Anaesthetic Management of Acute Liver Failure for Liver Transplant

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Abbreviations

ALF	Acute liver failure
CPP	Cerebral perfusion pressure
CRRT	Continuous renal replacement therapy
CSF	Cerebrospinal fluid
FFP	Fresh frozen plasma
ICP	Intracranial pressure
IVC	Inferior vena cava
MAP	Mean arterial pressure
OLT	Orthotopic liver transplant
t-PA	Tissue plasminogen activator
VVB	Venovenous bypass

33.1 Background

Acute liver failure represents a rare but complex syndrome, characterised by acute liver dysfunction without evidence of any underlying chronic liver disease. It comprises of coagulopathy of liver aetiology and altered mentation due to hepatic encephalopathy, and may progress to multi-organ dysfunction.

ALF has been defined as the severe acute liver injury with encephalopathy and impaired synthetic function (INR of 1.5 or higher) in a patient without cirrhosis or pre-existing liver disease and with an illness of fewer than 26 weeks duration [1].

Although, with improved critical care therapy rate of transplant free survival has shown significant improvement in recent years, still liver transplant remains to be the only definite remedy available for patients with acute liver failure who do not improve with conservative management.

Early identification of acute liver failure and its aetiology with major advancements in intensive care therapy and identifying potential candidates for liver transplantation have greatly improved the survival rate of patients with ALF—Liver assist devices have too contributed as a "bridging therapy" to liver transplant or spontaneous recovery.

Identification of patients who are too sick to survive liver transplantation surgery or carry a guarded prognosis for postoperative recovery is as important, to avoid futile liver transplants and thereby improve outcome figures.

Liver transplantation for acute liver failure poses varied challenges for the perioperative anaesthesiologist in terms of the urgency of surgery, underlying multi-organ dysfunction and possible use of marginal grafts in emergency surgery where waiting for an optimum graft could jeopardise the patient outcome.

Protocols have been described to aid in the intensive care management of patients with acute

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liver failure. The literature pertaining to intraoperative management of these patients is limited, but it is in essence continuation of critical care management-especially avoiding manoeuvres during the course of surgery which would raise intracranial pressure.

Comprehensive preoperative evaluation should include detailed past medical and surgical history often elicited from relatives (due to the presence of advanced hepatic encephalopathy) and clinical examination to rule out any condition that may impact the decision to proceed with emergency liver transplant.

33.2 Specific Concerns

Multi-organ dysfunction is a major cause of morbidity associated with acute liver failure. Presence of established extra-hepatic organ failure at the time of surgery makes the context for liver transplant for patients with acute liver failure different from elective orthotopic liver transplant. Understanding of the various systems involved, careful monitoring and appropriate management of organ dysfunction is essential for a successful outcome.

33.3 Central Nervous System

Acute cerebral oedema resulting in subsequent rise in intracranial pressure with a decrease in cerebral perfusion pressure resulting in brainstem herniation is one of the major causes of mortality in patients with acute liver failure.

Cerebral blood flow in patients with acute liver failure have altered response to both arterial pressure and partial pressure of CO_2.

These patients exhibit impaired cerebral autoregulation, wherein cerebral blood flow (CBF) varies passively with mean arterial pressure (MAP) [2, 3]. Larsen et al. described "*dissociated vasoparalysis*" [4]—suggesting that CBF has blunted response to hypercapnia but shows preserved response to hypocapnia (cerebral vasoconstriction). These observations suggested that the brain vasculature in patients with ALF is in a state of *constant vasodilatation*.

Despite the state of "luxury perfusion" [5] brain hypoxia is still a possibility in cases of decreased cerebral perfusion pressure due to intracranial hypertension or episodes of severe systemic hypotension in the absence of cerebral autoregulation. In order to optimise neurological outcome, balance needs to be maintained between adequate cerebral blood flow to support brain metabolism as well as avoiding hyperperfusion that may lead to intracranial hypertension.

Brain injury as a consequence of acute rise in intracranial pressure during various phases of liver transplant can result in irreversible brain damage. Therefore, there is a need for continuous monitoring of ICP in the intraoperative period as an essential component of anaesthetic management.

33.4 Cardiovascular System

Circulatory dysfunction in patients with acute liver failure is characterised by a state of hyperdynamic circulation with high cardiac output, low mean arterial pressure (MAP), and low systemic vascular resistance (SVR) [6]. Hemodynamic derangements in these patients may be attributed to hypovolemia- due to poor oral intake or loss of fluids and decreased effective circulating volume due to systemic vasodilatation-as a result of toxins released from the failing liver or other inflammatory mediators [7]. Cardiac function is essentially well preserved in these patients, except in some cases of hypoxic hepatitis that may have evidence of both right and left sided cardiac dysfunction with or without valvular abnormalities.

