BLEEDING AND USE OF BLOOD PRODUCTS AFTER HEART OPERATIONS IN INFANTS

Recent studies have suggested that postoperative bleeding is decreased in pediatric heart operations if fresh whole blood instead of blood component therapy is used for postoperative transfusions. Because this is in contrast to our practice to use whole blood for only the priming of the cardiopulmonary bypass circuit and then to use blood components for additional transfusion requirements, it was our interest to analyze the bleeding complications and the use of blood products after heart operations in infants. The patient records of the 73 infants operated on in 1992 were reviewed. The chest tube drainage varied from 3 to 51 ml/kg per 6 hours (mean 10 ml/kg) and it did not correlate with any of the tested clinical or laboratory parameters. One infant underwent reoperation because of surgical bleeding. Disseminated intravascular coagulation developed in another patient. Sixty-eight patients (93%) needed red blood cell supplementation. Sixty-eight percent of patients between 1 month and 1 year old could be treated without any other postoperative transfusion except for red blood cell supplementation. In contrast, in the neonates, platelet concentrates or fresh frozen plasma, or both, were used in 61% of the patients. In addition to the known immaturity of the hemostatic system, the increased need for platelet concentrates in the neonates was attributed to longer cardiopulmonary bypass time, deeper hypothermia in association with circulatory arrest, larger dosages of heparin, and more extensive plasma dilution during cardiopulmonary bypass. In conclusion, a low rate of bleeding complications and acceptably low general blood loss can be achieved postoperatively with blood component therapy. (J THORAC CARDIOVASC SURG 1995;109:524-9)

Jari Petäjä, MD, Ulla Lundström, MD, Mauri Leijala, MD, Kaija Peltola, MD, and Martti A. Siimes, MD, *Helsinki, Finland*

From Children's Hospital, University of Helsinki, Finland.

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Address for reprints: Jari Petäjä, MD, Children's Hospital, University of Helsinki, Stenbäckinkatu 11, FIN-00290 Helsinki, Finland.

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Cardiac operations are often associated with bleeding complications, and resternotomy because of bleeding is needed in 3% to 5% of patients.[1, 2] The cause of bleeding after cardiac operations is multifactorial with contributions from problems with surgical hemostasis and hemostatic alterations involving platelets, coagulation, and fibrinolytic systems.[2-5]

Transfusion requirements in heart operations have decreased,[6-8] but still blood transfusions constitute both remarkable economic cost and a medical risk of adverse reactions including viral infections. However, it seems that blood product policies are highly variable in different centers and only partly dependent on sound medical indications.[6, 9, 10] Development of blood-saving techniques has made heart operations possible even without homologous blood transfusions.[11] The general development in transfusion medicine including transfusions after cardiac operations has been toward use of blood components instead of unfractioned blood. However, in pediatric cardiac operations, the situation is more unclear. In a recent study, use of fresh whole blood instead of stored blood components after termination of cardiopulmonary bypass (CPB) in children younger than 2 years old resulted in a 46% decrease in the postoperative blood loss.[12] Later, the use of fresh whole blood was also recommended by others.[13, 14] In our hospital, the transfusion requirements after CPB have almost exclusively been met with component therapy for several years. Therefore it was of interest to analyze the bleeding complications and the use of blood products in infants less than 1 year old who underwent heart operations. In addition it was our aim to characterize the potential risk groups of patients with higher transfusion requirements.

Patients and methods

The patient series comprised all of the 73 infants, younger than 1 year of age, who had initial open heart operations in our hospital in 1992. Of them, 23 were younger than 4 weeks old and were called neonates. The others were called older infants. There were 32 boys and 41 girls. Of the patients, 9 were born before 38 weeks of gestation.

The cardiac defects of the patients are shown in Table I. Standardized surgical and CPB techniques were used

with core cooling to 18° to 20° C. In association with circulatory arrest ($n = 23$) hypothermia varied from 18° to 15° C. Cold potassium (5° C) crystalloid ($n = 55$) or blood ($n = 18$) cardioplegia for myocardial preservation was used. In 65 patients, the anesthesia was done by high doses of intravenous fentanyl and pancuronium. Whole blood, donated 20 to 28 hours before the operation (except for operations on Mondays, when the blood was donated on the previous Saturday), tested for antibodies against human immunodeficiency virus and hepatitis C virus and presence of hepatitis B surface antigen, and 4% human albumin solution were used for priming of the CPB circuit. The dilution was calculated to achieve a hematocrit of 25%. The whole volume of cardioplegia was hemofiltrated and during rewarming the hematocrit value was elevated to the target value by adding whole blood to the CPB circuit and continuing the hemofiltration. Occasionally, red blood cell concentrates (RBCs) were used in addition to the whole blood, if the target hematocrit was not achieved conveniently with whole blood and hemofiltration.

