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Bacterial Culture Reduces but Does Not Eliminate the Risk of Septic Transfusion Reactions to Single Donor Platelets

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Abstract

BACKGROUND—Transfusion associated bacterial sepsis has been a significant risk of morbidity and mortality related to platelet transfusion therapy. Previously we determined the rate of septic transfusion reactions (SPTRs) to single donor platelets (SDPs) in our hospital to be 1 in 15,098 transfusions. The goal of this study was to determine if there has been a reduction in the rate of SPTRs in our hospital since the implementation of bacterial testing of SDPs.

STUDY DESIGN AND METHODS—An automated microbial detection system was implemented at our regional blood supplier in February 2004. We performed a retrospective examination of the number of SPTRs that have occurred to SDPs at our hospital since that time, using the same criteria we used prior to bacterial screening. Transfusions over a three and a half year period were examined. Clinical and laboratory data were gathered and correlated from transfusion reaction files and three independent computer documentation systems.

RESULTS—From 3/1/04 through 8/31/07, there were 49,625 transfusions of SDP with 1,096 transfusion reactions reported. Only one reaction detected the same organism in two of three sites, meeting the criteria we set for a SPTR. Consequently we identified our rate of SPTRs in SDPs as 1 in 49,625.

CONCLUSION—Although not statistically significant we did observe in our institution a decrease in the rate of STRs to SDPs from to with the implementation of bacterial testing.

Keywords

SPTR(s) septic transfusion reaction(s); SDP(s) single donor platelet(s)

Introduction

Transfusion associated bacterial sepsis has been a long standing risk of morbidity and mortality related to platelet transfusion therapy. Although estimates of its incidence vary greatly, it is universally acknowledged as the most frequent infectious risk from transfusion in the United States. To reduce this risk the AABB required implementation of Standard 5.1.5.1 by March 1, 2004. The standard published in its 22nd edition of Standards for Blood Bank and Transfusion Services reads, ‘the blood bank or transfusion service shall have methods to limit and detect bacterial contamination in all platelet components’. On February 22, 2004 our supplier, the Greater Chesapeake and Potomac Region (GCPR) of the American Red Cross (ARC), began using the BacT ALERT 3D, (bioMerieux, Durham, NC)

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microbial detection system to meet the new standard mandated by the AABB. Previously, we had documented the rate of septic transfusion reactions (SPTRs) in our hospital when transfusing single donor platelets (SDP) as being 1/15,098.[1] The goal of this study was to determine if there has been a reduction in the rate of SPTRs at our hospital since the implementation of this screening for bacterial contaminated products.

Materials and Methods

This retrospective study evaluated the number of SPTR that occurred in our hospital from March 2004 through August 2007, the first 3.5 years our local blood supplier had the BacT ALERT system in place. The ARC uses a standard procedure to test for bacterial contamination. The products are sampled and cultured in aerobic bottles 24 to 36 hours post collection. Inoculated bottles are placed in the BacT ALERT Microbial Detection Instrument. The culture bottles are incubated for greater than 12 hours before the product is labeled and released. The cultures continue to be incubated and monitored for the presence of microorganisms for 5 days after the initial sampling.[2] In December 2006, the amount of inoculant was increased from 4 mls to 8 mls due to data suggesting increased sensitivity with larger sample size.[3] The larger sample size was used to screen for bacteria in 77.3% or 38,354 of the transfusion episodes in this study.

We established the number of transfusions that occurred in our hospital during this time period from files generated by our computer-based Blood Ordering System (BOS). These numbers were checked against billing files from our blood supplier. The type of patient transfused was determined by the location in which the transfusion occurred. The number of reactions was obtained from the transfusion medicine computer system by searching ‘transfusion reactions’ and sorting by product type.

All clinically suspected transfusion reactions are standardly evaluated by our transfusion medicine laboratory. In early 2004, before the dates of this study, the evaluation of all reported reactions, regardless of symptoms, was modified to include a clerical check, a review of documented clinical symptoms with confirmation of the history and patient status by a transfusion medicine physician and a gram stain and culture of the residual content of the platelet container or infusion set. Our microbiology laboratory has a standard operating procedure for performing an evaluation of a product implicated in a transfusion reaction. The plates and bottles inoculated depend on the volume remaining in the product. As a minimum all products have: 1.) two unspun slides prepared, one is Gram stained, the second is saved for future staining if needed, 2.) the residual content is plated. With a 3 ml syringe, two free falling drops of product are used to inoculate two chocolate agar plates. One is held at room temperature, approximately 25°C for 48 hours, the other plate is placed in a 4°C refrigerator for the same amount of time. If the unit contains < 5 mls, a third chocolate agar plate is inoculated and incubated at 35°C in CO_2 for 48 hours. For products that contain more than 5 mls the laboratory is able to do additional testing. If the product contains 5 to 10 mls the third plate is inculated and stored at 35 °C in an anaerobic atmosphere (increased nitrogen) for 48 hours, and one aerobic BacT/Alert bottle is inoculated with the remainder of the product. The bottle is incubated at 35 °C for at least 5 days. If there is more than 10 mls remaining in the product the laboratory inoculates both and aerobic and anaerobic BacT/ Alert bottle and they are both stored for at least 5 days at 35°C.

