Original Article

Perioperative use of allogenic blood components in live-related donor orthotopic liver transplantation: A cross sectional study

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Abstract:

Background: In spite of many improvements that have reduced the blood component requirements, substantial numbers of transfusions are still needed in liver transplantation. **Aims:** The objective of the present study was to analyze the perioperative usage of allogenic blood components and predict the preoperative factors as predictors of red cell transfusion in live-related donor liver transplant recipients. **Materials and Methods:** The retrospective data on utilization of allogenic blood components were analyzed for a total of 150 liver transplant procedures. The data on utilization of blood components during surgery and till 48 hours of ICU stay was collected from the blood bank record and hospital information system (HIS). **Results:** Red cell concentrate was commonest blood component used in liver transplant recipient and most of the transfusion took place during surgery. During intraoperative period 92.7% (N = 139) of the cases utilized red cell components with the median number of five whereas in postoperative period only 38% (N = 57) of patients received blood with the median number of one. This study demonstrates that the preoperative hemoglobin and platelet count are the predictors of utilization of red cell concentrates during surgery. There were a total of 11 (7.3%) recipients who didn't receive allogeneic blood transfusion in any form.Utilization of blood components was negligible among organ donors. **Conclusion:** Our study demonstrates the pattern and predictors of usage of allogeneic blood components in liver transplant recipients at a tertiary healthcare center in India.

Key words:

Allogeneic blood components, orthotopicliver transplantation, transfusion

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Introduction

Live-related donor orthotopic liver transplantation (OLT) is an extensive operative procedure where the diseased liver of recipient is replaced by a healthy liver from a live-related donor. Due to limited availability of cadaveric liver and a large number of patients dying during waiting period, live-related liver transplant procedures have emerged as successful treatment option for end-stage liver disease cases. Continuous improvements over the last few decades in surgical techniques in reducing blood loss, use of pharmacological alternatives of blood and availability of potent immunosuppressive agents have remarkably improved the survival outcome of solid organ transplants. The liver is an extremely vascular organ and the site for synthesis of various coagulation factors and protein. Disease associated preoperative hypo-coagulopathy, portal hypertension, thrombocytopenia and considerable blood loss during transplant procedure creates a challenge to blood transfusion services.[1] Bloodless kidney transplantation is common[2] but bloodless liver transplantation is a challenge. Thus, in spite of many developments liver transplant procedures still require substantial support of blood components during and immediately after the surgical procedure.[3] In liver transplant cases, at majority of instances, it's difficult to predict the perioperative requirement of blood transfusion.[4] The primary objective of the present retrospective study was to analyze the perioperative usage of allogeneic blood components in live donor related orthotopic liver transplant recipients and liver donors in liver transplant procedures performed at our tertiary healthcare center. The secondary objective of this study was to assess the preoperative parameters that can predict the utilization of red cell concentrates during the liver transplant procedures.

Materials and Methods

This study was carried out at Department of Transfusion Medicine, between July 2010 to Feb 2011 (eight months) at a tertiary healthcare center situated in the national capital region of India. All live-related donors liver transplant procedures utilizing allogeneic blood components were included in the study. Those patients who received autologous blood transfusion were excluded from the study. As

a hospital policy, for all patients we use blood components in form of Red Cells- in additive solutions (RC), Platelet Concentrate (PC), Fresh Frozen Plasma (FFP) and Cryoprecipitate (Cryo). In brief, according to the departmental Standard Operating Procedures (SOP) only 450 ml of whole blood was collected from the donors weighing more than 50kg. At the Department of Transfusion Medicine, we have facility for plateletpheresis (COM.TEC, Fresenius Kabi, Germany) in case patient requires single donor platelets (SDP). Every unit of Red Cells and Platelet Concentrates were three log leuko-depleted before storage using red cell filter (BioR 01 max BBS, Fresenius Kabi, Germany) and platelet filter (BioP plus BBS PF, Fresenius Kabi, Germany) using departmental standard operating procedures (SOP). Analysis of perioperative utilization of blood components was performed in all patients irrespective of their outcome (discharge or death during the period of observation). Platelets utilized in liver transplant cases were mainly single donor platelets. Platelet concentrates were used only in those circumstances where single donor platelets were not available. Therefore, platelet concentrates were excluded from the final analysis of the data. The retrospective data on utilization of blood components was collected from the blood bank record and hospital information system (HIS). As hospital policy, blood components were issued from the blood bank only when it is required for transfusion. None of the blood components were issued for the anticipatory use of blood components because we didn't have storage facility for blood components at Operation Theatre. The peri-operative period in our study was defined from the date of surgery until 48 hours of the ICU stay. For liver transplant recipients data were collected, analyzed and presented separately for intraoperative and for post-operative utilization of first 48 hours whereas in case of liver donor the data were collected, analyzed and presented cumulatively for intraoperative and perioperative utilization. To assess the factors affecting utilization of blood components during the liver transplant procedures we divided the total population of patients into two groups. group one contained those patients who received less than or equal to five red cell concentrates while those patients who utilized more than five red cell concentrates were positioned in group two. All the data were stored in Microsoft excel sheets (Microsoft Corp, USA) and were finally analysed using the SPSS version 16 software. For assessing the factors influencing the utilization of red cell concentrate during the period of surgery the significance of difference of mean demographic, haematological and coagulation parameters were assessed between the two groups in terms of p value. The difference of each parameter was found to be highly significant when the p value was <0.01. For the comparison of blood used during surgery and blood used during 48 hours of surgery in a particular group paired t-test was applied by taking the mean and SD difference in to account.

