Anesthesia eJournal /AEJ
Volume 2 Issue 2 2014

OPEN ACCESS

Perioperative Management To Prevent Allogeneic Blood Transfusion In Liver Surgery

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Abstract

Considerable surgical blood loss is a recognized complication of hepatic surgery. Allogeneic blood product transfusion can be used to treat anemia related to surgery. However, research has shown that transfusing blood products exposes the patient to multiple risk factors. Methods of surgical and anesthetic management of blood loss such as establishing acute normovolemic hemodilution and maintaining low central venous pressure can prevent the need for a transfusion. This case study outlines the use of acute normovolemic hemodilution and low central venous pressure to prevent allogeneic blood transfusion in a patient undergoing hepatic resection.

Keywords:

Allogeneic transfusion; central venous pressure, hemodilution, hepatic resection, hepatectomy.

Acknowledgments
The authors thank Ben Lindsey, CRNA, MS, for his guidance and encouragement in this case and for his continued efforts to educate future certified registered nurse anesthetists at the University of Southern California.

INTRODUCTION

Advances in the operative and anesthetic techniques of hepatic resection have decreased associated morbidity and mortality. Administration of allogeneic blood products to correct anemia and coagulopathy is routine in this surgical population, although adverse events occur with significant frequency. Immunosuppression, infection, transfusion reactions, and early recurrence of cancer have all been associated with allogeneic blood transfusions.[1-3] The incidence of these complications may be as high as 1 in 2000 units of red blood cells (RBC) transfused. Furthermore, the incidence of transfusion errors has been estimated at 1 in 14,000 units of blood transfused.[4]

Anesthesia practitioners must focus on careful perioperative management to reduce RBC loss and prevent allogeneic blood transfusions. Techniques traditionally used to prevent allogeneic transfusion during hepatic resection include clamping the major hepatic vessels, decreasing retrograde hepatic blood flow, and diluting the circulating RBC concentration.[1,2] In this case report, acute normovolemic hemodilution (ANH) and maintenance of a low central venous pressure (CVP) were implemented to reduce the concentration of RBC lost, decrease overall blood loss, and prevent allogeneic blood transfusion.

CASE SUMMARY

A 53-year-old woman with an American Society of Anesthesiologists (ASA) Physical Status 3 presented for open surgical resection of a liver mass. She was 163 cm tall and weighed 83 kg. Her medical history included type 2 diabetes mellitus, hypertension, and rectal cancer. Preoperative medications were metformin and valsartan. The patient's surgical history included transrectal excision of rectal cancer in 2009. Preoperative laboratory values were as follows: hemoglobin 13.4g/dL, hematocrit (HCT) 40.2%, blood urea nitrogen 13 mg/dL, creatinine 0.66 mg/dL, glucose 162 mg/dL, protime (PT) 10.4 seconds, international normalized ratio 1.0, and partial thromboplastin time (PTT) 28 seconds. The chest x-ray showed no acute disease; the electrocardiogram (ECG) showed a possible inferior infarct. A myocardial perfusion scan was performed after the ECG. The scan showed normal perfusion, ventricle size, and ejection fraction and no wall motion abnormalities. The ECG results did not clinically correlate with the perfusion scan, and the patient was cleared for surgery. The preoperative vital signs were: heart rate 106 beats per minute, blood pressure 116/80 mm Hg, respiratory rate 19 breaths per minute, and temperature 36.6°C.

The patient was given 2 mg midazolam intravenously (IV) before entering the operating room. Standard ASA monitors were connected to the patient, and a face mask delivering 6 L/min oxygen was applied. The patient was placed in a seated position, and the regional anesthesia team inserted a thoracic epidural at the level of T8 without complications. The patient was positioned supine, pre-oxygenated for 5 minutes, and induced with 100 mg lidocaine, 100 mcg fentanyl, 150 mg propofol, and 10 mg cisatracurium. A 7.0-mm endotracheal tube (ETT) was inserted into the trachea. General anesthesia was maintained with desflurane 5%-6% inspired concentration in a mixture of 0.5 L/min oxygen and 0.5 L/min air.

