Large-scale use of red blood cell units containing alloantibodies

M.R. COMBS, D.H. BENNETT, AND M.J. TELEN

Many transfusion services are reluctant to accept red blood cell (RBC) units containing antibodies. We evaluated the impact of accepting routine shipments of our region's inventory of alloantibody-positive RBC units over a 4-month period. All patients' samples received up to 30 days after transfusion of such units were evaluated for the presence of passively acquired antibody, and labor and reagent costs were determined. During the study period, we received 259 alloantibody-containing RBC units, and 253 of these were transfused to 187 patients. Follow-up samples were received on 99 of these187 patients, and 10 of these patients had detectable passive antibody in posttransfusion antibody screening tests. Two patients had anti-C and -D and eight patients had anti-D. Due to our negotiation of a small discount for antibody-containing units and the use of 20 units based on labeled phenotype rather than antigen typing in our laboratory, we experienced a net savings of $3814 over the 4-month period. This savings was achieved despite some additional costs incurred, including costs of data entry and additional testing on patients' samples. We concluded that large-scale use of RBC units from donors with alloantibodies is safe and likely to have a minimal impact on a busy transfusion service's workload and costs. Furthermore, nationwide use of such units would help alleviate projected blood shortages. ***Immunohematology* 2000;16:120–123.**

Key Words: red blood cells (RBCs), passively acquired alloantibodies, cost-saving, antigen phenotyping

Reports have estimated that as many as 24,000 red blood cell (RBC) units from donors with unexpected alloantibodies are discarded annually in the United States. However, almost half of these units can be expected not to have detectable antibody in the final RBC product.[1] A major cause of this wastage is the reluctance of many transfusion services to accept RBC units containing alloantibodies. This unwillingness has several potential causes, including concerns that the detection of passive antibody in posttransfusion samples will lead to additional testing, such as antibody identification panels, phenotyping of RBC units, and antiglobulin-phase crossmatches, if passively acquired antibody were found in a posttransfusion sample. Another concern is the possibility of minor incompatibility and consequent hemolysis if the patient's RBCs are positive for an antigen against which a passively acquired antibody is directed. As a result, some institutions will only transfuse antibody-positive units if they are washed free of the antibody-containing plasma, or if the patient's RBC's are known to lack the antigen to which the antibody is directed. These limitations result in the performance of additional pretransfusion testing and handling by the blood center or transfusion service. Thus, it is often difficult for blood centers to find transfusion services willing to use products containing alloantibodies, and many antibody-positive units expire before being used.

Because we are a large transfusion service that issues more than 40,000 RBC units per year, we hypothesized that our ability to use antibody-positive units could contribute substantially to the efficient use of blood products in our region. We further reasoned that, due to the low plasma volumes in these packed RBC units, detection of passively acquired antibody and minor incompatibility would be rare. Finally, we felt that any additional testing involved could be incorporated easily into our already large testing volume. Therefore, we set up an agreement with our sole blood supplier, the Carolinas Region American Red Cross, to receive all of their otherwise acceptable RBC units containing alloantibodies. We then evaluated the impact of accepting these units over a 4-month period.

Methods

During the study period, antibody-positive units were shipped weekly at a discounted price $14 less per unit than our standard price. Antibody-positive units were handled as routine inventory, except that we recorded the identities of the recipients of all antibody-containing units for the purposes of this study. For 30 days following receipt of these units, we recorded and analyzed the results of all posttransfusion type and screen samples from patients who had received antibody-positive units, in order to identify the frequency of detectable passively acquired antibody. Direct antiglobulin tests were not routinely performed on these posttransfusion samples, consistent with our routine procedures. No blood samples were requested or drawn specifically for this study. Posttransfusion samples were only received when the physicians providing care to the patients felt that further transfusion might be needed. In addition, labor and supply costs incurred due to the use of antibody-containing

units and subsequent additional testing necessitated by presence of passively acquired antibody were determined.

Results

Transfusion of antibody-positive RBC units.

We received 259 RBC units containing a total of 312 alloantibodies; of these, 233 (90%) contained potentially clinically significant antibodies. As shown in Table 1, more than half of these antibodies were anti-D or anti-K. These proportions are consistent with a survey of 1000 antibody-positive units from our region performed during a 1-year period (Rebecca Bullock, Carolinas Regions Red Cross, personal communication). Of the 259 antibody-positive units received, 253 were transfused to 187 patients. Of the six units not transfused, two were mishandled by the patient care unit and four units expired without being dispensed from the transfusion service. The four expired units included three group A, D– with anti-D and one group B, D– with anti-D.

