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Advantages of Autologous Blood Transfusion in Off-Pump Coronary Artery Bypass

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ABSTRACT

Background: In this randomized controlled study, we investigated the effects of autologous Hemobag blood transfusion (AHBT) and allogenic blood transfusion (ABT) in off-pump coronary artery bypass (OPCAB) surgery.

Methods: Sixty patients who underwent surgery between February 2008 and August 2008 were randomized into 2 groups. The AHBT group (n = 30) consisted of patients who received autologous Hemobag blood transfusion, and the ABT group (n = 30) consisted of patients who received allogenic blood transfusion. All patients underwent OPCAB via sternotomy. The time to extubation, chest tube drainage volume, postoperative white blood cell counts, amount of blood transfusion, sedimentation rate, C-reactive protein concentration, postoperative temperature, and the presence of atelectasis were recorded in the intensive care unit.

Results: Intraoperative bleeding and fluid resuscitation were similar in the 2 groups ($P > .05$); however, there were significant decreases in postoperative blood loss, extubation period, postoperative white cell counts, sedimentation rate, incidence of atelectasis, C-reactive protein, and fever in the AHBT group compared with the ABT group ($P < .05$). The rate of atrial fibrillation in the AHBT group tended to be lower than in the ABT group.

Conclusion: Autologous blood transfusion in OPCAB may be beneficial in certain cardiac surgery patients; however, these beneficial effects require further study to be proved.

INTRODUCTION

Coronary artery bypass grafting (CABG) is one of the most frequently performed major operations and is highly effective in improving life expectancy and quality of life in patients with coronary artery disease [Samolyk 2005]. Off-pump CABG (OPCAB) is a form of open heart surgery in which clogged arteries are bypassed while the heart is still beating. OPCAB is gaining widespread acceptance as the preferred choice for myocardial revascularization in certain patient groups with coronary artery disease [Casati 2004; Banbury 2006]. Although the number of surgical procedures is continuing to decline with the advances in interventional cardiology, the proportion of higher-risk patients requiring complex surgical procedures is likely to continue to increase in the near future [Karamanoukian 2000; Ascione 2001; Puskas 2001; Banbury 2006]. Some studies have found that blood transfusion may be performed less often in OPCAB compared with on-pump CABG [Ascione 2001; Purskas 2001; Casati 2004; Staton 2005].

Transfusion needs are determined not only by the surgical methods but also by volume manipulations. One such manipulation is acute normovolemic hemodilution (ANH). ANH allows the physician to conserve blood withdrawn from the patient preoperatively and then retransfuse it into the patient postoperatively [Jamnicki 2003]. Although autotransfusion has been familiar to physicians for a long time, its popularity has increased in the last 2 decades with the increase in transfusion-induced diseases [Puskas 2001]. Over the last 20 years, the potential benefits of avoiding homologous blood transfusion and optimizing oxygen delivery to vital organs have led to a renewed interest for ANH in major surgery [Casati 2004]. Perioperative blood-conservation modalities can affect the necessity of homologous blood transfusion in patients undergoing surgery via reducing postoperative surgical hemorrhage, augmenting patient coagulation function, and preserving the autologous transfusion [Rastan 2006]. The putative effects of ANH are reportedly related to the preservation of red cell mass, because the loss of red blood cells with surgical hemorrhage will be smaller after hemodilution [Popovsky 1985]. In addition, intraoperative provision of fresh whole blood containing platelets and coagulation factors theoretically augments coagulation and reduces surgical blood loss [Allain 2003].

OPCAB has been argued to reduce the inflammatory response during CABG [Mack 2004]. On the basis of this argument, it is believed that OPCAB surgery could reduce end-organ damage seen after conventional CABG, leading to less morbidity. Numerous reports in the literature have described studies comparing the outcomes of off-pump and on-pump

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coronary artery revascularization techniques [Gwozdziewicz 2008; Feng 2009]; however, to our knowledge, the effects of autologous and allogenic blood transfusion (ABT) have not been investigated in OPCAB patients. In this prospective study, we investigated whether autologous Hemobag blood transfusion (AHBT) can conserve blood, decrease morbidity, and improve patient outcomes compared with ABT in OPCAB patients [Scott 2008].