A 20-gauge right radial arterial catheter and a 7F triple-lumen central venous catheter (CVC) were placed under sterile conditions. The CVP was transduced through the CVC. The patient was placed in a 15-degree Trendelenburg position. Two citrate phosphate dextrose (CPD) bags were attached to the CVC for phlebotomy. About 700 mL blood were collected between both bags, which were stored in a cooler and agitated periodically to prevent clotting. Albumin 5% (500 mL) and plasmalyte (600 mL) were administered IV over 30 minutes. Post-phlebotomy and hemodilution lab specimens were processed in the main hospital laboratory and resulted in HGB 11.5 g/dL and HCT 35%. Before the intraparenchymal dissection, the surgeon clamped the hepatic arteries and portal vein. During resection, CVP was maintained at ≤4 mm Hg with administration of a nitroglycerin (NTG) infusion. As blood loss increased, IV fluids and phenylephrine were needed to maintain the blood pressure within 10%-20% of preoperative values. Total administration of NTG was 2100 mcg, and administration of phenylephrine was 2450 mcg. Total IV fluid administration was 3 L crystalloid and 500 mL albumin. Total blood loss for the operation was estimated at 500 mL, and urine output was 250 mL.

Before extubation, 700 mL whole blood in the CPD bags were transfused to the patient over 30 minutes, and the phenylephrine infusion was adjusted downward and turned off. Epidural morphine (3 mg) was administered before tracheal extubation. Return of neuromuscular function was determined by train-of-four monitoring with 4/4 twitches and sustained tetany. The patient met extubation criteria to maintain spontaneous ventilation, and the ETT was removed. The patient was transferred to the postanesthesia care unit (PACU) with 6 L/min oxygen administered via face mask. After 30 minutes in the PACU, the blood pressure began to decline but responded to administration of 500 mL normal saline. The patient did not complain of pain.

To prevent further decline in blood pressure, epidural infusion of local anesthetic was not initiated. After 30 minutes in the PACU, the patient reported pain at the surgical site. She was given IV hydromorphone for pain management in the PACU and throughout her hospitalization. Postoperative hematology results in the PACU were HBG 8.7 g/dL and HCT 25.5%. On postoperative day 2, the patient's HGB increased to 9.0 g/dL and HCT to 26.1%. The epidural was used only for morphine administration at the end of surgery and was discontinued on postoperative day 3 with no sequelae. No allogeneic blood products were transfused during hospitalization.

DISCUSSION

Hepatic resection is the preferred management for malignant and benign masses of the liver.[3] Over the past few decades, advances in intraoperative management have reduced morbidity and mortality associated with this surgical population.[3] However, acute blood loss remains a significant challenge for both surgeons and anesthetists. Often, these losses result in the transfusion of allogeneic blood products.[2] Serious complications such as renal injury, immunosuppression, sepsis, hemolytic reactions, acute lung injury, and infection can occur after these transfusions.[4,5] To prevent these complications, anesthetic management should focus on interventions to minimize surgical blood loss. In this case, the following plan was implemented to accomplish this goal: before incision, ANH would be used and, during liver parenchymal resection, CVP would be maintained at ≤4 mm Hg.

