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Local Hemostasis with Fibrin Glue after Intracardiac Repair of Tetralogy of Fallot and Transposition of the Great Arteries

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Summary

In the last year fibrin glue Tissucol®[1] was used for local hemostasis in 21 patients subjected to correction of tetralogy of Fallot (ToF) and in 10 patients subjected to Senning-procedure in transposition of the great arteries (TGA). The postoperative blood loss was compared with the blood loss of 20 ToF-patients and 10 TGA-patients who had undergone correction one year ago without fibrin glue. Between the 2 groups were no differences in age, sex, bodyweight (BW), coagulation state or operative management.

Two hours postoperatively the blood loss with fibrin glue was 2.2 ml/hr/kg BW in ToF-patients and 2.4 ml/hr/kg BW in TGA-patients, whereas without fibrin glue it was 4.2 ml/hr/kg BW in ToF ($p<0.01$) and 4.5 ml/hr/kg BW in TGA ($p<0.01$). The same significant difference ($p<0.01$) was found 6 hours postoperatively with 1.4 versus 2.2 ml/hr/kg BW in ToF and 1.9 versus 2.5 ml/hr/kg BW in TGA. Over the following 18 hours the secretion from the chest tubes was identical in both groups.

Six patients with ToF and one patient with TGA required reoperation for bleeding. The blood loss per kg BW per hour at reoperation was 6.9 ml with and 8.2 ml without fibrin glue (N.S.). The blood loss of patients who did not require reoperation at the same time was 4.6 times lower with fibrin glue and only 3.7 times lower without fibrin glue.

Fibrin glue reduces blood loss after intracardiac repair of ToF and TGA by local hemostasis at patches and suture lines. The application of fibrin glue can facilitate differentiation of surgical bleedings and the indication for reoperations.

Key Words: Local hemostasis – Fibrin glue – Tetralogy of Fallot – Transposition of great arteries – Reduced postoperative blood loss

Introduction

After intracardiac repair of ToF and the Senning-procedure in TGA, prolonged postoperative hemorrhage may be present due to long suture lines, porous patches and prostheses, preexistent disturbances of coagulation and, last but not least, coagulation disturbances following heparin-application during cardiopulmonary bypass. Similar problems are found in patients undergoing cardiac surgery for other reasons or replacement of different parts of the aorta or other arteries with unsealed prostheses. These conditions result in increased postoperative blood loss through chest tubes, risk of pericardial tamponade, and hematomas in other regions.

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The discrimination between surgical bleedings and hemorrhages due to coagulation disturbances is difficult in such cases, however, necessary for indication to reoperate in surgical bleedings.

Many methods for the sealing or preclotting of highly porous vascular prostheses or patches, gluing anastomoses, and efficient local hemostasis in different organs have been described (2, 3, 6, 7, 8, 9, 10, 11, 12, 15, 18). Good results have been reported but never the actual decrease in blood loss. A decreased blood loss, however, is indicative of the efficiency of these methods. Further, simple intraoperative application is mandatory. Other risks must be excluded or minimal.

Material and method

Since May 1980 we have used fibrin glue for local hemostasis, and sealing porous patches and prostheses in cardiac and vascular surgery at the Department of Thoracic and Cardiovascular Surgery of the University Surgical Hospital in Tübingen. In a retrospective study we compared 2 groups of patients undergoing 2 different surgical procedures with and without fibrin glue. Since May 1980, 21 patients with ToF have undergone intracardiac repair with patch-closure of the ventricular septal defect (VSD), patch-enlargement of the right ventricular outflow tract (RVOT), and commissurotomy of the pulmonary valve (PV). In 8 patients the RVOT-patch was extended across the PV to the main pulmonary artery (MPA) because of severe PV stenosis, and one conduit was used from the RVOT to the MPA because of PV atresia. In the same period 10 patients with simple TGA were subjected to the Senning-procedure. In all these patients fibrin glue was used for local hemostasis and patch-sealing. The postoperative blood loss through the chest tubes of these patients was compared with 20 patients with ToF and 10 patients with TGA who had undergone intracardiac correction a year ago without fibrin glue. In ToF cases, patch-closure of VSD and patch-enlargement of RVOT with PV commissurotomy was performed in 7 patients. An extension of the RVOT-patch to the MPA was necessary in 13 cases. Senning-procedure was performed in 10 patients with simple TGA.

The mean age in ToF patients was 84 ± 114 months with fibrin glue and 86 ± 86 months without fibrin glue, in the TGA group with fibrin glue it was 17 ± 11 months, and without fibrin glue 15 ± 6 months.

