TRANSFUSION PROFILE OF THE FIRST ONE HUNDRED PATIENTS UNDERGOING LIVER TRANSPLANT IN FORTALEZA

Perfil transfusional dos cem primeiros pacientes submetidos a transplante hepático em Fortaleza

Perfil de transfusión de los primeros cien pacientes sometidos a trasplante de hígado en Fortaleza

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ABSTRACT: Objective: To identify the profile of the first hundred transfusion patients undergoing liver transplantation at a university hospital in Fortaleza, Ceará. **Method:** An observational, analytical, and retrospective study was performed. **Results:** There were 10 retransplantations among the 100 patients initially enrolled in the study. One patient was excluded from the study owing to the inability to access the medical records. For this reason, 89 medical records were analyzed. **Conclusion:** Most patients were male adults with an average age of 47 years, and a high prevalence of previous abdominal surgeries were observed among them. The most common blood group was group A, and the leading cause of transplantation was cirrhosis induced by alcohol. On average, patients received 6 units of blood components, and the most frequently transfused were packed red blood cells.

Keywords: Liver cirrhosis. Liver transplantation. Blood transfusion. Perioperative nursing.

RESUMO: Objetivo: Traçar o perfil transfusional da primeira centena de pacientes submetidos a transplante hepático em um hospital escola, em Fortaleza, Ceará. **Método:** Trata-se de um estudo observacional, analítico e retrospectivo. **Resultados:** Dentre os cem pacientes inicialmente incluídos no estudo, houve dez retransplantes. Um paciente foi excluído do estudo por impossibilidade de acesso ao prontuário. Por esses motivos, 89 prontuários foram analisados. **Conclusão:** Os pacientes, em sua maioria, eram adultos com idade média de 47 anos, do gênero masculino e com grande prevalência de cirurgias abdominais prévias. O grupo sanguíneo mais prevalente foi o grupo A, e a principal causa do transplante, a cirrose por álcool. Em média, os pacientes receberam seis unidades de hemocomponentes, sendo o concentrado de hemácias o mais frequentemente transfundido.

Palavras-chave: Cirrose hepática. Transplante de fígado. Transfusão de sangue. Enfermagem perioperatória.

RESUMEN: Objetivo: Trazar el perfil de transfusión de los cien primeros pacientes sometidos a trasplante de hígado en un hospital universitario en Fortaleza, Ceará, Brasil. **Método:** Se realizó un estudio de observación, analítico y retrospectivo. **Resultados:** Entre los 100 pacientes incluidos inicialmente en el estudio, hubo 10 re-trasplantes. Se excluyó un paciente del estudio porque no había acceso a sus registros médicos. Por estas razones, se analizaron 89 registros médicos. **Conclusión:** La mayoría de los pacientes eran adultos con una edad promedio de 47 años, sexo masculino y con un alto predominio de cirugías abdominales previas. El grupo sanguíneo más frecuente fue el grupo A y la principal causa del trasplante fue la cirrosis inducida por alcohol. En promedio, los pacientes recibieron seis unidades de componentes sanguíneos, siendo el concentrado de glóbulos rojos el más frecuentemente transfundido.

Palabras clave: Cirrosis hepática. Trasplante de hígado. Transfusión de sangre. Enfermería perioperatoria.

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INTRODUCTION

Liver transplantation has become an alternative in the treatment of patients with end-stage liver disease. However, owing to the systemic effects of end-stage liver disease, the patients with liver cirrhosis usually present with involvement of multiple organs and systems, which imposes several challenges to the transplantation services[1].

One of the main problems in these patients is their hematologic management, especially concerning the transfusion therapy. Patients with liver cirrhosis frequently present with anemia and have a complex hemostatic system. In addition, transplantation surgery often involves several factors that contribute to bleeding, such as extensive surgical dissection, presence of vast network of collateral blood vessels, tendency to develop hypothermia, hypocalcemia, hyperfibrinolysis, anemia, and production of heparinoids, in addition to the phase of the surgery in which the patient cannot rely on the role of the liver in coagulation (anhepatic phase)[2].