Establishment of ANH involves the removal of blood cells, resulting in RBC dilution and lower HGB and HCT, followed by return of the patient's original blood concentrated with RBCs and coagulation factors. By replacing the blood that was removed with colloid or crystalloid, the blood lost is diluted. This results in a decrease in the number of lost RBCs during intraoperative bleeding and maintains intravascular volume and cardiac output.[3,6] Transfusing blood at the end of surgery can increase RBC count, restore blood volume, and improve coagulability.[4] For this patient, 2 CPD bags were used to remove about 700-800 mL. However, larger volumes of blood can be safely removed during ANH.[3,6,7] Hemodilution to HGB levels of 8.0 g/dL can easily be achieved if the patient's hemodynamic status is maintained during the procedure. The amount of blood that needs to be removed to achieve a target HGB or HCT can be estimated by applying the equation in Figure 1.[3,6] Substituting the patient's pre- and post-phlebotomy HCT confirms that the estimated amount of blood removed in the 2 CPD bags was accurate.

The effectiveness of ANH in reducing allogeneic blood transfusion has been debated. Table 1 includes a number of studies for review. A 2004 meta-analysis reviewed 42 randomized controlled trials using ANH and concluded that there was no significant reduction in the incidence or relative risk of allogeneic blood transfusion. The volume of blood transfused in the ANH group was significantly less than in the usual-care groups. Although the volume of blood transfused was decreased by 1-2 units, it did not affect the incidence of allogeneic transfusion.8 However, this meta-analysis had limitations; most of the studies were not conducted in the United States, and only 12 had the outcome evaluator blinded to the study group. In addition, only one study was specific to hepatic surgery. A 2002 study specific to ANH in hepatic surgery showed a significant increase in the incidence of allogeneic transfusion when ANH was not used.9 Four patients in the ANH group received an allogeneic blood transfusion, compared with 14 patients in the control group. Half the patients in the control group received only 1 unit of blood. This could have been avoided by using ANH.[9]

In 2006, the ASA conducted a research review and published its guidelines for perioperative blood transfusion. The ASA concluded that there is statistically significant evidence to support using ANH to reduce perioperative allogeneic blood transfusion.[10] More recent research also supports these findings. Jarnagin et al, who studied patients undergoing hepatic resection, demonstrated a 50% reduction in RBC transfusion using ANH.[3]

Guo's 2013 study compared 30 elderly patients undergoing hepatic resection randomly assigned to either ANH or a control group.[7] This study also identified a significant decrease in blood transfusion in the ANH group by more than 100 mL RBC. Although fibrinogen was decreased and PT/PTT were prolonged after ANH, these values were within normal limits and improved to values similar to the control group after transfusion of homologous blood.[7] ANH facilitated a reduction in the concentration of RBCs lost, and allogeneic blood transfusion was not necessary, possibly due to ANH therapy.

Maintenance of a low CVP (≤5 mm Hg) has been identified as a potential means to reduce blood loss during hepatic resection.[2,11] A low CVP results in a decrease in retrograde pressure and flow through the dissected liver parenchyma. The surgical steps involved in hepatic resection include an initial clamping of the hepatic arteries and portal vein, causing total hepatic inflow occlusion before parenchymal dissection. The increase in pressure from the retrograde blood flow into the hepatic veins increases bleeding through the hepatic sinusoids. Lowering the CVP can reduce these pressures and blood flow to the liver to decrease overall blood loss (Table 2). A research trial to evaluate this phenomenon studied two groups of 50 patients undergoing hepatic resection (CVP ≤5 mm Hg or CVP >5 mm Hg). Demographic data and transfusion thresholds were equivalent in both groups. The low CVP group recorded a roughly 80% reduction in blood loss and significantly fewer blood transfusions.[11] Multiple methods can be used to reduce CVP while maintaining normotension.

A 2006 study of 50 patients undergoing hepatic resection used IV NTG infusion and the Trendelenburg position, limited IV fluid administration, and used IV furosemide to maintain CVP at 2-4 mm Hg. Compared with the control group, the low CVP group had a 69% reduction in blood loss and a 32% reduction in allogeneic transfusion.[12] In 2008, a trial of 46 patients used similar methods to reduce CVP to 2-4 mm Hg. This trial evaluated the volume of intraoperative blood loss and blood product administration and monitored renal function to postoperative day 7. The low CVP group demonstrated a 49% reduction in intraoperative blood loss and a 44% decrease in volume of blood product administration compared with the control group. There were no differences in postoperative renal function in either group.[13] In this case, CVP was maintained at ≤4 mm Hg using both the Trendelenburg position and IV NTG infusion. These interventions may have been responsible for the lower intraoperative blood losses.

