The Use of Fibrin Glue in Thoracic Organ Transplantation: Analysis of 4-Year Experience

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Abstract

From November 1985 to May 1992, 261 heart (247 orthotopic, 7 heterotopic) and 11 heart-lung transplantations were performed in our institution. In the first 116 cases of heart transplantation (group A) the operations were carried out without the use of fibrin glue (FG), while in the last 145 cases (group B) a protocol of FG application was introduced. FG was also used in all patients who underwent heart-lung transplantation (group C). The protocol for FG application in heart transplantation requires: preparation of 5 cc FG (Tissucol) at the beginning of the operation, sealing of the atrial pulmonary artery and aortic sutures leaving the operative field dry for 4 min before aortic cross-clamp removal. In the case of reoperation 2 cc FG is sprayed onto the pericardial surfaces. In heart-lung transplantation, after thorough hemostasis of the posterior mediastinum, 5 cc FG is sprayed over mediastinic and pleural surfaces keeping the patient in circulatory arrest for 5 min at 25 °C body temperature. After completion of the tracheal anastomosis FG is applied to the suture line. No wrapping techniques are used. Right atrial and aortic anastomoses are sealed as in HTx. In all patients after protamine administration the blood is collected from the field and processed by a cell-saver. In group A 250 ± 70 ml and in group B 55 ml ± 25 ml packed red cells (hematocrit 55%) per patient were obtained from the field ($p < 0.001$). The time required to complete the operation after protamine administration was 85 ± 15 and 30 ± 12 min in groups A and B, respectively ($p < 0.001$). No significant difference was observed in postoperative bleeding concerning the need for reoperation [four cases (3.5%) in group A and three cases (1.4%) in group B]. In group C the amount of packed red cells collected during the operation (before heparinization and after protamine administration) varied from 225 to 4500 ml (mean 1100 ml). Mean blood loss from chest drainage tubes was 650 ml (range 350–2250 ml). Reoperation for bleeding was performed in one case. Healing of the tracheal anastomosis was normal in all cases; in two patients small leaks (0.5 and 1 cm) were observed on the suture line at the intraoperative fibroscopic control. In both cases the trachea appeared normal at the second postoperative month. In conclusion, from our experience FG can be considered a useful tool during surgery for thoracic organ transplantation on account of its hemostatic and biostimulating effects.

It significantly contributes to reducing both the duration of operation and postoperative blood loss.

Introduction

Bleeding is a common event during and after open heart surgery which can be troublesome for the patient because of unpredicted prolongation of surgical time, necessity of homologous blood transfusion, and possible requirement of reoperation in 3 % of cases [1]. Many attempts to reduce surgical bleeding have been made in the past. Rational protocols have recently been proposed that are based on a complex approach to the problem of saving blood, including autotransfusion, red cell collection from the surgical field, reinfusion of drained blood, and careful normalization of coagulating factors. The introduction of aprotinin as an antifibrinolytic agent has dramatically reduced the problem of hemostasis in the majority of cases, almost eliminating the contraindication to repeat a cardiac operation for "technical reasons" [2, 3].

Fibrin glue (Tissucol) was introduced in cardiothoracic surgery 15 years ago and in many centers has proved to be a useful tool in enhancing local hemostasis, reducing blood loss and consequently the need of emergency resternotomy for postoperative bleeding. Since January 1988 Tissucol has been an essential part of our protocol for reducing transfusion, with satisfactory results. This report discusses our experience with Tissucol in thoracic organ transplantation, high-lighting its importance in reducing operative time, facilitating surgical hemostasis, and contributing to airway anastomosis healing.

Materials and Methods

From November 1985 to October 1992, at our institution 272 heart transplantations were performed (258 orthotopic, 7 heterotopic) on 265 patients (238 men, 34 women; mean age 47 years, range 8–64). These included: 125 dilated, 111 ischemic, 18 valv, 8 hypertr, 1 myocarditis, 1 ARVD, 1 amyloidosis, and 7 retx. In-hospital mortality (30-day) was 5.9 %, and the long-term actuarial survival rate was 77 % at 7 years (mean follow-up 30 months). In January 1991 we started our lung program which, at the end of October 1992, consisted of 14 heart-lung and 3 single lung transplantations. In six heart-lung transplantations a "domino" procedure was adopted. In-hospital mortality for heart-lung transplantation was 12.5 %; the 1-year actuarial survival rate was 80 % (mean follow-up 6 months).

General guidelines currently used at our institution to reduce homologous blood transfusion are the following:

Preoperative management

Normalization of coagulating factors
Avoidance of antiplatelet agents
Autologous blood predonation (technically impossible)

Abbreviations:
valv = valvular cardiomyopathy; hypertr = hypertrophic cardiomyopathy; ARVD = arrhytmogenic right ventricle dysplasia; retx = retransplantation

Intraoperative management
Thorough surgical hemostasis
Aprotinin administration
Tissucol application
Red cell collection from the surgical field and the ECC system using the cell saver

Postoperative management
Aprotinin administration
Reinfusion of drained blood (Pleurevac system)
Normalization of coagulating factors

In transplant candidates withdrawal of antiplatelet agents and autologous blood predonation are impossible due to the predictability of the time of the operation. The reinfusion of drained blood with the Pleurevac system is sometimes avoided in these patients to reduce problems of sterility and hemolysis.