Results

The data were analyzed for a total of 150 patients who utilized allogeneic blood components during surgery and in first 48hrs of intensive care unit (ICU) stay. The common indications for liver transplantations were alcoholic cirrhosis, chronic liver disease associated with viral hepatitis and cryptogenic chronic liver disease [Table 1]. The median age of liver transplant recipients and donors were 49 and 32 years respectively with a wide age range in recipients varying from six months to 78 years. Majority of the liver transplant recipients were male (M:F=4.2) and majority of liver donors were females (data not shown in Table). In present study, among 150 patients, we observed that during intraoperative period 92.7%(N=139) of the cases utilized red cell components with the median number of five and with a wide range (range 0-20). Similarly, during the intraoperative period there were a total of 136 patients (90.7%) who received transfusion of FFP with median number of four and remaining 14 cases (9.3%) did not utilize even a single unit of FFP. Only 24.7% (N=37) of the total patients utilized single donor platelets with the mean number of 0.3. Cryoprecipitate was a sparingly used blood component [Table 2]. There were a total of 11 cases (7.3%) who did not utilize even a single unit of allogeneic blood components (bloodless liver transplantation) [Table 2].

The difference of mean between the two groups was found to be statistically highly significant (<0.01) for haemoglobin and platelet count. We observed no statistical significance for parameters like PT, INR and APTT [Table 3].

Unlike the utilization of blood in liver transplant recipient during surgery the utilization of blood components during first 48 hrs of ICU stay was very low. Only 38% (N=57) of the total recipients received blood transfusion in any form during post-op period and that was mainly in the form of red cell concentrate. The median utilization of FFP, SDP and other components was zero as shown

Table 1: Indications for liver transplantations (N = 150)

Indications	Number (%)
Hepatitis B related chronic liver disease (HBV-CLD)	27 (18)
Hepatitis C related chronic liver disease (HCV-CLD)	23 (15.3)
Alcoholic liver disease (ALD)	28 (18.7)
Cryptogenic chronic liver disease	27 (18)
Fulminant hepatic failure (FHF)	07 (4.7)
Non-alcoholic fatty liver disease (NAFLD)	08(5.3)
Autoimmune CLD	07(4.7)
Primary sclerosing cholangitis (PSC)	06(4)
Others	17(11.3)
1. CLD associated with hemochromatosis	03(2)
2. Hepatocellular carcinoma	03(2)
3. Drug induced CLD	02(1.3)
4. Repeated sub-acute bacterial peritonitis with decompensated CLD	02(1.3)
5. Primary biliary atresia	02(1.3)
6. Extrahepatic biliary atresia with post kasai	01(0.7)
7. Factor VII deficiency	01(0.7)
8. Recurrent oriental cholangitis	01(0.7)
9. Allogille syndrome	01(0.7)
10. CLD with multiple hemangiomas	01(0.7)

Table 2: Utilization of allogeneic blood components (N = 150)