Other preoperative data, early mortality, and frequency of rethoracotomy are shown in Tables 1 and 2.

There were no differences between groups with and without application of fibrin glue in: perfusion time, aortic cross-clamping time, and temperature at the time of ischemia (Tables 3 and 4). Methods of cardioplegia, however, were different; since 1980, Bretschneider's infusion-cardioplegia with the HTP-[2] or the LK

[2] Dr. F. Köhler Chemie KG. D-6146 Alsbach

Table 1 Preoperative data, early mortality and frequency of rethoracotomy in patients with ToF undergoing intracardiac repair with and without fibrin glue

	With fibrin glue		Without fibrin glue	
	n	%	n	%
Total	21	100	20	100
Male	12	53	12	60
Previous operation	5	24	7	35
Rethoracotomy	3	14	3	15
Early mortality	3	14	1	5

Table 2 Preoperative data, early mortality and frequency of rethoracotomy in patients with TGA undergoing Senning-procedure with and without fibrin glue

	With fibrin glue		Without fibrin glue	
	n	%	n	%
Total	10	100	10	100
Male	5	50	5	50
Previous operation	2	20	2	20
Rethoracotomy	1	10	–	–
Early mortality	1	10	1	10

Table 3 Perfusion time, aortic cross-clamping time and temperature at time of ischemia in patients with ToF

	With fibrin glue		Without fibrin glue	
	Mean	SE	Mean	SE
Perfusion time (min)	77	16	77	14
Aortic cross-clamping time (min)	43	14	41	12
Temperature at ischemia (°C)				
Venous blood	21.6	2.1	21.0	1.8
Esophageal	21.9	2.9	21.9	3.3
Rectal	26.0	3.0	28.5	2.0

Table 4 Perfusion time, aortic cross-clamping time and temperature at time of ischemia in patients with TGA

Perfusion time (min)	With fibrin glue		Without fibrin glue	
	Mean	SE	Mean	SE
Perfusion time (min)	86	15	85	9
Aortic cross-clamping time (min)	48	12	44	6
Temperature at ischemia (°C)				
Venous blood	19.6	2.8	19.8	1.7
Esophageal	20.5	3.6	19.5	2.8
Rectal	25.9	3.1	26.6	2.8

352-solution[3] with a single dose of 30 ml/kg BW has been used, and previously Kirsch's injection-cardioplegia with a single dose of 3 ml/kg BW of Cardioplegin[3] was used.

Changes in clinical findings which are dependent on and necessary for hemostasis and blood coagulation are demonstrated in Tables 5 and 6 for each group.

[3]Dr. F. Köhler Chemie KG, D-6146 Alsbach

In all patients with fibrin glue application both components of the glue were placed on patches and suture lines before releasing aortic cross-clamping.

The postoperative blood loss through chest tubes was measured in periods of 2 hours in each patient and related to his body weight and one hour. Differences in postoperative blood loss in both groups were analyzed statistically by Student's t-test.

Table 5 Changes in clinical findings and coagulation state preoperatively and 6 hours postoperatively in patients with ToF

	With fibrin glue		Without fibrin glue	
	Preoperative	Postoperative	Preoperative	Postoperative
Hemoglobin (g/100 ml)	17.1 ± 2.3	16.8 ± 1.6	17.3 ± 2.6	17.1 ± 2.7
Hematocrit (%)	9 ± 7	47 ± 6	49 ± 9	47 ± 7
Platelets (1000/mm^3)	226 ± 67	119 ± 67	235 ± 95	86 ± 65
Quick (%)	90 ± 16	61 ± 19	86 ± 16	65 ± 11
PTT (sec)	36 ± 5	55 ± 38	47 ± 15	52 ± 11

Table 6 Changes in clinical findings and coagulation state preoperatively and 6 hours postoperatively in patients with TGA

	With fibrin glue		Without fibrin glue	
	Preoperative	Postoperative	Preoperative	Postoperative
Hemoglobin (g/100 ml)	18.6 ± 2.9	17.9 ± 2.3	18.2 ± 1.7	17.8 ± 1.9
Hematocrit (%)	51 ± 6	50 ± 6	58 ± 8	50 ± 6
Platelets (1000/mm^3)	200 ± 108	97 ± 37	143 ± 38	85 ± 41
Quick (%)	86 ± 22	60 ± 11	62 ± 38	55 ± 13
PTT (sec)	32 ± 3	56 ± 22	46 ± 23	61 ± 19

