Original Article

Anaesthesia for Live Related Liver Transplantation: Experience at a Teaching Hospital in Abroad

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Abstract :
ordinary, challenging and very much special for anaesthesiologists. The liver transplantation programme at Indraprastha Apollo Hospital, Delhi, India has been running since 1998. Both live related and cadveric liver transplantations are performed and it is about 100 to 120 per year. In this prospective study, the anaesthetic aspects of 10 live related liver transplantations are reviewed.
Here we focused on anaesthetic technique used; indications for liver transplantation and type of graft transplanted; survival rate; duration of anaesthesia and cost; intra-operativeLive related liver transplantation is no longer experimental. It is the therapeutic option for patients with chronic liver failure. Adequate logistic and prompt laboratory service, availability of blood products, maximum invasive and non invasive monitoring is mandatory for better outcome.

Key words: Anesthesia; Intraoperative complications; Liver transplantation :

Introduction

Liver transplantation or hepatic transplantation is All patients received general anaesthesia with rapid sequence induction. Most adult recipients had cirrhosis from various causes, whereas biliary atresia was the cause of the paediatric case. Only live related liver transplantations were performed. Veno-venous bypass was not used; a cell saver device was used for only one adult recipient. All transplant recipients had acidosis, coagulation profile alteration and hypotension during the

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biochemical changes, changes associated with major transfusion; coagulopathy, and reperfusion; frequency of use of cell saver devices, veno-venous bypass, and a rapid infusion system; and associated complications.
All patients received general anaesthesia with rapid sequence induction. Most adult recipients had cirrhosis from various causes, whereas biliary atresia was the cause of the paediatric case. Only live related liver transplantations were performed. Veno-venous bypass was not used; a cell saver device was used for only one adult recipient. All transplant recipients had acidosis, coagulation profile alteration and hypotension during the operation. One out off 10 patients died in 15th post operative day due to rejection followed by multi organ failure.

operation. One out off 10 patients died in 15th post operative day due to rejection followed by multi organ failure. the replacement of a diseased liver with a healthy liver allograft. The most commonly used technique is orthotopic transplantation, in which the native liver is removed and replaced by the donor organ in the same anatomic location as the original liver. Liver transplantation nowadays is a well accepted treatment option for end-stage liver disease and acute liver failure. It is also one of the most expensive treatments in modern medicine.
The first human liver transplant was performed in 1963 by a surgical team led by Dr. Thomas Starz1 of Denver, Colorado, United States. Dr. Starz performed several additional transplants over the next few years before the first short-term success was achieved in 1967 with the first one-year survival post transplantation.
Live related liver transplantation has emerged in recent decades as a critical surgical option for patients with end stage liver disease, such as cirrhosis and/or hepatocellular carcinoma often attributable to one or more of the following: long-term alcohol abuse, long-term untreated Hepatitis C infection, long-term untreated Hepatitis B infection. The concept of live related liver transplantation is based on the remarkable regenerative capacities of the human liver and the widespread shortage of cadaveric livers for

patients awaiting transplant. In live related liver transplantation, a piece of healthy liver is surgically removed from a living person and transplanted into a recipient, immediately after the recipient's diseased liver has been entirely removed. Historically, live related liver transplantation began as a means for parents of children with severe liver disease to donate a portion of their healthy liver to replace their child's entire damaged liver. The first report of successful live related liver transplantation was by Dr. Christoph Broelsch at the University of Chicago Medical Center in November 1989, when two-year-old Alyssa Smith received a portion of her mother's liver.2

Orthotopic liver transplantation has been shown to be the best therapeutic option for those with chronic liver failure.3 Liver transplantation involves the following three stages: stage I (pre- anhepatic phase), which involves dissection and mobilisation of the native liver; stage II (anhepatic phase), which represents the time when there is no circulation to the liver, and during which veno venous bypass (VVB) can be used in adult recipients to lessen the haemodynamic effect of the inferior vena cava cross-clamping; and stage III (post-anhepatic phase), which is marked by reperfusion with the re-establishment of portal and caval blood flow. Liver transplant surgery carries the risk of massive haemorrhage, hence the use of cell saver devices and a rapid infusion system. Anesthesia considerations for liver transplantation include the management of severely deranged physiology, pharmacology, and biochemistry, as all organ systems may be affected adversely by the failing liver. Anaesthetic management of liver transplant surgery is extra ordinary, challenging and very much special for anaesthesiologists. The liver transplantation programme at Indraprastha Apollo Hospital, Delhi, India has been running since 1998. Both live related and cadeveric liver transplantations are performed and it is about 100 to 120 per year. In this prospective study, the anaesthetic aspects of 10 live related liver transplantations are reviewed.