	Intraoperative utilization			
	RC	FFP	SDP	Cryo
Number (%) of cases received transfusion	139(92.7)	136 (90.7)	37(24.7)	5(3.3)
Median (Range)	5(0-20)	4(0-16)	0(0-3)	0(0-4)
Mean±SD	6±3.9	4.4±2.8	0.3±0.6	0.1±0.5
	Utilization during first 48 hours of ICU stay			
Number (%) of cases received transfusion	57(38)	25(16.6)	28(18.6)	2(1.3)
Median (Range)	1(0-18)	0(0-10)	0(0-5)	0(0-4)
Mean±SD	1.3±2	0.6±1.7	0.3±0.8	0.1±0.5

in Table 3. The difference of utilization of red cell concentrate and FFP during and 48 hours after surgery was found to be highly significant (P<0.01) in group of patients who utilized less than five red cell concentrate. However, no statistical significance was observed in case of SDP and cryoprecipitate utilization. Similarly, the difference of utilization of red cell concentrate and FFP during and 48hrs after surgery was found to be statistically highly significant (P<0.01) in group of patients who utilized more than five red cell concentrates. However no statistical significance was observed in case of SDP and cryoprecipitate utilization [Table 4]. We also observed that the patients having preoperative hemobglobin less than 10 gm%, had high probability of utilization of red cell concentrate than those patients had hemoglobin more than 10gm% both introperatively and postoperative 48 hours after surgery (odds ratio Odds Ratio = 87.229, Chi Sq Value=27.47, P<.01). In contrast to above, we could not found any statistical significance when we took into account the preop platelet count 75000/cmm as the cutoff (results not shown in Table). Liver organ donor rarely utilized blood components during and after surgery as shown in Table 5.

Table 3: Demographic and Haematological Variables of Recipients of Two Groups

Variables	≤5 units of RC	>5 units of RC
Number	78	72
Gender (M/F)	60/18	61/11
Age(yrs)-Median (Range)	46(0.5-65)	46(1-78)
RC utilized-Mean±SD	3.12±1.34	9.07±3.36
FFP utilized-Mean±SD	3.37±2.15	5.58±3.05
SDP utilized- Mean±SD	0.10±0.31	0.56±0.78
Preoperative INR	1.94±1.19	1.90±0.61
Preoperative Hb (gm/dl)	10.31±1.47	8.12±1.12
Preoperative platelet count (10^9/L)	89.45±55.05	61.77±36.59
Preoperative APTT	39.80±12.66	41.86±11.29

Table 4: Comparison of utilization of blood components during surgery and during first 48 hours of ICU stay in two groups of patients

	≤5 RC (*N* = 78)			
	RC	FFP	SDP	CRYO
Mean Difference	1.88	2.90	-0.14	-0.05
SD Difference	2.80	2.35	0.82	-0.57
T value	5.94	10.89	-1.52	-0.57
P Value	<0.01	<0.01	-0.1286	-0.5686
>5 RC(*N*=72)				
	RC	FFP	SDP	CRYO
Mean Difference	7.78	4.82	0.19	0.12
SD Difference	3.35	3.38	1.05	0.60
T value	19.84	12.19	1.56	1.76
P Value	<0.01	<0.01	0.1188	0.0784

Table 5: Total Usage of allogeneic blood components in liver donors (*N*=150)

	Blood components			
	RC	FFP	SDP	Cryo
Number (%) of Cases received Transfusion	55 (36.7)	6 (4)	0	0
Median	0	0	0	0
Mean	0.4	0.08	0	0
Range	0-10	0-3	0	0

Discussion

In this study we retrospectively evaluated the transfusion of blood components in orthotopic liver transplant cases performed during the period of eight months at our center. Over the last decade the requirement of blood transfusion has decreased amazingly but the role of transfusion facility is still indispensible. For a successful transplant program a good coordination between transplant team and transfusion facility is must because ultimately at the end of the day it's a team work. At the moment only few centers in India are having a transplant program and our institute is apparently doing the largest number of liver transplant procedures in the country.

Liver transplantation procedures are associated with relatively high amount of blood and blood products usage during transplantation. There are a lot of factors during pre-operative, intraoperative and post-operative period that are associated with utilization of large amount of blood products.[5] Preoperative factors are basically related to the underlying disease process. Liver failure patients usually have a moderate to severe derangement of coagulation profile due to failure in synthesis of factor II, VII, IX, and factor X.[6] Liver cirrhosis is usually associated with decreased synthesis of Vit K which may lead to abnormal bleeding not correctable with Vit. K infusion.[7] Thrombocytopenia is invariably associated to chronic liver disease and the cause is multifactorial. Liver is the main site for the synthesis of thrombopoietin (TPO), the growth factor for the synthesis of platelets in bone marrow. In case of liver failure there is a decreased synthesis of TPO which leads to decreased production of platelets in bone marrow. In addition to decreased synthesis of platelets, splenomeagaly may add fuel to fire due to increased sequestration and destruction. Sometimes patient exhibit qualitative platelet abnormalities that may further lead to increased blood loss and blood requirements during surgery.[1,8] Factors during intraoperative period which may lead to increased demand of blood components are primarily due to the surgery over the collateral vessels and oozing from the raw surface of liver.[9] Decreased uptake (clearance) of tissue plasminogen activator (serine protease involved in breakdown of clots) during anhepatic and post anhepatic phase may lead to fibrinolysis which may consequently lead to aggravation of bleeding.[10] During the post operative period coagulopathy due to graft failure could be an important cause of bleeding. Again thrombocytopenia due to multiple factors may lead to aggravation of bleeding in postoperative period.[1,11]

