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An Unexpected Bystander Effect: a RBC Focused Patient Blood Management Program Resulted in Reduced Plasma and Platelet Utilization

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Abstract

Background: A computerized order for red blood cell (RBC) transfusion was modified to include clinical decision support (CDS) to enforce our restrictive RBC transfusion policy. These changes were focused exclusively on RBCs. The goal of this retrospective observational study was to evaluate whether RBC decision support implementation resulted in decreased utilization of non-RBC blood products.

Study design and Methods: The Blood Utilization Committee, a subgroup of the Vanderbilt University Medical Center Transfusion Committee, developed and implemented CDS within the order entry system computerized provider entry (CPOE) to support restrictive RBC transfusion practices. These changes occurred from November 2011 to December 2012. Data on transfusion and pre-transfusion laboratory testing were collected from January 2011 to December 2014. Data were normalized to number of transfusions per 1000 hospital discharges. Descriptive data were represented by median interquartile range (IQR) and Mann-Whitney *U* test was used to compare data.

Results: The comparison between the pre-implementation group and post-implementation group demonstrated a decrease in plasma (313 versus 203 units, *p* value<0.001) and platelets (184 versus 162 units, *p* value<0.001); cryoprecipitate use increased (13 versus 21 units, *p* value<0.001). Pre-transfusion laboratory values showed an increase in international normalized ratio (INR) (1.7 versus 1.8, *p*-value=0.002), decrease in platelet count (32,500/mcL versus 30,000/mcL, *p*-value=0.188), and increase in fibrinogen (149 mg/dL versus 163 mg/dL, *p*-value=0.009).

Conclusion: Implementation of CPOE guided CDS for RBC transfusions resulted in a bystander effect with respect to reductions in plasma and platelet utilization. Pre-transfusion laboratory changes were variable.

Keywords: Bystander effect; Plasma; Platelet

Introduction

A growing number of clinical trials indicate that liberal versus restrictive use of red blood cell (RBC) units does not confer clinical benefit and often is harmful to patients [1-5]. RBC utilization, approximating 12 million units annually, far exceeds the utilization of other blood products [6]; approximately 7 million platelets and 2 million plasma doses are transfused each year in the United States [6]. Between 2008-2011, our institution spent over 13 million dollars annually procuring RBC units for transfusion. Given the risks and cost of RBC transfusions and encouragement from professional societies, most hospitals, including ours, focused initial efforts at improving patient blood management (PBM) on inappropriate RBC utilization [1].

Randomized clinical trials providing guidance on transfusion triggers for platelet, fresh frozen plasma (FFP) and cryoprecipitate outside of specific clinical scenarios are sparse, making it difficult to establish recommendations to guide transfusion triggers [5,7-11]. Yet, since most platelet and FFP transfusions are prophylactic, and published reports indicate a wide variation in clinical practices, there is likely opportunity to eliminate unnecessary transfusions [12,13].

Vanderbilt University Medical Center is a 900-bed adult and 350 bed pediatric hospital. It is a level I trauma center and also has a large hematopoietic and solid organ transplant program in both the adult and pediatric hospitals. Combined annual RBC, platelet and FFP transfused is approximately 7000 units each month. In an effort to improve blood product utilization and promote restrictive RBC transfusion practices, a patient blood management program was implemented using an interdisciplinary, multimodal approach focused exclusively on decreasing RBC utilization. The goal of this retrospective observational study is to assess if there were any concomitant changes in utilization of platelets and FFP in the setting of an RBC-focused PBM program.

Materials and Methods

In order to improve evidence based RBC transfusion practice in patients with symptomatic anemia, a multidisciplinary patient blood management committee was established including providers from transfusion medicine, critical care and anesthesiology, and quality improvement at Vanderbilt University Medical Center (VUMC), a tertiary care academic medical center in Nashville, Tennessee (TN). The committee developed an evidence-based consensus recommending RBC

transfusion in patients with symptomatic anemia at hemoglobin less than 7.0 g/dL, with exceptions for chemotherapy induced bone marrow failure or chronic anemia (hemoglobin<8.0 g/dL) and active coronary artery disease or cerebral vasospasm (hemoglobin 9-10 g/dL), in addition RBC ordering was restricted to a single unit at a time [14]. Moreover, we developed a computerized provider entry (CPOE) system with associated clinical decision support (CDS), which consisted of best practice alerts at the CPOE and requested a reason for RBC orders outside of suggested transfusion guidelines. Following education, the CPOE changes and CDS were phased in across the inpatient units of both the adult and children's hospitals from September 2011 to December 2012. After implementation of the guidelines, monitoring of compliance data was conducted monthly. No real-time or retrospective provider-specific alerts were sent for ordering products outside of guidelines, however, re-education of residents and nurses were provided to directed areas with poor compliance.

