ORIGINAL INVESTIGATION
ÖZGÜN ARAŞTIRMA

Yoğun Bakım Derg 2019;10:(3)90–94
https://doi.org/10.33381/dcbybd.2019.2200

Blood Transfusion Practice in Critically Ill Patients and Clinical Outcomes

Kritik Hastada Kan Transfüzyonu Uygulamasi ve Klinik Sonuçlar

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Cite this article as: Gönderen K, Gönderen A. Blood Transfusion Practice in Critically Ill Patients and Clinical Outcomes. Yoğun Bakım Derg 2019; 10(3):90-95.

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Received: June, 30, 2019
Accepted: August 29, 2019
Available online: 01.12.2019

ABSTRACT

Aim: The aim of this study is to quantify the red blood cell (RBC) transfusion threshold in critically ill patients and to examine the relationship between RBC transfusion and clinical outcomes.

Materials and Methods: Five hundred and twenty patients who were admitted to the internal medicine intensive care unit (ICU) between February 2018 and May 2019 were included in this study. The collected data included patients' demographic characteristics, admission diagnostic categories, co-morbidities, the ICU admission Simplified Acute Physiology Scores (SAPS) II, numbers of RBC transfusion, ICU admission and pretransfusion hemoglobin levels, and requirements of invasive mechanical ventilation and vasoactive drugs during the ICU stay. The primary endpoint of the study was to determine the RBC transfusion threshold in critically ill patients. Secondary outcomes were the ICU length of stay and mortality.

Results: A total of 89 (17.1%) patients received RBC transfusion during the ICU stay. The transfusion threshold hemoglobin was 6.9 g/dL in transfused patients. Transfused patients had higher SAPS II scores at ICU admission than non-transfused patients ($p<0.001$). The number of patients requiring invasive mechanical ventilation and vasopressor support was higher in transfused patients ($p<0.001$). ICU mortality rates were higher in patients who had received RBC transfusion during the ICU stay than in those who did not (ICU mortality rates were 51.7% and 23.9%, respectively).

Conclusion: This study showed that one-fifth of ICU patients received RBC transfusion during the ICU stay. Transfused patients had higher disease scores and lower hemoglobin levels on the day of ICU admission. Transfused patients stayed longer in the ICU and had higher mortality rates than non-transfused patients.

Keywords: red blood cell transfusion, mortality, intensive care, critically ill patients

ÖZ

Amaç: Kritik hastalarda eritrosit süspansiyonu (ES) transfüzyonu eşiğini belirlemek ve ES transfüzyonunun klinik sonuçlarla ilişkisini incelemektir.

Gereç ve Yöntemler: Çalışmaya Şubat 2018-Mayıs 2019 arasında İç hastalıkları yoğun bakım ünitesinde (YBÜ) yatan 520 hasta alınmıştır. Hastaların demografik özellikleri, yatış tanıları, ek hastalıkları, yoğun bakım kabulünde hesaplanan Basitleştirilmiş Akut Fizyoloji Skoru (SAPS) II puanları, yoğun bakıma yatış anındaki ve transfüzyon öncesi hemoglobin seviyeleri, ölüm oranları, mekanik ventilasyon ve vazopressör ihtiyaçları, YBÜ'de kalış süreleri kaydedilmiştir. Çalışmanın birincil sonlanım noktası, kritik hastalarımızdaki ES transfüzyon yapılma eşiğinin belirlenmesidir. İkincil sonlanım noktası ise yoğun bakımda yatış süresi ve mortalitesidir.

Bulgular: Hastaların 89 (%17.1)'na ES transfüzyonu yapılmıştır. Transfüzyon yapma eşiği 6.9 g/dL olarak bulunmuştur. ES transfüzyonu yapılan hastalar ile yapılmayan hastalar karşılaştırıldığında SAPS II skoru daha yüksek, invaziv mekanik ventilasyon ve vazopressör uygulama oranı daha fazla bulunmuştur ($p<0.001$). Yoğun bakım yatışında transfüzyon yapılan hastaların mortalite oranı transfüzyon yapılmayan hastalara göre daha yüksek bulunmuştur (%51.7 vs %23.9, $p<0.001$).

