LIVING DONOR HEPATECTOMY (LDH)

- Comparative Study Between Two Different Anesthetic Techniques -

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Abstract

Background: Living donor hepatectomy (LDH) is now widely used to meet the need for liver grafts due to the shortage of cadaveric livers. Donor safety and perioperative anesthetic management are our major concern. The aim of our study was to compare two anesthetic techniques for management of living donor hepatectomy.

Patients & Methods

After ethical committee approval and informed written consent, 20 donors ASA I physical status undergoing hepatectomy for living-relative liver transplant were allocated randomly to one of two groups. Group A where anesthesia was induced with fentanyl 2µg/kg and propofol 2-3 mg/kg^{-1}, and maintained with isoflurane 0.8-1.2% and fentanyl infusion 1-2$mcg/kg^{-1}/h^{-1}$. In group B anesthesia was induced with sufentanyl 0.2mcg/kg^{-1}, and propofol 2-3mg/kg^{-1}, and maintained with propofol infusion 6-12 $mg/kg^{-1}/h^{-1}$, and sufentanyl infusion 0.2-0.4$mcg/kg^{-1}/h^{-1}$. Atracurium was the muscle relaxant for intubation and maintenance in both groups.

Results: There were no perioperative mortality in both groups, no

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significant statistical differences between both groups as regard demographic data, duration of surgery, duration of anesthesia, hospital stay, intraoperative hemodynamics, blood loss, liver function tests (PT, AST, & ALT) measured in the first, third, and seventh days postoperative.

Conclusion: In conclusion, our study demonstrated that both anesthetic techniques were well tolerated for living donor hepatectomy, with no blood transfusion required, with short and safe discharge from PACU and short hospital stay, but with significant laboratory changes reflecting transient impairment in metabolic liver function. These procedures have proven useful as an important alternative to the cadaveric liver transplantation. Both techniques can be used as fast tract technique for living donor hepatectomy.

Key words: Liver resection; hemodynamic, TIVA, liver function

Introduction

Living donor hepatectomy (LDH) is now widely used to meet the need for liver grafts due to shortage of cadaveric livers[1,2]. Adult to adult living donor liver transplantation (LDLT) grew rapidly over the past few years[3]. Significant improvements in the outcomes have been seen over recent years, however LDLT still comprises <5% of adult liver transplantation[4].

Optimal preoperative preparation of both the donor liver and the recipient allow the procedure to be done as an elective operation. Living-relative liver transplantation has the advantage of relatively shorter ischemia time of the graft.

The living-relative liver transplantation programme was reactivated in King Faisal Specialist Hospital & Research Center in April 2001. Right hepatectomy was performed in 20 adult donors between February 2002 and August 2004 to provide adequate liver graft for adult recipients.

The term right hepatectomy as defined by the Terminology Committee of the International Hepato-Pancreato-Biliary Association is surgical excision of hepatic segments 5 to 8[5]. Adequate liver volume must be left in place to avoid hepatic dysfunction[6]. This depends on preoperative radiological studies of vascular and biliary anatomy as well as computed tomographic volumetry. Donor safety and perioperative anesthetic management are of major concern as well as surgical preparation of an optimal liver graft to be transplanted. Advances in anesthetic and surgical management over the past few years have made it possible to perform liver resections with minimal risk to the donors[7].

The aim of the present study was to compare two different anesthetic techniques of anesthesia during living donor hepatectomy (LDH) and its implications on the intraoperative hemodynamic, postoperative liver and coagulation function and hospital stay duration.

Patients & Methods

After ethical committee approval and informed written consent, 20 donors ASA physical status I to undergo hepatectomy for living-relative liver transplant, were enrolled in our study. There were 9 male and one female in Group (A) and 8 male and two female in Group (B). The mean age group was 26.8 ± 5.3, 24.6 ± 4.5 in Groups A & B respectively as shown in Table (1).