During CPB 10 patients needed less than 500 ml of whole blood (1 donor), 62 between 500 and 1000 ml (2 donors), and 1 patient more than 1000 ml (3 donors). At the end of bypass, factor IX concentrate (375 to 500 IU) was added to the CPB circuit of 15 patients with preoperative low prothrombin time (PT) values (less than 30%). Hemostasis during the operation had to be supported by giving fresh frozen plasma ($n = 4$), platelet concentrates ($n = 5$), or cryoprecipitate ($n = 1$) to 9 patients. Aprotinin was given (50,000 to 100,000 IU/kg) to 20 patients, 18 of whom were neonates. Our current strategy is to give aprotinin to all neonates, deeply cyanotic older infants, and all patients undergoing reoperation. During 1992 this routine was just being introduced, which explains why occasional neonates did not receive aprotinin. CPB time varied from 22 to 232 minutes (mean ± SD* 105 ± 43 minutes). The heparin effect was neutralized by giving protamine (at first 2 mg/kg and then additional doses according to the activated clotting times). The postoperative stay at the intensive care unit varied from 1 to 36 days (7.5 ± 5.8 days). Of the 73 patients, 11 have died; 7 patients died during the postoperative intensive care unit stay in intimate relation to the complex operation and 4 patients died later.

We recorded 51 parameters concerning the preoperative medical history, cardiac problems, anesthesia, operation, and postoperative course from the patient records. In addition, 19 preoperative laboratory parameters were recorded. The preoperative screening of coagulation consisted of activated partial thromboplastin time (APTT), PT, and platelet count. After operation, APTT and PT were measured when clinically indicated. Hemoglobin, hematocrit, and platelet count were analyzed until the eighth postoperative day.

Five clinical subgroups of patients were also analyzed. These were those who subsequently died, the neonates, and the three subgroups of cardiac defects. For the latter, a pediatric cardiologist divided the patients as to those with and those without cardiac failure (54 versus 17 patients), profound preoperative hypoxia (19 versus 53 patients), and a cardiac defect with increased turbulence of blood flow (22 versus 50 patients). When the division was made, the cardiologist did not have knowledge of the postoperative bleeding or blood product use of the patients. The subgroups of the cardiac defects were not mutually exclusive. The surgical procedures were also divided into categories of simple, intermediate, and complex.

*Standard deviation.

Table I. *Cardiac defects and classification of operative procedures in the 73 infants*

Diagnosis	*n*
Simple	
Aortic stenosis	3
Atrial septal defect	3
Intermediate	
Atrioventricular septal defect	20
VSD	11
Complex	
Simple TGA	10
Complex TGA (TGA + VSD)	8
Total anomalous pulmonary venous drainage	3
Left heart hypoplasia	2
Univentricular heart connection	1
Other	12

TGA, Transposition of the great arteries; *VSD,* ventricular septal defect.

The drainage from chest tubes during the first 6 postoperative hours was taken as a measure of the postoperative bleeding. This arbitrary limit was chosen because later the secretion from the chest tubes gradually and variably turns from blood into a mixture of blood and serous exudate. The plasma dilution during and immediately after CPB was calculated by the formula:

$$F = \frac{(100 - Hct_{preoperative}) \cdot Hct_t}{(100 - Hct_t) \cdot Hct_{preoperative}} \cdot 100$$

where Hct_t presents the lowest hematocrit value measured during CPB (maximal dilution) or the hematocrit value at the end of the operation (postoperative dilution).[15]

Two-tailed Student's t test for independent samples and χ^2 test were used for comparisons and Spearman R correlation test was used to calculate correlation coefficients. A value of $p < 0.05$ was regarded as significant.

The study protocol was approved by the ethics committee of the Children's Hospital, University Central Hospital of Helsinki.

Results

Bleeding. Of the 73 patients, only 1 patient had a recognizable bleeding complication. This patient underwent reoperation because of defective surgical hemostasis. Another patient had, after repeated resuscitations necessitated by low cardiac output, gastrointestinal tract bleeding and laboratory evidence of disseminated intravascular coagulation. This patient died of these multiple complications.