Sonuç: Bu çalışmada yoğun bakım hastalarının beşte birine YBÜ'de kalış süresi boyunca ES transfüzyonu yapıldığı gösterilmiştir. Transfüzyon yapılan hastalar daha yüksek hastalık skoruna ve yoğun bakıma yatış gününde daha düşük hemoglobin seviyelerine sahip hastalardır. ES transfüzyonu yapılan hastalar yapılmayan hastalara göre YBÜ'de daha uzun kalış süresine ve daha yüksek ölüm oranına sahiptir.

Anahtar Kelimeler: eritrosit süspansiyonu transfüzyonu, mortalite, yoğun bakım, kritik hasta

Introduction

Anemia is commonly observed in the intensive care unit (ICU). Therefore, red blood cell (RBC) suspension transfusions are frequently performed in patients in the intensive care unit. The risk of infection and even death associated with excessive and unnecessary RBC transfusion is an important problem for patient safety and quality of care (1,2). Furthermore, blood products are costly and have limited availability.

Although anemia development in critically ill patients depends on many reasons, taking blood samples for examination is one of the important risk factor contributing to the development of anemia (3,4). In addition, infiltration from injury sites, invasive procedures, losses caused by gastrointestinal bleeding, and hemodilution due to excessive fluid administration, nutritional deficiencies, decreased red blood cell production due to hemolysis and inflammation, and shortened red blood cell life span may also be considered among other reasons (5-7).

The guidelines recommend restrictive transfusion in the ICU (when Hb <7 g/dL). By comparing the restrictive transfusion strategy and the liberal transfusion strategy, it was shown that the incidence of adverse situations, such as cardiac events, hemorrhage, bacterial infection, and total mortality were lower in patients using restrictive transfusion strategies (8). Data collected from randomized studies using less restrictive transfusion strategies (when Hb >7 g/dL) showed no significant effect on patient outcomes (9).

The aim of this study was to determine current transfusion practices in our intensive care unit and to investigate the effect of RBC transfusion on the clinical outcomes of critically ill patients.

Materials and Methods

This is a retrospective study carried out in an eight-bed internal medicine intensive care unit which provides tertiary care in a tertiary level hospital. Five hundred and twenty patients hospitalized for over 24 hours in the internal medicine intensive care unit between February 2018 and May 2019 were included in the study, and their files were reviewed retrospectively. Patient outcomes were determined as discharge from the intensive care unit or mortality. The first hospitalization data of patients with multiple ICU admissions were included in the study. The exclusion criteria are being <18 years of age, pregnancy, brain death, death within the first 24 hours, multitrauma, and terminal disease. Medical records and electronic laboratory database files of each patient were used to obtain information. The study protocol was approved by the Ethical Evaluation Committee of Kütahya Health Sciences University on 23.05.2019 with the decision number 2019/06-4. Informed consent was not obtained from the patients because it was a retrospective file review.

Patients' demographic characteristics, hospitalization diagnoses, comorbidities, the Simplified Acute Physiology Scores (SAPS II) at the time of admission to ICU, hemoglobin levels at the time of admission to ICU and before transfusion, mortality rate, mechanical ventilation and vasopressor requirements, and length of stay in ICU were recorded. The length of stay of the patients until discharge from intensive care unit or death was calculated. The primary endpoint of the study was to determine the threshold for RBC transfusion in critically ill patients. The pre-transfusion threshold was defined as the lowest hemoglobin measurement obtained within 24 hours prior to transfusion. The second endpoint is the length of stay in ICU and mortality.

Admission diagnoses were classified as follows. The diagnosis of sepsis; is sepsis developing due to lung, gastrointestinal system, urinary system, central nervous system, soft tissue or blood/catheter-related infections. The diagnosis of respiratory failure; is hypoxia developing due to chronic obstructive pulmonary disease, interstitial lung disease, asthma attack, pulmonary embolism, and pneumothorax. The diagnosis of metabolic disorder includes; electrolyte disorders (such as hypernatremia, hypercalcemia), ketoacidosis, hypoglycemia, and hepatic encephalopathy. Cardiac disease includes heart failure and heart rhythm disorders. The diagnosis of neurological disease includes status epilepticus, intracranial hemorrhage, and ischemic stroke. The diagnosis of post-CPR includes patients whose spontaneous circulation is restored after cardiopulmonary resuscitation.

