

A Rapid Platelet Function Assay Used to Regulate Platelet Transfusion Prophylaxis Following Cardiopulmonary Bypass Surgery

Kathy E. Shaffer, MT, (ASCP);* David T. Pearman, BS;† Robert S. Galen, MD, MPH;‡
David G.M. Carville, PhD§

*Aultman Blood Center, Canton, Ohio; †Point-of-Care Division, Helena Laboratories, Beaumont, Texas; ‡College of Pharmacy, University of Georgia, Athens, Georgia; §Department of Chemistry, Indiana University South Bend, Indiana

Abstract: Subsequent to cardiac surgery with cardiopulmonary bypass (CPB), patients are at risk of postoperative bleeding caused by acquired defects associated with the procedure. As such, many patients receive prophylactic blood product transfusion. The effectiveness of measuring platelet function using a near-patient platelet function analyzer for the purpose of regulating platelet transfusion and potentially modulating other blood products including fresh frozen plasma (FFP) and cryoprecipitate (CRYO) transfusion was evaluated prospectively in patients undergoing CPB. A 6-month prospective study was designed that encompassed all CPB patients at Aultman Hospital (Canton, OH) during 2001. Each patient was assessed postoperatively for platelet count and function using a point-of-care analyzer. Data were used to help determine whether a platelet

transfusion would be administered. Transfusion of CRYO and FFP was also recorded. The data were then compared to the retrospective same 6-month period in the preceding year for the purpose of determining the value of this system in guiding transfusion triage. There were 1770 platelet packs transfused during the study period, representing a 34% reduction in platelet usage. Platelet transfusions were reduced by 51% (5.75 in 2001 vs. 11.75 in 2000) per patient. CRYO/FFP usage was also substantially reduced. During the study period, the patient caseload had increased by 72 (310 vs. 238). Monitoring platelet count and function as a result of CPB and administering an appropriate transfusion protocol can positively impact transfusion outcome. **Key-words:** cardiopulmonary bypass, platelet function, transfusion triage. *JECT. 2004;36:145-148*

The concept of blood conservation in cardiac surgery is not new and is continually under scrutiny (1,2). Indeed, there is considerable scientific and clinical literature reporting a reduction in institutional expenditures because of rising blood costs via conservation (1-5). Increasing availability issues, which are further exacerbated by the need for cross-matched and leukocyte-reduced products, fuels this frugality. The primary goal of healthcare providers is to offer better patient care by reducing risks of exposure and preventing hypervolemia in both cardiac and other surgeries (1,2,5). According to the Bacterial Contamination (BaCon) of blood products study conducted by the American Association of Blood Banks (AABB), the American Red Cross (ARC), the Centers for Disease Control and Prevention (CDC), and the Department of Defense (DOD), it has been estimated that the bacterial contamination rate of platelet packs is approximately 10%

(6). With these underlying concerns, the ultimate goal for the regulatory bodies and healthcare providers should be to establish a transfusion algorithm, elucidating the underlying etiology for platelet-derived bleeding (6). However, an understanding of all the contributing factors coupled with a reliable, robust, user-friendly platelet function assay remain unmet clinical needs.

Open-heart surgery activates platelets and elicits a decrease in platelet number and function with a potential increase in postoperative bleeding. The magnitude of thrombocytopenia and platelet dysfunction is variable both among perfusion systems and patients and is a major cause of hemorrhage (7). Upon initiating CPB, generation of thrombin potentially activates platelets resulting in some of the circulating discoid platelets to become activated, express glycoprotein IIb/IIIa receptor complexes, aggregate, adhere to surface-adsorbed fibrinogen, and release the contents of their dense granules. As CPB continues, other factors, including activated complement (C5b-9), plasmin, hypothermia, platelet-activating factor (PAF), cathepsin G, serotonin, epinephrine, play a significant role in activating platelets and contribute to their loss and dysfunction (8). Unfortunately, traditional methods

This work was completed at Aultman Blood Center, Canton, Ohio. Address correspondence to: David G.M. Carville, PhD, Department of Chemistry, Indiana University, South Bend (NS067), 1700 Mishawaka Avenue, South Bend, IN 46634. E-mail: dcarvill@iusb.edu

for evaluating platelet count and function (platelet-rich plasma (PRP) aggregometry and cell counting platforms) do not lend themselves well to the acute setting of cardiac surgery and, as such, platelets are transfused following National Institutes of Health (NIH) guidelines, which include a platelet count of $<50 \times 10^3/\mu\text{L}$ or $<100 \times 10^3/\mu\text{L}$ with concomitant microvascular bleeding (9). Moreover, other tests that have demonstrated clinical utility in the assessment of the coagulation profile require specialized equipment and training and are, in some cases, laborious. These include fibrin and d-Dimer enzyme-linked immunosorbent assays (ELISA), flow cytometry, and the thromboelastograph (TEG).

