommended to continue CRRT intraoperatively and for a few days after the transplantation as well.

34.10.3 Maple Syrup Urine Disease (MSUD)

MSUD is a rare genetic disorder characterized by a unique set of perioperative challenges to the anesthesiologist. It is an autosomal recessive condition caused by a deficiency of the enzyme Branch Chain Alpha Ketoacid Dehydrogenase (BCKDH). This results in excessive accumulation of branch chain amino acids, leucine, and isoleucine. Neurotoxicity is caused by these increased leucine levels with most children presenting in infancy with obtundation and coma leading to cerebral edema. These children are put on a protein-restricted diet and also requires avoidance of catabolic states like prolonged fasting and dehydration [11].

It is important to avoid catabolic states during the pre-operative fasting of these patients. This involves administration of specialized TPN which includes concentrated dextrose solutions. The plasma BCAAs should be normalized prior to surgery and dehydration and acidosis if any should be corrected. Lipid infusion can be used intraoperatively to provide calories avoiding overhydration and hemodilution, thus preventing cerebral edema.

34.11 Conclusion

It has been around 4 decades since the first successful pediatric liver transplantation. In these 4 decades huge advances have been made in the surgical and anesthetic techniques, perioperative care and immunosuppression. Very few children die intraoperatively and in the early postoperative period. However, further studies are

required especially for immunosuppression where chronic rejection and lymphoproliferative disorders still cause significant loss of graft. Fast tracking is an exciting concept and is fast catching up with major pediatric transplant centers with significant improvement in outcomes.

Key Points

- Pediatric Liver Transplant necessitates the anesthesiologist to deal with distinct physiology of infants and children.
- Children are more vulnerable to hypothermia and the harmful effects associated with them.
- Managing coagulopathy is extremely important owing to the small calibre of pediatric vessels and the tendency to have thrombosis.
- The success of pediatric liver transplant depends on a multidisciplinary approach including the pediatric hepatologist, transplant surgeon, anesthesiologist, and intensivist.

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