Table 1. Specificities of antibodies contained in RBC units received

Antibody Specificity	Number (%)
D	101 (39)
K	67 (26)
C	38 (15)
E	37 (14)
Fy^a	16 (6)
c	13 (5)
Le^a	13 (5)
M	10 (4)
Le^b	6 (2)
S	5 (2)
Jk^a	4 (2)
Kp^a	1 (<1)
Js^a	1 (<1)

Posttransfusion testing and detection of passively acquired antibodies

Posttransfusion samples were received from 99 (53%) of the 187 patients who had received antibody-positive units. Ten patients (10% of those for whom posttransfusion samples were received) had detectable passively acquired antibody in posttransfusion samples. Of these 10 patients, six had each received one antibody-positive unit, three had each received two antibody-positive units, and one patient had received four antibody-positive units. Thirteen posttransfusion samples received from these 10 patients had positive antibody screens using polyethylene glycol (PEG), which is our standard antibody detection method (Table 2). Two patients had passively acquired anti-C and -D and eight patients had passively acquired anti-D. All 10 patients were D–. No hemolytic transfusion reactions were reported in any patients receiving antibody-positive units during this period. In addition, no autocontrols were positive in the posttransfusion samples for which antibody panels were performed. During the 4-month study period, 34 transfusion reactions were reported to the Transfusion Service. Four of these were in patients that had received antibody-positive units, but none were in patients (listed in Table 2) who had passively acquired antibody detected at any time. The four reported transfusion reactions in the 187 patients who had received antibody-positive units were evaluated as being febrile (two patients), allergic (one patient), and a reaction consisting of transient hypotension with no apparent cause (one patient).

Table 2. Posttransfusion samples containing passively acquired alloantibodies

Patient	Date (number of RBCs received)	Posttransfusion sample dates	Presence of passively acquired antibody
1	1/15/98 (1)	1/18/98	Positive
2	1/28/98 (1)	2/12/98	Positive
		2/17/98	Positive
		3/9/98	Negative
3	2/2/98 (1)	2/8/98	Positive
		2/20/98	Positive
4	2/17/98 (1)	2/18/98	Positive
		2/25/98	Negative
		3/5/98	Negative
5	2/24/98 (1)	2/28/98	Positive
6	3/11/98 (2)	3/25/98	Positive
		3/29/98	Positive
7	3/12/98 (1)	3/16/98	Positive
		4/1/98	Negative
8	3/24–26/98 (3)	3/27/98	Positive
		4/4/98	Negative
		4/7/98	Negative
	4/8/98 (1)	4/11/98	Negative
9	4/16–17/98 (2)	4/20/98	Positive
10	4/19/98 (1)	5/16/98	Positive

Additional testing resulting from detection of passively acquired antibody included 10 antibody identification panels, two antigen typing tests, and 30 antiglobulin-phase crossmatches. The number of additional antibody identification panels was relatively limited due to our longstanding policy of not performing panels on samples with previously identified antibodies as long as there is no indication in the three-cell antibody screen or crossmatch that a new antibody is present.

Costs incurred and overall financial impact

To determine the financial impact of accepting antibody-positive RBC units, we calculated labor as well as supply costs (Table 3). The 259 units were received at a discount of $14 per unit, for a total savings of $3626.

Table 3. Financial impact of accepting 259 antibody-positive RBC units

Savings	
Discount from supplier	$3626.00
Antigen typings not required	$488.00
Total	$4114.00
Costs	
Data Entry	$73.00
Antibody identification	$114.50
Antigen typing	$25.80
Antiglobulin crossmatches	$86.40
Total	$299.70
Net Savings	$ 3814.30

Additional savings of $488 were due to the use of 20 units for patients with known alloantibodies; the labeled antigen-negative phenotype for these units obviated the need to perform antigen typing in our laboratory. By accepting antibody-positive units with determined RBC phenotypes, we were able to use these 20 units for 16 patients with anti-K, -E, -C, -c, -Jk^a, and -Fy^a. We calculated the savings achieved based on the frequency of the antigen and the number of units and controls necessary to find the required antigen-negative units. We based our calculations on a cost of $9.81 for antigen typing tests using the indirect antiglobulin test and $6.45 for direct agglutination tests. We were also able to use six units containing anti-D for four patients with anti-D. Even though this did not provide savings in terms of phenotyping—as with phenotyped units for patients alloimmunized against other antigens—we were able to use these units without concern for additional testing due to detection of passively acquired antibody.

Additional costs incurred by the use of antibody-positive units included $73 for data entry. This cost was based on one additional minute of technologist time per unit at an average rate of technologist pay of $16.28 per hour. Labor and supply costs for the additional antibody identification panels, antigen typings, and antiglobulin crossmatches for those patients with detectable passively acquired antibody was $227 (10 antibody panels at a total cost of $114.50, two antigen typings at a total cost of $25.80, and 30 antiglobulin crossmatches at a total cost of $86.40.)