In the look back we examined the results of gram stains and cultures on all SDP products sent from transfusion medicine to microbiology implicated in a clinical reaction regardless of the clinical symptoms demonstrated by the patient. Monthly transfusion reaction reports generated by the Pathology Data System (PDS) were reviewed. This report captures the results of gram stains and cultures on all products sent from transfusion medicine to the

microbiology lab implicated in a transfusion reaction. The transfusion reaction file in the BOS was searched for the key word **SEPTIC**. Any positive result discovered on either system was investigated. Descriptions of transfusion reactions were found and reviewed in the BOS, the transfusion medicine system and in the patient clinical notes and lab results. Autopsy reports were examined if relevant. _____Febrile reactions were defined by a 1°C rise in oral temperature within one hour of transfusion or the occurance of chills and rigors within one hour of transfusion in patients on antibiotics or antipyretic therapy.[(1)] The symptoms of allergic reactions were those of hypersensitivity such as hives, rash, urticaria, flushing and or tachycardia. SPTRs were defined as reactions with clinical symptoms of a febrile reaction and identification of the same organism from two of the following three sources: gram stain of the product at the time of reaction, culture of the product at the time of reaction, blood cultures from the patient after the reaction.

Results

There were 49,625 transfusions of SDP products to 5,701 different patients in the 3.5 year period we examined. The majority of these, 70%, were transfused in our cancer center to inpatients and outpatients being treated for hematological disorders and solid tumors. The remaining 30% were used by trauma, operating room, intensive care unit, extracorporeal membrane oxygenation (ECMO) and non-oncology medical patients.

There were 1,096 possible reactions reported to SDPs. Approximately 70% had allergic manifestations, 26% had a febrile component and the remaining 4% were classified as '*other*' to include possible transfusion associated circulatory overload (TACO), transfusion associated acute lung injury (TRALI), or atypical reactions.

The products from the 1,096 suspected transfusion reactions were each cultured as part of the transfusion reaction evaluation. Twenty cases had organisms isolated by plating or culturing of the product. In only one case, #11, was the same organism identified in two sources; the gram stain was positive for gram positive cocci and the culture plates were positive for heavy *coagulase negative Staphylococcus* (CONS) at 24 hours.

Case #11 was a 78 year old with refractory leukemia. He was receiving palliative care in the outpatient department with hydroxyurea and blood transfusion support. His total white cell count was 36,140 with an absolute neutrophil count of zero. He was receiving clindamycin prophylactically three times daily. He was issued two separate bags of platelets from the same donation at noon on the fifth day of storage. His symptoms of severe shaking chills, a fever of 41.5°C and tachypnea developed rapidly after infusion of only part of bag one. The infusion was stopped and the remainder of bag one and all of bag two were returned to transfusion medicine. When the gram stain on bag one was found to be positive, bag two was destroyed. Cultures were not obtained before it was destroyed. The patient required admission and IV antibiotics. He died several days later with refractory leukemia and other complications.

As part of our transfusion reaction procedure the status of other components from the donation is determined. It was discovered that bag one had an aliquot removed earlier in the day. At 8:30 am, four hours prior to case #11's transfusion, the aliquot had been issued to an 8 month old female, case #11-A who was being treated for *Streptococcus Pneumoniae* sepsis with meropenem and vancomycin. No transfusion reaction was noted although the patient was febrile and hypotensive. Routine monitoring blood cultures, drawn from the patient several hours after the infusion of platelets, grew CONS at five days with a sensitivity pattern consistent with the organism isolated in the reaction experienced by case

#11. This infant developed purpura fulminans associated with her S*treptococcus Pneumoniae* sepsis and gangrene of her extremities requiring amputation.