MATERIALS AND METHODS

After the study was approved by the local ethics committee, we obtained written informed consent from all patients scheduled for OPCAB and who met the eligibility criteria. Inclusion criteria were as follows: a hematocrit >35%; stable angina (Canadian Cardiology Society classes I and II); a left ventricular ejection fraction >45%; an absence of significant coexisting diseases, including valvular disease, recent myocardial infarction (< 6 weeks), significant carotid stenosis (>70%) or recent stroke (<3 weeks), renal insufficiency (estimated creatinine clearance <20 mL/min), chronic respiratory disease (arterial oxygen pressure >60 mm Hg on room air), or liver insufficiency (aspartate transaminase or alanine transaminase ≥2 times the upper reference limit); preoperative use of heparin; preoperative use of Coumadin or anti-inflammatory drugs; uncontrolled hypertension; or diabetes mellitus.

Sixty patients who underwent their operations between February 2008 and August 2008 were randomized into 2 groups. The AHBT group (n = 30) consisted of patients who received autologous transfusion and the ABT group (n = 30) consisted of patients who received allogenic transfusion. All patients underwent OPCAB surgery via sternotomy. The allocations were generated from random-number tables by an independent observer and concealed in sealed envelopes.

Anesthesia Protocol

On the morning of surgery, the patients were premedicated (midazolam, 0.05 mg/kg intravenously) and received their usual cardiac drug regimen, except for aspirin, heparin, diuretics, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers, which were withdrawn at least 24 hours before surgery. In the operating room, cannulae were inserted in a peripheral vein, a radial artery, and the right jugular vein. Standard monitoring included pulse oximetry, leads II and V5 of the electrocardiogram for heart rate and automated ST-segment trend analysis, continuous measurements of mean arterial and central venous pressures, nasopharyngeal temperature, end-tidal capnography.

A balanced anesthesia technique included fentanyl (bolus of 1-2 µg/kg, followed by an intermittent bolus of 1-2 µg/kg hourly), etomidate (bolus of 0.2-0.3 mg/kg), Esmeron (a bolus of 1 mg/kg and an intermittent bolus of 0.3 mg/kg hourly), and inhaled sevoflurane (2%-3% in the prebypass period and 1%-1.5 % in the bypass period), and ventilation was modified with each patient to reach a partial arterial oxygen pressure >150 mm Hg and a partial arterial carbon dioxide pressure of 35 to 45 mm Hg.

Perioperative Intervention in the AHBT Group

After anesthesia induction and before systemic heparinization, blood was withdrawn (40-70 mL/min) from a central vein by gravity into citrate-phosphate-dextrose collection Hemobags (Fenwal; Baxter HealthCare, Irvine, CA, USA). In parallel, poly(0–2-hydroxyethyl) amidon (hydroxyethyl starch; mean molecular weight, 200,000; 50% substitution degree; C2/C6 ratio, 5) (HAES-steril; Kabi-Fresenius, Hamburg, Germany) was infused through a 14-gauge peripheral catheter on the opposite arm to a ratio of 1.10:1 to the donated blood. The blood volume to be removed was calculated according to a standard formula to reach a hematocrit of 28% [Matot 2002]. The whole-blood/colloid exchange procedure lasted approximately 15 minutes (range, 10-20 minutes), and it could be interrupted if there were signs of myocardial ischemia and/or unresponsive hypotension. All autologous blood was retransfused to the patients in the operating room, and heparin was not neutralized. Packed red blood cells (PRBC) were transfused in both groups when the hemoglobin concentration was <8 g/dL and the hematocrit was <25% after on-demand reinfusion [Staton 2005].

Perioperative Intervention in the ABT Group

Autologous blood was neither withdrawn from nor retransfused to these patients; however, PRBC were transfused in the intensive care unit (ICU) when the hematocrit was <25% during the ICU period.