Methods

Between 15 May 2009 and 17 June 2009, 10 liver transplants were performed in Indraprastha Apollo Hospital, Delhi, India. Their records were kept. The anaesthetic technique used, the indications for liver transplantation, duration of anaesthesia, hospital stay, cost and mortality were reviewed. Intra-operative changes such as haemodynamic changes when the inferior vena cava was cross-clamped and during reperfusion, changes in electrolytes, acid-base balance, clotting profile before and after reperfusion were analyzed. The frequency of use of cell saver devices and a rapid infusion system, and the associated complications were also recorded.

Anaesthetic technique

All patients who had undergone liver transplantation received general anaesthesia with rapid sequence induction to prevent any aspiration of gastric contents. Induction was accomplished by the administration of fentanyl 1 to 2 mg/kg, propofol 1-2 mg/kg, and suxamethonium 1.5 mg/kg. Anaesthesia was maintained by metabolic flow of oxygen, atracurium infusion, fentanyl infusion and isoflurane. After induction, additional monitoring including that of inspiratory and expiratory gases, invasive blood pressure, nasopharyngeal temperature, and urine (using a urinary catheter) were initiated. All intravenous lines were placed in the upper limbs, as clamping of the inferior vena cava was required during the procedure. All except two adult recipients had two 8.5-French vascular sheaths inserted into the right internal jugular vein. One of the sheaths was used for the insertion of the flow-directed, balloon-tipped pulmonary arterial catheter (Arrow, International Inc., Philadelphia, US). Central venous pressure and wedge pressure were

monitored through the pulmonary arterial catheter, and cardiac output was measured by the thermodilution technique. Both sheaths were subsequently connected to the rapid infusion system. After the insertion of central and arterial lines, blood was drawn to determine arterial blood gas tensions, haemoglobin level, platelet counts, prothrombin time, partial thromboplastin time, and serum osmolality, as well as levels of glucose, serum sodium, serum potassium, and ionized calcium. These measurements served as a baseline blood profile for each patient. Hourly laboratory measurements were performed before reperfusion. After reperfusion, it was done half hourly. Thromboelastography was performed at various intervals to guide the replacement of blood products and a cell saver was used to salvage blood

for autologous transfusion. A rapid infusion pump was used in adult recipients to facilitate fluid resuscitation. Air-warming blankets were used to maintain body temperature, sequential compression device were used for every patient and the theatre temperature was set to greater than 24°C.

Results

Indications for liver transplantation and anthropometric measurement

Table 1 summarizes the patients' diagnoses and indications for transplantation. Most of the adult recipients had cirrhosis, with hepatitis B being the most common cause of this. In descending order of frequency were alcoholic cirrhosis, cryptogenic cirrhosis and hepatitis B cirrhosis. One patient had fulminant hepatic failure at the time of transplantation and one paediatric patient had primary biliary atresia that was the main indication for liver transplantation in paediatric group. Nine liver transplantations were performed during the study period. The patients ranged in age from 6 years to 60 years. The maximum weight was 80 kg and minimum weight was 50 kg for adult and paediatric patient was 22kg.

Table 1: The various diagnoses that necessitated a liver transplantation and anthropometric measurement

Diagnosis	No.of patients	Agerange (years)	Body Weight range (kg)
Hepatitis B cirrhosis	2	(42.0- 51.0)	(55.0- 80.0)
Cryptogenic cirrhosis	3	(43.0- 58.0)	(56.0- 67.0)
Alcoholic cirrhosis	3	(41.0-60)	(50.0- 71.0)
Primary billiaryatresia	1	6	22.0
Hepatitis B fulminant hepaticFailure	1	40	64.0

Duration of anaesthesia, hospital stay, cost and mortality

Most of the surgical starting times were within normal working hours. The median anaesthetic time for adult recipients was 14 hours (range 12-18 hours). The median hospital stay was 21 days with ranges from 21 days to 30 days. The cost was 35,00,000 to 50,00,000 BDT (median 40,00,000 BDT). Among them only one adult patient was died in multi organ transplant unit.

Special equipment

All recipients required the rapid infusion system for fluid resuscitation. Only one recipient received salvaged blood through the use of a cell saver. Venovenous bypass machine was not used at all. Sequential compression device, temperature control machine and body warmer were used for all patients.