Table II. *Blood loss (mean ± SD) by age and surgical difficulty*

	Blood loss (ml/kg)
By age	
Neonates (n = 23)	10.0 ± 9.6
Older infants (n = 50)	10.8 ± 5.4
By surgical difficulty	
Simple (n = 6)	8.8 ± 3.4
Intermediate (n = 31)	11.3 ± 3.9
Complex (n = 36)	10.2 ± 9.1

None of the differences are statistically significant.

The mean drainage from the chest tubes was 10 ml/kg during the first 6 postoperative hours. It was less than 8 ml/kg (10% of the estimated mean blood volume of 80 ml/kg) in 33% of patients and less than 20 ml/kg (25% of blood volume) in 96% of patients. The amount of drainage from chest tubes did not correlate with any of the tested clinical or laboratory parameters. The chest tube drainage was also analyzed according to the complexity of the operation (Table II). No significant differences were found between simple, intermediate, and complex operations. The drainage did not differ between the neonates and the older infants (Table II).

Postoperative use of blood products. During the intensive care unit stay three patients did not receive any blood products. RBCs were given to 68 (93%), whole blood transfusions to 10 (14%), platelet concentrates to 20 (27%), and fresh frozen plasma to 8 (11%) of the patients. The previously mentioned patient with disseminated intravascular coagulation also received factor IX concentrate and cryoprecipitate. Of the 20 patients who received platelets, 13 were neonates. Forty-three patients (59%) were treated throughout the intensive care unit stay without any blood product other than RBCs. Of these, 9 were neonates (39% of all the neonates) and 34 were older infants (68% off all the older infants).

To find possible preoperative and perioperative indicators of postoperative blood product need, the patient material was analyzed for associations between the use of blood products and clinical and laboratory parameters (Table III). A further approach was made by first dividing the patient series into clinical subgroups as described in the *Patients and methods* section. Then the use of RBCs and platelet concentrates was studied in these subgroups (Table IV).

The use of platelet concentrates but not RBCs was clustered in the neonates. Of the neonates 57% and of the older infants 14% received platelet concentrates ($p < 0.001$). In the search for a mechanism for this, all the factors associated with the use of platelet concentrates in the patient series as a whole (Table III) were found to be more unfavorable in the neonates than in the older infants (Table V). To test whether these factors (namely, CPB time, circulatory arrest time, degree of hypothermia, dose of heparin, perioperative and postoperative dilution, preoperative platelet count, and hematocrit value had any indicator value of subsequent platelet concentrates need for outside the neonatal period, the analysis was repeated after exclusion of the neonates (Table VI). The postoperative dilution, preoperative hematocrit value, CPB time, and circulatory arrest time were significantly increased in the older infants receiving platelet concentrates when compared with these variables in the older infants who did not receive platelet concentrates.

A new finding in the present study was the association between postoperative hemodilution and later use of platelet concentrates and RBCs (Fig. 1).

Discussion

The first objective of the present study was to analyze the frequency and type of bleeding complications. Somewhat surprisingly, such complications were rare. Only one patient had to undergo reoperation because of excessive bleeding caused by a surgical defect in a vascular anastomosis. Also, general postoperative blood loss, measured as drainage from chest tubes during the first 6 postoperative hours, was low and did not correlate with any of the tested parameters.

Our study was stimulated by recent reports that recommended the use of fresh whole blood throughout the operation and postoperative period in infants undergoing heart operations[12, 14] and indicated no further need for transfusion therapy in these infants.[14] In their study Manno and associates[12] found the mean 24-hour blood loss to be 96 ml/kg (120% of blood volume) if reconstituted blood was used and 52 ml/kg (65% of blood volume) if fresh whole blood was used. They concluded that fresh blood should be used to achieve less bleeding in children younger than 2 years old.[12] The present study is a retrospective analysis, whereas the study by Manno and associates[12] was prospective and randomized. In addition, we recorded chest tube drainage for only 6 hours. These differences make a direct comparison of the studies impossible. However, in light of the figures reported by Manno and

Table III. *Spearman R correlation coefficients and corresponding significance levels for use of RBCs and platelet concentrates and relevant clinical or laboratory parameters*