Table 1

Demographic data, Anesthesia & surgical durations, blood loss. (Mean ± SD)

PACU = Post Anesthesia Recovery & hospital discharge times

	Group (A)	**Group (B)**
Age	26.8 ± 5.3 27 (19-34)	24.6 ± 4.5 24.5 (18-35)
Sex	9 M/1 F	8 M/2 F
Anesthesia Time (min)	428 ± 52.5	442 ± 77.4
Surgical Time (min)	394.3 ± 60.8	398.9 ± 70.3
Blood Loss (ml)	768 ± 225.1 (775)*	829.9 ± 174.7 (825)*
PACU Discharge Time (min)	739.2 ± 48.2	753.6 ± 55.4
Hospital Discharge (days)	6.8 ± 0.78	7.2 ± 0.63

* Median.

All donors underwent a full preoperative evaluation including biochemical, radiological studies as well as psycho-social and anesthetic evaluation. CT was used for preoperative volumetric calculation of the estimated residual hepatic volume of the donors. Graft Recipient Weight Ratio (GRWR) >0.8 was intended for recipients and remaining liver volume was ≥32% in all donors.

In addition to the standard monitors, intraoperative monitoring included intra-arterial (radial artery catheter), central venous (an internal jugular catheter) pressure monitoring electrocardiogram, urine output, and (esophageal) central temperatures. Hypothermia was prevented during surgery by using warming blanket, Bair Hugger and perfusion warming. The surgical technique was also similar for all patients. Minute ventilation was titrated to maintain normocarbia.

Patients were randomly allocated into two groups. Group A where anesthesia was induced with fentanyl 2μg/kg^{-1} and propofol 2-3mg/kg^{-1}, and maintained with isoflurane 0.8-1.2% in air/oxygen (FiO2 = 0.4-0.5) and fentanyl infusion 1-2 mcg/kg^{-1}/h^{-1}. In Group B anesthesia was induced with sufentanyl 0.2mcg/kg^{-1}, and propofol 2-3mg/kg^{-1}, and maintained with propofol infusion 6-12 mg/kg^{-1}/h^{-1}, and sufentanyl infusion 0.2-0.4 mcg/kg^{-1}/h^{-1}. Atracurium was the muscle relaxant for intubation and maintenance in both groups.

CVP was maintained ≤5cm H_2O during hepatic parenchymal transection. For all patients, hemodynamic measurements (MABP, HR, and CVP) were recorded as baseline after establishing monitoring, before removal of the graft and at skin closure. Liver function test, hemoglobin, hematocrit as well as coagulation data were obtained as a base line preoperatively, first, third and seventh day postoperative. Intraoperative Cavitron Ultrasonic surgical Aspirator (CUSA system 200; Vallelylab Inc., Boulder, CO), Argon beam and bipolar electrocautary were used by the surgeons to reduce blood loss. Surgical field blood was collected and processed by a hemonetics cell saver system. Total blood loss and transfusion were measured as well as other fluid replacements. The permissible lowest hemoglobin 70g/L^{-1}.

Statistical analysis

Results were expressed as mean ± SD, analyzed using tests of significance to identify the variables significantly to differences in different groups: Paired t-test, student t-test. Statistical significance was considered at the level of $p<0.05$.

Results

There was no perioperative mortality or morbidity in both groups. There were no significant statistical differences between both groups as regard demographic data, duration of anesthesia and duration of surgery.

The mean duration of surgery was 394.3 ± 60.8, 398.9 ± 70.3 minutes and duration of anesthesia was 428 ± 52.5, 442 ± 77.4 minutes.

No Packed Red Blood Cell (PRBCs) transfusion was needed for all patients in both Groups. There was insignificant difference in the blood loss between both Groups. The mean blood loss was 768 ± 225.1ml and 829 ± 17.4ml in Groups A & B respectively. There was hemodynamic stability in both groups throughout the operation as shown in Fig 1. Only the mean CVP values during the dissection period were lower than initial and the end of operation ($p<0.05$). Table (2).