In a retrospective single institution study[4] it was demonstrated that preoperative haematological parameters like INR, Hemoglobin and platelet count can influence requirement of red cell transfusion during liver transplantation. According to this study, INR was found to be a most sensitive parameter for predicting utilization of blood components. In our study we also demonstrated that those patients having low Hb and low platelet count demonstrated high utilization of blood components than those patients having high Hb and high platelet count. However, in our study the difference of mean INR was insignificant between the two groups. Thus we could not demonstrate the effect of INR on red cell transfusion requirement. We also observed that the patients having preoperative hemoglobin less than 10 gm%, had high probability of utilization of red cell concentrate but we did not found any preoperative platelet cutoff below which probability of high utilization of blood could be predicted.

In a previous study[12] it has been established that the median usage of blood components varies from institution to institution and surgeon to surgeon and to some extent varies due to institutional variability in transfusion policy. In our study we observed that red cell concentrate was the most common blood component used in liver transplant recipient and most of the transfusion took place during intraoperative period only. We observed that 92.7% of liver transplant recipients' utilized red cell concentrates during intraoperative period with the median number of five while it was used only by 38% of the cases during first 48hrs of ICU observation with the median number of one. Similarly, we observed that approximately 91% of patients required FFP transfusion during surgery with the median number of four units while majority of patients did not require FFP transfusion during the postoperative period. Platelet transfusion was required only by few patients, both during the intraoperative period as well as during postoperative period. Cryoprecipitate has remained as most sparingly used blood components in our observation. Since the present study is the single institution study where all liver transplant procedures were performed by a single team, we did not have opportunity to assess inter institutional and interpersonal variability in transfusion practice.

Over the last few decades it has been observed that there is considerable decrease in the requirement of blood but still there is a wide range of utilization of red cell concentrate which varies from 4.3 to 43 units per patients.[4,12-14] We are able to state that there is almost similar pattern of utilization of blood components in liver transplant recipients in procedures performed at our center. The median usage of FFP at our center was found to be relatively low compared to previous study[12] and the possible explanation could be the real time monitoring of coagulation profile with thromboelastography (TEG). Use of thromboelastography[15,16] and antifibrinolytic agents[17] have dramatically decreased the requirement of blood components during the liver transplant procedures and consequently improved the outcome.

In our study we observed that approximately 7% of liver transplant recipients did not receive even a single unit of allogeneic blood component in any form during and after the procedure. Blood less liver transplant procedures has been performed in patients of Jehovah's witness and studies published[4,14,18] from the various institutions have demonstrated that 19 to 25% of the liver transplant procedures did not utilize allogeneic blood components in any form. The possible explanation for this finding could be the better intraoperative and postoperative care of the patient. The second possible explanation could be the vast experience of the liver transplant surgeon and a very good team support. In contrast to recipients, obviously the requirement of blood components in liver organ donor was almost negligible and furthermore we did not find any published data to compare our findings with. Thus, overall if we see the median utilization of blood components are almost similar to the published data.[12] There could be two possible explanations for this.

After a thorough exploration of literature, we realized that there is no existing data with regard to utilization of allogeneic blood components in liver transplantation recipients and liver organ donor from the Indian subcontinent thus this study is just an effort to find out the pattern of utilization of blood components in liver transplant recipient and donor. The most important limitation of this study was that we analyzed retrospectively the median utilization of blood components in live donor related liver transplant recipients and donors. Secondly, the sample size was relatively small. Thus, with the background of this study we need to plan a study where prospectively we can evaluate the median utilization of blood components and the different preoperative factors which can affect the amount of blood requirements in a relatively larger number of transplant cases.

In conclusion, our study shows the pattern and predictors of usage of blood components in liver transplant recipients and donors at a center in India where liver transplantation has a state of the art facility for organ transplantation and results are comparable to international standards. In due course improvement in surgical techniques, use of intraoperative blood salvage and pharmacological alternatives to blood transfusion has remarkably reduced the utilization of blood components in liver transplant cases.

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