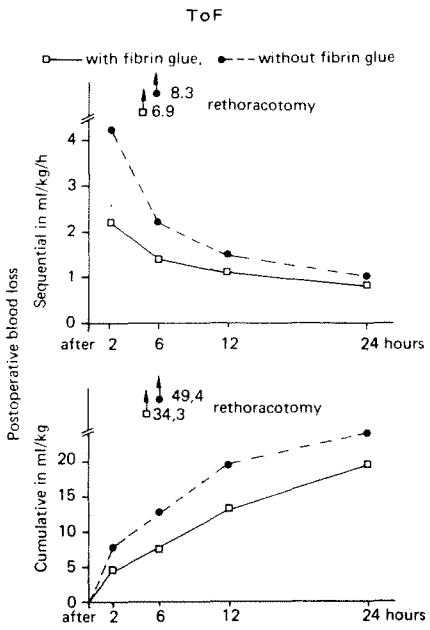

Fig. 1 Postoperative blood loss in sequential and cumulative demonstration in patients with ToF in the first 24 hours

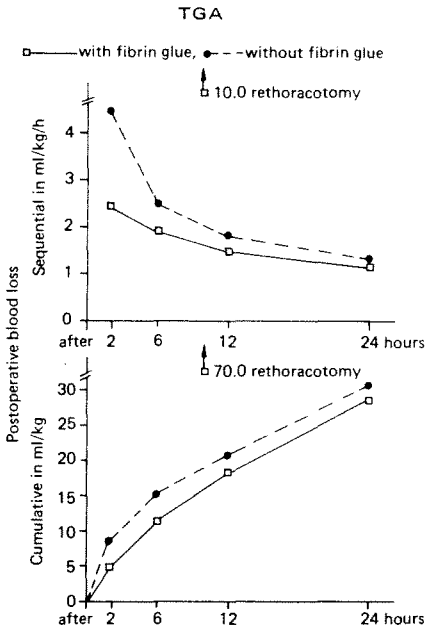

Fig. 2 Postoperative blood loss in sequential and cumulative demonstration in patients with TGA in the first 24 hours

Results

Significant differences of blood loss between the patients with application of fibrin glue and those without were found 2, 6, and 12 hours postoperatively in both groups of operations (ToF and TGA). Two hours postoperatively the blood loss in ToF patients was 2.2 ml/hr/kg BW with fibrin glue, and 4.2 ml/hr/kg BW without fibrin glue ($p < 0.01$); 6 hours postoperatively the difference was 1.4 ml/hr/kg BW with, and 2.2 ml/hr/kg BW without fibrin glue ($p < 0.01$); and 12 hours postoperatively 1.1 ml/hr/kg BW with, and without fibrin glue 1.5 ml/hr/kg BW ($p < 0.05$). In patients with TGA the blood loss was, 2 hours postoperatively, 2.4 ml/hr/kg BW with and 4.5 ml/hr/kg BW without fibrin glue ($p < 0.01$); 6 hours postoperatively, 1.9 ml/hr/kg BW with and 2.5 ml/hr/kg BW without fibrin glue ($p < 0.01$); and 12 hours postoperatively with fibrin glue 1.5 ml/hr/kg BW and 1.8 ml/hr/kg BW without fibrin glue ($p < 0.05$).

The blood loss during the following 12 hours showed no significant differences between groups with and without fibrin glue. The first 24 hours postoperatively in total did not demonstrate a significantly lower blood loss in patients using fibrin glue for local hemostasis or patch-sealing. These data were found in patients without rethoracotomy.

Blood loss in ToF patients requiring reoperation due to surgical bleeding showed differences between patients with fibrin glue, 6.9 ml/hr/kg BW, and without fibrin glue, 8.3 ml/hr/kg BW. The difference, however, was not significant. A comparison of blood loss in patients requiring reoperation due to surgical bleeding, and patients without reoperation at the same time showed a greater difference of blood loss in patients with fibrin glue. The blood loss at the time of reoperation in ToF patients not requiring reoperation was 4.9 times lower with fibrin glue, and only 3.8 times lower without fibrin glue, than in patients with rethoracotomy. One patient with TGA had be to reoperated due to hemorrhage. His blood loss was 6.4 times the average of other TGA patients in whom fibrin glue was applied. Reoperations were caused by surgical bleedings at the site of cannulation for extracorporeal circulation in 3 cases, from retrosternal vessels in 3 patients in both groups and in one patient without fibrin glue from the RVOT-patch. Nevertheless the rate of rethoracotomies could not be reduced in the group with fibrin glue treatment. Sealing patches and suture lines with fibrin glue cannot be expected to influence early mortality. The sequential and cumulative data of blood loss in different postoperative periods are demonstrated in Tables 7 and 8 and in Fig. 1 and 2.

