CASE REPORT

Anaesthetic management of liver transplantation in patients with fulminant hepatic failure

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Abstract

Acute Liver Failure (ALF) is associated with rapidly progressive multiorgan failure and may even lead to death. Although liver transplantation (LT) has emerged as the only viable treatment option, there are many challenges associated with LT. The literature available from developed countries mainly focuses on the prognosis of ALF with limited focus on the anaesthetic management of LT. In the developing world particularly, the facility and experience of LT is relatively new. This case report presents the first case from Pakistan regarding the anaesthesia management of ALF. It discusses the management of a 46-year-old female who underwent emergency LT which includes initiation of Total Intravenous Anaesthesia, steps to reduce intra-cranial pressure, continuous Renal Replacement Therapy, and correction of coagulopathy using thromboelastography. To conclude, a holistic understanding of pre, intra, and post-operative anaesthetic management of liver transplantation requires a multi-disciplinary team management and can significantly improve the survival rates.

Keywords: Liver Transplant, Anaesthesia, Liver Failure.

DOI: https://doi.org/10.47391/JPMA.9055

Introduction

Acute Liver Failure (ALF), with an average annual incidence of approximately 5.5–6.2 people per million population, is known to be an uncommon condition.[1] ALF is classified by the time difference between the appearance of jaundice and the development of encephalopathy; hyperacute (0–7 days), acute (8–28 days) and subacute (29–84 days).[2] Moreover, when a person without any previous history of liver disease develops encephalopathy and coagulopathy within the 8 weeks following the appearance of jaundice, it is characterised as Fulminant Hepatic Failure (FHF).[2] Aetiology of ALF has a geographical diversity, and many cases have an unknown origin. In developing countries, viral hepatitis is the leading cause and in the Western world, most cases are drug-induced.[3]

Liver transplantation (LT) remains the only viable treatment option that can improve the survival rate in ALF patients. In a recent cohort study, the short-term survival rate was 93.7% before discharge. However, in older patients, the in-hospital survival rate decreased to 80%. One of the leading causes of mortality (20-35%) in these patients is intracranial hypertension because of cerebral oedema secondary to hyperammonaemia.[4]

Studies from developed countries mostly discuss the prognosis of the disease with limited literature regarding the anaesthesia aspect of liver transplantation in the management of ALF. Furthermore, the facility of liver transplantation in Pakistan is relatively new. Thus, this is one of the first case reports regarding anaesthesia management of ALF from Pakistan.

Case Report

A 46-year-old female with no previous history of liver disease, presented to the Emergency Department (ED), Shifa International Hospital, Islamabad, Pakistan in June 2021 with a history of jaundice for eight weeks and unconsciousness for one day. She had a previous history of diabetes mellitus, hypertension, and ischaemic heart disease. Her past surgical history included percutaneous coronary intervention stenting and thyroidectomy. On arrival, she had Grade IV Hepatic Encephalopathy and was immediately intubated to protect her airway using Propofol (1 $\mu g \cdot kg^{-1}$) and Rocuronium ($mg \cdot kg^{-1}$). Her baseline workup revealed deranged liver function tests, coagulopathy, and hyperammonaemia as shown in Table 1. Her viral serology was negative. She was diagnosed as a case of acute liver failure with an unknown cause. MRI brain showed encephalopathic change, T2 Flair diffuse cortical oedema, and hyperintensity with minimum electrical activity on Electroencephalography. In ED, she remained haemodynamically stable and after initial management, she was shifted to the intensive care unit (ICU). Continuous Renal Replacement Therapy (CRRT) was started on the first day in the ICU to prevent worsening hyperammonaemia and to control cerebral oedema.[5] Stress ulcer prophylaxis with omeprazole was started. Rifaximin in combination

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Submission completed: 01-02-2023 **First Revision received:** 25-08-2023
Acceptance: 12-10-2024 **Last Revision received**: 11-10-2024

with lactulose was started to reduce ammonia absorption from the bowel. Following the European Society for Clinical Nutrition and Metabolism guidelines, a low-dose enteral feeding via nasogastric tube was started with daily ammonia levels.[6] Despite aggressive medical management, her condition continued to deteriorate. After adequate fluid resuscitation, Norepinephrine (0.05 - 0.1 µg/kg/min) was commenced to maintain MAP greater than 75 mmHg via central line (8.5 Fr Multicath 4- VYGON) inserted in the right internal jugular vein to maintain cerebral perfusion pressure. Echocardiography demonstrated no significant abnormality and other causes of hypotension were ruled out. She was offered an emergency liver transplant based on King's College criteria.[7] Finally, one of her family members was compatible with liver donation, and she underwent an emergency living-related liver transplant on her third admission day.