Maintaining optimal hemodynamic parameters becomes imperative in the face of intracranial hypertension or compromised renal function as may be present in cases of acute liver failure. Patient volume status needs to be adequately assessed and corrected before administration of vasopressors.

33.5 Coagulation

Coagulopathy is an integral component of acute liver failure and is indicative of the key role liver plays in haemostatic pathway.

Conventional coagulation tests such as PT/INR are often misleading and can be misconstrued as haemorrhagic tendency, thereby leading to unwarranted transfusion of blood products [8].

Most coagulation factors including fibrinogen and factors II, V, VII, IX, X, XI, and XII—synthesised by the hepatocytes—are markedly decreased except for factor VIII and vWF which are derived from endothelium, and are substantially increased [9, 10]. Decreased production of procoagulants as well as short half-life of these coagulation factors contribute towards underlying coagulopathy in cases of acute liver failure. Simultaneously, there is a decreased synthesis of anticoagulant factors by the liver such as protein C, protein S, protein Z, protein Z-dependent protease inhibitor, antithrombin, heparin cofactor II, and α2-macroglobulin, that may help offset the effect of depleted procoagulant factors [11].

Therefore, decreased synthesis of procoagulants, anticoagulant factors, impaired fibrinolytic system and platelet dysfunction- all contribute towards impaired haemostasis in acute liver failure [12]. Any disturbance in this fine balance can lead to either bleeding or thrombotic complications.

33.6 Renal Function

Renal dysfunction is a frequent complication associated with acute liver failure [13, 14]. Acute kidney injury(AKI) when present with ALF augurs a poor prognosis and is associated with increased length of hospital stay and mortality. Cause of renal insufficiency is often multifactorial, ranging from hypotension caused from volume depletion, hepatorenal syndrome or acute tubular necrosis. Risk factors for AKI include increased age, paracetamol-induced ALF, hypotension, the presence of the systemic inflammatory response syndrome (SIRS) and infection [15, 16].

33.7 Too Sick To Be Considered for Liver Transplant

The only ***absolute contraindication*** to liver transplant is irretrievable brain injury and any signs suggestive of it-such as presence of bilateral dilated non-reactive pupils, absence of spontaneous respiratory efforts, loss of middle cerebral artery flow or evidence of uncle herniation on CT should be actively used out.

Progressive vasoplegic shock with increasing requirement of vasopressor support, presence extensive bowel ischemia, severe hemorrhagic pancreatitis and poorly controlled ARDS - are considered to be ***relative contraindications*** for liver transplant.

Presence of bacteraemia, responding to treatment is not considered to be a contraindication. Relative changes in the prognostic variables should be taken into consideration before proceeding for liver transplant [17].

33.8 Shifting from ICU to Operating Room

Patients with acute liver failure are nursed and managed in intensive care units while being prepared for liver transplantation. Thereby, proper communication with detailed handover between the intensivist and anaesthetist in regard to the preoperative management is imperative to continue the required care during intraoperative period as well.

Patients with ALF in view of advanced stage of hepatic encephalopathy are often mechanically ventilated and are maintained with continuous infusions of sedative, analgesic with/without paralysing agents, and vasopressor agents if needed.

Intracranial hypertension is one of the major causes of morbidity associated with ALF and its management is of paramount importance to prevent any acute surges in it, not only during intraoperative period but during transit to OR as well.

Different strategies to keep ICP in check ranges from specific ventilatory settings to use of osmotic therapy.

Use of portable ventilators should be preferred as opposed to manual ventilation to avoid any gross changes in pCO2, as well as maintaining head end elevation, thereby, minimising rise in ICP.

During transfer, adequate sedation, analgesia, and muscle paralysis should be ensured to minimise chances of patient bucking or coughing on ET tube.

Due care should be taken of all the vascular accesses along with vasopressor infusions to prevent cardiovascular instability during the transfer.

Special monitoring devices such ICP monitor, if present, should be carried to the OR to aid in intraoperative management.

Often, patients of ALF are managed with CRRT in the preoperative period and the decision to continue the same during intraoperative period is individualised on per case basis.