In the last two decades, we witnessed a reduction in demand for blood components during liver transplantation, probably owing to the development of surgical and anesthetic techniques, and the use of intraoperative blood savage (Cell Saver). However, the demand for transfusion in these patients is still high nowadays, and the occurrence of massive transfusion is not uncommon[3].

In addition, the potential deleterious effects that such transfusions may have on patient and transplantation outcomes, the high demand for blood components is a major challenge to the maintenance of adequate stocks of blood in the blood banks. Therefore, knowing the transfusion needs of these patients, their possible predictors and the impact of the use of the Cell Saver facilitate better maintenance of stocks of components and adequate blood bank logistics. Moreover, the assessment of the impact of transfusions on patient and transplantation outcomes raises the awareness of the professionals involved in the surgery and enables the consequent rational use of the transfusion therapy.

In addition to the recognized undesirable consequences of transfusions, more recently, various studies have also demonstrated the deleterious role of transfusions in morbidity and mortality of patients undergoing orthotopic liver transplantation (OLT) and in the graft survival[4].

Given the scarcity of national studies to clarify the aforementioned issues, this study intended to evaluate the transfusion demands of the first hundred patients undergoing liver transplantation in a university hospital, to identify possible predictors of transfusion requirements, and to assess the impact of the Cell Saver on the transfusion of allogeneic red blood cell concentrates.

METHODS

An observational, analytical, and retrospective study was carried out in a specialized and reference hospital for liver transplantation. This institution assists patients of the public Unified Health System (SUS). Data collection was conducted from November 2014 to January 2015. Data were collected from medical records and transferred to a data collection tool developed by the researcher, using all the records of the first one hundred patients undergoing liver transplantation at the *Hospital Geral de Fortaleza* as the object of study. Data collection was initiated after the approval of the Research Ethics Committee of the *Hospital Geral de Fortaleza* under the opinion (CAEE) 33999914.9.0000.5534, and the signing of the *bona fide* depositary term. The rules of the Resolution number 466/12 of the National Health Committee[5] were followed.

During the OLT, the piggyback technique was used. This technique comprises the anastomosis between the suprahepatic vena cava of the donor liver and the suprahepatic veins of the receiver, with subsequent connection of the lower stump of the vena cava of the graft, which can shorten anhepatic phase and consequently the bleeding[6].

The blood lost during the surgery is collected, immediately anticoagulated (continuously irrigated by a solution of 30,000 sodium heparin units in 1000 mL of saline solution), processed by the Cell Saver, and then immediately returned to the patient.

With regard to the use of blood components, the following protocol was used: packed red blood cells (PRBCs) when hemoglobin is <7 g/dL, fresh frozen plasma (FFP) when prothrombin time (PT) or activated partial thromboplastin time (aPTT) is >1.5 x control, platelet concentrate (PC) if platelets are <50,000 mm^3, and cryoprecipitate when bleeding and fibrinogen are <80 g/dL, and there is bleeding caused by von Willebrand disease unresponsive to Desmopressin (DDAVP)[7].

The absolute and relative frequencies were calculated for categorical variables, and means and standard deviations were calculated for the numeric variables. Comparisons between two numerical variables were carried out using both the

Pearson correlation coefficient and the test of significance of the variables. Comparisons involving a numeric and a categorical variable were performed by the nonparametric Mann–Whitney test (due to the nonnormality of the figures). Finally, the comparison of two categorical variables was performed using the χ^2 test and odds ratios. The tests were performed considering a 5% significance level.

RESULTS

Among the 100 patients initially included in the study, there were 10 retransplantations. In addition, one patient was excluded from the study for the inability to access the medical records. For these reasons, 89 records were analyzed.

Table 1 shows that the majority of the transplanted patients (71.9%) were male. Almost half of patients (46.1%) had undergone previous abdominal surgeries. The most prevalent blood groups were groups A (41.6%) and O (39.3%). With regard to the liver disease leading to the transplantation, alcoholic cirrhosis was the most prevalent cause (29.2%).

