Anaesthesia for liver transplantation: experience at a teaching hospital

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Objective. To assess the anaesthetic aspects of liver transplantation.
Design. Retrospective study.
Setting. University teaching hospital, Hong Kong.
Patients. The first 55 patients who received liver transplantations between 5 October 1991 and 14 June 1997.
Main outcome measures. The anaesthetic technique used; indications for liver transplantation and type of graft transplanted; survival rate; duration of anaesthesia and surgical starting time; intra-operative changes associated with major transfusion; frequency of hypothermia, coagulopathy, and reperfusion; frequency of use of cell saver devices, veno-venous bypass, and a rapid infusion system; and associated complications.
Results. All patients received general anaesthesia with rapid sequence induction. Most adult recipients had cirrhosis from various causes, whereas biliary atresia was the most common condition in the paediatric population. Both cadaveric and living-related liver transplantations were performed, and the overall 1-year survival rate of patients who received a transplantation before June 1996 was 85%. Veno-venous bypass was used in 84% of adults, but in none of the paediatric patients; a cell saver device was used for all adult patients and 92% of paediatric patients. All transplant recipients had acidosis, hypothermia, and hypotension during the operation.
Conclusions. Liver transplantation is no longer experimental. It is the therapeutic option for patients with chronic liver failure. Good anaesthetic support is an essential element of a liver transplantation service.

HKMJ 1999;5:27-33

Key words: Anesthesia; Intraoperative complications; Liver transplantation; Postoperative complications

Introduction

Orthotopic liver transplantation has been shown to be the best therapeutic option for those with chronic liver failure.[1] 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.

The liver transplantation programme at the Queen Mary Hospital has been running since 1991. Over the past 7 years, both cadaveric and living-related liver transplantations have been successfully performed. In this report, the anaesthetic aspects of the first 57 liver transplantations are reviewed.

Methods

Between 5 October 1991 and 14 June 1997, 57 liver transplants were performed on 55 patients at the Queen Mary Hospital. Their records were retrospectively reviewed.

The anaesthetic technique used, the indications for liver transplantation, and anaesthetic time were

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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, and body temperature before and after reperfusion were analysed. The frequency of use of cell saver devices and a rapid infusion system, and the associated complications were also reviewed.

Results

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 μg/kg, thiopentone sodium 3 to 5 mg/kg, and suxamethonium 1.5 mg/kg. Anaesthesia was maintained by giving a mixture of air, oxygen, and isoflurane. Atracurium besylate was the drug of choice for muscle relaxation. Analgesia was achieved by fentanyl infusion. 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. The left external jugular vein was cannulated with a triple-lumen catheter for the purposes of drug infusion and blood sampling. All paediatric patients had their left internal jugular vein cannulated with a double-lumen catheter. A right internal jugular cut-down was performed by the surgeon to facilitate the insertion of a Broviac catheter through which postoperative total parental nutrition was given. 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 ionised calcium. These measurements served as a baseline blood profile for each patient. Hourly laboratory measurements were performed throughout the operation. 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, and the theatre temperature was set to greater than 24°C.

Indications for liver transplantation

Table 1 summarises 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, primary biliary cirrhosis, and cirrhosis due to Wilson's disease. Nine patients had fulminant hepatic failure at the time of transplantation. In the paediatric group, primary biliary atresia was the main indication for liver transplantation.