Discussion

Over the 4-month evaluation period, we had a net savings of $3814 through the use of 253 antibody-positive RBC units. Without a discounted price for these units, however, our net savings only would have been $188. Moreover, our net savings may actually be less due to the expiration of four of the antibody-positive RBC units provided by the Red Cross. The antibody-positive units had a 1.5 percent attrition rate (4/259), slightly higher than our overall attrition rate for all products of 1 percent. It is difficult to determine if the presence of alloantibody was a factor in red cell wastage. Because all of the expired units contained anti-D and were non-group O, they were more difficult to assign to patients and may not have been selected for D+ recipients by technologists who were fearful of minor incompatibility. However, our net savings also may be underestimated, because additional testing related to the detection of passive antibody was charged to the patient. The budgetary impact of costs passed on to the patient is difficult to determine, as collected revenues may differ substantially from charges billed. Furthermore, in a managed care or capitated environment, the hospital and transfusion service may not receive compensation for such additional costs. Primary savings may be realized through the negotiation of a discounted price for the antibody-positive units as well as through the use of labeled phenotype information on antibody-positive units to select RBCs for alloimmunized patients.

We concluded that the large-scale use of RBC units containing alloantibody is a safe practice that had minimal impact on the workload of our busy transfusion service. First, the receipt of posttransfusion samples containing passively acquired antibody occurred in less than 6 percent of the patients transfused with units containing alloantibody, as only 10 percent of those patients with posttransfusion samples had detectable antibody. Second, as indicated previously, more than half of the antibodies found in these units were anti-D or anti-K. When these antibodies are detectable in a posttransfusion sample, they are easily identified, and units that lack the antigen can be found easily. Because most units containing anti-D will be transfused to D– recipients and the frequency of the K antigen is only 9 percent, these antibody specificities rarely would be involved in minor incompatibility. Antibodies of other specificities (such as anti-C, -E, and -Fy^a) would more likely result in minor incompatibility based on antigen frequencies; however, the generally low titer of these antibodies and the small plasma volume remaining in RBC units made significant reactions due to passively acquired antibody unlikely. Furthermore, there is not a convincing report of non-ABO antibodies passively acquired from RBC units causing significant hemolysis of a recipient's antigen-positive RBCs; but interdonor incompatibility leading to limited hemolysis has been reported.[2–5] Because antibody screens are performed on all samples and antiglobulin crossmatches are performed if antibody is present, there

is a theoretical risk of interdonor incompatibility only if administration of an antigen-positive unit follows administration of an antibody-positive unit before the next sample is obtained.

Most important, the routine use of antibody-positive units should help reduce the number that are discarded rather than transfused. Given the prediction that our blood supply may fail to meet our needs in the coming years as demand continues to outpace donations, a strategy for using antibody-positive RBC units should be useful in maximizing use of this limited resource.

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Martha R. Combs, BS, MT(ASCP)SBB, Transfusion Service, Duke University Medical Center, Durham, NC; Donald H. Bennett, BS, MT(ASCP), Transfusion Service, Duke University Medical Center, Durham, NC; and Marilyn J. Telen, MD (corresponding author), Professor of Medicine, Duke University Medical Center, DUMC 2615, Durham, NC 27710.

BOOK REVIEW

Current Issues in Platelet Transfusion Therapy and Platelet Alloimmunity. Thomas S. Kickler, MD, and Jay H. Herman, MD, eds. Bethesda, MD: American Association of Blood Banks (AABB) Press, 1999. 306 pp. Domestic: member $99, nonmember $119. International: member $139, nonmember $159. ISBN: 1-56 395-105-3. To order: e-mail: sales@aabb.org or fax: (301) 951-7150.

It is hard to believe that, not so long ago, controversies regarding platelet transfusion therapy centered around issues such as the relative merits of platelet transfusions in patients undergoing splenectomy for idiopathic thrombocytopenic purpura or the practice of empiric platelet therapy in trauma patients receiving massive red cell transfusions. The areas of discussion have changed such that we currently debate the very content of platelet products (e.g., platelet dosage and leukoreduction) but the issues are no less contentious. So this textbook on current issues in platelet transfusion therapy is a welcome addition to sources of information to guide clinical therapy and laboratory practice. The authors are an esteemed roster of experts in platelet transfusion who have done a very good job of providing the reader with an up-to-date bibliography in this rapidly evolving field.

Because the book focuses on "current issues," controversies on any given topic often require some depth of discussion along with summaries of the authors' opinions. This is done particularly well in the chapter critiquing the clinical trials to prevent alloimmunization to platelets. The published data are summarized in an approachable, helpful manner that show the reader how the thought processes have evolved along with the data. Through clear exposition and, in one chapter, useful case examples, the reader quickly progresses through the wide variety of issues that now confront anyone attempting to decide what type of platelet component to transfuse to which patient on what indication. In other areas, however, additional pages devoted to further exploration of topics might have provided not only a good introduction but a thorough review of key fields. For example, lack of discussion of the problem of hypotension associated with kinin activation by bedside leukoreduction filters in patients taking angiotensin-converting enzyme inhibitors is an important omission of an admittedly rare phenomenon. The text's brief discussion of platelet transfusion indications do not explore some areas of controversy thoroughly, such as platelet transfusion in cardiac surgery, nor provide the reader insight into how clinical practices have come to be so varied.