OPCAB Surgical Technique

The perfusionist was ready during OPCAB surgery. Blood pressure was optimized carefully, and vasoconstrictors were used when needed. A sternotomy was performed in all patients. In addition to left-sided deep pericardial retraction sutures and table rotation, a right vertical pericardiotomy on the right-sided diaphragmatic surface was performed toward the inferior vena cava to enter the right pleural cavity. This procedure facilitated exposure of the circumflex artery without compromising the patient's hemodynamics. Local stabilization of the coronary artery was achieved with a mechanical stabilizer (Immobilizer™, Genzyme, Cambridge, MA, USA; Octopus 4, Medtronic, Minneapolis, MN, USA). We used an intracoronary shunt in all anastomoses for bleeding control. First, revascularization was performed to the left anterior descending coronary artery, because it generally contained a critical lesion. In subsequent grafting, the proximal anastomosis was constructed so that the blood supply to the coronary artery could be established immediately after completion of the anastomosis, for which we used 7-0 or 8-0 monofilament continuous suture.

Postoperative Monitoring

Extubation times, chest tube drainage volumes, postoperative white blood cell counts, amounts of blood transfused, the sedimentation rate, the C-reactive protein (CRP) concentration (measured with a BN II nephelometer; Siemens Healthcare Diagnostics/Dade Behring, Deerfield, IL, USA), and postoperative temperature were recorded in the clinic. Extubation time was defined as the time from the entrance

Table 1. Preoperative Patient Data*

	AHBT Group (n = 28)	ABT Group (n = 29)	Normal Range	*P*
Age, y	64.2 ± 8.3	62.1 ± 7.4		NS
Female sex, n (%)	6 (27)	5 (23.3)		NS
Congestive heart failure, n (%)	3 (11)	3 (10)		NS
Previous CVA, n (%)	2 (7)	3 (10)		NS
COPD, n (%)	3 (11)	4 (14)		NS
Diabetes mellitus, n (%)	10 (36)	11 (38)		NS
Hypertension, n (%)	14 (50)	15 (52)	120/80 mm Hg	NS
Ejection fraction, %	58.89 ± 5.75	56.75 ± 6.95		NS
Previous PCI, n (%)	15 (53)	1 (25.6)		NS
EuroSCORE	8.6 ± 11.3	8.3 ± 11.5		NS
Hemoglobin, g/dL	15.1 ± 1.9	14.7 ± 1.8	12-17	NS
Hematocrit, %	46.3 ± 5.2	44.1 ± 4.9	33-50	NS
Platelet count, ×103/μL	218 ± 71	225 ± 63	160-450	NS
Prothrombin time, s	15.7 ± 1.21	15.1 ± 2.1	9-13	NS
INR	1.23 ± 0.38	1.18 ± 0.94	0.8-1.4	NS
PTT, s	73 ± 26	67 ± 14	23-36	NS

*Data are presented as the mean ± SD where indicated. AHBT indicates autologous Hemobag blood transfusion; ABT, allogenic blood transfusion; NS, not statistically significant; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; INR, international normalized ratio; PTT, partial thromboplastin time.

of the intubated patient into the ICU to the extubation of the patient. The amount of drainage from chest tubes was defined as the volume of blood collected from the chest tubes until the tubes were removed. Blood loss was recorded during the first 24 hours, and chest-drainage cannulae were removed when bleeding was <100 mL in the preceding 4 hours. Surgical reexploration was performed with a normal coagulation profile and when bleeding was >300 mL/h in the ICU for the first 2 hours and >200 mL/h thereafter. Hematocrit values were measured as the patient entered the ICU and at 24 hours postoperatively. Neither the AHBT group nor the ABT group received PRBC transfusions perioperatively. Sedimentation rates and CRP measurements were performed on the first and fifth postoperative days. Postoperative temperature follow-ups were performed every hour in the ICU and every 4 hours in the cardiovascular clinic. Fever was defined as the number of times temperatures were >38.0°C during the clinical course of each patient. Pulmonary complications were assessed by chest radiography. The Chest Radiographic Scoring System Protocol was used for evaluating the atelectasis rate and total atelectasis scores [Goodnough 1993]. Chest radiographs were examined by a blinded radiologist. Two patients in the AHBT group were excluded from the study because they received PRBC for having a hematocrit <25% postoperatively in the ICU. One patient in the ABT group underwent reoperation because of high drainage from chest tubes and was excluded from the study. One of the patients in the ABT group did not require PRBC.