With regard to the use to Tissucol during transplant surgical procedure, our patients are divided into three groups: group A; 116 heart transplantations, performed before January 1989, without the use of Tissucol and aprotinin (the other strategies are those listed above); group B, 156 heart transplantations performed from January 1989 to October 1992, in which Tissucol and aprotinin were used; group C, 14 heart-lung and 3 lung transplantations performed since January 1991, in which Tissucol and aprotinin were used.

Royston's aprotinin protocol [4] provides for the administration of 2×10^6 aprotinine KIU in cardiopulmonary bypass prime, 2×10^6 in bolus before sternotomy, 0.5×10^6/h during operation, and 0.5×10^6 every 6 h on the first postoperative day. The cell-saver protocol is based on the collection of blood from the operating field before heparinization and after protamine administration and on the use of residual blood in the oxygenator. By means of Dideco autotrans equipment, red cells are separated from debris, washed, and concentrated: the mean hematocrit of retransfused blood was 56 %.

Protocols of Tissucol Application

Group B (heart transplantation)
- Preparation of 5 ml Tissucol.
- On completion of surgical procedure, before aortic cross-clamp removal, the operative field is dried, and the atrial pulmonary artery and aortic sutures are sealed.
- In cases of reoperation 2 ml Tissucol is sprayed on the pericardial surface.

Group C (heart-lung transplantation)
- Preparation of 10 ml Tissucol.
- After removal of heart and both lungs and hemostasis of the posterior mediastinum, on circulatory arrest for 5 min at 25 °C body temperature, 5 ml Tissucol is sprayed over mediastinal and pleural surfaces.

- After completion of tracheal anastomosis (PDS 4/0 running suture) 2 ml Tissucol is applied on the suture line and then the nearby mediastinal tissue is stitched on; no omental wrapping is used.
- Tissucol is applied on right atrial and aortic sutures.

Group C (single lung transplantation)
- Preparation of 5 ml Tissucol.
- Pneumonectomy and Tissucol spray on pleural scar in case of adhesions.
- Bronchial anasthomosis (pars membranacea PDS 4/0 running suture, pars cartilaginea PDS 4/0 interrupted suture) and Tissucol application. No omental wrapping is used, but the anastomosis is covered with local connective tissue.
- Tissucol is applied on left atrial and pulmonary artery anastomoses.

Results

In comparing the groups of patients one must remember that in groups B and C the difference in results must be related to the combined use of aprotinin and Tissucol. The favorable effect on surgical hemostasis by the association of the two substances is demonstrated by the significant difference in the amount of blood collected from the operative field and processed according to the cell-saver protocol (group A 250 ± 70 ml, group B 55 ± 25 ml; $p < 0.001$) and by the difference in operation time after protamine administration (group A 85 ± 15 min, group B 30 ± 12 min; $p < 0.001$). The incidence of reoperation for bleeding was not significantly different: 4/118 cases (3.4%) and 3/156 cases (1.9%) in groups A and B, respectively. Problems directly related to Tissucol application were not found.

In 1 of the 13 patients of group C, operated for heart and lung transplantation, reoperation was necessary for bleeding. The mean amount of packed red cells collected from the operative field was 1100 ml (range 225–4500), and the blood loss from chest drainage tubes was 650 ml (range 350–2250). No dehiscence of tracheal anastomosis was encountered, nor major leaks requiring specific treatment. In the three patients operated for single lung transplantation the healing of bronchial anastomosis was normal.

Discussion

Tissucol is a biological sealing system containing a high concentration of many plasmatic and tissue coagulative and reparative factors (fibrinogen, XIII coagulation factor, fibronectin, other coagulative human proteins, thrombin, and aprotinin).

The efficacy of fibrin sealant in facilitating hemostasis in cardiothoracic surgery has been demonstrated by several investigators. In cardiothoracic transplantation bleeding is a major problem due to the alteration of coagulative factors in low cardiac output patients and to the length and complexity of the

operation (such as in cardiopulmonary transplant) requiring lengthy cardiopulmonary bypass, considerable extension of suture lines. The necessity of optimizing hemostasis in these patients is essential because the reduction in operative time and the limitation of transfusions limit the possibility of infection transmission, the incidence of pulmonary and renal complications, and ultimately the incidence of multiorgan failure.

Our protocol of surgical hemostasis was reviewed in 1988, and from January 1989 aprotinin and extensive use of Tissucol were introduced. This may complicate the interpretation of our results because both substances have proved effective in independent studies. Nevertheless we consider Tissucol a valuable tool in facilitating the management of bleeding problems for several reasons: (a) it eliminates blood oozing from around stitches on the suture lines allowing easier control of the true surgical bleeding; (b) it stiffens the tissue around the suture, improving the efficiency of the hemostatic additional stitches; (c) it almost eliminates biological bleeding from extended surfaces after adhesion dissection; and (d) it dramatically facilitates the hemostasis on the posterior mediastinum during cardiopulmonary transplantation.

In airway anastomosis the use of Tissucol has been recommended by many authors [5], underlining its efficacy in sealing small leaks, avoiding local contamination, and contributing by its biostimulating action to tissue healing in this poorly vascularized area. Our experience with the use of Tissucol around tracheal and bronchial anastomosis is favorable; we think that its sealant effect, which eliminates oozing of contaminated material, combined with its incentive to vascularization may significantly contribute to the success of the operation.

In conclusion, we consider the use of Tissucol highly recommendable in cardiothoracic transplantation; it is one of the essential items in the protocol of hemostasis and blood saving, and it can effectively contribute to airways anastomosis healing.

References

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