Table 1. The various diagnoses that necessitated a liver transplantation

Diagnosis	No. of patients	Median age (years) [range]	Median body weight (kg) [range]
Hepatitis B cirrhosis	9	43.0 (22.0-51.0)	60.0 (35.0-80.0)
Hepatitis C cirrhosis	2	55.0 (54.0-56.0)	57.0 (56.0-58.0)
Alcoholic cirrhosis	6	50.0 (41.0-60.0)	56.0 (50.0-71.0)
Cryptogenic cirrhosis	5	29.0 (20.0-63.0)	58.0 (50.0-61.0)
Primary biliary cirrhosis	3	56.0 (41.0-62.0)	47.0 (44.0-56.0)
Cirrhosis due to Wilson's disease	2	28.0 (20.0-36.0)	76.5 (63.0-90.0)
Autoimmune cirrhosis	1	45.0	56.0
Polycystic liver disease	1	59.0	38.0
Polycystic liver and kidney disease	1	55.0	70.0
Drug-induced fulminant hepatic failure	3	37.0 (20.0-46.0)	66.0 (53.0-68.0)
Hepatitis B fulminant hepatic failure	4	21.5 (17.0-34.0)	64.0 (54.0-73.0)
Unknown fulminant hepatic failure	1	26.0	59.0
Fulminant hepatic failure due to Wilson's disease	1	28.0	89.0
Chronic active hepatitis B	5	39.0 (19.0-47.0)	65.0 (58.0-100.0)
Post-transplant hepatitis	2	12.0 (2.0-22.0)	31.0 (12.0-50.0)
Biliary atresia	11	1.0 (0.7-11.0)	7.0 (6.0-25.0)

Table 2. Use of special equipment during the liver transplantation procedure

Equipment	Adult transplantations, n=45 No. (%)	Paediatric transplantations, n=12 No. (%)
Veno-venous bypass	38 (84)	0
Rapid infusion system	40 (89)	0
Cell saver	45 (100)	11 (92)

Patient population and causes of death

Fifty-seven liver transplantations (45 adult and 12 paediatric transplantations) were performed on 55 patients (44 adult and 11 paediatric patients) during the study period. The patients ranged in age from 8 months to 63 years. Thirty-four patients received a cadaveric liver graft and 23 received a living-related donor graft. The latter group comprised 10 paediatric and 13 adult recipients. Of the adult recipients, five had left lobe grafts and eight had extended right lobe grafts. The overall 1-year survival of patients who received a liver transplant before June 1996 was 85%. Eight patients died; the causes of death included intracerebral haemorrhage, myocardial infarction, systemic candidiasis, lymphoma, and graft failure.

Surgical starting time and duration of anaesthesia

Most of the surgical starting times for living-related liver transplant recipients were within normal working hours, whereas the starting times for recipients of a cadaveric transplant were usually in the early morning. The average anaesthetic time for adult recipients was (mean [standard deviation, SD]) 15.37 (3.92) hours while for paediatric recipients, it was longer: 16.72 (4.64) hours.

Special equipment

Table 2 shows the frequency with which special equipment was used during the transplantation procedure. Eighty-four percent of adult recipients underwent VVB, but none of the paediatric patients had this procedure. One patient experienced transient VVB pump failure during the anhepatic phase, which resulted in electro-mechanical dissociation of the heart. Most of the adult recipients (89%) required the rapid infusion system for fluid resuscitation. All recipients received salvaged blood through the use of a cell saver except for one paediatric recipient owing to equipment failure.

Consumption of blood products

The average consumption of red cells, platelets, and fresh frozen plasma (FFP) is shown in Table 3. 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 average number of units (mean [SD]) of packed cells, FFP, and platelet concentrate used in adult recipients were 11.8 (9.0) U, 17.8 (13.1) U, and 14.8 (12.0) U, respectively. The volume (median [range]) of packed cells, FFP, and platelet concentrate used in the paediatric group were 275 mL (0-1750 mL), 320 mL (0-2200 mL), and 0 mL (0-700 mL), respectively.

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 42% of the adult recipients (Table 4), but only in 9% of the paediatric patients. The mean blood pressure at graft reperfusion was 60.55 (14.55, SD) mm Hg in adult recipients and 46.72 (11.46) mm Hg in paediatric patients. A drop in the mean blood pressure was seen when the inferior vena cava was cross-clamped; the drop in adult patients ranged from 0% to 18% (median, 5%). In the paediatric group, the drop in mean blood pressure was similar, ranging from 0% to 23% (median, 5%).