The patient was shifted to the operating room on non-invasive monitoring, which included non-invasive blood pressure, pulse oximeter, capnography, ECG, and temperature. Ventilator support was continued in the same ICU settings (Mode: volume control ventilation, Tidal volume:500 ml, Respiratory Rate 12- 16 breaths per minute, FiO2: 50% and Positive End-Expiratory Pressure: 5 cmH_2O). On arrival in the operating room, arterial cannulations were done in the left radial and left femoral artery for intra-arterial blood pressure monitoring and pulse contour cardiac output monitoring (PiCCO) (Pulsion Medical System, Munich, Germany) respectively. Another central venous cannulation was performed in the right internal jugular vein with a 9-Fr Advanced Venous Access catheter (Edwards Lifesciences, Irvine, CA, USA). A Bispectral Index® monitor (Aspect Medical Systems. Inc., Norwood, USA) was attached. A Foley catheter and nasogastric tube were already in place. As per the protocol of the institution, defibrillator pads were attached. For maintaining the core body temperature, a forced-air patient warming blanket was applied before surgical draping.

Total Intravenous Anaesthesia (TIVA) was started and maintained with Propofol (50 - 100 µg·kg−1·min−1), and Fentanyl (2 µg·kg−1·hr−1) to maintain BIS values between 40 and 60. Atracurium infusion (0.5 mg·kg−1·hr−1) was used for neuromuscular blocking. Noradrenaline infusion (0.05-0.1 µg·kg−1·min−1) was used for haemodynamic stability. For renal protection and to reduce intracranial pressure, the patient received mannitol and furosemide. The patient was given 20% human albumin and Terlipressin bolus followed by infusion for renal protection. Prophylactic antibiotics were given as per institutional protocol to prevent surgical site infection. The patient was kept in a slight head-up position throughout the procedure. Thromboelastography (TEG) based coagulation management was performed. Continuous Renal Replacement Therapy (CRRT) was continued during the dissection and anhepatic phase to control the blood ammonia levels. CRRT was discontinued thirty minutes before reperfusion.

During the dissection phase, restrictive fluid therapy along with diuretics was used to maintain low Central Venous Pressure (2-4 cmH2O) to prevent an increase in portal pressure and bleeding from variceal veins whilst avoiding hypovolaemia and hypotension. Tight glycaemic control was maintained using a Variable Rate Intravenous Insulin Infusion (VRIII) Protocol. She remained haemodynamically stable during the anhepatic period. In preparation for the reperfusion phase, 2-gram magnesium sulphate was given

Table: Significant investigations during admission

Significant Investigations					
Test	**Normal Value**	**Admission**	**Post-op day 0**	**Post-op day 3**	**Post-op day 5**
Total Bilirubin (mg/dL)	Up to 1.2	33	13.2	20.25	17.81
Direct bilirubin (mg/dL)	Up to 0.3	23	7.2	13.1	11.9
Alanine transaminase (U/L)	Up to 50	222	962	480	388
Aspartate aminotransferase (U/L)	Up to 50	297	807	256	167
Alkaline phosphatase (IU/L)	40 -130	195	49	87	143
ammonia (µ/dL)	19-87	268	105	57	73
International Normalized Ratio (INR)	0.8- 1.3	4.8	1.8	1.5	1.38
Platelets (/µL)	150,000-400,000	150,000	29000	26000	39000
Haemoglobin (g/dl)	12.5 -16	13.6	8.2	8.8	9
White blood cell (/µL)	4000 - 10500	6980	4360	10250	12530
Sodium (mEq/L)	136-145	147	153	150	149
Potassium (mEq/L)	3.5 – 5.1	4.1	3.3	3.5	3.5
Bicarbonate (mEq/L)	22 – 29	26	25	28	27
Creatinine (mg/dL)	0.57 – 1.11	1.6	0.44	0.91	0.7
Fibrinogen (mg/dL)	200 - 400	80	131	258	
Lactate (mmol/L)	0.5 – 2.2	5			

as it is associated with lower post-reperfusion arterial lactate levels.[8] Sodium bicarbonate was also given and $Fi0_2$ was temporarily increased to 1.0. The right lobe graft without the middle hepatic vein from the living donor was transplanted in the recipient. During the reperfusion phase, the portal vein clamp was released, and the donor graft was reperfused leading to a drop in the mean blood pressure to 59 mmHg, and Systemic Vascular Resistance to 400 dynes.sec-1.cm5-1. This was normalized within minutes with adrenaline and noradrenaline boluses. Cold and warm ischaemia times were sixty-four and forty-three minutes respectively. No temporary portocaval shunt was performed. Total blood loss was 4 litres and she received 1250 ml of red blood cells, 200 ml of platelets, 1800 ml of fresh frozen plasma, and 600 ml of cryoprecipitate.