Data regarding utilization of both RBC and non-RBC products along with concurrent laboratory data were collected as a routine part of clinical care and quality assurance function of the VUMC Transfusion Committee and was deemed quality improvement activity by the VUMC Institutional Review Board. Severity of illness for the study population was determined during the control and study intervals. Case-mix index (CMI), based on the Centers for Medicare and Medicaid Services cost weights, was assessed and compared during the control and study intervals to further ensure that findings were not attributed to differences in severity of illness between pre and post implementation cohorts.

Data regarding inpatient blood product utilization included plasma, cryoprecipitate and platelet utilization per 1000 patient discharges. For patients receiving plasma, cryoprecipitate or platelet transfusion, relevant pre-transfusion laboratory data were obtained: INR, plasma fibrinogen concentration, or platelet count. The primary outcome measure was non-RBC blood product transfusions per 1000 patient discharges. The secondary outcome measure was observation of laboratory trends prior to transfusion.

Blood product utilization and laboratory data for patients admitted to VUMC was collected from January 2011 to December 2014. Data were analyzed using SPSS version 23. Descriptive analysis for continuous variables included mean, median and range. Comparison of blood product utilization (median number of blood products transfused per 1000 discharges) prior to protocol implementation (calendar year 2011) and after full protocol implementation (calendar years 2013 and 2014) was performed using Mann Whitney *U* test.

Results

The study period (January 2011-December 2014) demonstrated a period of growth for the medical center in regards to number of admissions (52,961 in 2011, 55,173 in 2012, 59,750 in 2013, and 58,717 in 2014). Despite this increase, the case mix index and patient populations remained steady throughout the study period. In addition, the gender and age distributions were consistent throughout the study period (Table 1).

	2011	2012	2013	2014
Cases	52,961	55,173	59,750	58,717
CMI	1.8426	1.8617	1.8414	1.8541
Gender				
Female	26,844 (51%)	28,383 (51%)	30,556 (51%)	30,025 (51%)
Male	26,116 (49%)	26,788 (49%)	29,192 (49%)	28,691 (49%)
Admission Age				
<1 year	6733 (13%)	7314 (13%)	7500 (12%)	7314 (13%)
1-17 years	7351 (14%)	7372 (14%)	8666 (14%)	8422 (15%)
18-50 years	18855 (35%)	19134 (35%)	20327 (34%)	19383 (33%)
51-74 years	16261 (31%)	16977 (31%)	18628 (31%)	18373 (31%)
>75 years	3761 (7%)	4367 (7%)	4740 (8%)	4780 (8%)

Table 1: Hospital demographics for the study period (2011-2014)

The use of CPOE and CDS, coupled with hospital-wide educational efforts to encourage a restrictive RBC transfusion policy, resulted in a steady and sustained decrease in RBC utilization as well as unanticipated alterations to plasma, platelet and cryoprecipitate usage. Blood product utilization throughout the period was recorded monthly, and comparisons of the median number of units transfused per 1000 discharges were calculated. Comparisons were made between the pre-implementation group (2011) and post-implementation group (2013+2014). Throughout the study, RBC transfusions per 1000 discharges decreased from a median of 722 (IQR 69) units prior to protocol implementation to 545 (IQR 32) units after protocol implementation (p value<0.001). Retrospective review of non-RBC products demonstrated significant decrease in plasma (313 (IQR 77) versus 203 (IQR 60) units, p value<0.001) and platelets (187 (IQR 53) versus 162 (IQR 21) units, p value<0.001). By contrast, we observed an increase in cryoprecipitate use (13 (IQR 7) versus 21 (IQR 10) units, p value<0.001) (Figure 1). Thus, following implementation of a blood management initiative focused solely on RBCs, we observed an associated decline in the use of both plasma and platelets decreased throughout the study period, while the use of cryoprecipitate increased, albeit the utilization numbers are relatively low in comparison to other components (Figure 1).