33.9 Anaesthetic Management

Most of the patients with acute liver failure arriving in the operating room are being mechanically ventilated. Continuous infusion of sedatives and muscle relaxants if already present can be continued in the intraoperative period as well. In cases where patients are not mechanically ventilated, anaesthesia is induced with rapid sequence induction with fentanyl 1–2 mcg/kg, propofol 1–2 mg/kg and a rapid onset muscle relaxant either suxamethonium 1–2 mg/kg or rocuronium 0.6–1.2 mg/kg.

Suxamethonium may cause transient rise in ICP and hyperkalemia [18], therefore should be avoided if feasible.

Due care needs to be taken to attenuate any acute rise in ICP associated with the stimulus of laryngoscopy and intubation.

Anaesthesia technique includes continuous infusion of fentanyl 1–2 mcg/kg/h, propofol infusion, non-depolarising muscle relaxant (preferably cis-atracurium since its metabolism is independent of hepatic function and does not produce laudanosine as in case of atracurium).

Propofol has long been used as a sedative agent in patients with intracranial hypertension due to its potential to decrease cerebral metabolic rate and oxygen demand [19]. Propofol reduces cerebral blood flow and subsequently lower the intracranial pressure in patients with acute liver failure [20]. Due to its shorter duration of action, anticonvulsant properties as well as potential to decrease intracranial pressure, it is used as an adjunct to inhalational agent.

Anaesthesia is maintained with air/oxygen/isoflurane or sevoflurane.

Ability of isoflurane to preserve Hepatic artery buffer response and splanchnic blood flow has made it the preferred inhalational agent [21].

Primary volatile anaesthetic technique is discouraged due to their tendency to cause increase in cerebral blood flow over 1 MAC and thus leading to rise in intracranial pressure. Therefore, maintenance with volatile anaesthetic in combination with a sedative (propofol being used most commonly) is preferred.

Depth of Anaesthesia Bispectral index (BIS) monitoring has been used extensively to monitor the depth of general anaesthesia. It is a non-invasive modality based on frontal electroencephalographic parameters. Various studies have utilised BIS monitoring to evaluate the level of consciousness in patients of liver failure with hepatic encephalopathy in the peritransplant period.

Advanced hepatobiliary disease causes increased levels of endogenous opioid peptides, which in addition to altered neurotransmission caused by bilirubin contributes to decreased anaesthetic requirement in patients with liver disease [22, 23].

Patients with hepatic encephalopathy tend to have lower anaesthetic requirements which can be reflected by lower MAC required to attain BIS values of less than 60 [24, 25].

33.10 Vascular Access

Since liver transplant as a surgery is associated with major fluid shifts with risk of massive blood loss, adequate venous access is vital to facilitate multiple drug infusions as well as rapid fluid

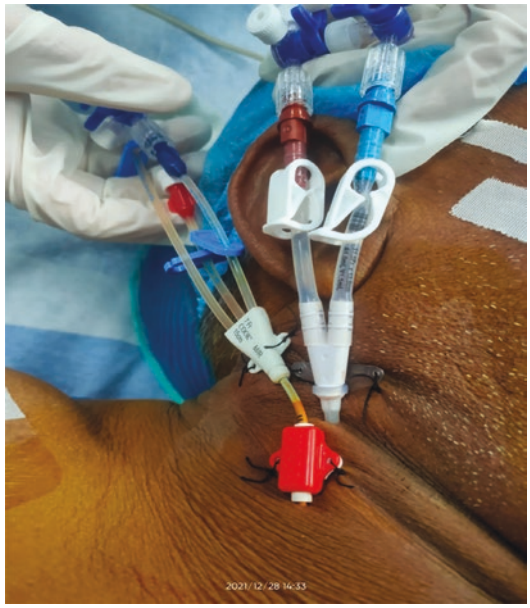

Fig. 33.1 Central venous catheter and Dialysis catheter inserted in IJV

infusion when necessary. For this purpose, two central venous catheters are placed- triple lumen 7Fr catheter- used for drug infusion, and advanced venous access/HD catheter (double lumen 11Fr) for rapid infusion of fluids. USG guided right sided IJV cannulation is preferred (Fig. 33.1).

In paediatric patients, two central venous catheters of the same size (appropriate for age) can be used.

Radial artery is frequently used for invasive blood pressure monitoring. In event of extreme hemodynamic instability or vasodilation, radial artery may underestimate central aortic pressure, in such instances, femoral artery cannulation may be contemplated.