The purpose of the current study was to determine whether the use of a point-of-care platelet analyzer (Plateletworks[®], Helena Laboratories POC, Beaumont, TX) to evaluate platelet function and count, as part of a complete blood count (CBC), in postoperative CPB patients would enhance transfusion triage.

DESCRIPTION

Plateletworks[®] Background

The *in vitro* diagnostic platelet function assay, Plateletworks[®] (PW), has been described in detail elsewhere (10,11). In brief, this system uses an impedance-based type cell counter (hematology analyzer). The patented technology comprises hematology type tubes; one of which is a K₃ EDTA tube for a baseline platelet count, and the other, containing an agonist such as ADP or other typical platelet agonists. Each sample is then passed through the cell counter and the platelet count is determined. In the agonist tube, the functional platelets aggregate. As the aggregated platelets exceed the threshold limitations for platelet size and/or the platelet clumps are left at the lowest portion of the tube beyond reach for aspiration, they are no longer counted as individual platelets (i.e., the non-functional platelets are those that are counted). By calculating the difference between the baseline tube and the agonist tube, the number of functional platelets is determined. This number can, therefore, be used for transfusion decision. The ratio of the platelet count between the agonist tube and baseline tube can also be calculated as percentage platelet aggregation. Results are available within 4 minutes. The PW test system has been shown to be substantially equivalent to the current gold standard of platelet function testing (i.e., PRP aggregometry) (10).

Quality control testing of hematology analyzers used to perform the PW assay should be completed during each shift the instrument is used to ensure the instrument is functioning properly. Tri-level control material and calibrators are available from the manufacturer. It is recommended that each laboratory establish its own normal range.

Patients and Study Protocols

The institutional review board from Aultman Blood Center approved the protocol, and written informed consent was obtained from each subject before enrollment. During this study, conducted between 08/01 to 01/02, a total of 310 CPB cases were performed. Postoperatively, patients were evaluated for platelet count and function using PW. Here samples were drawn from an arterial line, using a two-syringe technique; the extracorporeal blood access line was flushed by withdrawing 2.0 mL of blood into a syringe and discarding. Then a second syringe was used to obtain a 2.5 mL sample of fresh whole blood for testing (1.0 mL each for the baseline and agonist tube).

The protocol for platelet transfusion was based upon the AABB/WHO guidelines (i.e., a platelet count $<50 \times 10^3/\mu\text{L}$ or $<100 \times 10^3/\mu\text{L}$ in the presence of microvascular bleeding guided the decision to transfuse platelets). In addition, the decision to transfuse FFP or CRYO was based on observational bleeding and/or the platelet function result. Specifically, if platelet function (as per the quantitative PW test) was in an acceptable range and bleeding persisted, FFP/CRYO were transfused. The number of platelets transfused was recorded per patient. All apheresis platelets that were transfused were counted as seven random donor platelet (RDP) packs. In the absence of bleeding, no products were transfused. Beside administration of transfusion products, no other parameters were altered between the study group and the retrospective comparative group implemented under the guidelines of the institutional policies in place.

RESULTS

As indicated, in conjunction with platelet function testing, transfusion data were collected between 08/01 and 01/02 and were compared directly to that period from the previous year. During the study period, 72 additional CPB cases were performed for a total of 310. In this patient group, a total of 1770 platelet packs were transfused. This was compared to the retrospective time period where 2676 platelet packs were used, for a savings of 906 platelet transfusions. These data are represented as a line chart in Figure 1. A reduction of platelet transfusions per patient was also realized. The units of platelets transfused per patient fell from 11.75 in 2000 to 5.75 in 2001. The individual monthly comparisons are shown in Figure 2. FFP and CRYO usage was reduced by greater than 80% in the study period, which is represented in the line chart in Figure 3.

DISCUSSION

CPB induces mechanical and physiological effects on platelet count and function that may contribute to signifi-