We also noted changes in the laboratory triggers that led to transfusion of plasma and cryoprecipitate. Comparisons were made between median laboratory values in the pre-implementation group (2011) and post-implementation group (2013+2014). Measurements to INR prior to transfusion of plasma (obtained in 87.2% of cases) were noted to demonstrate an increasing trend over the study period (1.7 (IQR 0.1) versus 1.8 (IQR 0.1), p-value=0.002). While the median platelet count prior to transfusion (obtained in 97.6% of cases) demonstrated a downward trend during the study period, this change was not statistically significant (32500 (IQR 9500) versus 30000 (IQR 9400) per micro liter, p-value=0.188). In contrast, an increase in the value of fibrinogen at the time of cryoprecipitate transfusion (obtained in 80.3% of cases) was observed (149 (IQR 19) versus 163 (IQR 21) mg/dL, p-value=0.009).

Discussion

This retrospective study shows that implementation of hospital-wide educational efforts to encourage a restrictive RBC transfusion policy was associated with a decline in utilization of platelet and plasma utilization. Real-time decision making support has been demonstrated to improve RBC utilization [1], and the observation has been noted that plasma and platelet transfusions decrease in the setting of RBC CPOE and CDS [1]; however, to our knowledge, the overwhelming majority of RBC PBM studies have not quantitatively reported on the utilization of other blood products or laboratory trends unless their blood management strategy included a multifaceted program targeting all transfusions in general [3]. Our study demonstrated that improved education in regards to RBC utilization for symptomatic anemia not only resulted in an overall, statistically significant decreased use of plasma and platelets, but also shifted the laboratory triggers that result in transfusion orders. It is interesting to compare our results to the utilization data from the most recently available 2011 National Blood Collection and Utilization Survey (NBCUS), which reported that 30% of the responding institutions reported a PBM program. The NBCUS survey reported a reduction in RBC and FFP of 8.2 and 13.4%, respectively, but an increase in platelet use of 7.3%. Thus, at least in this broad sampling, a parallel reduction in FFP and platelet did not accompany a utilization reduction in RBCs. An important factor for this difference is narrowing our findings to a category of symptomatic anemia, thereby eliminating practices that exhibit unpredictable transfusion practices that are typically outside of PBM scope (i.e. requirement for exchange transfusions and acute bleeding).

