Quality control of red cell filtration at the patient's bedside

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Background: Concern has been raised about the quality of white cell (WBC) reduction in blood components when it is performed by filtration at the patient's bedside. Thus, the quality of red cell (RBC) filtration performed at the bedside through two new flatbed WBC-reduction filters was evaluated.

Study Design and Methods: In the laboratory, 25 and 10 RBC units suspended in additive solution were stored for 1 to 2 and 14 to 21 days, respectively, and filtered through each filter. At the end of filtration, an automated complete blood count and a manual WBC count (Nageotte chamber) were determined in two samples collected from 1) a segment clamped at 5 and 25 cm below the filter along the line connecting prefiltration and postfiltration bags and 2) the postfiltration bag. In addition, 10 of the 11 nurses of the hematology outpatient clinic administered to hematologic patients 25 RBC units stored for 1 to 2 days through each type of filter. At the end of transfusion, a segment was collected from the transfusion set and a WBC count was performed as described above. No filter priming or rinsing with saline was done.

Results: WBC counts obtained after laboratory filtration in the segments were similar to those obtained from the postfiltration bags and from the segments collected at the bedside in all cases, with the exception of 14- to 21-day-old RBCs filtered in the laboratory through one of the filters, which produced slightly higher WBC counts in the segments than were seen in the postfiltration bags. The difference was not significant. In no case was the count in the postfiltration bag higher than that in the segment. Nurse training was easy, and bedside filtration was associated with no untoward effects.

Conclusion: The RBC filtration at the patient's bedside can be equal in quality to that performed in the laboratory, at least in such clinical settings as hematology and oncology departments in which blood transfusion is common practice, and if simple training is provided to the nursing staff. Under the conditions of this study, it seems that quality control of RBC bedside filtration is feasible and simple. TRANSFUSION 1994;34:26-30.

Abbreviations: NHFTR = nonhemolytic febrile transfusion reactions; RBC(s) = red cell(s); WBC(s) = white cell(s).

Established indications for the use of white cell (WBC)-reduced blood components include the prevention of recurrent nonhemolytic febrile transfusion reactions (NHFTR) in recipients of red cells (RBCs) and the prevention or delay of alloimmunization to WBC antigens in selected patients who are candidates for transfusion on a long-term basis.1 Other indications currently under review include the prevention of the transmission of cytomegalovirus to seronegative transfusion recipients and the prevention of the platelet refractory state.1 Technology involved in WBC reduction in RBCs and platelet concentrates can significantly increase the workload in the blood transfusion center if the WBCs are removed by filtration procedures carried out in the laboratory. A possible alternative consists of performing filtration at the patient's bedside. Advantages of the bedside approach include, in addition to decreased workload in the laboratory, no delay in the provision of WBC-reduced blood components that may be necessary outside the usual working hours and no blood wastage if the transfusion of units prepared with open systems is delayed or cancelled.2 These advantages induced us to use bedside filters since 1985, when we developed the spin-cool-filter technique.3 This technique was successfully used in combination with a microaggregate filter (SQ40S, Pall, Glen Cove, NY) to prevent NHFTR in a group of approximately 80 thalassemic patients who received multiple transfusions at our hospital.4 More recently, flatbed polyester filters suitable for use both in the laboratory and at the patient's bedside became available. These filters do not require prefiltration unit centrifugation and cooling, as the spin-cool-filter technique does. We thus adopted these new filters because of their increased effectiveness and ease of use. Since 1990, WBC-reduced RBCs are routinely obtained in our hospi-
tial by filtration performed at the bedside with flatbed polyester filters.6

Recently, concern has been expressed about the quality of bedside filtration. In particular, the possibility has been raised that filtration protocol violations could be more frequent in a clinical setting than in the laboratory, which would result in unpredictable WBC removal at the patient’s bedside. This is probably not so critical for the prevention of NHFTR, where the threshold of WBCs capable of evoking NHFTR (100-200 x 10^6/ transfusion) is well above WBC residuals attained with modern filters (<5 x 10^6/unit). However, this could be relevant, for example, for the prevention of cytomegalovirus transmission, which seems to depend on a critical residual dose of 5 to 10 x 10^6 WBCs.6-10

We thus performed a study aimed at comparing the quality of filtration through the latest generation of flatbed polyester filters in the laboratory and in the clinical setting of our hematology department.