Table 2 shows an average age of 47 years, average weight of 76.1 kg, and an average model for end-stage liver disease (MELD) of 26±9. On average, conventional tests (PT, aPTT, and platelet count) presented alterations in relation to the reference values. An average cold ischemia

Table 1. Profile of the patients – Part 1, Fortaleza, Ceará, 2015.

Variable	n (%)
Gender	
Female	25 (28.1)
Male	64 (71.9)
Previous abdominal surgery	
Yes	41 (46.1)
No	39 (43.8)
Blood group	
A	37 (41.6)
O	35 (39.3)
B	13 (14.6)
AB	04 (4.5)
Cause of transplantation	
OH	26 (29.2)
CRYPTO	13 (14.6)
Other	12 (13.5)
HVC	10 (11.2)
Fulminant	09 (10.1)
AH	05 (5.6)
HC	04 (4.5)
HVC + OH	04 (4.5)
OH + HC	02 (2.2)
HVB	01 (1.1)
HVC + HC	01 (1.1)
HVB + HC	01 (1.1)
Not informed	01 (1.1)

HC: hepatocellular carcinoma; CRYPTO: cryptogenic cirrhosis; Fulminant: fulminant hepatitis; AH: autoimmune hepatitis; OH: cirrhosis by alcohol; HVB: hepatotropic virus B; HVC: hepatotropic virus C.

Table 2. Profile of the patients – Part 2, Fortaleza, Ceará, 2015.

Variable	n	Mean ± standard deviation
Age (years)	89	47±15
Weight (kg)	82	71.6±14.1
MELD score	81	26±9
Preoperative platelet count (/mm^3)	87	106.9±73.8
Preoperative PT (seconds)	84	29.5±19.7
Preoperative aPTT (seconds)	83	62.5±38.2
Cold ischemia time (hours)	78	5.5±1.5
Warm ischemia time (hours)	75	51±0.6
Duration of transplantation surgery (hours)	89	5.1±1.2
Red blood cell concentrate (units)	89	3±3
Fresh frozen plasma (units)	89	2±2
Cryoprecipitate (units)	89	1±3
Platelet concentrate (units)	89	0±1
Blood components transfused (units)	89	5.5±7.0
Colloids volume* (units of 550 mL)	89	7.2±4.5
Diuresis volume (mL)	88	358.9±343.8
Highest value of SGOT (U/L)	87	2,172±2,754
Highest value of SGPT (U/L)	87	1,444±1,596
Length of stay in ICU (days)	89	6±8
Time until hospital discharge or death (days)	87	19.9±20.8

MELD: model for end-stage liver disease; PT: prothrombin time; APTT: activated partial thromboplastin time; SGOT: glutamic oxaloacetic transaminase; SGPT: glutamic pyruvic transaminase, *Ringer's lactate solution (500 mL) combined with human albumin 20% solution (50 mL).

time of 5.5±1.5 hours and a mean warm ischemia time of 51 minutes were observed. The mean duration of surgery was five hours and six minutes. The use of colloids during the intraoperative period was equivalent to an average of 3,600 mL, which intended to prevent hypovolemic shock by increasing the intravascular oncotic pressure, with a smaller volume of liquid. The average volume of diuresis was 358.9 mL. The average values of serum glutamic oxaloacetic transaminase (SGOT) (2,172) and serum glutamic pyruvic transaminase (SGPT) (1,444) are sensitive indicators of liver damage. Considering that these values are from postoperative period, they do not indicate liver necrosis, but a delayed functioning. With regard to the care procedures, these patients had an average length of stay in the intensive care unit (ICU) of 5 days and length of stay in the hospital until the discharge of 20 days.

Table 3 shows a statistically significant difference between the averages of total blood components transfused and the occurrence, or not, of tracheal extubation within six hours after the surgery. A correlation between the means of all transfused blood components and the occurrence of in-hospital deaths was also found.