33.11 Hemodynamic Monitoring and Management

Apart from clinical assessment, other invasive techniques should be used to assess the need for volume therapy/vasopressors in these patients. Use of invasive monitoring (such as pulmonary artery catheter or pulse contour analysis) provides measures of cardiac index. Due to invasiveness of pulmonary artery catheter (PAC) and its potential hazards, PAC should be reserved for high risk patients with significant cardiac comorbidities. Non-invasive cardiac output monitors using pulse power analysis through the pulse CO algorithm or arterial pressure-based cardiac output (APCO) method for continuous cardiac output monitoring are commonly used.

In recent times, trans-oesophageal echocardiography (TEE) has emerged as an invaluable tool for intraoperative hemodynamic monitoring. TEE provides direct measurement of the cardiac filling therefore allowing real time assessment of fluid status during the surgery. It offers additional benefit of diagnosing intraoperative complications such as pulmonary embolism, myocardial ischemia or strain. Despite its advantages, absence of technical skill and expertise to operate TEE precludes its routine use.

Waveform analysis allowing continuous measurements of stroke volume variation (SVV) and pulse pressure variation (PPV) helps in assessment of volume status and allows prediction of the likely response to fluid challenge.

Persistent positive fluid balance has been found to be associated with higher mortality patients in many cohorts. Fluid overload can cause elevated venous pressure that may lead to tissue oedema and impaired microcirculatory flow [26–28]. Therefore, it is important to avoid volume overload as much as volume depletion.

Vasopressors are recommended in event of severe hypotension (SBP < 90 mmHg or MAP<65 mmHg) or in order to maintain a cerebral perfusion pressure of more than 50 mmHg.

Norepinephrine is the preferred vasopressor since it provides a more consistent and predictable increase in cerebral perfusion [29]. Epinephrine may decrease mesenteric blood flow and therefore compromise hepatic blood flow in cases of ALF. Vasopressin and its analogues are not routinely recommended in cases of acute liver failure due to their potential to cause celebrate vasodilatation and thereby exacerbating underlying intracranial hypertension. Although, this risk has not been substantiated in recent studies [30].

There is no general consensus on the target MAP but in patients without pre-existing hyper-

tension MAP>60 mmHg is considered to be adequate. In patients with chronic hypertension who are at a risk of developing renal dysfunction, maintaining a MAP>75 mmHg should be considered [31]. Due to underlying impaired cerebral autoregulation, intraoperative hypertension should also be avoided to prevent cerebral hyperaemia that may worsen intracranial hypertension.

33.12 Neurologic Monitoring and Management

Different phases of liver transplant are associated with changes in ICP and can lead to catastrophic consequences if such changes go unrecognised and untreated.

Dissection and reperfusion phase are associated with rise in ICP and consequently decreased cerebral perfusion pressure, whereas anhepatic phase shows a decrease in intracranial pressure [32].

Intraoperative neurologic management in cases of ALF ranges from certain general supportive measures to specific targeted therapies to attenuate any overt surge in ICP. ICP should maintained below 25 mmHg. Mean arterial pressure should be optimised to ensure cerebral perfusion pressure between 50–80 mmHg.Higher cerebral perfusion pressures can cause cerebral hyperaemia, thereby worsening intracranial hypertension.

33.13 ICP Monitoring

It is imperative to monitor changes in icp intraoperatively to detect any untoward surges in intracranial pressure which otherwise may remain undetected and cause irreversible brain damage and cerebral herniation. The objective of ICP monitoring is to maintain ICP < 25 mmHg as well as ensure adequate cerebral perfusion pressure.

ICP monitors require implantation of catheters in the epidural, subdural-subarachnoid or intraventricular spaces through a burr hole. They provide real time as well as continuous data. Although invasive intracranial pressure monitors are considered to be the gold standard, overall survival benefit with their use has not been proven [33]. Due to their potential hazards, are no longer considered to be the standard of care.

Due to safety concerns associated with invasive ICP monitors, non-invasive modalities to monitor ICP have gained popularity and are commonly being used for intraoperative monitoring. Various modalities that have been used in this regard are-.

Optic nerve sheath diameter (ONSD) Optic nerve sheath is a continuation of dura mater of the brain, with the subarachnoid space of optic nerve communicating with subarachnoid space of the brain. Therefore, any pressure changes in CSF in cranial cavity are reflected in optic nerve sheath diameter (ONSD). A linear correlation has been observed between ICP and ONSD measurements (Fig. 33.2). Recent studies have suggested that an estimated increase in ONSD in the range of 4.5–5.5 mm is indicative of increased ICP (>20 mmHg) [34].