Materials and Methods

We determined the WBC counts in samples collected from 1) the filtered units processed in the laboratory; 2) a segment along the tubing connecting the prefiltration and postfiltration units processed in the laboratory; and 3) a segment along the transfusion set of units filtered at the patient’s bedside. We used two recently developed filters (RC400, Pall Corp.; and BioR-01-Plus, Biofil, Medolla, Italy) for WBC reduction in RBCs. We followed manufacturers’ instructions and performed filtrations by gravity, without applying additional pressure to the bags. We used the Wilcoxon two-sample test statistic to compare WBC counts.11

Laboratory protocol

We collected 450 ± 45 mL of blood in a multiple blood bag, with 63 mL of CPD in the primary bag and 100 mL of saline-adenine-glucose-mannitol as an RBC additive solution in a satellite bag. We centrifuged the unit within 2 hours of collection at 5000 x g for 5 minutes and transferred plasma to a satellite bag. We did not remove the buffy coat. We added 100 mL of the saline-adenine-glucose-mannitol additive solution to the RBCs and stored the unit at 4°C. Twenty-five RBC units stored for 1 to 2 days and 10 units stored for 14 to 21 days were evaluated with each filter. Immediately before filtration, we carefully resuspended the unit by agitation on a platelet reciprocator for 15 minutes, determined the net weight of the RBCs, and performed a complete blood count with an automated counter. All laboratory filtrations were started within 20 to 30 minutes of the unit’s removal from the refrigerator. We then filtered the unit without priming or rinsing the filter with saline. The RC400 and BioR-01-Plus filters were primed with RBCs by squeezing of the bag and by spontaneous gravity, respectively. We did not modify the maximum spontaneous flow obtained under gravity during filtration. We did not vent the filters at the end of the procedure. At the end of filtration, we clamped the tubing connecting the filter to the postfiltration bag at 5 and 25 cm below the filter and collected this segment (Sample A). We determined the net weight of filtered RBCs and collected a sample from the postfiltration bag (Sample B). Finally, we performed a complete blood count with an automated counter and a WBC count with a Nageotte chamber equipped with a 50-µL grid (Brightline, Paul Marienfeld, Bad Mergentheim, Germany) in Samples A and B after a 1-in-10 dilution with Türk’s solution.12 The total number of WBCs per filtered unit was obtained by multiplying the number of WBCs per µL obtained in filtered RBCs times the volume of the postfiltration unit. In this calculation, both the WBC counts determined in Samples A and B were used. Residual platelets were not counted in the filtered units because of a lack of sensitivity and accuracy of counting methods. The RBC yield was determined by the ratio of postfiltration-to-prefiltration total unit hemoglobin.

Bedside protocol

We discussed the bedside filtration procedure with the 11 nurses in the hematology clinical department. Of them, 10 carried out bedside filtrations. We prepared and stored RBC units to be filtered at the bedside as described above, except that the 15-minute resuspension of the RBC units was not done.

Table 1. Prefiltration data* on RBC units filtered in the laboratory and at the patient’s bedside through RC400 and BioR-01-Plus