Table 7 Postoperative blood loss in ml/hr/kg BW in different periods of time in patients with ToF

Postop. period	With fibrin glue		Without fibrin glue
Hours 0 – 2	2.2 ± 1.4	($p < 0.01$)	4.2 ± 2.3
Hours 3 – 6	1.0 ± 0.8	($p < 0.05$)	1.2 ± 0.9
Hours 7 – 12	0.8 ± 0.5		0.9 ± 0.7
Hours 13 – 24	0.5 ± 0.2		0.4 ± 0.3
Hours 0 – 6	1.4 ± 1.0	($p < 0.01$)	2.2 ± 1.4
Hours 0 – 12	1.1 ± 0.5	($p < 0.05$)	1.5 ± 0.8
Hours 0 – 24	0.8 ± 0.3		1.0 ± 0.5
Patients with rethoracotomy	6.9 ± 3.2		8.5 ± 5.3

Discussion

In the contemporary literature, many methods for sealing or preclotting patches and prostheses and for local hemo stasis have been described. Good results have been report

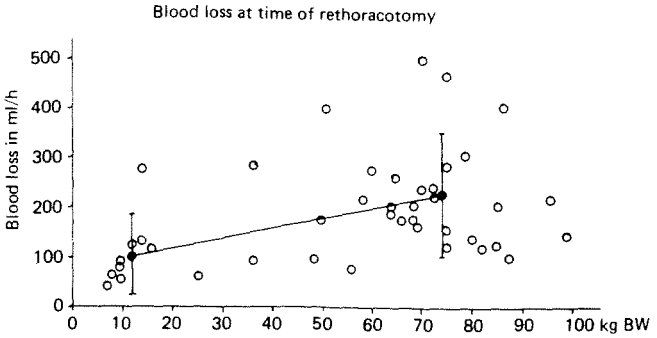

Fig. 3 Blood loss at time of reoperation in 50 patients undergoing rethoracotomy due to bleeding after open-heart surgery in ml/hr related to patients BW

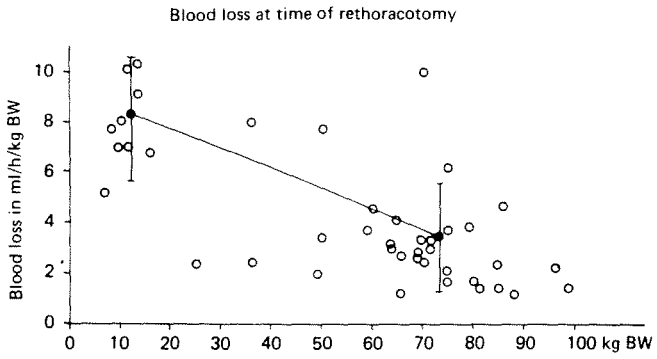

Fig. 4 Blood loss at time of reoperation in 50 patients undergoing rethoracotomy due to bleeding after open-heart surgery in ml/hr/kg BW related to patients BW

Table 8 Postoperative blood loss in ml/hr/kg BW in different periods of time in patients with TGA

Postop. period	With fibrin glue		Without fibrin glue
Hours 0 – 2	2.4 ± 1.2	($p < 0.01$)	4.5 ± 2.2
Hours 3 – 6	1.7 ± 0.9		1.6 ± 0.7
Hours 7 – 12	1.1 ± 0.7		0.9 ± 0.6
Hours 13 – 24	0.8 ± 0.5		0.8 ± 0.5
Hours 0 – 6	1.9 ± 1.0	($p < 0.01$)	2.5 ± 1.1
Hours 0 – 12	1.5 ± 0.7	($p < 0.05$)	1.8 ± 0.8
Hours 0 – 24	1.2 ± 0.6		1.3 ± 0.5
Patients with rethoracotomy	7.0 –		– –

ed however, a decreased postoperative blood loss has not been definitely established (2, 3, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 18). In all investigations a reduction of used blood transfusions has been shown. The overall blood consumption included transfusions for preoperative blood loss, i.e. dissection and perforation of an aortic aneurysm, intraoperative blood supply, i.e. priming volume for cardiopulmonary bypass and blood loss during operation; and lastly postoperative blood loss caused by incorrect local hemostasis, coagulation disturbances or surgical bleedings. Transfusion units of 500 ml of blood are too large for comparison when discussing the blood loss in children.