Statistical Analysis

Statistical analysis was done with SPSS statistical software (version 13.0; SPSS, Chicago, IL, USA). Descriptive analyses were made, and data are presented as the mean ± SD. Differences between the groups for nominal data were analyzed with the χ^2 test, and continuous variables were evaluated with the Student *t* test and the Mann-Whitney *U* test. *P* values <.05 were considered statistically significant.

RESULTS

Twenty-eight patients in the AHBT group and 29 patients in the ABT group [Staton 2005] completed the study. The 2 groups were similar with respect to sex, age, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, previous myocardial infarction, preoperative ejection fraction (Table 1), operative time, the number of distal anastomoses, the amounts of intraoperative fluid replacement, and bleeding. Compared with the ABT group (Table 2), the patients in the AHBT group had significantly less fever (the number of times the temperature was >38.0°C during the clinical course of each patient; 5.4 ± 1.2 versus 7.9 ± 1.0; P < .03), lower white blood cell counts (13 ± 1.2 × 10^3/μL versus 15.8 ± 2.3 × 10^3/μL; *P* < .01), lower sedimentation rates (20.3 ± 3.6 mm/h versus 24.4 ± 3.7 mm/h; *P* < .02), and lower CRP levels (21.6 ± 7.2 mg/L versus 26.2 ± 8.9 mg/L; *P* < .02). The AHBT group had a significantly shorter time to extubation (5.7 ± 1.9 hours versus 8.2 ± 2.3 hours; *P* < .01) and

Table 2. Postoperative Patient Data*

	AHBT (n = 28)	ABT (n = 29)	P
Operation time, min	155.78 ± 21.70	160.72 ± 23.29	.52
Extubation time, h	5.71 ± 1.90	8.17 ± 2.34	.01
Chest tube output, mL	258.52 ± 38.47	388.11 ± 45.91	.01
Distal anastomoses, n	2.81 ± 0.71	2.88 ± 0.61	.43
White blood cells, /μL			
Day 1	13,122.68 ± 1413.68	15,844.00 ± 2266.00	.01
Day 50	12,112.73 ± 1234.15	14,106 ± 1768.44	.01
Sedimentation rate, mm/h			
Day 1	20.31 ± 3.57	24.45 ± 3.67	.02
Day 50	15.65 ± 3.20	15.98 ± 3.34	.24
C-reactive protein, mg/L			
Day 1	21.55 ± 7.22	26.21 ± 8.94	.03
Day 50	15.92 ± 4.01	20.88 ± 5.47	.02
Packed red blood cells, units	1.64 ± 0.52	0.53 ± 0.46	.01
Operative drainage, mL	388.63 ± 104.85	346.11 ± 65.15	.39
Operative fluid, mL	1223.21 ± 245.24	1145.88 ± 143.55	.16
Fever, n	5.4 ± 1.2	7.9 ± 1.0	.03
Atelectasis, n	2 (10.5%)	7 (38.9%)	.04
Atrial fibrillation, n	10	3	0

*Data are presented as the mean ± SD where indicated. AHBT indicates autologous Hemobag blood transfusion; ABT, allogenic blood transfusion.

a significantly lower amount of chest tube bleeding (258.5 ± 38.5 mL versus 388.1 ± 45.9 mL; $P < .01$). The atelectasis rate was 2 of 28 patients in the AHBT group and 7 of 29 patients in the ABT group ($P < .04$) (Table 2). The total atelectasis score for the AHBT group was 2 points, and the total atelectasis score for the ABT group was 13 points ($P < .01$). The atrial fibrillation rate was 13.6% (3/28) in the AHBT group and 24.1% (10/29) in the ABT group ($P < .09$).

DISCUSSION

To our knowledge, the current study is the first double-blinded prospective study to assess the effectiveness of acute ANH in OPCAB patients.