Consumption of blood products

The average consumption of red cells, platelets, fresh frozen plasma (FFP), cryoprecipitate, crystalloid and colloid is shown in Table 3. For one patient blood loss was hard to estimate, as the use of salvaged blood from the cell saver made it difficult to measure accurately. However, the consumption of banked blood reflects the degree of blood loss. The median units of packed red cells, platelets, fresh frozen plasma (FFP), cryoprecipitate, crystalloid and colloid are 4, 3, 1 and 1 unit respectively. The median crystalloid and colloid were 9 liter and 0.5 liter respectively.

Table 2: Duration of anaesthesia, hospital stay, cost and mortality

Duration of anaesthesia(H) (Median/Range)	Mortality (No of pt)	Hospital stay (Days) (Median/Range)	Cost (BDT) (Median/Range)
14(12-18)	1	21(21-30)	40, ,00,000(3 5,00,000- 0,00,000)

Table 3: Use of special equipment during the liver transplantation procedure

Equipment	Veno – venous bypass	Rapid Infusion system	Cell saver	Sequential compression device	Temperature control machine	Body warmer
No. of patients	0	10	1	10	10	10

Table 4: Type and amount of blood products and other fluids used during the transplantation procedure

No. of patients	Packed cells (units) (Median/Range)	(Median/Range) plasma (units) (Median/Range)	Platelets (units) (Median/Range)	Cryoprecipitate Cryoprecipitate (Median/Range)	Crystalloid (L) (Median/Range)	Colloid (L) (Median/Range)
10	4 (2- 12)	3 (3- 12)	1 (0- 2)	1 (0- 8)	9 (3-16)	0.5 (0.5-1)

Intra-operative haemodynamic changes

Post-reperfusion syndrome (a 30% or more drop in blood pressure from baseline just before reperfusion that lasts for 1 minute or more and occurs within 5 minutes of reperfusion) was seen in 6 recipients. A drop in mean blood pressure >30% was seen when the inferior vena cava was cross-clamped in 7 patients.

Table 5: Intra-operative haemodynamic changes when the inferior vena cava was clamped and during reperfusion

Haemodynamic change	No. of patients (total no 10)
>30% Mean blood pressure fall at the time of inferior vena cava cross-clamping	7
Post-reperfusion syndrome	6

Intra-operative changes in electrolytes, acid-base balance and clotting profile

Intra-operative changes in pH, PaCO2, PaO2, StHCO3, SBE, Hct, Hb, Platelate, PT, INR, APTT, Na+, K+, Ca++, B. Glucose and Lactate are shown in Table 6. Critical changes usually occurred at reperfusion; hence, data obtained before and after reperfusion are shown for comparison purposes. A rise in potassium level and a drop in pH should be anticipated at reperfusion. Table 6 shows a rise in potassium level. However, the expected drop in pH after reperfusion was not observed due to vigorous correction of acidosis by sodium bicarbonate, which was given just before and after reperfusion. Calcium chloride infusion was given routinely to all patients to maintain normal calcium levels when they received FFP and salvaged blood from the cell saver. Table 6 also shows that calcium levels were well maintained before and after reperfusion. A rapid rise in sodium level is a known complication in liver transplant recipients due to the administration of blood products, saline, and sodium bicarbonate. PT, INR and APTT decreased after reperfusion. Table 6 shows a rapid rise of blood glucose level after reperfusion indicates liver is working nicely.

Table 6: Intra-operative changes in electrolytes, acid-base balance and clotting profile

Parameters	Before anaesthesia (Mean±SD)	30 minutes Before reperfusion (Mean±SD)	30 minutes After reperfusion (Mean±SD)
pH	7.40±0.10	7.25±0.11	7.26±0.12
$PaCO_2$	36.11±7.54	34.33±6.20	32.45±6.02
PaO_2	187.69±97.49	145.84±90.30	140.75±85.80
$StHCO_3$	22.45±3.63	12.40±2.87	11.65±2.45
SBE	-2.46±4.00	-12.45±3.60	-11.56±3.20
Hct	29.63±4.93	24.40±4.80	25.50±4.85
Hb	9.4±1.56	8.20±1.02	8.50±1.05
Platelate	54875±23757.33	60598±22987.20	61983±23934.54
PT	21.93±4.42	24.75±4.87	22.54±4.67
INR	2.3±1.85	2.5±1.88	2.00±1.24
APTT	55.35±8.77	85.54±9.80	60.80±8.90
Na+	128.89±7.38	133.65±7.28	134.50±7.90
K+	3.43±0.54	4.10±0.30	4.50±0.50
Ca++	1.04±0.14	1.06±0.11	1.08±0.12
B glucose	104.75±30.42	110.80±25.90	140.90±26.75
Lactate	2.11±1.96	3.78±1.80	3.50±1.50