<table>
<thead>
<tr>
<th>Filters</th>
<th>RC400</th>
<th>BioR-01-Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory filtration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1- to 2-day-old RBCs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unit volume (mL)</td>
<td>314 (259-351)</td>
<td>305 (266-404)</td>
</tr>
<tr>
<td>Unit hematocrit (%)</td>
<td>57 (52-61)</td>
<td>57 (50-66)</td>
</tr>
<tr>
<td>Total number of WBCs (x 10^6/unit)</td>
<td>2420 (1015-4597)</td>
<td>2442 (1584-4703)</td>
</tr>
<tr>
<td>Total number of platelets (x 10^6/unit)</td>
<td>60 (41-117)</td>
<td>69 (27-115)</td>
</tr>
<tr>
<td>14- to 21-day-old RBCs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unit volume (mL)</td>
<td>324 (285-350)</td>
<td>313 (290-349)</td>
</tr>
<tr>
<td>Unit hematocrit (%)</td>
<td>62 (57-77)</td>
<td>61 (59-64)</td>
</tr>
<tr>
<td>Total number of WBCs (x 10^6/unit)</td>
<td>522 (247-1512)</td>
<td>495 (117-1426)</td>
</tr>
<tr>
<td>Total number of platelets (x 10^6/unit)</td>
<td>48 (30-81)</td>
<td>35 (18-76)</td>
</tr>
<tr>
<td>Bedside filtration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unit volume (mL)</td>
<td>313 (269-348)</td>
<td>326 (286-338)</td>
</tr>
<tr>
<td>Unit hematocrit (%)</td>
<td>57 (52-61)</td>
<td>58 (55-62)</td>
</tr>
<tr>
<td>Total number of WBCs (x 10^6/unit)</td>
<td>2728 (1147-4281)</td>
<td>2880 (1839-3934)</td>
</tr>
<tr>
<td>Total number of platelets (x 10^6/unit)</td>
<td>67 (57-108)</td>
<td>70 (57-122)</td>
</tr>
</tbody>
</table>

* Median (range)
and that only 1- to 2-day old RBC units were used. RBC units were issued from the blood transfusion service at approximately 9 to 10 AM. A total of 25 units per filter type were evaluated. In most cases, 2 units per transfusion were given. In the clinical ward, the nurses kept the units at room temperature until transfusion was started. This was done within approximately 45 minutes of unit issue. RC400 and BioR-O1-Plus filters were connected to the bags and primed with RBCs approximately 45 minutes after unit issue. Only 1- to 2-day old RBC units were used. RBC units were connected to the bags and primed with RBCs until transfusion was started. This was done within approximately 45 minutes of unit issue. RC400 and BioR-O1-Plus filters were connected to the bags and primed with RBCs by manual squeezing of the bag and by spontaneous gravity, respectively. The transfusion of each unit was accomplished in an interval ranging from approximately 0.5 hour to 3 hours. A new filter and transfusion set was used for each RBC unit. Filters were not vented at the end of transfusion, when the nurses clamped the tubing along the transfusion set at 5 and 25 cm below the filter. The segment was sent to the blood transfusion service where a technologist performed a complete blood count and a WBC count with a Nageotte chamber as described above.

### Results

The characteristics of RBC units before and after filtration are reported in Tables 1 and 2, respectively. In Table 1, it is seen that the number of WBCs detectable in RBC units stored for 14 to 21 days is significantly lower than that in 1- and 2-day-old RBC units. Table 2 shows that WBC counts obtained in the segments after laboratory filtration were similar to those obtained in the postfiltration bags and in the segments collected at the bedside in all cases, except for the 14- to 21-day-old RBCs filtered in the laboratory through BioR-O1-Plus, which produced slightly higher WBC counts in the segments than in the postfiltration bags. The difference was not significant. In no case was the count in the postfiltration bag higher than in the segment. All units processed through RC400 and 1- to 2-day-old units processed through BioR-O1-Plus contained less than 350 x 10^3 WBCs. The remaining counts never exceeded 5 x 10^6 per unit.

The time from unit issue and the start of transfusion and time required for the different filtration procedures are reported in Table 3. It is seen that the filtration times of BioR-O1-Plus were longer than those of RC400 and that the BioR-O1-Plus filter clogged on two occasions. In addition, Tables 2 and 3 show that WBC reductions obtained with short filtration times in the laboratory or with longer filtration times at the bedside were not significantly different. The nurses reported easier RBC priming of the BioR-O1-Plus than of the RC400. As expected, no reaction was shown by recipients of the RBC units.