Fig. 1
Intraoperative change in Mean Blood Pressure (MBP)

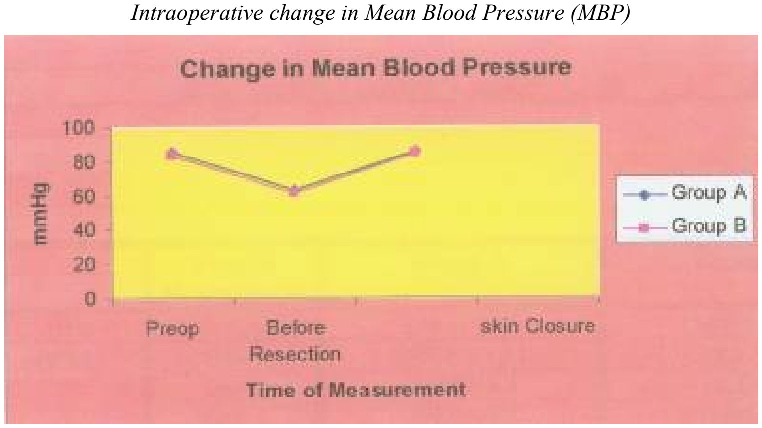


Table 2

Perioperative hemodynamic course in both groups. (Mean ± SD)

	Preoperative			**Before Resection**			**Skin Closure**		
	MBP mmHg	HR bpm	CVP cmH_2O	MBP mmHg	HR bpm	CVP cmH_2O	MBP mmHg	HR bpm	CVP cmH_2O
Group (A)	85.1±8.1	77.6±10.3	7.2±1.75	62.9±2.9	74.4±6.8	3.9±1.1	85.5±3.6	80.8±7.7	7.2±1.0
Group (B)	83.1±7.3	78.7±5.8	7.8±1.31	61.7±2.7	69.2±5.9	4.1±.7	84.4±7.1	78.9±3.1	7.0±1.9

The mean hemoglobin concentration and hematocrit (%) decreased significantly as shown in Table 3 from a preoperative values 140 ± 14.6g/L, 0.42% ± 0.03%, and 134.8 ± 14.0, 0.40% ± 0.03% to 103.7 ± 12.1, 0.3% ± 0.01%, and 109.1 ± 8.9, 0.31% ± 0.02% in day 1, 108.8 ± 8.1, 0.32% ± 0.05%, and 105.1 ± 8.5, 0.31% ± 0.02% in day 3 and 110.5 ± 9.1, 0.33% ± .05%, and 106.2 ± 11.1, 0.31% ± 0.03% in day 7 in Groups A & B respectively, but there was insignificant statistical differences between both groups throughout the study period.

Table 3

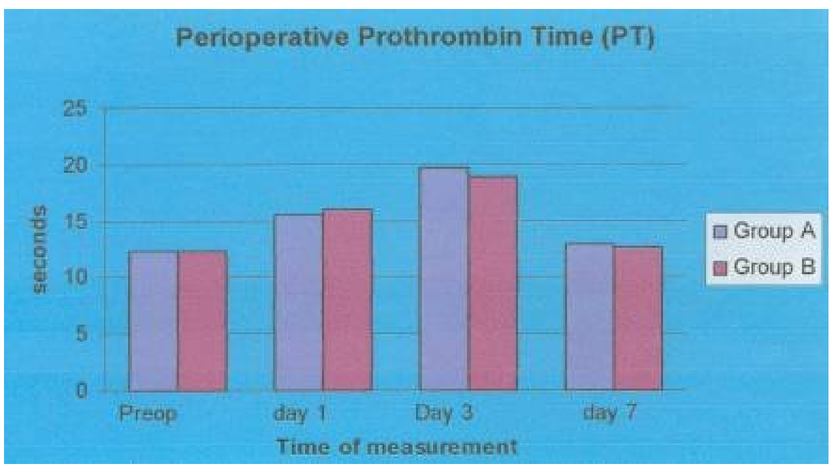
Perioperative hemoglobin concentration (Hb), hematocrit values (Hct), Prothrombin Time (PT) and International Normalized Ratio (INR) (Mean ± SD)