Other intra-operative changes

Intra-operative changes in electrolyte levels, acid-base balance, and body temperature are shown in Table 5. Critical changes usually occurred at reperfusion; hence,

Table 3. Type and amount of blood products used during the transplantation procedure

Patient group	Packed cells (units)*	Fresh frozen plasma (units)*	Platelets (units)*
Adult patients			
mean (SD)	11.8 (9.0)	17.8 (13.1)	14.8 (12.0)
maximum	41.0	66.0	53.0
minimum	1.0	4.0	0.0
Paediatric patients			
median	0.8	1.6	0.0
maximum	5.0	11.0	14.0
minimum	0.0	0.0	0.0

*1 U of packed cells, fresh frozen plasma, and platelets is approximately 350 mL, 200 mL, and 50 mL, respectively

Table 4. Intra-operative haemodynamic changes when the inferior vena cava was clamped and during reperfusion

Haemodynamic change	Adult transplantations, n=45	Paediatric transplantations, n=12
Post-reperfusion syndrome (%)	42	9
Mean blood pressure change at the time of inferior vena cava cross-clamping (%) [median (range)]	-5 (0 to -18)	-5 (0 to -23)
Mean blood pressure during graft reperfusion (mm Hg) [mean (SD)]	60.55 (14.55)	46.72 (11.46)

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 5 shows a rise in potassium level in both the adult and paediatric groups. However, the expected drop in pH after reperfusion was not observed in the adult group due to vigorous correction of acidosis by sodium bicarbonate, which was given just before and after reperfusion. The lowest pH was usually seen after reperfusion (pH 7.16 [0.08] in the adults and 7.21 [0.06] in the paediatric group).

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 5 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. The average rise in sodium level was 8.78 (4.44) mmol/L and 9.55 (3.36) mmol/L in adult and paediatric groups, respectively. None of the patients developed central pontine myelinolysis. Hypothermia was a significant complication, with body temperature falling more in adult recipients.

Discussion

Patients receiving orthotopic 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 living-related liver transplantations usually fell within normal working hours, as most of these were semi-elective procedures. In contrast, the usual starting time for cadaveric graft recipients was in the late evening or early morning hours. 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 15.37 (3.92) hours for adults and 16.72 (4.64) hours for the paediatric patients. 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.[2] As a result, it is not advisable to have the same team complete an operation. The system at the Queen Mary Hospital consists of a staff roster that is dedicated solely to liver transplant activities to facilitate

Table 5. Intra-operative changes in electrolytes, acid-base balance, clotting profile, and temperature

Measure	Adult patients (mean [SD])		Paediatric patients (mean [SD])	
	Value before reperfusion	Value 10 min after reperfusion	Value before reperfusion	Value 10 min after reperfusion
Ionised calcium (mmol/L)	1.08 (0.20)	1.07 (0.22)	0.92 (0.28)	1.11 (0.16)
Potassium (mmol/L)	3.47 (0.61)	3.61 (0.69)	3.18 (0.24)	3.78 (0.33)
Base excess (mmol/L)	-11.20 (3.47)	-11.80 (3.20)	-9.05 (2.18)	-9.90 (2.45)
pH	7.06 (1.13)	7.23 (0.06)	7.31 (0.07)	7.22 (0.66)
Lowest pH	7.16 (0.08)		7.21 (0.06)	
Worst base excess (mmol/L)	-14.53 (3.68)		-12.48 (2.16)	
Worst international normalised ratio	2.62 (0.55)		2.65 (0.25)	
Mean rise in sodium level (mmol/L)	8.78 (4.44)		9.55 (3.36)	
Temperature (°C)	33.80 (1.20)		35.40 (0.80)	

the treatment of sick patients and to minimise any disruption of service, thus making it possible to involve two senior anaesthetists.

