Impact of a Transfusion-Free Program on Non–Jehovah’s Witness Patients Undergoing Liver Transplantation

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Background: Orthotopic liver transplantation (OLT) is associated with a large amount of blood loss. This article examines the impact of the initiation of a transfusion-free program in January 2000 for Jehovah’s Witnesses (JWs) on the overall use of blood products in non-JW patients undergoing OLT.


Setting: University of Southern California University Hospital.

Patients: A total of 272 OLTs were performed on non-JW adults. This number includes 216 (79.4%) deceased donor and 56 (20.6%) living donor liver transplantations. Thirty-three OLTs were performed before January 2000 (ie, before the initiation of a transfusion-free program) (group 1), and 239 OLTs were performed after January 2000 (group 2). In group 2, all patients underwent OLT using cell-scavenging techniques and acute normovolemic hemodilution whenever feasible. Demographic, laboratory, and clinical data were collected and matched for severity of disease (model of end-stage liver disease [MELD] score). Transfusion records of packed red blood cells (PRBCs), platelets, and fresh frozen plasma (FFP) were obtained from the University of Southern California blood bank.

Results: In comparing group 2 with group 1, the mean MELD score was statistically significantly higher ($P < .001$), whereas the mean number of intraoperative PRBC and FFP transfusions was significantly lower ($P = .03$ and $P = .004$, respectively). The number of preoperative and postoperative PRBC, FFP, and platelet transfusions between the 2 groups was not statistically different.

Conclusion: The development of a transfusion-free surgical program for JW patients has had a positive impact on reducing the overall blood use in non-JW patients undergoing OLT, despite the increase in MELD score.

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cine and Surgery Program at USC in January 2000. Group 1 consisted of recipients who received the liver transplant before January 2000. Group 2 included all patients who underwent transplantation after January 2000. Recipients in group 1 underwent OLT without intraoperative blood-saving or salvaging techniques, whereas all transplant recipients in group 2 underwent intraoperative cell salvage (ICS) and acute normovolemic hemodilution (ANH) whenever feasible. The broad term ANH indicates a therapeutic initiative that involves simultaneously removing the patient’s blood and replacing it with nonblood products and has been previously described by our team. Rarely, ANH has been used for the DD transplant recipient population. Unlike with the JW patients, this is primarily because we do not have the luxury of preoperatively optimizing every patient going to the operating room before liver transplantation, and there were no protocol-driven regimens for increasing their red blood cell (RBC) mass with erythropoetin. On the other hand, we were able to optimize some of the LD transplant recipients, and 15% underwent ANH. For the purposes of ANH, blood was removed from the central line and drained to a citrate-phosphate-dextrose bag before incision. The volume of blood withdrawn for ANH usually ranged from 400 to 1500 mL, depending on the original hemoglobin level and patient tolerance. In adults, hemoglobin levels decrease 1 g/dL for each unit of blood removed. In our patient population, the lowest hematocrit value after ANH was 21% (range, 21%-26%). Hemodynamic monitoring of heart rate, blood pressure, arterial blood gases, pulmonary artery pressures, central venous pressures, and transesophageal echoes to monitor cardiac contractility and ventricular filling are routinely used during the ANH process as a measure of tolerance to the procedure. The ANH blood volume is replaced with 5% albumin and crystalloid solution. The ANH blood is later reinfused after washing. All liver transplantations were performed by the same surgical and anesthesiology teams at USC-UH.

The following preoperative data were collected and reviewed: demographic, Child-Pugh score, model of end-stage liver disease (MELD) score, primary diagnosis, type of transplantation, and laboratory data. The MELD score describes survival probability of a patient with end-stage liver disease and is estimated based on the following variables: international normalized ratio, creatinine level, and bilirubin level. It was introduced by the United Network for Organ Sharing (UNOS) in 2002 and is calculated based on a logarithmic equation: 10(0.957ln[serum creatinine] + 0.378ln[total bilirubin] + 1.12ln[international normalized ratio] + 0.643). The MELD score was obtained from the UNOS database. All other patients who underwent transplantation before that time had the MELD score calculated retrospectively. Transfusion records of packed RBCs (PRBC), platelets, and fresh frozen plasma (FFP) were obtained from the USC blood bank. Records were further classified into intraoperative (before 6 months of transplantation), intraoperative, and postoperative (after 6 months of transplantation) data. The t test was performed using SAS statistical software, version 8 (SAS Institute Inc, Cary, NC). P<.05 was considered statistically significant.

