Heparin-Bonded Cardiopulmonary Bypass Circuits Reduce the Rate of Red Blood Cell Transfusion During Elective Coronary Artery Bypass Surgery

Kenneth R. Kreisler, MD,* Robert A. Vance, MD,† Jose Cruzzavala, MD,‡ and Jonathan D. Mahnken, PhD§

Objective: **This study compared the transfusion rates of patients treated with heparin-bonded circuits with the transfusion rates of patients treated with standard bypass circuits with and without ϵ-aminocaproic acid (EACA).**

Design: **Prospective double-blind (drugs), open trial (cardiopulmonary bypass circuits).**

Setting: **University medical center.**

Participants: **Seventy-one patients undergoing elective AM admission coronary artery bypass graft surgery.**

Measurements and Main Results: **Patients were randomized to receive either heparin-coated cardiopulmonary bypass circuits (HBCPB), nonheparin-coated cardiopulmonary bypass circuits and EACA (EACPB), or nonheparin-coated bypass circuits and placebo (control). Patients were transfused if their hematocrit was <18% while on cardiopulmonary bypass or <25% at any time after the cardiopulmonary bypass period. The rate and number of transfused packed red blood cells (pRBCs), platelets, fresh frozen plasma, and cryoprecipitate were measured. A Fisher exact test showed that the transfusion rate was as follows: the HBCPB group (5.0%), the EACPB group (18.2%), and the control group (36%), ($p = 0.034$).**

Conclusions: **The heparin-bonded cardiopulmonary bypass–treated patients in this study received fewer pRBCs than did the control group. A nonsignificant reduction in the pRBC transfusion rate was found between those with heparin-bonded bypass circuits and those with standard circuits who received ϵ-aminocaproic acid.**

KEY WORDS: heparin-bonding, Amicar, cardiopulmonary bypass, transfusion rates, coronary artery bypass surgery

A COMMON COMPLICATION of cardiac surgery requiring cardiopulmonary bypass is postoperative hemorrhage. The Society of Thoracic Surgeons database for 1998 to 2001 reveals that 41% to 44% of all patients undergoing isolated coronary artery bypass graft (CABG) surgery received blood products of some type.[1] Multiple strategies have been used to reduce postoperative bleeding and transfusion of allogeneic blood products. The use of treatment algorithms based on laboratory data significantly reduces the rate of transfusion of both red blood cell and non–red blood cell products.[2] Aprotinin and ϵ-aminocaproic acid (EACA) have been shown to reduce bleeding and transfusion requirements.[3] Heparin-bonded cardiopulmonary bypass circuits (HBCPB) also reduce postoperative chest tube drainage and blood transfusion requirements.[4,5] These circuits also reduce complement activation and attenuate the systemic inflammatory response associated with cardiopulmonary bypass (CPB).[6-8]

In this double-blind (EACA), open trial (cardiopulmonary bypass [CPB] circuits) investigation, the authors prospectively compared the transfusion rate of 71 patients treated with an HBCPB with a placebo infusion, standard bypass circuits with an EACA infusion, or standard bypass circuits with a placebo infusion. The authors used a clinical picture with laboratory-based algorithm to determine which patients would be transfused with red cell or non-red cell blood products.

METHODS

After obtaining institutional review board approval and informed consent, 71 patients who had not received platelet inhibitors, including aspirin, or anticoagulants within the past 5 days and were undergoing elective primary CABG surgery with systemic hypothermia (32°C) on the day of admission to the hospital were randomized to 1 of 3 groups. HBCPB patients were treated with tip-to-tip heparin-coated CPB circuits, including the cardiotomy reservoir, arterial filter, aortic and venous cannulas (Carmeda Bonded Maxima; Medtronic, Inc, Minneapolis, MN), and a placebo infusion. EACPB patients were treated with nonheparin-coated CPB circuits (Maxima, Medtronic, Inc) and EACA (75 mg/kg load, 12.5 mg/kg/h infusion, 5 g in CPB priming fluid). The EACA load was given over 10 minutes after induction of anesthesia and prior to skin incision. The maintenance infusion was started immediately on completion of the EACA loading dose. Control patients received nonheparin-coated circuits (Maxima) and a placebo (0.9% normal saline) load and maintenance infusion given in the same manner as the EACA-treated patients. The infusion was continued for 2 hours after arrival in the intensive care unit. The investigators were blinded to the type of infusion (placebo *v* EACA). Randomization was accomplished through the use of a computer-generated table of random numbers. The investigators were not blinded to the type of bypass circuitry intraoperatively. Heparin-bonded circuits are easily differentiated from standard bypass circuits because of the inherent tactile and visual characteristics.