We investigated the clinical and microbiological information on any additional bags or aliquots transfused from the 20 donations that had positive bacterial cultures. Table II indicates the recipient of these products, whether or not a transfusion reaction occurred and the results of any cultures from the products or patient that were available. The first product is the aliquot received by case #11-A discussed above. Five of the recipients were the same case listed in Table I and are referred to by case number. Both bags one and two from a split donation had been given as one transfusion episode and infused consecutively. Both bags were gram stained and cultured as part of the transfusion reaction evaluation. In all five of these cases only one bag from the split donation grew an organism, the second bag had negative cultures. Case #12-Areceived an aliquot from the product transfused in case #12. Case #12-A experienced a transfusion reaction with rigors and a greater than one degree rise in temperature from 37.3°C to 38.6°C, but gram stain, product culture and patient culture were all negative. Lastly, case #20-A received the second bag of the donation from case 20. No transfusion reaction was experienced and therefore no microbial data was available.

Only one case, #11, met our definition of a septic transfusion reaction, having the same organism detected from two sources: a gram stain positive for gram positive cocci and a product culture positive for CONS. The rapid onset of the patient's severe symptoms of fever to 41.5°C, shaking chills and tachypnea further substantiated the likelihood that this was a septic transfusion reaction.[4, 5] The remaining 19 cases having positive product cultures were thought to be post transfusion contaminants of processing. Six of the 19 cases involved split donations and gram stain and culture from the second bag were negative. Ten of the remaining cases had allergic or other non-febrile manifestations of a reaction making it unlikely that a SPTR had occurred. Cases 8, 9 and 13 each manifested a change in temperature and or chills but the maximum temperature reported was 38.3°C and none of the three patients experienced hemodynamic instability.

Discussion

Since the ARC implemented bacterial screening, SPTRs in our institution have decreased but have not been eliminated. In 1987–1988 when we used a mixed inventory of SDP and whole blood derived platelets, our SPTR rate was 1/4,818. After converting our inventory to 99.4% SDP our SPTR rate changed to 1/15,098.[1] Now with bacterial screening in place we are seeing an incidence rate of 1/49,625 SPTRs to SDPs, a reduction of 70% attributable to bacterial culture.

In the first 10 months of implementation, the ARC reported an overall rate of confirmed positive bacterial contaminated SDPs identified by the BacT Alert system to be 1/5,157 with at least three high probability septic reactions occurring in the screened negative products.[2] The Blood Systems Incorporated (BSI) experience with the BacT Alert System is comparable to the ARC data. They identified 1/5,856 true positive contaminated SDP in the first two years of bacterial screening and acknowledged that SPTRs continue to occur.[6] The ARC subsequently summarized their findings from March 1, 2004 through May 31, 2006.[7] With the implementation of bacterial screening, they identified bacterial contamination as 1/5,399 donations. During this same study period, they estimated that the residual risk of SPTRs was 1/74,807 per distributed component based on voluntary reporting by transfusion facilities. Our finding of a reduced, yet residual risk of septic reaction is consistent with the experience of the ARC and BSI.

Our study takes advantage of a consistent process for reporting and evaluating suspected transfusion reactions at our institution. We used this methodology both before and after the implementation of bacterial screening. Our criteria for defining a SPTR has also been consistent pre and post bacterial testing. We feel that this consistent method of active surveillance within a single institution is advantageous in assessing the impact of bacterial testing on the rate of SPTR as compared to the blood center process of voluntary reporting of events from numerous institutions with differing processes for managing transfusion-related adverse events.

With the publication of their initial experience, the Red Cross hypothesized that a longer than 24 hour waiting time before sampling products or a larger volume of inoculation sample may increase the sensitivity of testing.[2] Indeed it was suggested in May 2006 that doubling the sample size to 8 mls would improve detection of bacterial contaminated SDP products by approximately 25%.[3] In December 2006, our supplier initiated this change in their inoculation procedure. Our data at this point includes only eight months of observation after the enhancement of bacterial screening with a larger sample size and the one septic reaction in this study occurred before December 2006.

We report here one SPTR in 49,625 transfusions that occurred in the first 3.5 years of bacterial screening. Although it is highly suggestive that bacterial testing has decreased the number of SPTRs in our institution, it is difficult at this time to know the true incidence rate of breakthrough cases and the overall effectiveness of current screening since we have only identified a single case in this time period. Longer follow up is required.