Discussion

Patients receiving live related liver transplants have severe liver disease characterised by multisystem disorders that provide many anaesthetic challenges. In addition, logistical problems such as coordinating patient transport and ensuring operating theatre readiness need advance planning. Appropriate timing of the recipient skin incision is essential and requires the notification of donor acceptability from the harvest team. All of these elements depend on the establishment of good communication between all the parties involved. Unpredictable starting times and the long duration of the procedure can potentially disrupt the operating theatre schedule for elective cases. In this series, the starting time of live related liver transplantations usually fell within normal working hours, as most of these were semi-elective procedures. Nevertheless, minimal disruption of the operating theatre services was achieved because a well-established system was in place. The average anaesthetic time (from induction to the end of the operation) was 12 hours to 18 hours with median 14 hours. Such long operating times often meant that more than one anaesthetic team was required for the management of a single recipient. Fatigue has been attributed as one of the most frequently quoted contributors to critical incidents.4 As a result, it is not advisable to have the same team complete an operation. The system at the Indraprastha Apollo Hospital, Delhi, India consists of a staff roster that is dedicated solely to liver transplant activities to minimise any disruption of service. The cell saver and rapid infusion system should be available during pre-anhepatic phase. The use of the cell saver can help to minimise the complications associated with massive blood transfusion, which includes hyperkalaemia, citrate toxicity, and acidosis. Moreover, most liver transplant centres use this technique to reduce dependence on banked blood. The reduction in transfusion needs has been reported to be as high as 30%.5 Consequently, most of the recipients required potassium and calcium supplementation to maintain normal potassium and calcium levels whenever the cell saver was used. In spite of the cell saver, the average amount of banked blood required by the patients was still considerable when compared with other centres .5,6,7 Possible causes include differences in surgical technique and patient condition. As a result of donor shortage, many patients in this series had very poor liver function when they underwent liver transplantation. The use of blood products was guided by coagulation tests. However, as most standardised laboratory coagulation testing is performed at the normothermic temperature of 37°C,8 the results do not reflect the in vivo situation of a hypothermic patient, which is a common observation in adult liver recipients. Both laboratory9 and clinical10 findings suggest that hypothermic patients have more extensive coagulation defects than those indicated by in vitro laboratory tests.11,12 Every effort should thus be made to maintain normothermia in a liver transplant recipient. Despite active measures, which included ensuring an ambient temperature of 25°C, infusing warm intravenous fluid, and using air-warming blankets for all recipients, all still developed intra-operative hypothermia. Heat is lost through many mechanisms: the VVB circuit, large volumes of fluid replacement, decreased oxygen consumption and metabolism during the anhepatic phase, and the infusion of an iced flush solution through the cold allograft as the infrahepatic caval anastomosis is being constructed.13 In the event of massive blood loss, the use of a rapid infusion system that can maintain infusion rates up to 1 L/min can be life-saving in adult recipients. Although it may not always be required, it should be available for use in all patients.14 Large-bore venous catheters, such as the 8.5-French introducer sheaths, were used in the patients in this series to achieve the rapid infusion of intravenous fluids. Avoiding the use of additional resistors such as three-way stopcocks is highly recommended for effective performance of the system.15 The clamping of the caval and portal circulations marks the beginning of the anhepatic phase. Post-reperfusion syndrome is defined as a 30% or more drop in blood pressure from baseline that lasts for 1 minute or more and occurs within 5 minutes of reperfusion.13,16 Estrin et al17 have suggested that the lower incidence of post-reperfusion syndrome observed in patients without VVB can be attributed to the maintenance of increased intravascular volume before reperfusion. However, at present, no definite explanation can be offered for the syndrome; acidosis, hypothermia,

and hyperkalaemia do not seem to be responsible.18 Possible causes include isolated right ventricular dysfunction,14 marked fluid shift, and the release of vasoactive substances such as prostaglandins, kallikrein, and leukotrienes into the systemic circulation during reperfusion, which results in a decrease in cardiac output. For those who exhibit extreme arterial hypotension, bradycardia, or cardiac arrest on graft reperfusion, multiple aetiological factors are likely to be involved. Treatment of post-reperfusion syndrome includes the maintenance of adequate filling pressures, hyperventilation, and the administration of calcium chloride and sodium bicarbonate for hyperkalaemia and acidosis. These are administered just before reperfusion. Table 6 shows the changes in electrolytes that occurred just before and after reperfusion in recipients. The dosage of calcium chloride and sodium bicarbonate were adjusted according to the blood gas tensions and electrolyte levels just before reperfusion. As a result, severe acidosis was not observed in any of the recipients. Noradrenaline and dobutamine have been used for their positive inotropic effect, whereas phenylephrine has been used to reverse the vasodilatative effect of the vasoactive substances.13 There was a substantial increase in the sodium level of recipients. Possible causes include the use of normal saline as maintenance fluid and the use of sodium bicarbonate to treat metabolic acidosis.

