Use of fibrinogen and thrombin sponge in pediatric split liver transplantation.

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Introduction: Pediatric liver transplantation is associated with good results, however, it is difficult to find deceased liver donors with suitable grafts for small recipients¹. Some techniques have been developed as surgical alternatives to increase the number of viable liver grafts available for liver transplantation and reduce the mortality rates in liver transplant waiting lists. One such technique is split-liver. In this technique, a liver graft from a cadaver donor is divided on an auxiliary table respecting the anatomical liver segments while preserving their vascular structures, yielding two partial grafts suitable for transplantation into two distinct recipients, with survival rates similar to those obtained with whole graft transplants². However, the split technique may be associated with complications such as increased bleeding in the wound area, greater requirement of red blood cell transfusion, and occurrence of biliary leak³. The human fibrinogen and thrombin sponge (TachoSil®, Takeda, Linz, Austria)⁴ is a useful tool in surgical hemostasis that consists of a collagen matrix with a layer of plasma components such as clotting factors, fibrinogen, and fibrin. The sponge has been used in pediatric patients undergoing liver transplantation, in a case series in which two children received the left segment of the liver from a living donor, while two others received a reduced graft. In all four cases, the sponge was used in the open area of the graft with optimal and effective hemostasis⁵. The objective of this study was to analyze the use of the human fibrinogen and thrombin sponge in pediatric patients undergoing split-liver transplantation.

Methods: The project of this study was approved by the Ethics Committee at Universidade Federal de São Paulo (UNIFESP), number 38311, 18 June 2012. This was a retrospective study conducted from September 2009 to April 2016 including pediatric patients undergoing split-liver transplantation at Hospital São Paulo, UNIFESP. The study included 35 patients divided into two groups according to the use of the sponge during transplantation: 18 patients allocated to Group A (without the sponge) and 17 to Group B (with the sponge). Potential donors for the split-liver transplantation were selected when matching most of the criteria established by our institution, as previously established in the literature: age below 50 years, hemodynamic stability, fewer than 4 days in the intensive care unit, levels of alanine aminotransferase (ALAT, U/L) and aspartate aminotransferase (ASAT, U/L) below twice the normal levels, gamma-glutamyltransferase (GGT) lower than 50 IU/L, serum sodium level below 160 mmol/L, and less than 20% of fatty infiltration of the liver on macroscopic analysis. The split technique was performed in a standard way, and the arterial trunk and left portal branch were dissected in order to remain within the graft comprising segments II and III. Following instructions from the manufacturer, we used pre-moistened sponges and applied their yellow side (the side which has the active ingredients) on the wound surface of the liver graft. Since the extension of the open area is greater than the surface of the sponge, we used, when necessary, more than one sponge and repeated the same process. This study evaluated the demographic characteristics of the recipients, use of red blood cell transfusion during split-liver transplantation (in mL/kg), reoperation due to wound bleeding, occurrence of biliary leak in the open area and graft, and patient survival at 30 days. The analyzed data are expressed as mean, median, standard deviation, and percentage. We used the tests Student's t, chi-square, Fisher's exact and Mann-Whitney, as well as Kaplan-Meier survival curves as indicated. We performed the statistical analysis using the software SPSS, version 2.0, and considered p values < 0.05 as significant.

Results: As shown in Table 1, both groups were comparable and had no significant differences in the evaluated parameters.

	Group A (n=18) Without the Sponge	Group B (n=17) With the Sponge	p
Age (years)	1.5 ± 1.2	1.4 ± 1.8	0.85
Sex	M: 7 F: 11	M: 9 F: 8	0.5
Weight (kg)	11.13 ± 14.30	10.42 ± 9.7	0.86
Height (cm)	68.26 ± 11.06	68.5 ± 13.32	0.95
PELD score	19.95 ± 8.91	25.58 ± 13.32	0.08

Table 1 Demographic characteristics of the study population. **M.** males; **F.** females; **PELD score.** Pediatric End-Stage Liver Disease score

Regarding the analyzed parameters (Table 2), the median volume of red blood cells transfused in Group A was significantly higher (73.4 ± 102.38 mL/kg) than that in Group B (35.1 ± 41.67 mL/kg; p = 0.048).

	Group A (n=18) Without Sponge	Group B (n=17) With Sponge	p
Red blood cells transfused (mL/Kg)	73.4 ± 102.38	35.1 ± 41.67	0.040
Reoperation due to bleeding in the wound area	10 (55%)	3 (17.6%)	0.035
Biliary leak in the wound area	2 (11.1%)	3 (17.6%)	0.65

Table 2 Results of analyzed parameters.

When we analyzed those cases that required reoperation due to bleeding in the wound area of the liver graft, we observed a significantly greater number of these patients in Group A (10 patients - 55.5%) than in Group B (3 patients - 17.6%; p = 0.035). Regarding biliary leak in the wound area, there was no statistical difference comparing both groups, with Group A rate showing a rate of 11.1% and Group B a rate of 17.6% (p = 0.65). At 30 days, patient survival rates were 75% in Group A and 87.5% in Group B (p = 0.36), while graft survival rates were 75% and 81.25%, respectively (p = 0.11).

Discussion: We observed a significantly higher rate of reoperation due to bleeding in the wound area in Group A when compared with Group B, showing that the sponge can improve hemostasis in the open area in pediatric patients undergoing split-liver transplantation. This finding is corroborated in the literature assessing the use of the sponge for hemostasis of the bleeding liver area after hepatectomy and liver transplantation with the split technique and / or living donor⁵. In the present study, there was no significant difference in biliary leak rates in the wound area when we compared Groups A and B. Biliary leak in liver transplantation is directly related to complications in the hepatic artery and an important cause of morbidity, with rates in the literature ranging from 5 to 10% in whole-liver transplantation⁶. In cases of liver transplantation with the split technique, these rates may increase⁷ reaching about 18.8%, as described by Diamond *et al.*⁸ The present study is limited by its retrospective design, although the data were prospectively collected in a spreadsheet. An important strength of the study was the fact that all the transplantations were performed by the same team in which all members had already completed their learning curves at the beginning of the study. **Conclusion:** The use of the human fibrinogen and thrombin sponge, when compared with no use of the sponge, required a lower volume of red blood cell transfusion during the procedure and presented lower reoperation rates due to bleeding in the wound area.

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