Vigilance and ingenuity are gradually decreasing the rate of SPTRs. Current methods of improvement to the skin cleansing process and phlebotomy technique, diversion of the first 10 mls of the donor blood, improved donor screening questions, preferential use of SDPs and continued bacterial screening inoculating with larger sample size are all contributing to the decreased frequency of these potential fatal reactions.[8,9] The transfusion community has successfully decreased the incidence rate of transfusion transmitted viral infections to very low rates with the development of highly sensitive and specific testing; HIV is estimated to occur 1/1,900,000, Hepatitis B 1/137,000 and Hepatitis C 1/1,000,000 transfusions.[10] Although the exact incidence of breakthrough septic reactions is unknown, we are reporting approximately 1 SPTR in 50,000 transfusions. There is still a need to improve on current techniques, potentially adding another process or test, to further decrease the residual risk. Pathogen inactivation and rapid bacterial testing prior to transfusion are methods whose clinical contributions have not yet been fully explored, but may be able to further decrease the incidence of this persistent transfusion risk.

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TABLE 1

Positive Bacterial Cultures from Reported Transfusion Reactions to SDPs

Case #	Date of Rxn	Age of SDP	Symptoms of Rxn	Gram Stain*	Product Culture Results	Pt. Culture Results	Outcome
1	3/10/2004	5	ALLERGIC	NEG	ANAEROBIC + 1 DAY CONS•; AEROBIC + 4 DAYS GPB	NS$^{\Delta}$	
2	5/17/2004	5	ALLERGIC	NEG	+ 5 DAYS PROPIONIBACTERIUM ACNES	NS$^{\Delta}$	
3	8/8/2004	5	ALLERGIC	NEG	+ 1 DAY STAPH. AUREUS	NS$^{\Delta}$	
4	11/10/2004	5	ALLERGIC	NEG	+ 1 DAY RARE CONS•	NS	
5	12/19/2004	5	OTHER	NEG	+ 3 DAYS CONS•	NS$^{\Delta}$	
6	12/29/2004	5	ALLERGIC	NEG	+ 4 DAYS PROPIOIBACTERIUM ACNES	NS$^{\Delta}$	
7	2/16/2005	5	ALLERGIC	NEG	+ 2 DAYS FEW BACILLUS CEREUS	NS$^{\Delta}$	
8	3/8/2005	3	FEBRILE	NEG	+ 1 DAY CONS•	NEGATIVE	
9	4/3/2005	4	FEBRILE	NEG	+ 2DAYS CONS•	NEGATIVE	
10	8/29/2005	5	FEBRILE	NEG	+1 DAY RARE CONS•	NS$^{\Delta}$	
11	9/12/2005	5	FEBRILE	GPC IN CLUSTERS	+1 DAY HEAVY CONS•	9/12–9/13/05 POS E.COLI	FATAL
12	11/30/2005	4	ALLERGIC	NEG	+ 6 DAYS PROPIONIBACTERIUM ACNES	NEGATIVE	
13	12/3/2005	4	FEBRILE	NEG	+1 DAY CONS•	NEGATIVE	
14	12/7/2005	5	ALLERGIC	NEG	+5 DAYS PROPIONIBACTERIUM ACNES	NS$^{\Delta}$	
15	2/10/2006	5	FEBRILE	NEG	+ 2 DAYS RARE CONS•	NEGATIVE	
16	7/3/2006	5	ALLERGIC	NEG	+ 4 DAYS PROPIONIBACTERIUM SPECIES	NS$^{\Delta}$	
17	8/30/2006	5	ALLERGIC	NEG	+ 1 DAY CONS•	NS$^{\Delta}$	
18	9/15/2006	5	OTHER	NEG	+ 5 DAYS PROPIONIBACTERIUM ACNES	NS$^{\Delta}$	
19	10/8/2006	5	ALLERGIC	NEG	+ 1 DAY STREP VIRDIANS	NS$^{\Delta}$	
20	3/26/2007	5	FEBRILE	NEG	+1 DAY CONS•	NS$^{\Delta}$	

TABLE 2

Microbial and Clinical Evaluation of Additional Aliqots/Splits from SDPs in Table 1

Case # from TABLE 1	Recipient	Split vs. Aliq.	TX RX	Gram Stain	Product Culture	Pt. Culture
11-A	BABY CC	A	NO	NS*	NS*	+ 5 DAYS CONS
10	CASE #10	S	YES	NEG	NEG	NS*
15	CASE #15	S	YES	NEG	NEG	NS*
17	CASE #17	S	YES	NEG	NEG	NS*
18	CASE #18	S	YES	NEG	NEG	NS*
19	CASE #19	S	YES	NEG	NEG	NS*
12-A	MR. TM	A	YES	NEG	NEG	NEGATIVE
20-A	MS. OB	S	NO	NS*	NS*	NS*

*NS = not sent