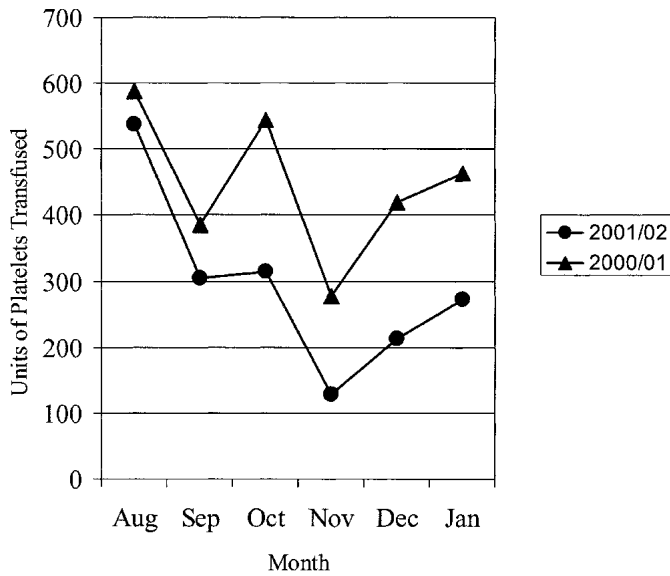


Figure 1. A comparison of prospective and retrospective platelet transfusion data. Each apheresis unit is converted to seven random donor units. Total PLT savings were 906 for a +72 increase in caseload. The data are compared on a monthly basis.

cant (and clinically relevant) postoperative bleeding. This may result in significant morbidity and mortality without the appropriate intervention. On the contrary, some patients will experience a suitable level of recovery because of several physiological mechanisms, including release of sequestered platelets from the spleen and rejuvenation of physiological agonists (12).

One of the major concerns during CPB is with regard to transfusion triage. Indeed, the National Institutes for

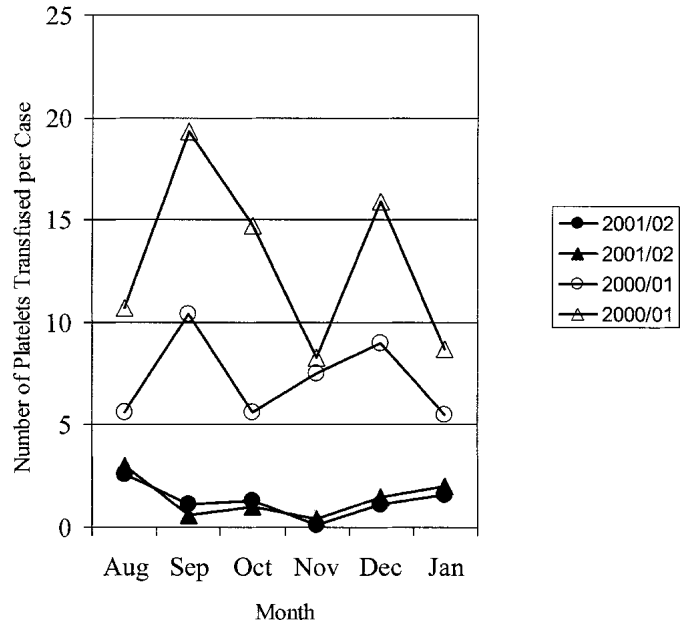


Figure 3. FFP (circles) and CRYO (triangles) transfused per case. Monthly comparative data as retrieved from blood bank records. Total savings were 82% for FFP and 88% for CRYO.

Health (NIH) and the AABB have published several Consensus Conference Statements regarding the appropriate transfusion regimen for platelets, red blood cells, and FFP (13). These recommendations have resulted in a trend to reduce the use of transfusion products that are recognized as posing an unnecessary risk to patients who do not require them (10,13).

Another concern is that transfusion practices are quite variable (ranging from 0–100% of procedures) and are dependent on the institution. Recently, benefit versus risk analyses have been undertaken to determine the need for adequate tissue oxygenation and coagulation versus adverse reactions associated with transfusion, including transmission of disease. Still other analyses have been performed to determine the cost versus benefit of transfusion practices, which have highlighted the significant expense associated with transfusion, which further compels a re-evaluation of transfusion practices (14).

CONCLUSION

In the current study, a total of 310 CPB procedures were performed at Aultman Hospital. This was an increase of 72 cases (25%) when compared with the retrospective time period. In this prospective study, all patients had platelet count and function evaluated using PW, in addition to a central laboratory CBC, performed perioperatively. During the course of the study, a total reduction in 906 platelet transfusions was observed, with a reduction of platelets transfused per patient of greater than 50%.

Unfortunately, although traditional laboratory tests

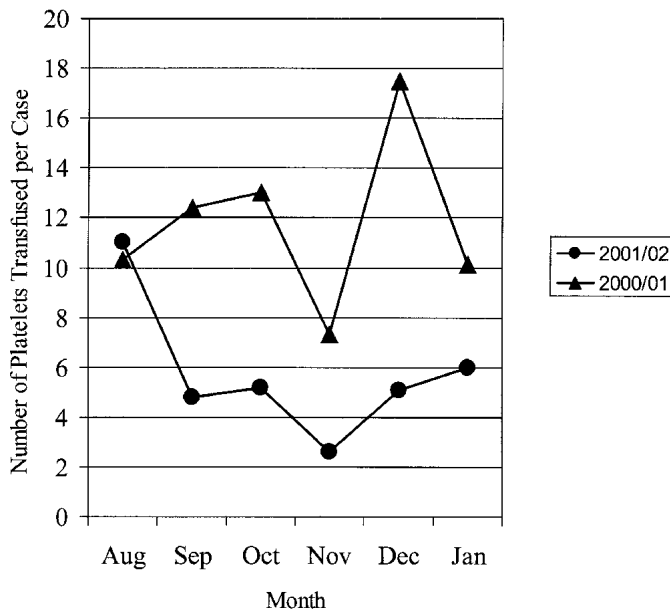


Figure 2. Number of PLT transfusions per case as illustrated on a monthly basis. Total savings were 50.9%.