A total of 365 OLTs were performed from January 1997 to December 2004 at USC-UH. Of these, 281 used DD transplants and 84 used LD transplants. After eliminating the pediatric and JW recipients, 272 adult non-JW OLTs were analyzed. Of these, 216 (79.4%) used DD transplants and 56 (20.6%) used LD transplants. There were 172 male (63.2%) and 100 female (36.8%) recipients. The mean±SD age of the study population was 53±10 years. The primary diagnoses of patients at the time of transplantation were hepatitis C cirrhosis in 78 (28.7%), hepatitis B cirrhosis in 44 (16.2%), autoimmune hepatitis in 35 (12.9%), primary sclerosing cholangitis in 17 (6.2%), primary biliary cirrhosis in 17 (6.2%), and other in 82 (30.0%). Thirty-three OLTs were performed before January 2000 (group 1) and 239 OLTs after that time (group 2).

At the time of transplantation, 111 patients (40.8%) had a MELD score of 25 or higher, and 161 patients (59.2%) had a MELD score of 24 or lower. A total of 85 patients (31.2%) had a MELD score higher than 30. The mean MELD score in group 2 was significantly higher than in group 1 (ie, 19 vs 11) (P<.001). Despite the increasing MELD score (Figure 1), the intraoperative use of PRBCs and FFP was significantly lower in group 2 compared with group 1 (P=.03 and P=.004, respectively) (Table 1 and Figure 2). Platelet use did not appear to be affected.

Preoperative and postoperative use of blood products was also compared. Preoperative requirements in the 6 months before OLT of PRBCs, FFP, and platelets showed no statistical difference for patients in either group (Table 1). However, there clearly appeared to be a trend toward increased use of preoperative FFP and platelets (Figure 3), perhaps related to the increased severity of the disease (higher MELD scores). Similarly, the postoperative use of blood products up to 6 months after OLT did not appear to show a statistical difference in the use of blood products between the 2 groups (Table 1). On further stratification of the patients into groups with MELD scores of above 25 or 25 or below, the results show that the intraoperative number of blood products used in these patients with higher MELD scores had significantly decreased (P=.001) (Table 2).
Liver transplantation for decompensating cirrhosis and unrecoverable acute liver failure is well accepted today and has come to be the standard of care. The operation is still fraught with technical challenges amid a field complicated by coagulopathy and significant portal hypertension. Therefore, colossal intraoperative blood loss that necessitates massive blood transfusion is not unusual, putting the patient and graft at risk and challenging the surgeon. Often these patients are sicker than they look because of additional comorbidities, such as malnutrition, cardiac problems, renal failure, and encephalopathy. The MELD score has pushed most centers, especially on the East and West Coasts, to perform transplantations in much sicker patients than what was done before 2002. This occurrence is seen in our own series, in which more than 30% of our patients had MELD scores higher than 30 (Table 1 and Figure 1). Such patients are undoubtedly more complex to treat because they require more transfusions before, during, and after surgery.

The literature is replete with studies aimed at predicting intraoperative need for transfusion and the correlation between the amounts of blood transfused and short- and long-term patient and graft survival. Findlay and Rettke1 performed a univariate analysis of intraoperative bleeding risk factors in 583 sequential adult patients undergoing OLT. They revealed significant associations between blood transfused and age, sex, primary diagnosis, presence and severity of encephalopathy, creatinine level, bilirubin level, activated partial thromboplastin time, platelet count, mean pulmonary artery pressure, and pseudocholinesterase level. Hendriks et al2 reported their experience with 164 consecutive OLTs and found that Child-Pugh classification, blood urea nitrogen level, year of transplantation, cold ischemia time, and autologous blood transfusion are independent predic-

