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Role of Transfusion in the Development of Urinary Tract-related Bloodstream Infection

Mary A.M. Rogers, PhD[1], **Neil Blumberg, MD**[2], **Joanna M. Heal, MD**[3], **Latoya Kuhn, MPH**[4], **M. Todd Greene, PhD**[1], **Emily Shuman, MD**[1], **Carol E. Chenoweth, MD**[1,5], **Robert Chang, MD**[1], and **Sanjay Saint, MD, MPH**[4,1]

Mary A.M. Rogers: maryroge@umich.edu; Neil Blumberg: Neil_Blumberg@urmc.rochester.edu; Joanna M. Heal: jmheal@gmail.com; Latoya Kuhn: lbernard@umich.edu; M. Todd Greene: mtgreene@umich.edu; Emily Shuman: emilyks@umich.edu; Carol E. Chenoweth: cchenow@umich.edu; Robert Chang: robchang@umich.edu; Sanjay Saint: saint@umich.edu

[1]Department of Internal Medicine, University of Michigan, Ann Arbor, MI

[2]Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, NY

[3]Hematology-Oncology Unit, Department of Medicine, University of Rochester, Rochester, NY

[4]Health Services Research & Development, Ann Arbor Veterans Affairs Medical Center, Ann Arbor, MI

[5]Department of Infection Control and Epidemiology, University of Michigan Health System, Ann Arbor, MI

Abstract

There is a growing body of evidence that transfusion alters host defenses against infection.[1] A meta-analysis of randomized controlled trials demonstrated that a restrictive approach to red blood cell (RBC) transfusion decreases the risk of infection by 24%.[2] This evidence has prompted changes in guidelines for the use of RBC transfusion.[3] The objective of this investigation was to examine whether transfusion affects the risk of developing a bloodstream infection from a urinary source.

METHODS

A matched case-control study was conducted at the University of Michigan Health System from January 1, 2000 through September 30, 2008. Cases (n=299) were adults who had both a positive urine and blood culture with the same microorganism during hospitalization. Patients with a positive urine culture within the first 2 days of admission or who were admitted for reason of septicemia or bacteremia were excluded. Controls (n=670) were selected by incidence density sampling and were a sample of adults with a positive urine culture who were at risk of a bloodstream infection but did not develop such an infection. Controls were matched to each case by calendar time (within 120 days) when the bloodstream infection occurred in the case. At maximum, there were 4 controls per case but, owing to constraints of the control definition, some cases were matched to 1 to 3 controls. A similar period was compared for cases and controls. That is, if the urinary tract-related bloodstream infection occurred on the 20th day after hospital admission for the case, a

CORRESPONDENCE: Mary A.M. Rogers, PhD, Department of Internal Medicine, University of Michigan, 300 North Ingalls, Room 7E07, Ann Arbor, MI 48109-0429, Telephone: 734-647-8851, FAX: 734-936-8944, maryroge@umich.edu.

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similar time period was evaluated in the matched control (from admission to the 20th day of hospitalization). For purposes of this investigation, this day was labeled the "index date."

Information was extracted from electronic medical records, with additional medical chart review by an infectious diseases physician. Conditional logistic regression was used, which accounted for the matched design. Adjusted models included RBC, platelets, fresh-frozen plasma, medication use during the 2 days prior to the index date (antibacterial, antifungal, antimicrobial, antiviral, statin, insulin, and immunosuppressants), age, race, sex, surgery (cardiovascular, gastrointestinal, other), cardiovascular disease, cancer and diabetes mellitus. To evaluate possible nonlinear associations between the volume of blood component and the outcome, fractional polynomials were used. For those analyses in which the age of the RBC unit was evaluated, some patients received multiple units and therefore, we used the expiration date for the oldest RBC unit given.

This study was approved by the University of Michigan Health System institutional review board.

RESULTS

Cases were younger than controls ($p=0.001$) and were more likely to be male ($p<0.001$). For those patients who developed a bloodstream infection, the median time between admission and bloodstream infection was 15 days. Patients with a principal diagnosis of cancer were significantly more likely to develop urinary tract-related bloodstream infection ($p<0.001$), as were patients who underwent surgery ($p<0.001$). Approximately a third of patients who developed urinary tract-related bloodstream infection (32.4%) died while in the hospital, compared with 4.5% in the controls ($p<0.001$).