	Time of Measurement	**Group A**	**Group B**
Hb (g/L)	Preoperative	140 ± 14.6	134.8 ± 14.0
	Day 1	103.7 ± 12.1	109.1 ± 8.9
	Day 3	108.8 ± 8.1	105.1 ± 8.5
	Day 7	110.5 ± 9.1	106.2 ± 11.1
Hct (%)	Preoperative	0.42 ± 0.03	0.40 ± 0.03
	Day 1	0.30 ± 0.01	0.31 ± 0.02
	Day 3	0.32 ± 0.05	0.31 ± 0.02
	Day 7	0.33 ± 0.05	0.31 ± 0.03
Prothrombin Time (PT) Seconds	Preoperative	12.4 ± 0.4	12.3 ± 0.6
	Day 1	15.6 ± 0.9	16.05 ± 2.02
	Day 3	19.6 ± 2.8	18.9 ± 1.9
	Day 7	13.08 ± 0.7	12.7 ± 0.59
International Normalized Ratio (INR)	Preoperative	0.9 ± 0.07	0.97 ± 0.06
	Day 1	1.47 ± 0.2	1.4 ± 0.9
	Day 3	1.52 ± 0.16	1.53 ± 0.14
	Day 7	1.22 ± 0.07	1.21 ± 0.05

Patients in both groups were successfully extubated in the operating room and transferred to PACU for overnight postoperative care and monitoring. The mean discharge time from PACU was 739.2 ± 48.2 and 753.6 ± 55.4 minutes in Group A & B respectively with insignificant statistical difference between both groups.

PT and INR were significantly elevated from the preoperative values 12.4 ± 0.4, 0.9 ± 0.07, and 12.3 ± 0.6, 0.97 ± 0.06 in both Groups A & B respectively with a maximal increase on (day 3) 19.6 ± 2.8, 1.52 ± 0.16, and 18.9 ± 1.9, 1.53 ± 0.14, but latter showed a gradual decrease during the first weak (Fig. 2). No blood products were required in both groups to achieve an INR <1.4.

Fig. 2
Perioperative Prothrombin Time



Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) increased significantly in both groups in the immediate postoperative period.

As shown in Table 4 but with insignificant statistical difference between the two groups, as shown in Fig. 3 & 4.

