Original Article

Effect of Autotransfusion on Fibrinolysis in Open Heart Patients

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ABSTRACT

Autotransfused blood is often used as an alternative to banked blood. The fibrinolytic consequences of autotransfused blood are undefined. This prospective study was designed to determine the effect of intraoperative autotransfused blood on fibrinolysis and other coagulation parameters.

Ten consecutive patients undergoing cardiopulmonary bypass (CPB) for open-heart procedures were studied. All patients received autotransfused blood intraoperatively and tolerated the procedure. Blood samples were taken preoperatively, intraoperatively, and at 6, 12, and 24 hours postoperatively. Coagulation parameters including prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen, fibrin degradation products, and D-dimer levels were measured at each time point. In addition, the quantity of autotransfused blood and additional standard blood products were recorded. Nonparametric repeated measures analyses with post hoc tests adjusted using the Bonferroni correction were used to analyze the data.

Mean PT increased from 13.9 ± 3.0 seconds preoperatively to 15.7 ± 1.6 seconds intraoperatively, but then gradually declined to 14.5 ± 1.1 seconds 24 hours postoperatively. A similar temporal pattern was observed for PTT, which reached a peak of 55.7 ± 33.0 seconds intraoperatively from a preoperative baseline of 44.0 ± 15.3 seconds. Adjusted post hoc comparisons of fibrinogen levels indicated a statistically significant difference between preoperative and 6 hour postoperative medians, (p < .0083). Fibrin degradation products had a modest and nonsignificant decrease over the 24-hour study period, (from 12.6 ± 6.7 mcg/mL preoperatively to 9.0 ± 1.6 mcg/mL 24 hours postoperatively), while D-dimer levels rose from a baseline of 0.54 ± 0.09 mcg/mL to 0.98 ± 0.48 mcg/mL 6 hours postoperatively, but declined nearly to baseline by 24 hours postoperatively, (0.62 ± 0.11 mcg/mL). We conclude that although autotransfused blood may activate the fibrinolytic pathway, its use remains safe and does not require the use of additional banked blood products.

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INTRODUCTION

Approximately 350,000 open-heart procedures are performed annually in the United States (1). Without autotransfusion, about 2.5 units of blood are used per case, totaling 875,000 units of blood in a single year (2). In addition, patients undergoing open-heart surgery not infrequently return to the operating room for bleeding. This magnitude of blood loss results from the requirement of inherent coagulopathies associated with cardiopulmonary bypass (CPB).

In addition to the platelet alterations that occur from contact with the surface of the oxygenator circuit, anesthesia, hemodilution, circulation temperature, and the use of suction devices all contribute to coagulopathy. Because of this propensity for hemorrhage, many cardiac surgery programs use a scavenging system to collect and reinfuse shed mediastinal blood during or after cardiac procedures. However, it remains unclear whether this reinfusion actually causes more postoperative bleeding because of activation of the fibrinolytic system. Consequently, this study addresses two questions: does the use of scavenged autologous blood activate fibrinolysis, and does this activation result in the need for additional blood products?

MATERIALS AND METHODS

Ten consecutive patients undergoing an open-heart procedure requiring CPB were prospectively studied. All patients were extensively questioned preoperatively concerning any bleeding abnormalities or hepatic dysfunction. Preoperative blood testing consisted of a complete blood count (CBC), platelet count, liver function tests (LFTs), prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen, fibrin split products (FSPs), and D-dimer levels. Intraoperatively, after heparinization, all patients were placed on normothermic bypass using a reverse hollow fiber membrane oxygenator. Shed mediastinal blood was collected in a solution containing 50,000 units of heparin per liter of normal saline. The blood then passed through a 120-micron filter into the cell-saving device. The blood was then washed with 1 liter of normal saline and centrifuged at 560 rpm. This packed red blood cell concentrate was then assayed for PT and PTT before passing through a 40-micron filter and into the patient. Prothrombin time, PTT, fibrinogen, FSPs, and D-dimer levels were measured at 6, 12, and 24 h postoperatively. The number of autotransfused units as well as any banked blood products infused during the first postoperative day were also recorded. In addition, the cross-clamp time, the amount of postoperative chest tube drainage, and platelet counts were recorded. This study was approved by the St. Luke’s Hospital Institutional Review Board.

Differences in values over time for partial thromboplastin, prothrombin, fibrinogen, D-dimer, and fibrinogen degradation products were assessed using Friedman tests followed by post hoc analyses using Wilcoxon signed ranks tests. Post hoc alpha levels were adjusted using Bonferroni’s inequality, in order to guard against the increased probability of making a Type 1 error. The Friedman test looks at differences in medians over multiple data collection periods and is analogous to a repeated measure analysis of variance (ANOVA) without a comparison group. The Wilcoxon signed ranks test is a nonparametric alternative to the paired t test and is commonly used in clinical research with small samples.