Table 4 shows that there was correlation between age and the number of cryoprecipitate units (p=0.027) and transfused platelets (p=0.032). However, the MELD score was correlated with the number of transfused units of red blood cells concentrates (p=0.021), FFP (p=0.017), and the total number of blood components transfused (p=0.009). Finally, the PT measured in the preoperative period correlated with the number of FFP units transfused (p=0.035).

Table 5 shows midsize surgeries, as most of the previous surgeries to the transplantation (29.2%). Consequently, there was no statistically significant association with the use of blood components (Table 6).

Table 7 shows from a statistical point of view that the use of the Cell Saver did not significantly influence the number of RBC concentrates transfused or the total number of blood components used, which can be explained by the protocol on the use of blood components followed

Table 3. Variables related to the use of blood components in the intraoperative period, Fortaleza, Ceará, 2015.

Variables	Blood components					p-value
	Total	0	1 a 3	4 a 9	>10	
	n (%)					
Tracheal extubation within 6 hours after the surgery						
Yes	36 (40.4)	16 (44.4)	06 (16.7)	10 (27.8)	04 (11.1)	0.015
No	53 (59.6)	08 (15.1)	17 (32.1)	14 (26.4)	14 (26.4)	
Need of hemodialysis in the ICU						
Yes	36 (40.4)	06 (16.7)	09 (25.0)	14 (38.9)	07 (19.4)	0.111
No	56 (59.6)	18 (34.0)	14 (26.4)	10 (18.9)	11 (20.8)	
Required reoperation because of bleeding in less than 12 hours after tp						
Yes	08 (09.0)	–	04 (50.0)	–	04 (50.0)	0.128
No	81 (91.0)	24 (29.6)	19 (23.5)	24 (29.6)	14 (17.3)	
Fail in the functioning of the graft						
Yes	15 (16.9)	02 (13.3)	05 (33.3)	02 (13.3)	06 (40.0)	0.162
No	74 (83.1)	22 (29.7)	18 (24.3)	22 (29.7)	12 (16.2)	
Retransplantation						
Yes	10 (11.2)	01 (10.0)	06 (60.0)	01 (10.0)	02 (20.0)	0.995
No	79 (88.8)	23 (29.1)	17 (21.5)	23 (29.1)	16 (20.3)	
Death before discharge						
Yes	33 (37.1)	04 (12.1)	09 (27.3)	10 (30.3)	10 (30.3)	0.026
No	55 (61.8)	19 (34.5)	14 (25.5)	14 (25.5)	08 (14.5)	

Mann–Whitney test.
ICU: intensive care unit; tp: transplantation.

Table 4. Correlation between different variables and the use of blood transfusions during surgery, Fortaleza, Ceará, 2015.

	Pearson correlation	p-value
Comparison with age (units)		
Red blood cells concentrate	-0.03	0.798
Fresh frozen plasma	-0.15	0.174
Cryoprecipitate	-0.23	0.027
Platelet concentrate	-0.23	0.032
Blood components transfused	-0.21	0.052
Comparison with MELD score (units)		
Red blood cells concentrate	0.26	0.021
Fresh frozen plasma	0.27	0.017
Cryoprecipitate	0.15	0.168
Platelet concentrate	0.19	0.083
Blood components transfused	0.29	0.009
Comparison with platelet count (units)		
Red blood cells concentrate	0.08	0.484
Fresh frozen plasma	0.06	0.552
Cryoprecipitate	-0.10	0.364
Platelet concentrate	-0.15	0.161
Blood components transfused	-0.02	0.832
Comparison with the preoperative PT (units)		
Red blood cells concentrate	0.17	0.118
Fresh frozen plasma	0.23	0.035
Cryoprecipitate	0.08	0.448
Platelet concentrate	-0.06	0.559
Blood components transfused	0.17	0.124
Comparison with preoperative aPTT (units)		
Red blood cells concentrate	0.148	0.181
Fresh frozen plasma	0,055	0,619
Cryoprecipitate	-0.036	0.745
Platelet concentrate	-0.074	0.504
Blood components transfused	0,045	0,685

Pearson's correlation test.
PT: prothrombin time; aPTT: activated partial thromboplastin time; MELD: model for end-stage liver disease.

by the team. It is also worth noting that the patient who underwent intraoperative cell savage (Cell Saver) had a major bleeding, which can recover up to 60% of the lost red blood cells.