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1</th>
<th>Group 2</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>54 (21-75)</td>
<td>53 (19-73)</td>
<td>.93</td>
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<tr>
<td>MELD score, mean</td>
<td>11</td>
<td>19</td>
<td>&lt;.001*</td>
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<td>Intraoperative, mean ± SD, U</td>
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<td>6.0 ± 6.6</td>
<td>.03*</td>
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<td>PRBCs</td>
<td>7.7 ± 6.5</td>
<td>4.9 ± 5.0</td>
<td>.004*</td>
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<td>FFP</td>
<td>3.1 ± 3</td>
<td>2.4 ± 2.8</td>
<td>.22</td>
</tr>
<tr>
<td>Platelets</td>
<td>3.9 ± 5.4</td>
<td>3.8 ± 7.1</td>
<td>.93</td>
</tr>
<tr>
<td>Preoperative, mean ± SD, U</td>
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<td>3.1 ± 7.2</td>
<td>.33</td>
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<tr>
<td>PRBCs</td>
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<td>1.3 ± 3.3</td>
<td>.14</td>
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<tr>
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<td>.11</td>
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<tr>
<td>Platelets</td>
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<td>.65</td>
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<tr>
<td>Postoperative, mean ± SD, U</td>
<td>1.9 ± 4.9</td>
<td>1.9 ± 5.9</td>
<td>&gt;.99</td>
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</table>

Abbreviations: FFP, fresh frozen plasma; MELD, model of end-stage liver disease; PRBCs, packed red blood cells.

*Statistically significant.
tors of transfusion requirements. Deakin et al8 showed that in their population of 300 adult liver transplantations, blood urea nitrogen level and platelet count had an independent correlation with transfusion necessity. Ramos et al9 showed that only preoperative hemoglobin level, UNOS score, and placement of portocaval shunts predicted the need for blood transfusion. However, much inconsistency occurred in the described preoperative variables, and the literature cites these variables to be poor predictors of intraoperative transfusion requirements and therefore of limited clinical use.1,5

On the other hand, it is imperative to take into account that massive intraoperative blood loss is a predictor of not only poor graft outcome but also poor long-term prognosis.20 Cacciarella et al21 reviewed 225 adult OLT recipients and showed a significant improvement in both patient and graft survival when less than 3 U of PRBCs was transfused intraoperatively. Ramos et al22 showed that even a moderate number of blood transfusions is associated with longer hospital stay and that transfusion of more than 6 U of PRBCs is associated with diminished survival. The Anemia and Blood Tranfusion in the Critically Ill (CRIT) studies by Corwin et al23 showed that in a setting of 284 intensive care units in the United States, patients who received transfusions had more complications and were at higher risk for mortality.

Excessive use of blood bank resources for liver transplantations puts pressure not only on the transplantation service but also on all other surgical fields. A long-term shortage of blood in hospitals, necessitating tapping into the resources of the Red Cross and other blood donor agencies, is not an unfamiliar setting for every practicing general surgeon. It is an unremittting problem for blood banks throughout the country, leading to delay or cancellation of elective cases, resulting in lost revenue. Heiss et al24 reported that autologous vs allogeneic blood transfusion decreases the recurrence of curable colon cancer. Allogeneic blood transfusion has been associated with an increased incidence of postoperative bacterial infections.24 Despite the current conviction among physicians that blood products are safer than they used to be, there are reports of transfusion-related transmission of hepatitis C and human immunodeficiency virus13,14 and emerging data of newer pathogens for bovine spongiform encephalopathy and West Nile virus. Blood can almost never be 100% safe. It often takes decades to demonstrate that disease was transmitted through allogeneic blood. For that reason, not only transplantation surgeons but also general surgeons should assume responsibility to minimize overall blood use.

Rapid development of novel drugs is also beginning to play a role in containing coagulopathy and increasing hemopoesis. Drugs such as human recombinant erythropoietin to increase the pretransplantation RBC mass, aprotinin,25 tranexamic acid,26,27 or ϵ-aminocaproic acid to inhibit fibrinolysis have now become mainstream strategies. We recently published our data on the utility of the novel drug recombinant factor VIIa in OLTs. Our data provided evidence of the potential usefulness and safety of this agent in the management of coagulopathy-related oozing.28 These drugs are not used routinely but rather on a case-by-case basis depending on objective cri-
the constant preoperative transfusion requirements, OLT continues to be successfully performed with the help of bloodless techniques and strategies. We surmise that the development of the Transfusion-Free Medicine and Surgery Program for JW patients has had a positive impact on overall blood use for all recipients undergoing OLT, even in the face of higher MELD scores. Successful decrease in blood use is an upshot of an advanced transfusion-free program.

Surgeons are the leading consumers of blood products, and it is important that we are leaders in promoting transfusion-free techniques. In conclusion, we propose that the recognized need to minimize the use of blood products be elevated to the same level as antibiotic and deep venous thrombosis prophylaxis.

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REFERENCES