When altering a patient's hemodynamic status with ANH and lower CVP, the impact on comorbidities must be addressed. In this case, the patient's hypertension was well controlled, without signs of compromised perfusion, as evidenced by a preoperative normal myocardial perfusion scan and normal chemistry values. An NTG infusion adjusted to a rate of 25 mcg/min was effective at reducing the CVP to ≤4 mm Hg. As surgical blood losses increased, the NTG infusion was discontinued and a phenylephrine infusion adjusted to 60 mcg/min, which maintained blood pressure at 89/48 to 115/60 mm Hg.

Constant communication between the surgeon and anesthetist enabled vigilant monitoring of current and anticipated blood losses, which informed decisions on vasoactive therapies and return of the patient's blood. When the vasopressor infusion was used to support blood pressure and the hepatic resection was completed, a decision was made to re-transfuse the patient. As blood pressure returned to baseline levels, the phenylephrine drip was discontinued. To reduce postoperative pain, the epidural was activated during incision closure with 3 mg morphine. The anesthetic management goals to maintain the patient's CVP at ≤4 mm Hg and blood pressure within 20% of the baseline were met throughout the surgery.

ANH and maintenance of low CVP reduced surgical blood loss and precluded the administration of allogeneic blood transfusion during hepatic resection. Current evidence supports the use of these methods in hepatic surgery.[1-3,6,10,11,14] The intraoperative management of hepatic resection should include ANH and low CVP to reduce the concentration of surgical RBC losses and overall intraoperative blood loss. These interventions can prevent exposing the patient to allogeneic blood products and the associated risks and complications.

Estimate amount of blood to be removed	VL = EBV x ((Hi – Hf)/Hav)
Apply equation to pre- and post-phlebotomy lab values	VL = (65 x 83) ([40.2 – 35.0] / 37.6) = 746 mL of blood removed

Figure 1.
EBV, estimated blood volume; Hi, initial hematocrit; Hf, target hematocrit after hemodilution; Hav, average between Hi and HF; VL, total volume to be removed.

Table 1. Methodology and outcomes of studies on use of acute normovolemic hemodilution during hepatic resection.

Author and date	Methodology	Outcomes
Segal et al - 20048	Meta-analysis of 42 trials: 18 cardiac surgeries, 13 orthopedic procedures, 4 radical prostatectomies, 3 spine surgeries, 2 aortic surgeries, 1 thoracic surgery, and 1 liver resection	No significant decrease in relative risk of receiving allogeneic blood transfusion (P = 0.3). Total volume of allogeneic blood transfused intraoperatively and postoperatively was significantly less in ANH group (P <0.001)
Matot et al - 20029	Prospective RCT of 78 patients undergoing hepatic surgery for tumor excision. Control group (n=39) did not undergo ANH therapy; ANH therapy group (n=39) underwent phlebotomy (HCT = 24%). Fluid administration was controlled in both groups to prevent increases in CVP values. Indication for blood transfusion was standardized in both groups to HCT = 20%	Intraoperative blood loss, CVP, and urine output were similar in both groups. 14 patients in control group received allogeneic blood transfusion, compared with 4 patients in ANH group (P = 0.014). 50% of patients in control group were transfused only 1 unit of blood. There were no differences in HCT, creatinine, PT, and pH between control group and ANH group
Jarnagin et al - 20083	Prospective RCT of 130 patients undergoing hepatic surgery comparing ANH with standard anesthetic management (65 patients/group). Target diluted HGB = 8.0 mg/dL. Low CVP was standardized in both groups. Transfusion trigger was HGB < 7.0 g/dL in both groups.	50% reduction in transfusion of allogeneic red cells and fresh frozen plasma in ANH group (P <0.05). 66.6% of standard management patients with ≥1500 mL blood loss were transfused intraoperatively compared with none in ANH group (P <0.01). Results showed 85% reduction in allogeneic transfusion requirement
Guo et al - 20137	Prospective RCT of 30 patients aged 60-70 undergoing hepatic surgery for tumor excision. Patients were randomly assigned to ANH group or control group (15 patients/group). Blood samples were drawn 5 times: before induction (T1), 30 min after ANH (T2), 1 hour after surgery start (T3), immediately after surgery (T4), and 24 hours after surgery (T5). ANH group target HCT = 28%. Transfusion threshold HGB = 8 g/dL or HCT = 25%	Intraoperative blood losses were similar in both groups. Volume of blood transfusion was significantly less in ANH group (350.5 ± 70.7 mL vs 457.8 ± 181.3 mL; P <0.05). Compared with data before ANH, PT and PTT were significantly prolonged in ANH group for times T2 and T3 (values were still within normal limits). Concentration of fibrinogen was significantly reduced after ANH (within lower limit). Fibrinogen values increased after transfusion of homologous blood removed by ANH