Preoperative demographic and laboratory studies included age, sex, weight, height, hemoglobin, hematocrit, platelet count, Ivy bleeding time, partial thromboplastin time (PTT), prothrombin time (PT), and international normalized ratio. Intraoperatively, the activated coagulation times, prebypass hematocrits, on-bypass hematocrits, total CPB times, and aortic cross-clamp times were recorded for each patient. Anticoagulation for the initial heparin dose and during the bypass period was maintained using heparin concentration-based management (Hepcon HMS, Medtronic) to achieve an activated coagulation time >480 seconds. Anticoagulation was monitored every 30 minutes while on CPB. Heparin was reversed with protamine sulfate (based on the Hepcon HMS system) upon discontinuation of CPB, and a sample of blood was tested for any circulating heparin. Blood from the surgical field and from the CPB circuitry was salvaged and processed using a cell saver (Frensensius C.A.T.S.; Frensenius USA, Walnut Creek, CA).

*From the *Department of Anesthesiology, University of Kansas, Kansas City, KS; Departments of †Anesthesiology and ‡Cardiothoracic Surgery, West Virginia University, Morgantown, WV; and §Department of Preventive Medicine and Public Health, University of Kansas Medical Center, Kansas City, KS.*

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Address reprint requests to Kenneth R. Kreisler, MD, Department of Anesthesiology, University of Kansas Hospital, 3901 Rainbow Boulevard, Kansas City, KS 66160. E-mail: kkreisler@kumc.edu

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Table 1. Demographics, Preoperative Laboratory Studies, and Bypass Events (Mean ± Standard Deviation)

	EACPB (n = 22)	HBCPB (n = 20)	Control (n = 25)	*p* Value
Age (y)	63.4 ± 7.2	59.6 ± 10.4	61.4 ± 8.8	0.3924
Male (%)*	17 (77.2)	17 (85.0)	17 (68.0)	0.4255
Weight (kg)	87.5 ± 14.7	85.3 ± 11.7	88.7 ± 17.8	0.7474
Hgb (gm/dL)	13.7 ± 1.4	14.0 ± 1.1	13.7 ± 1.2	0.6949
Hct (%)	40.3 ± 4.0	41.3 ± 3.5	40.5 ± 3.6	0.6345
Plt Count ($10^3/\mu L$)	227.6 ± 51.5	220.9 ± 44.3	232.5 ± 45.1	0.7119
BT (min)†	6.5 (5.0-8.0)	5.5 (4.3-6.8)	6.0 (4.0-7.0)	0.1336
PTT (s)†	28.4 (26.7-29.8)	28.4 (26.1-31.4)	29.4 (26.9-32.0)	0.5446
PT (s)†	11.0 (10.8-11.2)	10.9 (10.5-11.5)	11.2 (10.6-11.5)	0.4414
INR†	1.0 (1.0-1.0)	1.0 (1.0-1.1)	1.0 (1.0-1.1)	0.3607
ACT	143.7 ± 13.3	142.5 ± 10.0	142.7 ± 15.4	0.9514
CPB time (min)	100.9 ± 26.3	112.5 ± 25.1	118.2 ± 31.4	0.1077
Aortic cross-clamp time (min)	67.2 ± 21.2	69.5 ± 20.6	72.2 ± 20.9	0.7135
Bypass Hct (%)†	24.0 (22.0-28.0)	23.0 (21.0-25.0)	24.0 (21.0-27.0)	0.6935
Cell Saver volume (mL)†	675 (666-750)	813 (637-900)	710 (640-900)	0.2796
Operative Procedure (%)*				0.5738
2 veins	1 (4.6)	0 (0.0)	1 (4.0)	
3 veins	0 (0.0)	1 (5.0)	3 (12.0)	
4 veins	0 (0.0)	1 (5.0)	0 (0.0)	
6 veins	0 (0.0)	0 (0.0)	1 (4.0)	
Lima	1 (4.6)	0 (0.0)	0 (0.0)	
Lima & 1 vein	2 (9.1)	3 (15.0)	3 (12.0)	
Lima & 2 veins	8 (36.4)	6 (30.0)	4 (16.0)	
Lima & 3 veins	3 (13.6)	4 (20.0)	7 (28.0)	
Lima & 4 veins	2 (9.1)	3 (15.0)	4 (16.0)	
Lima & 5 veins	1 (4.6)	1 (5.0)	1 (4.0)	
Lima (×2) & 2 veins	1 (4.6)	0 (0.0)	0 (0.0)	
Lima, radial, & 3 veins	0 (0.0)	0 (0.0)	1 (4.0)	
Lima, radial, & vein	3 (13.6)	0 (0.0)	0 (0.0)	
Radial & vein	0 (0.0)	1 (5.0)	0 (0.0)	