	RBC transfusions		*Platelet transfusions*	
	R	*p Value*	*R*	*p Value*
Patient age	−0.29	0.013	−0.43	<0.001
CPB time	0.44	<0.001	0.33	0.005
Aortic clamping time	0.41	<0.001	0.18	NS
Arrest time	0.26	0.028	0.59	<0.001
Degree of hypothermia	−0.36	0.003	−0.42	<0.001
Hemofiltration	−0.13	NS	−0.17	NS
Dosage of fentanyl per kilogram	0.06	NS	0.04	NS
Dosage of protamine per kilogram	0.12	NS	0.08	NS
Dosage of heparin per kilogram	0.27	0.022	0.30	0.011
Maximal dilution	−0.22	NS	−0.27	0.020
Postoperative dilution	−0.38	0.001	−0.40	<0.001
APTT	0.43	0.001	0.25	NS
PT	−0.24	NS	−0.24	NS
Activated clotting time	0.02	NS	0.20	NS
Platelet count	−0.20	NS	−0.30	0.010
Hematocrit	0.27	0.021	0.52	<0.001

Laboratory values refer to those measured preoperatively. Activated clotting time refers to the value at the end of the operation. *NS,* Not significant.

Table IV. *Relative use of RBCs and platelet concentrates (mean of whole patient series, 1.00) in different subgroups of patients*

		RBC transfusions		*Platelet transfusions*	
	n	*Mean*	*p Value*	*Mean*	*p Value*
Deceased	11	1.58	0.027	2.20	0.025
Neonates	23	1.23	NS	2.00	0.001
Hypoxia	19	1.31	NS	1.80	0.034
Cardiac failure	54	0.90	NS	0.82	NS
Turbulence*	22	0.81	NS	0.80	NS

The *p* values calculated by two-tailed *t* test for independent samples.
*Cardiac defect with increased turbulence of blood flow.

Table V. *Comparison of neonates and older infants in respect to factors that correlated with use of platelet concuntrates*

	Neonates (mean ± SD)	*Older infants (mean ± SD)*	*p Value*
CPB time (min)	140 ± 45	89 ± 30	<0.001
Arrest time (min)	32 ± 28	5 ± 15	<0.001
Degree of hypothermia (° C)	16.0 ± 1.5	17.9 ± 2.3	<0.001
Dose of heparin (mg/kg)	6.5 ± 1.1	5.6 ± 1.1	0.002
Maximal dilution (%)	33 ± 14	51 ± 15	<0.001
Postoperative dilution (%)	59 ± 17	90 ± 29	<0.001
Platelet count (10^9/L)	315 ± 127	431 ± 104	<0.001
Preoperative hematocrit (%)	51 ± 7	39 ± 6	<0.001

associates[12] we believe that our strategy of using blood component therapy after operation was associated with an acceptable and manageable amount of postoperative blood loss.

It is our practice to use whole blood 20 to 28 hours after its donation for the CPB prime; the leftover content of the reserved 2 units are then used if needed during the operation for additional transfusions. This is essentially similar to the practice used by Jobes and coworkers,[14] who reported they could avoid further blood transfusions during and after operation even in neonates with this approach. In the present study this was clearly not the case: 12% of the patients received plasma or platelets, or both, during the operation and an additional 37% of patients needed these products during the intensive care unit stay. However, the clinical significance of this difference cannot be evaluated further, because in the present patient series the indications for individual postoperative transfusions were not predetermined but were partially dependent on the subjective judgment of the physician on duty. Suffice it to say that when the hemostatic capacity of the patient was judged subjectively by the surgeon and the anesthesiologist, the use of fresh whole blood during the operation did not abolish the frequent need for further blood products during and after the operation.

The use of factor IX concentrate in the prime for

Table VI. *Factors that correlated with use of platelet concentrates in whole patient series studied after exclusion of neonates*

	*Platelet concentrates** *(mean ± SD)*	*No platelet concentrates** *(mean ± SD)*	*p Value*
No. of patients	7	43	
CPB time (min)	119 ± 24	84 ± 29	0.004
Arrest time (min)	16 ± 7	0 ± 0	<0.001
Degree of hypothermia (° C)	16.4 ± 1.5	18.2 ± 2.4	NS
Dosage of heparin (mg/kg)	5.8 ± 0.9	5.6 ± 1.1	NS
Postoperative dilution (%)	70 ± 24	93 ± 29	0.048
Maximal dilution (%)	46 ± 19	52 ± 14	NS
Preoperative hematocrit (%)	45 ± 8	38 ± 5	0.001
Platelet count (10^6/L)	433 ± 91	431 ± 107	NS

NS, Not significant.

*The 50 patients are divided into those who received platelets and those who did not.