Transcranial Doppler (TCD) Klingelhofer et al. [35] first described relationship between ICP and TCD derived flow velocities. They correlated an increase in ICP with a decrease in TCD

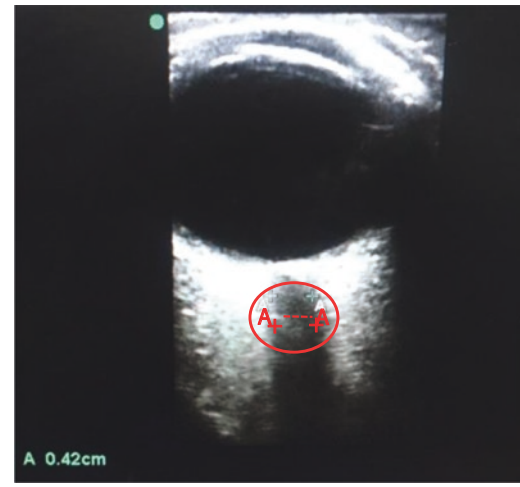

Fig. 33.2 Optic nerve sheath diameter

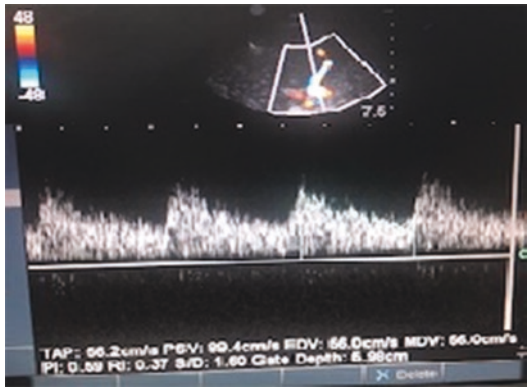

Fig. 33.3 Transcranial Doppler—*Calculation of Pulsatility index*

derived flow velocities and increase in *Pourcelot index* or *resistance index (RI)*. Middle cerebral artery is most commonly used for TCD measurement and Gosling pulsatility index (PI) (Fig. 33.3), most commonly used formula is PI = (systolic flow velocity − diastolic flow velocity)/(mean flow velocity).

Bellner et al. [36] proposed an equation to predict ICP values from pulsatility index and found that predicted ICP value was within ±4.2 mm Hg of the actual ICP, with a 95% confidence interval, in the ICP range of 5–40 mm Hg.(Equation-ICP = 10.972 × PI-1.284).

Operator dependent factors such as the ability to locate an acoustic window obtain a strong pulse signal with adequate depth and angle of insonation limit the reliability of TCD derived values. Reproducibility of the TCD also continues to be a limitation. Since TCD-ICP uses PI, which is a measure of systolic, diastolic and mean flow velocity, presence of anaesthetic agents can directly affect cerebral arteries and consequently the PI.

Electroencephalogram (EEG) This can be helpful in identifying seizure activity which occurs in up to 30% of patients and leads to characteristic change in EEG seen with increased intracranial pressure [37, 38]. Estimation of ICP from EEG is based on identification of slow high-voltage waves. Since most anaesthetic agents promote formation of delta or slow waves, identification of increased ICP levels under anaesthesia becomes difficult. Therefore, EEG is not routinely used in the intraoperative period.

Jugular Venous Oxygen Saturation (SJvO2) SJv02 has been used as surrogate marker for cerebral metabolism and brain oxygenation. Measurement of jugular bulb oxygen saturation helps to assess the arterio-venous oxygen difference (AVDO2), which in turn indicates metabolic demand in comparison to oxygenation. It involves placement of a retrograde catheter in internal jugular vein with tip at jugular venous bulb. In situations where cerebral oxygen demand exceeds supply, greater amount of oxygen is extracted by the brain, therefore, causing a decrease in SJv02. Conversely, SJv02 increases when supply exceeds metabolic demands. Under physiological conditions, ranges from 55% to 75%. In ALF, consistent values of SJv02 <60% or >80% are associated with raised intracranial pressure [39].

Decrease in SJv02 can be caused by reduced cerebral perfusion pressure as in acute surge in ICP [39], whereas increased values in SJv02 are indicative of cerebral hyperaemia. In situation, where both ICP and SJv02 are elevated, management should be aimed at reducing cerebral blood flow [40]. SJvO2 has been shown to have a utility in managing ALF patients with moderate hypothermia [41]. Similarly $SJvO_2$ has been utilised in managing ALF patients using hyperventilation to lower the intracranial pressure [42].