Less-invasive surgery will obviously decrease the morbidity and mortality rates in CABG patients; thus, OPCAB is gaining widespread acceptance as the preferred choice for myocardial revascularization in certain patient groups [Rastan 2006]. Blood transfusion is associated with increased resource utilization, morbidity, and mortality in cardiac surgery [Treib 1996]. Homologous blood transfusion during and after cardiac operations is associated with greater postoperative morbidity (including greater risks of disease transmission, infection, and immunosuppression) [Jamnicki 2003]. ANH during OPCAB is also a beneficial technique in reducing homologous blood transfusion [Treib 1996; Allain 2002]. Infusion of the Hemobag concentrate appears to safely recover substantial amounts of proteins, clotting factors, and cells in all types of cardiac procedures [Banbury 2006]. Since 1960, published reports in the literature have described >300 clinical studies that used ANH in a variety of surgical settings. These studies are characterized by considerable variation in patient-selection procedures, methodologies, and results. Recent metaanalyses of ANH by Bryson et al [Bryson 1998; Jamnicki 2003] and Segal et al [2004] according to strict inclusion criteria concluded that ANH was effective in reducing both the likelihood of exposure to allogenic blood and the volume of blood transfused.

Preoperative values for patient variables were similar for the 2 groups (Table 1). In addition, operative times, the numbers of distal anastomoses, and values for operative bleeding parameters that reflected bleeding during the operation, and operative fluids that consisted only of crystalloids were also statistically similar for the 2 groups (Table 2). We suggest that these parameters may not be responsible for the significant results found.

The 2 groups had significantly different values for inflammation parameters in the ICU. White blood cell counts, sedimentation rates, and CRP concentrations were significantly lower in the AHBT group. We suggest that the reason for increased values for inflammation parameters in the ABT group is the significantly increased use of allogenic transfusion in the ABT group. Although we have stated that ANH decreased postoperative bleeding, as measured by drainage of chest tubes, this finding was not supported by the study of Casati et al [2004] in OPCAB patients. These investigators stated that ANH did not decrease postoperative bleeding. However, their study design did not exclude patients who were on acetylsalicylic acid and/or heparin therapy. Thus, the different results of Casati et al may be attributed to platelet dysfunction or a bleeding diathesis. Furthermore, the autotransfusion reservoirs used by Casati et al may have adversely affected coagulation factors. Another contributing cause to the increased values for inflammation parameters may be the significantly increased chest tube output in the ABT group. Significantly increased fever may have been due to significantly increased values for inflammation parameters in the ABT group due to significantly increased allogenic transfusion. Although not statistically significant, the increased tendency of atrial fibrillation in the ABT group may have been due to increased values of inflammation parameters. Such inflammation mechanisms are considered the leading cause of atrial fibrillation [Aronson 2007].

The contributing findings of our study were improved patient outcomes with significantly decreased extubation times and atelectasis scores in the AHBT group. These 2 parameters may be related to each other, because lower extubation times may be the cause of decreased atelectasis scores. A previous retrospective study by Scott et al [2008] found that the mean time to extubation following surgery was 8.0 hours for the allogenic blood transfusion group and 4.3 hours for the nontransfused group ($P < .001$). In addition, Matot et al [2002] performed ANH in 39 patients who underwent major hepatic surgery and found that ANH allowed the use of allogenic blood to be avoided in a significant number of patients. These investigators concluded that transfusion-related acute lung injury is an important cause of transfusion-associated morbidity, which is probably often misdiagnosed. They also stated that ABT may have impaired postoperative pulmonary function and that any such adverse effect of ABT is probably mediated by the supernatant fluid of stored red blood cells [Matot 2002]. Thus, we suggest that the higher atelectasis scores in the ABT group may have been due to the aforementioned influences.

Our study was the first double-blinded, prospective study to search for the influence of AHBT in OPCAB patients. Our study may have some limitations, however. First, the smaller size of our samples made it difficult to interpret our findings. Second, our findings might have been supported by applications of pulse oximetry and monitoring of arterial blood gases, particularly while assessing atelectasis.

One may also argue that the use of 6% hydroxyethyl starch (molecular weight, 200,000 Da) might have influenced the results of the AHBT group; however, hydroxyethyl starch has adverse effects on the coagulation cascade [Stehling 1991], thrombocytes [Treib 1995], and the inflammatory cascade [Rittoo 2005]; thus, the significantly lower values for these parameters in the AHBT group may not be attributed to hydroxyethyl starch. We suggest that the use of hydroxyethyl starch minimally influenced our results.

In conclusion, autologous blood transfusion in OPCAB may be beneficial for certain cardiac surgery patients; however, these beneficial effects require additional study to be proved. Further studies with larger sample sizes for certain patient populations are needed to gain further insight regarding these issues.

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