Statistical Analysis

SPSS 22.0 packaged software was used in the analysis of the study data. The descriptive statistics used in the study include mean, standard deviation, frequency, and rates. The Kolmogorov-Smirnov test was used to determine whether the variables were normally distributed. Student's t-test was used to compare quantitative independent variables, while the chi-square test was used to compare qualitative independent variables. When the chi-square conditions were not met, Fisher's exact test was used for qualitative data. The value of $p<0.05$ was considered statistically significant. Significant data determined in univariate analyses were evaluated by multivariate analysis (logistic regression).

Results

A total of 520 patients were included in the study. More than half of the admissions to the ICU were from the emergency department. The most common history of the admitted patients was hypertension, diabetes mellitus, and coronary artery disease. The patients were most frequently admitted to the ICU with the diagnosis of sepsis/septic shock, metabolic disorder, and respiratory failure.

The patients were divided into groups as received transfusion/not received transfusion and those who died ICU or discharged. Sociodemographic characteristics of the groups are given in tables 1 and 2. Eighty-nine (17.1%) patients underwent RBC transfusion. The mean age of the patients who had received transfusion was 72.2 ± 13.8 years, and 58.4% of them were male. The mean age ($p=0.13$) and SAPS II scores were higher, and invasive mechanical ventilation and vasopressor utilization rates were higher in patients who had received transfusion ($p<0.001$).

Table 1. A comparison of some general characteristics of patients who had received and had not received erythrocyte suspension transfusion

	Univariate analysis			Multivariate analysis	
	Patients who had received transfusion n=431	Patients who had not received transfusion n=89	Chi-square Test		
	n (%)	n (%)	p*	OR	p
Gender					
Male	212 (49.2)	52 (58.4)	0.112		
Female	219 (50.8)	37 (41.6)			
Service of intensive care unit admission					
Emergency service	236 (54.8)	45 (50.6)			
Internal medicine service	75 (17.4)	17 (19.1)			
General surgery	16 (3.7)	0			
Palliative care unit	7 (1.6)	3 (3.4)			
Orthopedics	29 (6.7)	3 (3.4)			
Other intensive care units	60 (13.9)	19 (21.2)			
Other services	8 (1.9)	2 (2.2)			
Medical history					
Hypertension	232 (53.8)	47 (52.8)	0.520		
Diabetes mellitus	131 (30.4)	24 (27)	0.861		
Coronary artery disease	104 (24.1)	26 (29.2)	0.313		
Congestive heart failure	55 (12.8)	13 (14.6)	0.638		
Chronic renal failure	58 (13.5)	16 (18)	0.266		
Chronic obstructive pulmonary disease	80 (18.6)	20 (22.5)	0.394		
Malignancy	44 (10.2)	14 (15.7)	0.132		
Intensive care admission diagnosis					
Sepsis/Septic shock	98 (22.8)	29 (32.5)			
Metabolic disorder	73 (17.6)	4 (4.5)			
Respiratory failure	57 (13.2)	13 (14.6)			
Acute renal failure	51 (11.8)	9 (10.1)			
Postoperative follow-up	55 (12.8)	3 (3.4)			
Gastrointestinal hemorrhage	20 (4.6)	25 (28.1)			
Cardiovascular disease	22 (5.1)	3 (3.4)			
Suicide	22 (5.1)	0			
Post CPR	17 (3.9)	2 (2.2)			
Neurological disorder	16 (3.7)	1 (1.1)			
Invasive mechanical ventilation &					
Not applicable	281 (65.2)	39 (43.8)	<0.001		
Applicable	150 (34.8)	50 (56.2)			
Vasopressor &					
Not applicable	315 (73.1)	46 (51.7)	<0.001		
Applicable	116 (26.9)	43 (48.3)			
Intensive care unit mortality &					
Exitus	103 (23.9)	46 (51.7)	<0.001	4.490 (1.175-11.356)	0.002
Discharged	328 (76.1)	43 (48.3)			
	mean±SD	**mean±SD**	**Student's t-test**		
Age *(years)*	67.4±17.3	72.2±13.8	0.13		
SAPS II&	5.9±2.4	7.1±2.0	<0.001		
Length of ICU stay (*days*)	4.9±5.5	16.0±23.0	<0.001	1.149 (1.095-1.205)	<0.001
Basal hemoglobin levels&(*g/dl*)	11.3±2.3	8.2±2.1	<0.001	0.369 (0.292-0.466)	<0.001