After fourteen hours long surgery, the patient was eventually transferred to the ICU. On the fourth postoperative day, the patient was extubated, and her Glasgow Coma Scale (GCS) improved to 10/15. The Vasopressors were tapered off on the sixth post-operative day and on the tenth postoperative day, she was shifted to the ward bed. Subsequently, she was discharged home after thirty-five days of admission.

Discussion

Management aspects of ALF range from the use of hepatic dialysis systems to the introduction of xenotransplants. Yet, liver transplant remains the only curative option. The less the interval between the appearance of jaundice and the development of hepatic encephalopathy the better the prognosis. Conversely, in patients with subacute liver failure who develop hepatic encephalopathy only a few weeks after the onset of jaundice, there is a significantly low transplant-free survival.[9] Thus, it is important to note that this patient had an eight-week history of jaundice at the time of presentation, with grade IV encephalopathy.

Acute Liver Failure can progress rapidly, ranging from initial improvement to requiring an emergency liver transplant depending upon the aetiology. The overall death rate for ALF is around 30% but can rise to nearly 50% without a timely transplant.[5] Raised ammonia concentrations are closely associated with hepatic encephalopathy, cerebral oedema, and intracranial hypertension (ICH).[10] To control serum ammonia levels and prevent intracranial hypertension, mannitol or hypertonic saline and plasma exchange are used.[11] CRRT also lowers serum ammonia levels and improves 21-day transplant-free survival. It significantly helps in acute kidney injury management, which is another common manifestation. Thus, CRRT was started preoperatively in our patient to reduce the ammonia levels and to manage hypernatraemia.

Invasive intracranial pressure (ICP) monitoring is the gold standard. However, because ALF patients suffer from coagulopathy, there is an increased risk of life-threatening haemorrhage following ICP monitor catheter insertion so to avoid this and due to the lack of availability, any intervention to monitor ICP in this patient was not performed.

To manage intracranial pressure (ICP), recommended strategies include reducing cerebral oxygen consumption through adequate sedation with propofol or thiopental, maintaining normocapnia and normoglycaemia, minimizing venous congestion by head elevating, and avoiding hyperthermia. Propofol is effective in decreasing cerebral blood flow and ICP, and its pharmacokinetics remain stable even in liver failure.[12] Due to these benefits and to ensure continuity of anaesthesia, TIVA with propofol was maintained, monitored by BIS to ensure adequate depth of anaesthesia, and supplemented with opioids and neuromuscular blockers. For ICH that is resistant to conventional therapies, a brief period of hyperventilation to reduce PaCO2 to ≤ 30 mmHg can be employed. There is limited evidence supporting therapeutic cooling in the context of acute liver failure (ALF) and elevated ICP. The aim is to maintain a core temperature of 35–36°C.[13]

A pulmonary artery catheter for haemodynamic monitoring is not used commonly because of its invasiveness and known limitations in measuring preload. The Pulse Index Continuous Cardiac Output (PiCCO), a cutting-edge technology, uses algorithms to process and determine cardiac output, stroke volume, and pulse pressure variations.[14] Moreover, it can calculate the static preload indices. However, it must be noted that cardiac output measurements with PiCCO are not reliable during liver transplantation.[15]

Conclusion

In this case report, anaesthetic management of emergency living-related liver transplantation is discussed. Patients with acute liver failure refractory to medical management are left with the only option of liver transplant which can significantly improve survival rates. However, liver transplantation requires a collaborative effort from a multi-disciplinary team, including anaesthesiologists. This report provides an understanding of pre-, intra-, and post-operative management of such complex procedures.

Consent: Consent to publish the case report was obtained from the patient.

Disclaimer: None to declare.

Conflict of interest: None to declare.

Funding disclosure: None to declare.

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AUTHORS' CONTRIBUTIONS:

SAN: Concept, revision, final approval and agreement to be accountable for all aspects of the work.

SSP: Design, drafting, revision, final approval and agreement to be accountable for all aspects of the work.