ANH, acute normovolemic hemodilution; CVP, central venous pressure; HCT, hematocrit; HGB, hemoglobin; PPT, partial thromboplastin time; PT, protime; RCT, randomized controlled trial.

Table 2. Methodology and outcomes of studies on maintenance of low central venous pressure during hepatic resection.

Author and date	Methodology	Outcomes
Jones et al – 1998[11]	Prospective trial with 100 patients undergoing hepatic resection. Patients were categorized into 2 groups: CVP ≤5 and CVP >5. Transfusion threshold was HGB =10 g/dL for both groups	Median blood loss for CVP ≤5 = 200 mL; median blood loss for CVP >5 = 1000 mL (P = 0.0001). Group with CVP ≤5, 2 patients received blood transfusion compared with group with CVP >5 had 25 patients that received blood transfusion (P = 0.0008)
Wang et al – 2006[12]	Prospective RCT with 50 patients undergoing hepatic resection classified equally into low CVP group (CVP = 2-4 mm Hg and SBP >90 mm Hg) and control group (no CVP lowering). CVP was maintained in low CVP group by using Trendelenburg position, limiting fluid volume, IV NTG infusion, and IV furosemide if necessary. Transfusion thresholds were equivalent for both groups, at 8.0 g/dL	Total blood loss was significantly lower in low CVP group compared with control group (P <0.01) (904 mL vs 2329 mL). 56% of patients in control group received blood transfusion compared with 24% in low CVP group (P <0.05). Low CVP group had significantly shorter hospital stays (P <0.05). Postoperative complications were equivalent in both groups. There were no differences in postoperative hepatic and renal functions
Liu et al - 2008[13]	Prospective RCT of 46 patients undergoing liver resection classified equally into low CVP group (CVP = 2-4 mm Hg, SBP >90 mm Hg, and mean blood pressure >60 mm Hg) and control group (no CVP lowering). CVP was controlled in low CVP group by using Trendelenburg position, limiting fluid volume administration, and IV NTG infusion and IV furosemide. Transfusion threshold was same for both groups, at HGB <8.0 g/dL	Total intraoperative blood loss was significantly less in low CVP group (P <0.01) (375 mL vs 733 mL). RBC transfusion was significantly less in low CVP group, with average 206 mL vs 365 mL in control group (P <0.05). 7 patients in low CVP group required blood transfusion vs 13 patients in control group. There were no changes in BUN or creatinine on postoperative days 1, 3, or 7

BUN, blood urea nitrogen; CVP, central venous pressure; IV, intravenous; NTG, nitroglycerin; RBC, red blood cell; SBP, systolic blood pressure.

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