Fig. 3
Perioperative change in blood concentration of AST

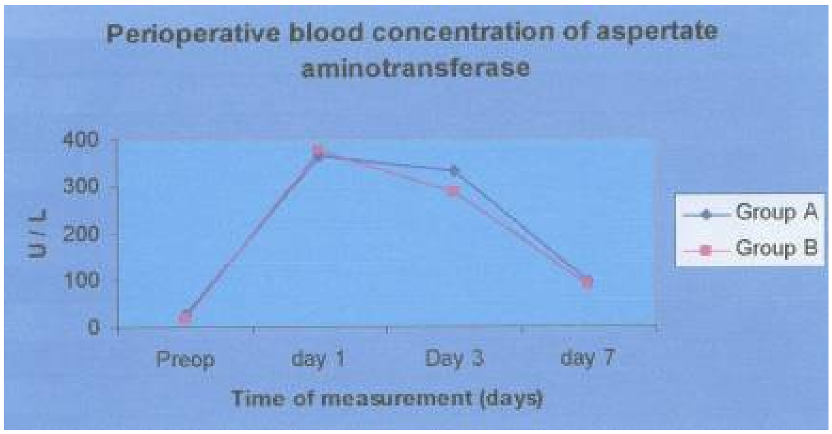
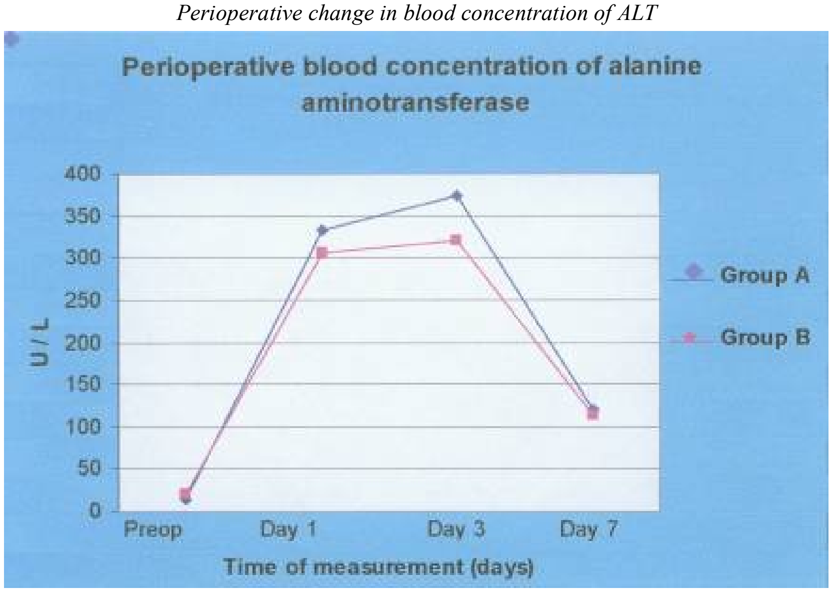


Fig. 4
Perioperative change in blood concentration of ALT



Albumin blood level decreased significantly from the preoperative mean values 43.3 ± 2.3, and 43.8 ± 2.2 g/L^{-1} in Group A & B respectively to 32.6 ± 3.6, and 30.3 ± 3.3 as shown in Table 4.

Table 4
Perioperative values of Aspartate Aminotranserase (ALT), Alanine Aminotransferase (AST) and albumin concentration. (Mean ± SD)

	Time of Measurement	Group A	Group B
AST (U/L)	Preoperative	27.1 ± 3.4	20.1 ± 2.3
	Day 1	364.2* ± 81.9	375.5* ± 116.8
	Day 3	331* ± 74.1	286.1 ± 106.5
	Day 7	93.9* ± 14.4	88.4* ± 14.7
ALT (U/L)	Preoperative	14.6 ± 2.6	20.3 ± 3.1
	Day 1	333.9* ± 94.5	306.8* ± 56.6
	Day 3	373.8* ± 166.7	320* ± 71
	Day 7	120.6* ± 28.9	112.9* ± 18.3
Albumin (g/L)	Preoperative	43.3 ± 2.3	43.8 ± 2.2
	Day 1	32.6 ± 3.6	30.3 ± 3.3
	Day 3	34.5 ± 4.3	34.2 ± 3.4
	Day 7	36.2 ± 4.8	35.1 ± 4.2

* $P<0.05$ significant when compared to preoperative values.

Most laboratory results were back to normal by the end of the first week. Patients were discharged home after 6.8 ± 9.78 days in Group A & 7.2 ± 0.63 days in Group B with insignificant statistical difference between both groups.

Discussion

Adult living donor liver transplantation offers hope to patients with end stage liver disease in an era where waiting time mortality is high and availability of decreased donor organs falls short of the need of the population.

Living donor hepatectomy (LDH) for living-relative liver transplantation is a challenging procedure, because a healthy individual undergoes a major operation for no physical benefit to him or herself[8].

Donor safety is paramount in living donor liver transplantation (LDLT). The most important risk to the donor during hepatectomy is bleeding which can be significant at the deep planes of liver transaction.