Conclusion

Live related liver transplantation is no longer experimental and has become an acceptable therapy for chronic liver failure. In this prospective study, we have highlighted the intra-operative problems that were encountered while treating patients for liver transplantation. Adequate logistic and prompt laboratory service, availability of blood products, maximum invasive and non invasive monitoring is mandatory for better outcome.

References

1. Starzl T, Marchioro T, Vonkaulla K, Hermann G, Brittain R, Waddell W. "Homotransplantation Of The Liver In Humans". Surg Gynecol Obstet 117: 659-76. PMID 14100514.

2.https://www.uktransplant.org.uk/ukt/statistics/presentations/pdfs/april_05/liver_life_expectancy.pdf

3. Starzl TE, Iwatsuki S, Van Thiel DH, et al. Evolution of liver transplantation. Hepatology 1982;2:614-36.

4. Garden AL, Currie M, Gander PH. Sleep loss, performance and the safe conduct of anaesthesia. In: Keneally J, Jones M, editors. Australasian anaesthesia. Melbourne: Australian and New Zealand College of Anaesthetists; 1996:43-51.

5. McNicol PL, Liu G, Harley ID, et al. Blood loss and transfusion requirements in liver transplantation: experience with the first
75 cases. Anaesth Intensive Care 1994;22:666-71.

6. Boylan JF, Kinck JR, Sandler AN, et al. Tranexamic acid reduces blood loss, transfusion requirements, and coagulation factor use in primary orthotopic liver transplantation.
Anesthesiology 1996;85:1043-8.

7. Halpern NA, Alicea M, Seabrook B, Spungen AM, McElhinney AJ, Greenstein RJ. Cell saver autologous transfusion: metabolic consequences of washing blood with normal saline. J Trauma 1996;41:407-15.

8. Bowie EJ, Thompson JH Jr, Didisheim P, et al. Mayo Clinic laboratory manual of hemostasis. Philadelphia: WB Saunders; 1971:65-73.

9. Douning LK, Ramsay MA, Swygert TH, et al. Temperaturecorrected thrombelastography in hypothermic patients. Anesth Analg 1995;81:608-11.

10. Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements HKMJ Vol 5 No 1 March 1999 33 Anaesthesia for liver transplantation during total hip arthroplasty. Lancet 1996;347:289-92.

11. Rutledge R, Sheldon GF, Collins ML. Massive transfusion. Crit Care Clin 1986;2:791-805.

12. Valeri CR, Feingold H, Cassidy G, Ragno G, Khuri S, Altschule MD. Hypothermia-induced reversible platelet dysfunction. Ann
Surg 1987;205:175-81.

13. Carton EG, Plevak DJ, Kranner PW, Rettke SR, Geiger HJ, Coursin DB. Perioperative care of the liver transplant patient: Part 2. Anesth

Analg 1994;8:382-99.
14. Rettke SR, Chantigian RC, Janossy TA, et al. Anesthesia approach to hepatic transplantation. Mayo Clin Proc 1989; 64:224-31.
15. Rothen HU, Lauber R, Mosimann M. An evaluation of the Rapid Infusion System. Anaesthesia 1992;47:597-600.
16. Aggarwal S, Kang Y, Freeman JA, Fortunato FL, Pinsky MR. Postreperfusion syndrome: cardiovascular collapse following
hepatic reperfusion during live rtransplantation. Transplant Proc 1987;19(4 Suppl 3):54S-55S.
17. Estrin JA, Belani KG, Ascher NL, Lura D, Payne W, Najarian JS. Hemodynamic changes on clamping and unclamping of major vessels during liver transplantation. Transplant Proc 1989;21:3500-5.
18. Blanot S, Gillon MC, Ecoffey C. Circulating endotoxins during orthotopic liver transplantation and post-reperfusion syndrome
[letter]. Lancet 1993;342:859-60.