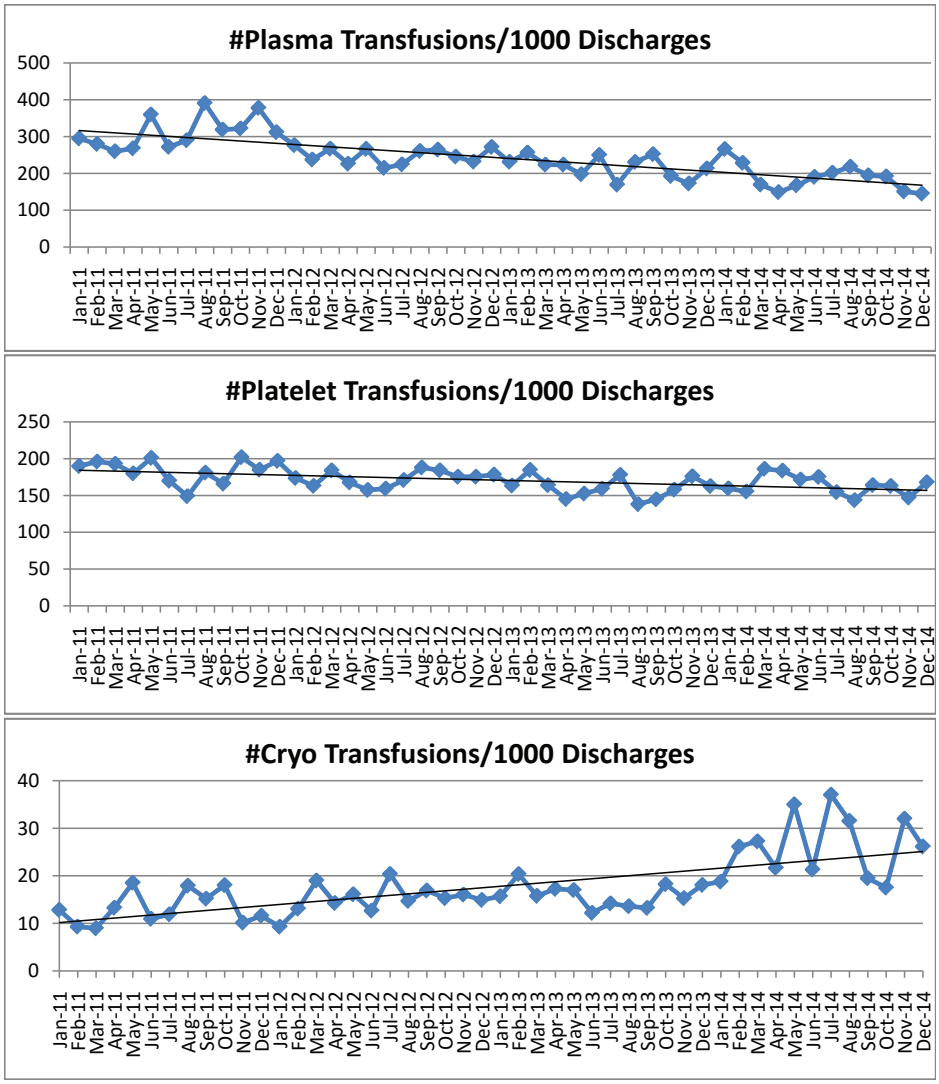

Figure 1: Transfusion data throughout the study period. Data is represented in number of transfusions per 1000 discharges each month of the study period.

The reasons are unknown for why directed education on transfusion triggers guiding RBC transfusion for symptomatic anemia may result in reduced transfusion of other blood components. The main indications to transfuse FFP and platelets are to correct deficiencies of clotting factors and to treat (or prevent) bleeding, respectively. We speculate that increasing sensitivity to inappropriate reasons for RBC transfusions (e.g. expansion of circulatory volume) and pursuing liberal triggers may have contributed. These findings are meaningful, not only from a financial perspective, but also in regards to patient safety. In comparing platelet and plasma utilization at our institution, the direct cost savings over one year was estimated at approximately $14,000. In addition, decreasing unnecessary blood product utilization has the potential to decrease transfusion related morbidity. In both adult and pediatric populations, both acute infectious and non-infectious transfusion reactions are most commonly associated with platelets [15]. Thus, reducing unnecessary platelet and plasma transfusions as a bystander effect of successful RBC utilization reduction would be expected to decrease overall risk from transfusion [16,17].

Unexpectedly, the use of cryoprecipitate demonstrated a statistically significant increase throughout the study period, and the trigger for transfusion of cryoprecipitate (fibrinogen activity) increased prior to transfusions throughout the study period. While contrary to our other observations, this observation is thought to be secondary to a shift in clinical practice that prioritized the use of cryoprecipitate over recombinant activated factor VII. Studies have suggested the need for increased fibrinogen thresholds prior to cryoprecipitate transfusion [18] which may also be contributing to our observation. The absolute increase in cryoprecipitate use was small, thus had little impact on blood product utilization. Further investigation into transfusion practices of cryoprecipitate in various hospital departments would be required to further elucidate the cause of this increase utilization.

Our study is limited by a number of factors. First, as in any retrospective study, we are unable to document a causal relationship between the implementation of our RBC utilization protocol for symptomatic anemia and the decrease in non-RBC blood product use. While we recognize this limitation, we feel that this observation is an important first step to understanding the factors that influence clinical decisions in blood product ordering. Second, the laboratory trends noted over the study period, while statistically significant, may not represent a true clinically significant change in patient care. Further investigation into clinical decision-making would be required to further understand this change. Finally, this study represents a time-limited single institution experience. While it is not clear if this change will be sustained or if it is generalizable,

our institution is a large sized academic referral medical center with a range of both medical and trauma services; we feel that it is reasonable to conclude that similar changes in practice would be noted at other similar institutions.

Conclusion

This study demonstrates that implementation of CPOE guided CDS to guide RBC transfusions for symptomatic anemia resulted in an unexpected bystander effect with respect to reductions in both plasma and platelet utilization.

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Conflict of Interest

No conflicts of interest to report.

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