With respect to Table 8, the in-hospital mortality and discharge time were not associated with the use of Cell Saver.

DISCUSSION

In the present study, several variables to characterize the most common profile of the first one hundred patients undergoing liver transplantation at the *Hospital Geral de Fortaleza*, Ceará, were outlined.

Generally, the various parameters of time evaluated (warm ischemia, cold ischemia, total duration of the transplantation surgery, length of stay in ICU, and time to hospital discharge) were within values usually described[8].

The reduced cold ischemia time obtained is important to highlight. This parameter is fundamentally determined by optimizing the logistics involved the harvesting process of organs, back-table surgery, anesthetic induction, and hepatectomy.

The average duration of the transplantation surgery can also be considered low, especially when considering that the first hundred surgeries for liver transplantation performed by the team of this hospital were assessed. This probably reflects the extensive planning and preparation for the service implementation. Other determining factors were probably the shared experiences and the previous training of various team members in other liver transplantation services and related surgeries. Finally, after the effective

Table 5. Distribution of the number of previous abdominal surgery to the liver transplantation, Fortaleza, Ceará, 2015.

Variable	n (%)
Umbilical hernia repair	12 (29.2)
Appendicitis	03 (7.3)
Cesarean section	03 (7.3)
Exploratory laparotomy	02 (4.8)
Splenectomy	02 (4.8)
Renal transplantation	01 (2.4)
Not informed	13 (56)

implementation of the service, it is necessary to maintain an alert, motivated, and committed team to achieve the best possible outcomes.

However, despite such remarkably positive results obtained, transfusion rates can be considered high. In addition to the high frequency, the number of transfused blood components was also considerable. In liver transplantation, blood loss is determined both by the extent of the surgical damage and by the degree of hemostasis impairment.

With regard to the extent of surgical damage, one of the main determinants is the adhesion resulting from previous surgeries. In this study, the prevalence of previous surgeries was 46.1%, which possibly hinders hepatectomy and increases the bleeding surface. The alcoholic etiology is another possible determinant. It was the most prevalent among the causes that led to transplantation and is commonly associated with adhesions and hypertrophy of the caudate lobe, which complicate the surgery.

Regarding the degree of hemostasis impairment, the main determinants were preoperative hemostatic reserve levels, the intensity of the damage to the hemostasis during surgery and the quality of the implanted graft. In this study, the variables age, MELD score, and preoperative PT were mapped as independent predictors of the use of blood components.

With regard to the variable age, it was observed that the older the patient was, the lower the number of concentrates was infused. The authors consider this finding counterintuitive and found no reasonable and feasible explanations for this result.

Table 6. Association of previous abdominal surgery with the use of blood components in the intraoperative period, Fortaleza, Ceará, 2015.

Variable (units)	Previous abdominal surgery			p-value
	n	Yes	No	
		Mean±standard deviation		
Red blood cell concentrate	80	2.2±2.4	2.9±3.1	0.475
Fresh frozen plasma	80	1.3±1.9	1.7±2.2	0.523
Cryoprecipitate	80	0.6±3.1	1.5±3.5	0.253
Platelet concentrates	80	0.1±0.3	0.5±1.7	0.216
Transfused blood components	80	4.2±4.5	6.5±8.4	0.442

Mann–Whitney test

Table 7. Analysis of the use of Cell Saver and the demand for red blood cells concentrates and the other blood components, Fortaleza, Ceará, 2015.

Variable	Used Cell Saver	Did not use Cell Saver	p-value
	Mean±standard deviation		
RBC concentrate	2.4±2.8	2.6±2.8	0.768
Total blood components	6.0±7.8	5.0±6.1	0.669

Mann–Whitney test.

Table 8. Analysis of the use of the Cell Saver and death before discharge and discharge time, Fortaleza, Ceará, 2015.