Liver donor shortage has been a chronic problem in Hong Kong. Only 34 cadaveric livers were donated for transplantation at the Queen Mary Hospital during the study period. As a result of this donor shortage and urgency, live donor grafts were used for patients with fulminant hepatic failure. So far, only one patient with fulminant hepatic failure has received a timely cadaveric graft. Reduced-sized and split partial liver transplantation from cadaveric donors have gained wide acceptance in other parts of the world as ways of increasing the donor pool.[3,4] At the same time, the feasibility of living-related liver transplantation in the paediatric population has been explored. Advantages include high-grade graft viability, superior immunohistocompatibility and better size-matching.[5]

The pre-anhepatic phase resembles simple hepatectomy. However, the procedure can be particularly bloody in the presence of previous upper abdominal surgery such as Kasai operation and previous liver transplantation.[6] The cell saver and rapid infusion system should be available during this phase. The use of the cell saver can help 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%.[7] In this series, all patients except those with hepatocellular carcinoma received salvaged blood through the use of the cell saver. Blood was washed with normal saline (0.9% sodium chloride). This practice commonly results in increased levels of sodium, while the potassium and total calcium levels are decreased.[8] These trends were observed in the recipients in this series (Table 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 (Table 3).[7,9,10] 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,[11] the results do not reflect the in vivo situation of a hypothermic patient, which is a common observation in adult liver recipients. Both laboratory[12] and clinical[13] findings suggest that hypothermic patients have more extensive coagulation defects than those indicated by in vitro laboratory tests.[14,15] 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. The average lowest core temperature of the paediatric group was 35.38 (0.80)°C. The problem was more severe in adults: the average lowest temperature was 33.80 (1.20)°C. 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.[16] The routine use of VVB in most of the adult recipients may explain the lower body temperature seen.

In the event of massive blood loss, the use of a rapid infusion system that can maintain infusion rates up to 1.5 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.[17] 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.[18]

The clamping of the caval and portal circulations marks the beginning of the anhepatic phase. Almost all adult recipients were given VVB during the anhepatic phase to minimise the haemodynamic changes associated with the clamping and transection of the supra- and infra-hepatic inferior vena cava. With the use of VVB, the maximum drop in mean blood pressure at the time when the inferior vena cava was clamped was only 18% in adult recipients (Table 4). A greater reduction in mean blood pressure would be anticipated in the absence of VVB. In addition, the use of this system may reduce the transfusion requirement as a result of portal decompression.[19] As paediatric patients can tolerate caval clamping without significant haemodynamic disturbances,[20] VVB was not used for the paediatric patients. The observed maximum drop in mean blood pressure in the paediatric series was 23% without the use of VVB. The advantages of VVB include haemodynamic stability with cardiac output

and renal perfusion maintained at preclamp values, and reduced portal venous pressures with less intestinal congestion and bleeding. Disadvantages include the need for additional surgery to insert the cannulae, thus increasing the surgical duration, and the potential hazards associated with the extracorporeal circuit, which include hypothermia, air embolism, thromboembolism, and trauma to cannulated vessels.[21,22] One of the patients had a transient electromechanical dissociation secondary to a decrease in venous return due to sudden pump failure of the bypass system.

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.[16,23] The adult recipients had a higher (42%) incidence of post-reperfusion syndrome than did the paediatric recipients (9%). Estrin et al[24] 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. This effect may explain the observed lower incidence of post-reperfusion syndrome in paediatric recipients, as no VVB was used. However, at present, no definite explanation can be offered for the syndrome; acidosis, hypothermia, and hyperkalaemia do not seem to be responsible.[25] Possible causes include isolated right ventricular dysfunction,[17] 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 5 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. Adrenaline and dobutamine have been used for their positive inotropic effect, whereas phenylephrine has been used to reverse the vasodilatative effect of the vasoactive substances.[16] 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. However, central pontine myelinolysis was not observed in any of the transplant recipients.

Conclusion

Liver transplantation is no longer experimental and has become an acceptable therapy for chronic liver failure. In this retrospective review, we have highlighted the intra-operative problems that were encountered while treating patients for liver transplantation. The results of this series are comparable to those of other well-established centres. However, as a significant number of the Hong Kong recipients had hepatitis B, regular surveillance must be maintained because of the possibility of graft recurrence of hepatitis B.

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