Fibrin glue has an influence on postoperative blood loss caused by incorrect local hemostasis only. Blood consumption is no measure of its efficiency.

To discover a correct measuring unit of postoperative blood loss, we looked at the blood loss at the time of reoperation in 50 of our patients who underwent rethoracotomy after open-heart surgery because of surgical hemorrhage during the last few years. In a comparison between blood loss per hour and kg BW in patients weighing less than 25 kg, the blood loss was, with 100 ml/hr, significantly ($p < 0.005$) lower than in patients over 25 kg BW, with 200 ml/hr, up to the time of reoperation (Fig. 3). But it was not a correct measurement in relationship to the circulating blood volume of these patients. A comparison considering the body weight of each patient showed a significantly higher ($p < 0.005$) blood loss of 8 ml/hr/kg BW in patients up to 25 kg BW than in patients with more than 25 kg BW, with 4 ml/hr/kg BW. This correlation is demonstrated in Fig. 4.

In our opinion, the postoperative blood loss must be measured in all cases in relationship to the bodyweight of the individual patient in short periods of time. Short-time sampling periods of blood loss through chest tubes in thoracic and cardiac surgery and correlation to patients' bodyweight guarantee, on one hand, a good determination of the amount of blood loss, and demonstrate the decrease of hematocrit in the tube secretion caused by decreased bleeding and increased exudation from hour to hour on the other hand. A decreased amount of blood loss was only found in the first postoperative hours using fibrin glue. The glue decreases bleeding by local hemostasis and sealing patches; a decreased exudation, however, cannot be expected.

The blood loss in the first 6 postoperative hours could be reduced in a child of 10 kg BW in ToF from 132 ml to 84 ml or 6.0% of his circulating blood volume, and in TGA from 150 ml to 114 ml or 4.5% of his circulating blood volume by using fibrin glue for local hemostasis. The rethoracotomy rate, however, could not be reduced. But no rethoracotomy because of bleeding at patches and suture lines sealed with fibrin glue was necessary.

The indication for reoperation for bleedings should result from a comparison between the blood loss of an individual patient and the blood loss of a group of patients after the same procedure. A decreased blood loss of the whole group through a better local hemostasis increases the difference from the individual patient with surgical bleeding. A greater difference of blood loss between patients requiring reoperation caused by bleeding and patients not requiring reoperation in the group with fibrin glue had facilitated the indication for reoperation.

In all cases of application of blood, or blood and plasma components, the risk of hepatitis must be discussed (5, 16, 17). No case of hepatitis was found in those patients with TGA and ToF using fibrin glue for local hemostasis. In our experience, with the application of fibrin glue for local hemostasis and patch-sealing in other patients did not increase the rate of hepatitis compared to those formerly treated without fibrin glue (17). Similar results were reported

by other investigators (13, 14). *Scheele* and co-workers (14) found no higher risk of hepatitis after application of fibrin glue in 2 comparable groups of 170 patients in general surgery. An increased risk of hepatitis was only associated with the number of transfused blood units (5, 13, 14, 16); therefore, to decrease the risk of postoperative hepatitis, a decrease of blood consumption is desirable. In our experience with ToF and TGA patients undergoing intracardiac repair, a significant decrease of blood consumption after the application of fibrin glue for local hemostasis was not evident. The postoperative blood loss, however, was small in total when compared to the volume of one transfusion unit of 500 ml. In other patients, especially in adults, a reduction of postoperative blood consumption is possible.

Hemorrhages could be prevented, even using low porous patches and prostheses. However, in recent studies, cases of restenoses of RVOT-enlargements and conduits have been reported caused not by adherent endothelial peel to the surrounding conduit and separation from the conduit, but by a layer of thrombus with fenestration and dissection (1, 4). That the endothelial peel will adhere better in sealed high porous patches and prostheses can be anticipated. *Cooley*'s method of autoclaving prostheses with autologous blood is rather complicated and time-consuming in comparison to the fibrin glue method and has not been proven to be effective in highly porous graft material (6, 9). Heat-denatured proteins must be implanted with the risk of immunological reactions. Both sealing suture lines and biological cross-linking of proteins are impossible with this autoclaving method. On the other hand the use of cryoprecipitated active human fibrinogen guarantees biological protein cross-linking (14) and makes it possible to seal grafts of low and high porosity (9) and suture lines independent of the coagulation state of the patient.

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