Used Cell Saver	In-hospital mortality	Discharge time	OR (95%CI)	p-value
	n (%)			
Yes	14 (42.4)	30 (54.5)	1.00	0.271
No	19 (57.6)	25 (45.5)	1.63 (0.68–3.89)	

χ^2 test; OR: odds ratio; 95%CI: 95% confidence interval.

The MELD score is calculated using three variables (serum bilirubin, serum creatinine, and international normalized ratio – INR) and thus reflects the degree of impairment of the hepatocellular function of the cirrhotic individual. Consequently, this score indirectly correlates with the hemostatic ability of the patient to control a vascular damage. In addition to this study, the correlation between MELD score and transfusion of blood components had already been demonstrated in other studies[9,10].

The PT is calculated using the plasma of the patient and adding to it calcium and a thromboplastin rich in tissue factor. Therefore, this test evaluates the coagulation factors involved in the extrinsic pathway (VII, V, X, II, and fibrinogen). As the liver is the main (or unique) site of synthesis of these factors, the PT is the examination which most commonly presents alterations in the liver diseases, although it assesses just some of the factors involved in coagulation. As a general impairment of hepatocellular function occurs in cirrhosis (that is, all the factors have a reduced synthesis), it is possible to infer that the PT is also correlated with the degree of impairment of hemostasis. Although in this study the PT has been shown as an independent risk factor for the use of blood components during the intraoperative period, its predictive capacity for bleeding during liver transplantation is usually poor. This apparent paradox can be explained by the fact that this test evaluates only few plasma coagulation components, whereas it is currently recognized that hemostasis must be widely assessed, as by means of the thromboelastography.

The great effort directed to the reduction of blood transfusion rates is explained by the recognized adverse effects related to the use of blood components[11]. This study showed that, among the evaluated postoperative variables, time to tracheal extubation and mortality were significantly affected by the use of blood components.

The exposure of the patient to the transfusion is associated with an inflammatory effect in different territories, especially in the lungs, resulting in increased pulmonary capillary permeability. Moreover, depending on the volume of administered blood components, a circulatory overload may occur. If these two factors (increased pulmonary capillary permeability and circulatory overload) are combined, a pulmonary edema occurs, which delay the tracheal extubation. Mortality associated with transfusions is due to multiple and intricate pathophysiological mechanisms; among them, immunosuppression and predisposition to infections may play an important role.

Surprisingly, the use of Cell Saver did not significantly influence the demand for red blood cell concentrates ($p=0.768$) or the overall demand for blood components ($p=0.669$). This can be attributed to other factors that determine the transfusion demands, such as preoperative hemoglobin level and the level of hemostasis. Since these factors were not compared between the two groups, it is not possible to further analyze them. Moreover, a formal sample size calculation to measure this effect was not carried out.

The use of Cell Saver also caused no significant impact on in-hospital mortality and on the discharge time ($p=0.271$). By reducing the demand for allogeneic red blood cell concentrates, it is intuitive to assume that the Cell Saver should result in improvements in postoperative outcomes. Owing to the same limitations described in the previous paragraph, to deeply explore this finding is not feasible.

CONCLUSIONS

The patients were mostly male adults, with an average age of 47 years, and a high prevalence of previous abdominal surgeries were observed among them. The most prevalent blood group was group A, and the main cause of transplantation was cirrhosis caused by alcohol consumption. On average, patients received six blood component units, and the concentrate transfused most often was RBCs. With regard to the hemostatic blood components, the FFP had the highest average number of transfused units.

The variables age, MELD score, and preoperative PT proved to be independent predictors of major transfusion demands. There was no significant impact of the use of the Cell Saver on the transfusion demands, and their use did not significantly alter in-hospital mortality.

Patients with higher average of transfused blood components had delayed extubation, increased demand for hemodialysis in the ICU, and higher in-hospital mortality.

It is worth noting that this study had some limitations such as the retrospective nature, which imposes all the difficulties inherent to the availability and quality of the evaluated records. Although this study is descriptive-analytic, it is valuable because it indicates the strengths and the aspects of improvement and optimization, which leads to a reflection on security, better quality of service, and the rational use of blood components.

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