*Chi-square test, quantitative data "n (percentage)", **SD:** Standard Deviation, **&** Significant data determined in univariate analysis were taken to multivariate analysis, **Post-CPR:** Patients with restored spontaneous circulation after cardiopulmonary resuscitation, **SAPS II:** Simplified Acute Physiology Score

Table 2. A comparison of some general characteristics of patients according to the outcomes of intensive care unit

	Univariate analysis			Multivariate analysis	
	Patients who died *n*=149	Patients who survived *n*=371	Chi-square Test	Multivariate analysis	
	n (%)	*n* (%)	p*	OR	p
Gender					
Male	70 (47)	194 (52.3)	0.273		
Female	79 (53)	177 (47.7)			
Service of intensive care admission					
Emergency service	65 (43.6)	216 (58.2)			
Internal service	40 (26.8)	52 (14)			
General surgery	1 (0.7)	15 (4)			
Palliative service	4 (2.7)	6 (1.6)			
Orthopedics	5 (3.4)	27 (7.3)			
Other intensive care units	33 (22.1)	46 (12.4)			
Other services	1 (0.7)	9 (2.4)			
Comorbidities					
Diabetes mellitus	39 (26.2)	116 (31.3)	0.251		
Hypertension	86 (57.7)	193 (52)	0.239		
Coronary artery disease	42 (28.2)	88 (23.7)	0.287		
Congestive heart failure	23 (15.4)	45 (12.1)	0.312		
Chronic renal failure[&]	29 (19.5)	45 (12.1)	0.030		
Chronic obstructive pulmonary disease	32 (21.5)	68 (18.3)	0.410		
Malignancy[&]	25 (16.8)	33 (8.9)	0.010		
Intensive care unit admission diagnosis					
Sepsis/Septic shock	54 (36.3)	73 (19.6)			
Metabolic disorder	20 (13.5)	57 (15.4)			
Respiratory failure	19 (12.8)	51 (13.7)			
Acute renal failure	17 (11.4)	43 (11.6)			
Postoperative follow-up	4 (2.7)	54 (14.6)			
Gastrointestinal hemorrhage	9 (6)	36 (9.7)			
Cardiovascular disease	7 (4.7)	18 (4.9)			
Suicide	1 (0.7)	21 (5.7)			
Post CPR	12 (8.1)	7 (1.9)			
Neurological disorder	6 (4)	11 (3)			
Invasive mechanical ventilation[&]					
Not applicable	33 (22.1)	287 (77.4)	<0.001	3.431 (1.848-6.369)	<0.001
Applicable	116 (77.9)	84 (22.6)			
Vasopressor[&]					
Not applicable	34 (22.8)	327 (88.1)	<0.001	10.853 (6.030-19.534)	<0.001
Applicable	115 (77.2)	44 (11.9)			
Transfusion[&]					
Not applicable	103 (69.1)	328 (88.4)	<0.001	3.320 (1.429-7.714)	0.005
Applicable	46 (30.9)	43 (11.6)			
	mean±SD	mean±SD	Student's t-test		
Age [&]**(** *years)*	72.8±13.6	66.4±17.6	<0.001		
SAPS II[&]	7.9±2.1	5.3±2.1	<0.001	0.957 (0.944-0.971)	<0.001
Length of ICU stay (*days)*	9.8±15.5	5.6±9.2	0.002		
Basal hemoglobin levels[&](*g/dl)*	10.4±2.3	11.0±2.6	0.019		