*Frequency (%) is displayed as the data are categorical. Fisher exact test was used to check for statistical significance because the assumptions for Pearson's chi-square test are not met.

†Median (1st quartile-3rd quartile) are displayed. The Kruskal-Wallis test was used to check for statistical significance because the assumptions for ANOVA are not met.

The volume of transfused cell saver blood was recorded. Before leaving the operating room, a final activated coagulation time/heparin detection cartridge was used to determine the adequacy of heparin reversal. The PT, PTT, hemoglobin, hematocrit, fibrinogen, and fibrin degradation products laboratory values were obtained after complete reversal of heparin by protamine was verified. The volume of chest tube drainage was recorded at 2, 4, and 12 hours after chest closure. A final postoperative hemoglobin and hematocrit were obtained on postoperative day 2.

Patients were transfused with packed red blood cells (RBCs) only if the hematocrit was less than 18% while on CPB and less than 25% after CPB or during the postoperative period until discharged from the hospital. Other blood products were used to treat postoperative bleeding if clinically indicated (chest tube output >200 mL/h) and the patient had abnormal laboratory values. If the postoperative PT was >15 seconds or the PTT was greater than 35 seconds, FFP was transfused; if the fibrinogen was less than 150, cryoprecipitate was given; or if the platelet count was less than 100,000, platelets were transfused in 6-unit increments.

The primary objective of this study was to compare the efficacy of HBCPB, EACA, and placebo in avoiding exposure to allogeneic RBCs. A corresponding secondary objective was to compare the efficacy of these treatments in avoiding and reducing exposure to other allogeneic blood components (eg, platelets, fresh frozen plasma, and cryoprecipitate).

Statistical analysis was conducted with SAS software (version 8.2; SAS Institute, Inc, Cary, NC). Differences in frequency of transfusion for each group were determined using a Fisher exact test. Too few patients requiring transfusion were observed to statistically compare differences in the number of packed RBC units and platelets transfused for each group. A Fisher exact test, analysis of variance, and the Kruskal-Wallis test were used to analyze the demographic, mean and median laboratory values, and chest tube drainage. The type I error rate (α) was set at 0.05.

RESULTS

Patient demographics in regard to age, sex, weight, height, preoperative hemoglobin, hematocrit, platelet count, ACT, PT, PTT, and international normalized ratio were similar in all 3 groups (Table 1). The average preoperative bleeding times

Table 2. Rate of pRBC Transfusion in the Postoperative Period

	EACPB (n = 22)	HBCPB (n = 20)	Control (n = 25)	*p* Value
Number of patients	4 (18.2)	1 (5.0)	9 (36.0)	0.0340
Number of patients	—	1	9	0.0271
Number of patients	4	1	—	0.3465