There was a significant relationship between RBC transfusion prior to the bloodstream infection but not platelet or fresh-frozen plasma transfusion (Table). The odds of developing a bloodstream infection were 4.91 times greater in patients who received a RBC transfusion compared with those who did not. When patients receiving platelet or fresh-frozen plasma transfusions were excluded, the odds of developing a bloodstream infection were 4.11 times greater in those who received RBC transfusion. There was a significant dose response; for those receiving RBCs, the probability of developing a bloodstream infection rose as the total volume of RBC transfusion increased during hospitalization. However, the relationship was nonlinear such that the greatest unit increase in the probability of bloodstream infection occurred between 1 unit (250 ml) and 2 units of RBCs (odds ratio, 1.77 for 500 versus 250 mL) and then gradually increased with greater RBC volume.

Prolonged RBC storage was associated with an increased likelihood of infection. In patients who received RBC transfusion, the odds of developing a bloodstream infection increased by 40% for every week of increased storage (Table). There was a significant correlation between the length of hospital stay and the age of the RBCs received in the case group (Spearman ρ, 0.25; $p=0.0003$) and in the control group (Spearman ρ, 0.13; $p=0.04$).

COMMENT

This study provides evidence that an infection originating in the urinary tract may be more likely to spread to the bloodstream in patients who receive a RBC transfusion. The odds of developing bloodstream infection increased nearly 5-fold with receipt of RBC transfusion. A dose-response was evident. A Cochrane meta-analysis of 4 randomized controlled trials designed to test the effect of RBC transfusion on infection (1788 patients) yielded results congruent to our study; restrictive RBC transfusion strategies reduced the rate of infection

by 24%.[2] However, our study was observational and as such, there is a possibility of residual confounding.

Our findings also suggest that in patients given a RBC transfusion, the risk of urinary tract-related bloodstream infection increases with the length of RBC storage, independent of the total volume of RBCs received. Changes in the morphology and biochemistry of stored RBCs have been extensively documented.[4] Evidence regarding the effects of aged RBC transfusion is conflictingand therefore, there are trials under way to assess hypotheses related to the age of RBCs.[5]

In conclusion, the decision to order a RBC transfusion in a patient with a urinary tract infection should involve careful deliberation, keeping in mind updated evidence-based guidelines. Our results suggest that if a RBC transfusion is needed, administering 1 unit of RBCs instead of the usual 2 RBC units at a given time may confer less potential risk of bloodstream infection. Our study also indicates that older RBCs may pose a greater infection risk, although ongoing randomized controlled trials should provide additional insight.

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Dr. Rogers had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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TABLE

Relative Odds of Developing a Urinary Tract-related Bloodstream Infection By Type of Blood Component Received

			Unadjusted		Adjusted[b]	
Blood Component	**n**	**Volume, Median [IQR], L[a]**	**OR**	**95% CI**	**OR**	**95% CI**
RBCs (yes/no)	969	1.5 (0.7 – 3.2)	6.87	4.66, 10.12	4.91	2.91, 8.27
RBCs without PLT or FFP (yes/no)[c]	695	0.7 (0.7 – 1.4)	3.76	2.23, 6.34	4.11	2.13, 7.92
RBCs length of storage, wk	449	1.5 (0.7 – 3.2)	1.36	1.13, 1.63	1.40[d]	1.02, 1.93
PLTs (yes/no)	969	0.7 (0.4 – 2.2)	5.94	4.05, 8.72	1.09	0.59, 2.01
PLTs, L	969	0.7 (0.4 – 2.2)	1.74	1.45, 2.07	1.16	0.996, 1.35
FFP (yes/no)	969	1.5 (0.6 – 3.1)	3.79	2.61, 5.51	1.52	0.86, 2.71
FFP, L	969	1.5 (0.6 – 3.1)	1.41	1.24, 1.60	1.13	0.9995, 1.29

Abbreviations: CI, confidence interval; FFP, fresh-frozen plasma; IQR, interquartile range; OR, odds ratio; PLTs, platelets; RBCs, red blood cells.

[a] Median volume and interquartile range for those who received the blood component.

[b] Models included RBC, PLT, FFP, age (centered on mean), gender, race, medications (antibacterials, antimicrobials, antifungals, antivirals, immunosuppressants, insulin, statin), diabetes, cardiovascular disease, cancer, and surgery (cardiovascular, digestive tract, other).

[c] Patients who received PLT or FFP were excluded.

[d] Adjusted model also included volume (liters) of RBC units. Only subjects receiving RBCs were included.

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