### Discussion

We designed this experiment after 8 years of positive experience with bedside filtration in a large group of thalassemic patients receiving transfusions at the outpa-
tient clinic of our Department of Pediatrics. More recently, we expanded bedside filtration to more general use for hematologic patients requiring WBC-reduced blood components and did not receive reports of significant inconveniences or difficulties. The education and involvement of hematology nurses in this procedure did not require special efforts, as it was mainly aimed at their training in the procedures for filter priming with RBCs and in avoiding manual squeezing of the bags to increase blood flow during the transfusion. In this regard, preliminary data from some filters evaluated in our laboratory suggest that manual squeezing can increase by 5 to 10 times the final WBC count in the filtered unit (Maragnoni F, unpublished observations, March 1993). The ease of the nurses’ training was not unexpected, because of the simplicity of bedside filtration compared to other procedures in which nurses are involved, such as the preparation and administration of chemotherapy. The study reported here confirmed our expectation that RBC filtration at the bedside is simple and effective, provided the staff is properly trained in the procedure. This is probably true in departments such as hematology and oncology, where blood transfusion is a routine component of patient treatment, while it could be less easy in other clinical departments, where the nursing staff is less routinely involved in the use of blood components.

It must be stressed that results could differ under other conditions, including the use of different filters. In this regard, the filters used in this study are among the most effective currently on the market. It is thus possible that WBC leaks could be found with other filters, and this could be particularly evident at the end of transfusion. A comment is warranted in regard to the finding that segment counts in 14- to 21-day-old RBCs filtered through the BioR-01-Plus were higher than those obtained from the bag. The causes for this finding are unclear. Although the increment was small and of doubtful biologic relevance, its systematic occurrence supports the appropriateness of additional investigations to clarify its cause. However, from the practical point of view, this slight difference is of limited interest, mainly for two reasons. First, WBC counts were always higher in the segment than in the bag, and therefore, counting in the segment per se does not determine increased risks to the recipient. Second, removing WBCs from stored RBCs for clinical transfusion cannot be recommended, because of the well-known disintegration of WBCs during blood storage. In fact, we do not support bedside or laboratory filtration of stored blood and agree that prestorage WBC reduction of RBCs in the laboratory should be preferred in settings where organizational or other reasons prevent the use of fresh blood for bedside filtration.

As far as the effectiveness of the new filters evaluated in this study is concerned, we found that both the RC400 and the BioR-01-Plus, using fresh RBC units, produced WBC residuals well below the lowest levels attainable in even the recent past with other filters. Even considering that the statistical error of the Nageotte WBC-counting method at such low levels can approach 100 percent, it is very unlikely that the true total-unit WBC counts exceed $1 \times 10^6$. If RBCs stored for 2 to 3 weeks also are considered, no WBC count exceeded $5 \times 10^6$ per unit, the widely accepted threshold for the prevention of some complications related to the transfusion of allogeneic WBCs.

With regard to flow characteristics of the two filters, the BioR-01-Plus clogged on 2 of 60 occasions and had filtration times longer than those of the RC400. These findings indicate that some modifications might improve the BioR-01-Plus.

In conclusion, our study showed that bedside filtration can be performed in a busy hematologic setting with the latest generation of flatbed polyester filters without practical inconvenience or unpredictable transfusion of unwanted WBCs to the recipients. Our data confirm our positive ongoing experience, begun in 1985, and show that reliable quality control can be done through the evaluation of a segment collected from the transfusion set at the end of transfusion. If our findings are confirmed in a larger series of units, we believe that our protocol can solve the problem of quality control of RBC filtration at the bedside in a simple and effective way.

As far as the cost of laboratory versus bedside filtration, the former requires a significant amount of a technologist’s time to be spent in filtering the units in the laboratory, whereas the latter requires a very limited amount of a nurse’s time to connect and prime the filter. This argument can be of use to those who share our concern about the cost of WBC reduction in blood components, a procedure that is being used in new categories of patients. Although we agree that the whole issue should be reconsidered if and when all blood components are issued as WBC-reduced, for the time being we believe that in certain settings, including hematology and oncology, and for specific indications, such as prevention of NHFR and cytomegalovirus transmission, the practical advantages of bedside filtration outweigh the disadvantages, without jeopardizing patient safety.

References


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