permit a rational approach to the management of periprocedural coagulation disorders during CPB, methods are laborious, require highly trained personnel, and turn-around times are long (10). Such reporting from central settings may result in inappropriate therapy; hence, the recent development of near-patient, user-friendly, rapid systems permits more accurate and timelier intervention. Studies have been conducted to evaluate the impact of near-patient coagulation systems on blood product usage, operation time, and the intraoperative management of microvascular bleeding (10,11). It was demonstrated that those patients managed "bedside" received significantly fewer blood products, including platelets, and also had significantly less adverse chest drainage as compared with those patients randomized to standard therapy.

The original goal of instituting this assay at Aultman Hospital was to improve patient care by either reducing the amount of transfusions or to establish a rationale for justification of transfusions. It was serendipitous that there were such substantial savings in platelet usage. The study also supports the recent findings that establishing a transfusion protocol or transfusion algorithm is the penultimate tool for successful transfusion triage. PW is a platform that requires a synergistic effort between the OR, the laboratory, and blood bank if it is to be effective. Not only is it imperative to operate expeditiously because of assay constraints (under 20 min), but results must also be rapidly available to decision makers to make transfusion decisions. When used appropriately, the PW assay has the potential to contribute substantially in improving patient care.

ACKNOWLEDGMENTS

This study was funded by Aultman Hospital. The authors ac-

knowledge support from patients and staff at Aultman Hospital for successful completion of this study.

REFERENCES

1. Walenga JM, Pifarre R. Blood preservation in cardiac surgery at Loyola Medical Center. In: Anticoagulation, Hemostasis, and Blood Preservation in Cardiovascular Surgery. Piffare R, ed. Philadelphia: Hanley and Belfus; 1993:77-84.
2. De Ritis S. Transfusion medicine: A state of constant change. *ADVANCE Med Lab Profs*. June, 2002;3:22-4.
3. Shore-Lesserson L, Manspeizer HE, DePerio M, Francis S, Vela-Cantos F, Ergin MA. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg*. 1999;88:312-9.
4. Speiss BD, Gillies BSA, Chandler W, Verrier E. Changes in transfusion therapy and reexploration rate after institution of a blood management program in cardiac surgical patients. *J Cardio Vasc Anesth*. 1995;9:168-73.
5. Borghi B, Stagni F, Bacchilega I. Blood salvage techniques to avoid homologous blood transfusion in orthopaedic surgery. *Intern Med*. 2001;9:30-5.
6. Kuehnert MJ, Roth VR, Haley NR, et al. Transfusion-transmitted bacterial infection in the United States, 1998 through 2000. *Transfusion*. 2001;41:1493-9.
7. Ellison N, Edmunds LH, Colman RW. Platelet aggregation following heparin and protamine administration. *Anesthesiology*. 1978;48:65.
8. Gluszko P, Rucinski B, Musial J, et al. Fibrinogen receptors in platelet adhesion to surfaces of the extracorporeal circuit. *Am J Physiol*. 1987;252:H615.
9. National Institutes of Health Consensus Conference. Platelet transfusion therapy. *JAMA*. 1987;257:1777-80.
10. Lau WC, Walker CT, Ogilby D, et al. Evaluation of a near patient platelet function assay— Performance and clinical utility. *Ann Cardiac Anaesth*. 2002;5:33-42.
11. Carville DG, Schleckser PA, Guyer KE, Corsello MF, Walsh MM. Whole blood platelet function assay on the ICHOR point of care hematology analyzer. *J Extra Corpor Technol*. 1998;30:171-6.
12. Tabuchi N, de Haan J, van Oeveren W. Rapid recovery of platelet function after cardiopulmonary bypass. *Blood*. 1993;82:29-30.
13. Goodnough LT, Johnson MFM, Ramsey G, et al. Guidelines for transfusion support in patients undergoing coronary artery bypass grafting. *Ann Thorac Surg*. 1990;50:675-83.
14. Gan TJ, Lubarsky D, Robertson K, et al. The hospital cost of perioperative transfusion of a unit of red blood cells and other blood products. *Anesth Analg*. 1996;82:S123.