Sudden bleeding is often associated with a decrease in hepatic blood flow and ischemic injury[9].

Our study showed that, during the LDHs, keeping the CVP ≤5cm H_2O renders the surgical transaction of the liver easier and provides better exposure. However, lower CVP levels may increase the risk of air embolism. No intraoperative complication occurred in the present study, due to meticulous surgical dissection, flooding of the surgical field with normal saline and head down position. We let the patients be hemodiluted to the extent possible, namely, Hb concentration ≥75g/L^{-1} (Hct values ≥0.25%) without abnormal bleeding, no blood products were required in both groups in the perioperative period.

This study demonstrated that both anesthetic techniques were comparable and produced intraoperative hemodynamic stability in both groups through out the surgical procedure.

Both low CVP technique[10,11] and meticulous surgical dissection resulted in the surgery that was well tolerated with a median blood loss of 775 and 825ml in Group A & B respectively. Although, Makuuchi et al.[12] reported a mean intraoperative blood loss of 748ml in their first 5 cases (similar to our finding), he reported that, they all received autologous fresh frozen plasma while 2 donors received packed red cells. Contrary to our study, in the Hamburg series, 20 out of the first 35 donors were transfused with packed red cells[13]. In contradistinction, Hong Kong living donor right hepatectomy series[14] reported that they rarely gave any blood transfusion despite a median blood loss of 600ml. This is close to the median blood loss of 775, 825ml in Groups A & B respectively reported in our study. The rationale beyond no blood transfusion given in our study is due to our strategy of accepting lower Hb concentration ≥75g/L^{-1} and Hct 0.25% which was well tolerated in young healthy donors. Living donor hepatectomy without blood transfusion is a realistic objective, and we were able to achieve this goal in all patients in both groups of the current study.

Although, Gelman et al[15] reported that the use of isoflurane is preferred due to its vasodilating properties and protective effect on hepatic flow, our study had shown that both anesthetic techniques we used had the same effect with regard to the protective effect on hepatic blood flow and liver functions.

In the present study, a colloid infusion (albumin 5%) was started after hepatic resection in order to replace the lost or dislocated amount of blood as a result of major surgery. Serum albumin has an important role in maintaining physiologic hemostasis as it has the ability to maintain normal colloid osmotic pressure[16]. Many studies have shown that it is important to administer sufficient exogenous albumin to achieve a level of more than 30g/L since serum albumin levels are a major determinant of morbidity[16,17]. Prevention of ischemic and hypoxic damage in isolated rat liver by albumin might be the result of albumin's antioxidant effect[17].

Significant changes in several laboratory values are reported in this study, which is an implication of transient impairment of liver function as a result of major surgery. These were significant intraoperative changes and was followed by a slow normalization postoperatively. These changes were insignificant between both groups and similar to the changes reported in several other studies[18-21].

Significant prolongation of prothrombin time was observed reached its maximum increase in the day 3 postoperatively, but slowly retumed to normal values within 4 to 7 days postoperatively, without the need to transfuse any blood product.

There have been wide ranges of complication rates reported in the literature in donors after LDLT. The over all complications rates ranged from 0 to 67%. Biliary complications have been reported in 0 top 7% of donors. Complications due to major abdominal surgery occur in 9 to 19% of donors including wound infections, small bowel obstruction, incisional hernia and pneumonia[22-25]. There were no short term complications reported in our study, however long term complications were beyond the aim of this study.

In conclusion, our study demonstrated that both anesthetic techniques were well tolerated for living donor hepatectomy, with no blood transfusion required, with short and safe discharge from PACU and short hospital stay, but with significant laboratory changes reflecting transient impairment in metabolic liver function. These procedures have proven useful as an important alternative to the cadaveric liver transplantation. Both techniques can be used as fast tract technique for living donor heptatectomy. However, we are in favour of maintenance of anesthesia with isoflurane and fentanyl infusion because it is less expensive than the other technique.

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