Cerebral oximetry It is a non-invasive method based on near infrared spectroscopy (NIRS) which measures haemoglobin saturation of arterial, venous, and capillary blood in the cerebral tissue. It is a new modality and is still awaiting validation through randomised control trials. Its use in acute liver failure is based on correlation of cerebral tissue oxygen saturation ($SctO_2$) with increase in intracranial pressure. *Cerebral desaturation*—decrease in $SctO_2$ can be the result of diminished oxygen supply to the brain or increase in oxygen demand by the brain tissue. The cause of change in $SctO_2$ has to be ascertained before management of cerebral desaturation can be initiated.

This modality has been studied more in patients undergoing cardiac surgery in the operating theatre. Cerebral oximetry guided therapy led to improved patient outcome in comparison to the control group [43]. This study of 1034 cardiac patients showed diminished incidence of stroke postoperatively in protocol guided maintenance of $Scto_2$ at or near the pre-induction baseline. Although preliminary results are encouraging, still there is no definite studies showing short-term and long-term outcome benefits (Fig. 33.4).

Fig. 33.4 Cerebral Oximeter

Pupillometry Pupillary examination and light reflex has very poor reliability. Pupillary reactivity can be more accurately assessed using a commercially available pupillometer (Fig. 33.5). Pupillary reactivity <10% correlates with raised ICP [44]. A case series of neurosurgical patients by Papangelou A et al. [45] revealed abnormal pupillometry observation in 73% of clinical herniation episodes and these were identifiable 7.4 h (median interval) before the event. The main advantage of pupillometry is that it can be performed quickly and frequently. Further studies are required to validate these findings in ALF patients.

Fig. 33.5 Pulpillometer

33.14 Strategies to Reduce Intracranial Pressure

- *Positioning*: Patients should be positioned with head end elevated to ~30° (to improve venous and CSF drainage) with head and neck in neutral position (to avoid compromise of jugular venous drainage).
- *Ventilation*: Lung protective ventilatory strategies should be adopted, although hypercapnia needs to be avoided to prevent any cerebral vasodilatation. $PaCO_2$ levels between 30 and 45 mmHg should be targeted. Hyperventilation causes pre capillary vasoconstriction and help in decreasing cerebral blood flow and ICP [46]. Hyperventilation has also been shown to restore impaired cerebral autoregulation in ALF, though this effect may be short-lived. Although, hyperventilation plays a key role in management of acute episodes intracranial hypertension, overzealous and prolonged periods of hypocapnia is discouraged as it can lead to cerebral ischemia. Therefore, despite being an indispensable tool in managing cerebral oedema, hyperventilation should be reserved only as an emergency rescue measure to terminate episodes of intracranial hypertension/imminent herniation.
- *Temperature regulation*: Hypothermia plays a neuro-protective role by decreasing cerebral metabolic rate and cerebral blood flow, thus reducing intracranial pressure. In acute liver failure, protective mechanism of hypothermia is multifactorial. Jalan et al. [47] demonstrated the beneficial role of moderate hypothermia (32–33 °C) in patients with refractory intracranial hypertension-unresponsive to mannitol or ultrafiltration therapy.

  Subsequent studies by Karvellas et al. [48] and Bernal et al. [49], however, failed to demonstrate any benefit of moderate hypothermia over 36 °C on prevention of intracranial hypertension.

  Potential complications associated with hypothermia include risks of infection, bleeding due to worsening of underlying coagulopathy and platelet dysfunction, arrhythmias, electrolyte imbalance as well as altered drug metabolism [50].

  These adverse effects are generally more common in event of severe hypothermia (<32 °C), and less severe at temperature <35 °C. Routine induction of hypothermia temperature <34 °C is, therefore, no longer recommended as a standard of care and should be considered only in management of refractory intracranial hypertension. In the absence of refractory intracranial hypertension, the reasonable approach, therefore, is to maintain normothermia (core body temp-35–36 °C) as well as avoid hyperthermia/fever [51].
- *Osmotic therapy*: Osmotherapy with mannitol, in the bolus dose of 0.25–0.5 g/kg over 10 min, can be effectively used in case of acute rise in ICP (>25 mmHg) intraoperatively. Lower doses of mannitol have proven to be equally efficacious, with reduced incidence of severe osmotic disequilibrium and dehydration. Hypertonic saline has also been successfully used in critical care settings in patients with intracranial hypertension, still data regarding its role in intraoperative setting is limited. Hyponatremia, of short duration, although is not a contraindication for using hypersonic saline, rate of correction should be inversely proportional to the duration of hyponatremia.