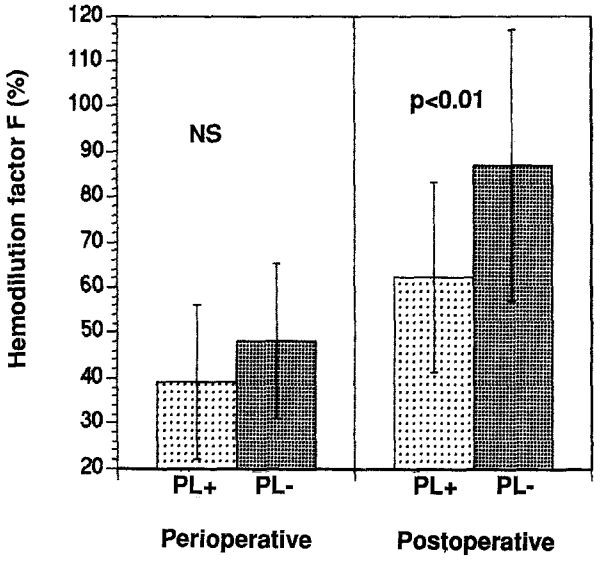

Fig. 1. Hemodilution factor F (mean ± SD) during and immediately after operation in patients who received platelet concentrates *(PL+)* and in those who did not *(PL−). NS,* Not significant.

the patients with low preoperative PT values is based on our clinical impression that this approach decreases the bleeding from the operative field with no experience of side effects. We prefer to use factor IX concentrate as the first choice of clotting factor concentrates because it is concentrated also for prothrombin and factor X. Cryoprecipitate would have the advantage of containing more fibrinogen, which may be of significance especially in the neonates.[13] However, in the absence of controlled studies between these two preparations, the question of superiority remains open.

The second objective of the study was to find clinical risk factors of bleeding tendency and indicators of blood product need. Regarding the chest tube drainage, the analysis was unrewarding. No significant associations between clinical parameters and the blood drainage could be found. However, the blood product use was found to correlate with several preoperative and perioperative clinical and laboratory parameters. This discrepancy of blood component use and recorded bleeding is explained by the fact that bleeding could be recorded only during immediate postoperative hours, whereas transfusions were analyzed for the whole period of intensive care. Further, bleeding is only one mechanism for blood product need. For example, platelets are consumed by infections and in the CPB circuit.[2] In infants the need for RBCs to replace the blood lost in blood samples makes RBC transfusions almost unavoidable in pediatric cardiac operations.[12]

The most interesting findings of the blood product use were those concerning the use of platelet concentrates. Platelets were given to 27% of patients, which is in accordance with the reported corresponding figures of between 19% and 24% for adults.[6, 10] Platelet use during intensive care was clustered in two subgroups of patients, the neonates and those with cyanotic cardiac defects, as could be expected.[14] Further analysis demonstrated the multifactor background of platelet need in the neonates. Long CPB time, deeper hypothermia in association with circulatory arrest, larger dosages of heparin, more extensive plasma dilution during CPB, and high preoperative hematocrit were more pronounced in the neonates than in the older infants. Further, the hemostatic system of the neonate is immature and thus prone to disturbances.[16-18] Aprotinin was given almost exclusively to neonates, but this could not abolish the more frequent use of platelets in the neonates.

After exclusion of the neonates from the data, platelet use was still associated with long CPB time, circulatory arrest, preoperatively high hematocrit, and extensive dilution after CPB. Cyanotic heart defects are known to be associated with both high hematocrit and increased bleeding. However, it was a new finding that high hematocrit value, irrespective of whether it was caused by cyanosis or a neonatal age, was associated with platelet use. The mechanism may be that those patients with high preoperative hematocrit value had greater relative reduction in hematocrit value during CPB. This resulted in greater dilution of all plasma proteins including clotting factors during and immediately after the operation.[15] These results indicate that it should be prospectively studied as to whether those patients with a high hematocrit value could have a higher target hematocrit value during and after CPB, bearing in mind the potential negative rheologic effects.

In summary, it was shown that the use of fresh whole blood in the CPB prime did not abolish the occasional need for perioperative platelet concentrates, fresh frozen plasma, and clotting factor concentrates. According to our experience it seems rational to make a fresh whole blood reservation of 2 units for CPB and then manage the occasional further perioperative transfusion needs with blood components. On the other hand, postoperative transfusion requirements could easily be met with conventional blood component therapy. Sixty-eight percent of patients between 1 month and 1 year old could be treated without any postoperative transfusion other than RBC supplementation. In the neonates, platelet concentrates or fresh frozen plasma, or both, were used in 61% of the patients. This transfusion practice was associated with no severe complications caused by bleeding and the general postoperative blood loss was acceptable. According to our experience, postoperative blood component therapy can safely be used throughout pediatric cardiac operations.

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