RESULTS

Eight patients underwent coronary revascularization, including two reoperations, one underwent a mitral valve replacement (MVR), and one patient received an MVR along with revascularization. There were six males and four females in the study group, ranging in age from 55 to 76 years, (mean 66.5 ± 7.3 years). Cross-clamp time ranged from 15 to 114 min, (mean 57.3 ± 27.6 min), and cardiopulmonary bypass time ranged from 35 to 166 min, (mean 92.2 ± 36.2 min). All patients tolerated the operative procedure well. No patient had any preoperative coagulopathy or hepatic dysfunction, nor were any patients taking anticoagulant medications. The mean units of cell saver (1 unit = 250 mL) used intraoperatively was 3.6 ± 0.7. The mean units of packed red blood cells used intraoperatively was 1.0 ± 1.5, and the mean units of blood used postoperatively 0.4 ± 1.0. Nonparametric correlation analysis revealed no statistically significant associations between units of autotransfused blood used and additional blood products used.

Mean international normalized ratio (INR) values were: preoperatively, 1.3 ± 0.07; intraoperatively, 1.7 ± 0.3; 6 h postoperatively, 1.5 ± 0.3; 12 h postoperatively, 1.4 ± 0.2; and 24 h postoperatively, 1.4 ± 0.2. Figure 1 demonstrates that mean PT increased from 13.9 ± 3.0 sec (normal range is 10.9–13.1) preoperatively to 15.7 ± 1.6 sec intraoperatively, but then gradually declined to 14.5 ± 1.1 sec 24 h postoperatively. The over-all difference among medians was statistically significant (p < .01), because of unadjusted differences between median times intraoperatively compared to 6 h (15.0 ± 1.4 sec), 12 h (14.5 ± 0.9 sec), and 24 h postoperatively. Unadjusted post hoc comparisons between these median times were statistically significant at p < .05; however, following the Bonferroni correction, statistical significance was not maintained. A similar but statistically nonsignificant temporal pattern was observed for PTT, which reached a peak of 55.7 ± 33.0 sec (normal range 22–32) intraoperatively from a preoperative baseline of 44.0 ± 15.3 sec and fell below baseline 24 h postoperatively, (33.9 ± 12.1 sec), (Figure 2).

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a Spiral Gold Oxygenator, Baxter Bentley, Irvine, CA 92713
b Cell Saver, Haemonetics, Braintree, MA
As might be expected, mean preoperative fibrinogen levels 538.0 ± 181.2 mg/dl, (normal range 202–430 mg/dl) initially decreased to a mean nadir of 316.9 ± 9.9 mg/dl at 6 h postoperatively and moved back toward the preoperative baseline within 24 h, (490.1 ± 98.8 mg/dl; over-all comparison, \( p < .001 \)), (Figure 3). Adjusted post hoc comparisons indicated a statistically significant difference between preoperative and 6 h postoperative medians, \( p < .0083 \).

Surprisingly, fibrin degradation products only had a modest and nonsignificant decrease over the 24-h study period, from 12.6 ± 6.7 mcg/mL preoperatively to 9.0 ± 1.6 mcg/mL 24 h postoperatively (normal range 0–15 mcg/mL) (Figure 4). D-dimer levels significantly rose from a baseline of 0.54 ± 0.09 mcg/mL to 0.98 ± 0.48 mcg/mL 6 h postoperatively, (normal range > 0.5 mcg/mL) but declined nearly to baseline by 24 h postoperatively (0.62 ± 0.11 mcg/mL), (\( p < .05 \)), (Figure 5). Statistical significance between median D-dimer levels was not observed following adjusted post hoc analyses.

**DISCUSSION**

The use of CPB for open-heart procedures is inherently associated with some degree of bleeding that is unlikely to be completely resolved. Because of the complications associated with blood product replacement, alternatives have been sought. These alternatives include blood substitutes such as Fluosol, modulating the artificial surface of the blood oxygenator and
extracorporeal circuit with bonded heparin, the use of drugs that either provide temporary platelet inhibition or that attenuate the fibrinolytic system [Aprotinin (3), Amicar], and the use of autotransfused blood (4–6).

Today, many cardiac surgery centers use a scavenging system to collect and reinfuse shed mediastinal blood during or after cardiac procedures. Considerable debate exists as to whether this reinfusion causes more postoperative bleeding from activation of the fibrinolytic system (7, 8). This pilot study sought to determine whether the use of scavenged autologous blood activated fibrinolysis requiring the need for additional blood products. In this patient population, the reinfused blood was washed and filtered, thereby eliminating plasma proteins that can cause hemostatic difficulties. Reinfusion of washed mediastinal blood was associated with activation of the fibrinolytic system, as shown by a statistically significant decrease in fibrinogen, (observable even though the sample size was small and following conservative adjustment to protect against a Type 1 error), and an increase, albeit not statistically significant, in D-dimer levels.

While the laboratory analysis demonstrated a coagulopathy, this study also sought to determine if this was a clinically relevant disturbance, as evidenced by excessive bleeding or increased utilization of banked blood products. All patients received between 3 and 5 units of autotransfused blood, and there was no correlation between the number of units trans-
fused and postoperative blood requirements. In addition, chest tube drainage was comparable to patients undergoing CPB without autotransfusion (2). Consequently, although autotransfused blood does not completely ameliorate the need for any blood product replacement, it does provide volume and oxygen-carrying capacity that is crucial during the immediate postoperative period (9). Thus, although limited by a small sample size, this study suggests that autotransfused blood (at least in the quantities given here) is a safe adjunct to banked blood during open-heart procedures.

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REFERENCES