33.15 Pre-emptive Hepatectomy

Pro-inflammatory cytokines released by the "failing liver" have been postulated to contribute towards cerebral hyperaemia and cerebral oedema. Pre-emptive hepatectomy (in the absence of a donor liver) has been reported in few cases to prevent neurological/cerebrovascular collapse [52]. This, however, provokes various ethical dilemmas. Although, in cases where donor liver is available, expeditious clamping of portal vein can be performed, rendering the patient anhepatic. This helps to stabilise the neurological as well cardiovascular status of the patient [53, 54].

In such scenarios, temporary portocaval shunt can be considered that prevents splanchnic congestion and helps to main portal venous return, thereby minimising systemic consequences associated with prolonged portal vein clamping.

33.16 Venovenous Bypass (VVB) and IVC Clamping

Due to lack of adequate collateral venous circulation in these patients, conventional caval clamping technique may lead to profound hemodynamic instability and thereby cause a significant impairment in cerebral and renal perfusion. In order to maintain required hemodynamic parameters, often large volume replacement is done which can further aggravate underlying cerebral oedema. Use of veno-venous bypass has been postulated to be associated with decrease in neurological sequelae due to cerebral oedema. Few authors, however, did not find any evidence of adverse neurological outcome in patients undergoing OLT without VVB. They demonstrated that with use of vasoconstrictors, MAP and CPP could be well maintained, deeming VVB unnecessary [55, 56].

33.17 Managing the Coagulopathy

Intraoperatively evidence of coagulopathy is evident by increased bleeding from cut surfaces and delayed clot formations.

Conventional coagulation parameters often poorly predict the risk of bleeding in such patients, pre-emptive correction of PT/INR values without any evidence of apparent bleeding is not routinely warranted. The inherent risks associated with FFP transfusion such as volume overload or TRALI should be carefully weighed but coagulopathy should be duly corrected.

Strategies to minimise heterologous transfusion should include the use of cell saver. To minimise blood loss maintaining permissive hypotension with controlled hypovolemia can be considered during dissection phase though these strategies are more relevant in chronic liver disease with portal hypertension and pooling up blood in splanchnic circulation. Additionally, permissive hypotension or hypovolemia can be counterproductive in such cases due to underlying compromised cerebral and renal perfusion.

Presence of minimal or no portal hypertension in ALF associated with absence of abdominal varices helps reduce the risk of surgical bleeding.

Recent studies have demonstrated other potential haemostatic mechanisms- thrombin generation, role of endogenous heparinoids, microparticles and relative role of platelets and fibrinogen in moderating the coagulation disturbances in patients with ALF [57].

Despite having reduced potential to generate thrombin, patients with ALF tend to show accelerated response to thrombin production- once initial amount to activate factors VIII, IX, and XI has been formed, and reduced thrombin inactivation due to activated protein-C resistance, consequently leading to thrombotic potential [58].

A heparin-like effect has also been demonstrated in patients with acute liver failure. Possible mechanism includes release of heparan sulphate from damaged endothelium, release of heparin from damaged liver and reduced renal clearance of heparinoids [59]. Heparinase-modified TEG therefore can be a valuable adjunct in the assessment of coagulopathy related to ALF. This heparin like effect is further enhanced during reperfusion.

Similarly, hyperfibrinolysis has also been observed in the immediate post-reperfusion phase and may be attributed to reduced clearance of t-PA during the anhepatic phase and its release in circulation during reperfusion [60, 61]. Spontaneous recovery from hyperfibrinolysis in the reperfusion phase generally commences 30–60 min but may take up to 2 h to normalise [62].

Viscoelastic tests not only provides information regarding the strength of clot formation but also reflect upon the presence of fibrinolysis. Global assays, thus, have proved to an invaluable tool to help towards a directed therapy and minimising injudicious transfusions and their associated risks.

33.18 Metabolic Derangement

With the failing liver, there is a propensity towards hypoglycaemia, therefore a continuous infusion of dextrose containing fluids with glucose monitoring is essential. Hyperglycaemia, on the other hand may exacerbate cerebral injury and therefore should be avoided.

Infusion of hypertonic saline to maintain S. Na + between 145 and 155 mmol/L in comparison to standard care has resulted in decrease in ICP.

However, liver transplant surgery often warrants large volume fluid administration, transfusion of blood and blood products and use of sodium bicarbonate solution, resulting in gross changes in serum sodium concentration intraoperatively. These changes are often more pronounced in the presence of hyponatremia. Therefore, hypertonic saline solution should be used with caution in these patient population. Due measures including the need for N/2 sodium chloride may be required to prevent rapid changes in sodium levels, ensuring that rate of correction does not exceed 10 mmol/L per 24 h [63].

Ongoing blood boss in the intraoperative period can worsen the underlying acidosis, if left uncorrected, can exacerbate hemodynamic instability. Therefore, metabolic acidosis needs to be addressed with intravascular volume correction or sodium bicarbonate infusion as required.

33.19 Renal Function Management

Intraoperative management of patients with liver failure with underlying renal dysfunction is complex. Conventional anaesthetic techniques such as maintaining "low CVP" and conservative fluid administration to avoid liver congestion and decrease portal pressures- to reduce bleeding and need for transfusion, can cause or worsen kidney injury [64, 65].

It is therefore imperative to maintain adequate blood pressure as well as euvolemia to ensure adequate renal perfusion. Volatile anaesthetics, positive pressure ventilation can further reduce cardiac output, renal blood flow, and consequently glomerular filtration rate. Increased transfusion of blood and blood products can further exacerbate renal injury.

Vasopressors need to be used to treat hypotension was required, with norepinephrine and arginine vasopressin, being most commonly used agents. However, in the background of cerebral oedema, arginine vasopressin analogues should be used with caution.

During the course of surgery, vascular occlusion of portal triad and inferior vena cava clamping, can cause a significant decrease in cardiac output, thereby further compromising renal blood flow. At times, patients with acute liver failure are rendered anhepatic earlier to promote neurological stability, which in turn may significantly alter acid-base balance. Correction of these acid-base derangements is important to prevent hypotension, myocardial depression or life threatening arrhythmias due to underlying hyperkalaemia.

In extreme cases of worsening renal function as reflected by decreased urine output and metabolic derangements (progressive acidosis/hyperkalaemia)—not responding to conventional measures, initiation of renal replacement therapy should be considered.

33.20 Use of Intraoperative CRRT

Continuous renal replacement therapy is often initiated in patients with acute liver failure in preoperative period. Use of CRRT has shown to be beneficial in reducing cerebral oedema, maintaining acid-base balance, maintaining fluid balance, and correcting metabolic derangements esp. in presence of underlying renal dysfunction.

Decision to continue CRRT in the intraoperative period further adds to the intricacy of procedure with need for additional machine, extra circuits, and technical staff to be present in the operating room.

Use of heparin anticoagulation is not recommended due to associated risks of bleeding and citrate anticoagulation can be used instead. Complications of circuit clotting has been reported in patients with ALF.

It is imperative for the anaesthesiologist to be well versed with the functioning of CRRT to avoid/troubleshoot any untoward instances that may arise intraoperatively such as kinking or malfunctioning of CRRT circuits. It is as important to take into account the effect of CRRT on intraoperative drug dosing esp. for drugs that undergo renal excretion, although protein binding and volume of distribution of drugs can also affect their clearance by CRRT. The extra corporeal circulation established with CCRT is prone to induce increased infection risk, hypothermia, thrombocytopenia, and coagulation abnormalities.

Therefore, the decision of continuing CRRT intraoperatively needs to be weighed against the inherent limitations of CRRT in addition to the limited experience of anaesthesiology team with it.

33.21 Postoperative Management

Despite a normal functioning graft, delayed recovery in the postoperative period is expected. Cerebral oedema leading to encephalopathy takes time to recover. Most patients would require postoperative ventilation for at least 24–48 h. Postoperative monitoring of cerebral status in the form of ONSD, Cerebral oximetry, and Pupillometry should continue pending documentation of resolving cerebral oedema. This could be in the form of improving neurological status and if required supported by decreasing cerebral oedema on CT.

After OLT, cerebral oedema resolves slowly and restoration of cerebral autoregulation may take up to 48 h with good allograft function.

Key Points

1. Acute liver Failure is acute liver dysfunction characterised by coagulopathy and hepatic encephalopathy.
2. Liver transplant continues to remain the only definitive therapy available.
3. Conventional coagulation test e.g. PT/INR are poor predictors of bleeding tendencies. Viscoelastic tests are more reliable.
4. Different phases of OLT are associated with changes in ICP.
5. Mild hypothermia has a neuroprotective effect.
6. Hyperventilation should be used as a rescue measure.
7. Intracranial pressure monitoring using surrogate markers like ONSD, TCD, $SJvO_2$ and Cerebral oximetry need to be validated.
8. Acute liver failure can be frequently complicated by presence of acute kidney injury.
9. Intraoperative CRRT, although promising, is not without hazards and should be considered on per case basis.
10. Delayed recovery in the postoperative period should be expected.

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