*Chi-square test, quantitative data "n (percentage)", **SD:** Standard Deviation, **&:** Significant data determined in univariate analysis were taken to multivariate analysis, **Post CPR:** Patients with restored spontaneous circulation after cardiopulmonary resuscitation, **SAPS II:** Simplified Acute Physiology Score

The basal hemoglobin levels (8.2 ± 2.1 g/dL) of the patients who had received transfusion on the first day of ICU admission were lower (11.3 ± 2.3 g/dL) (p<0.001). The number of patients with hemoglobin concentration <9 g/dL measured on the first day of ICU admission was 115 (22.1%). While 89 (17.1%) patients underwent RBC transfusion during the ICU stay, 40 (7.6%) patients underwent RBC transfusion on the first day of hospitalization.

The mean hemoglobin threshold of patients who had received transfusion was 6.9 ± 1.1 g/dL. The mean RBC transfusion per patient was calculated as 3.8 ± 4.1 units.

The mortality rate (51.7%) of the patients who had received transfusion in the ICU was higher compared to non-transfused patients (23.9%). The mean length of stay in the ICU was 16 ± 23 days in the patients who had received transfusion while the mean length of stay in the ICU was 4.9 ± 5.5 days in the patients who had not received transfusion.

When the patients included in the study were divided into two groups as those survivors and non survivors it was observed that the non-survivors group required higher rate of blood transfusison, vasopressor therapy and mechanical ventilation. In non-survivors, the mean age and SAPS II disease severity score were higher, the length of stay in ICU was longer, and the basal hemoglobin level measured on the first day of ICU admission was lower. When the data that were found to be significant in univariate analysis were taken into multivariate analysis. The prolonged hospital stay (OR:1.149 (1.095-1.205)) and low hemoglobin levels on the first day of ICU admission (OR:0.369 (0.292-0.466)) in ICU patients were found to be independent risk factors for transfusion (p<0.001).

The multivariate analysis of the survivors and non-survivors revealed that mechanical ventilation (OR:3.431 (1.848-6.369)), vasopressor therapy (OR:10.853 (6.030-19.534)), and RBC transfusion (OR: 3.320(1.429-7.714)) were found to be independent risk factors for increased mortality. Although the SAPS II score was statistically significant, it was not found efficacious on mortality due to OR: 0.957 (0.944-0.970).

Discussion

In this study, it was determined that the rate of the patients who had received transfusion during the ICU stay was 17.1% and the transfusion threshold was 6.9 g/dL. The transfusion rate was reported to be 37% in the ABC study, 44% in the CRIT study, 33% in the SOAP study, and 15-34.9% in the study conducted by Vincent et al.(10) in 2018 and evaluating transfusion practice in countries around the world (5,11,12). Soril LJJ et al. (13) reported that more than 40% of patients who were followed up in the surgical and medical ICU with no hemorrhage were transfused with hemoglobin levels between 7 g/dL and 7.9 g/dL. The rate of transfusion in our intensive care unit was lower compared to these studies. In the studies, the rate of the patients who had received transfusion on the first day of ICU admission was reported to be 7.1-19.4% (10). In our study, it was determined that 40 (7.1%) patients were received transfusion on the first day of ICU admission. This low transfusion rate appears to result from the use of a restrictive transfusion strategy in the ICU. The lowest threshold used for RBC transfusion was reported from the Middle East with 7.8 ± 1.4 g/dL, and the highest threshold was reported from Eastern Europe with 8.9 ± 1.9 g/dL. (10) Compared to these rates, the threshold hemoglobin level used to perform RBC transfusion in our intensive care unit was lower. The transfusion guidelines have recommended a transfusion threshold of 7 g/dL for stable adult patients without hemorrhage (14,15).

Studies evaluating the transfusion threshold of critically ill patients in the ICU showed that a decrease in patients' hemoglobin levels up to 7 g/dL can be tolerated and that the liberal RBC transfusion strategy can actually lead to worse clinical outcomes (16). In a meta-analysis of 18 randomized controlled studies comparing restrictive and liberal transfusion strategies, it was reported that the risk of developing severe infections such as pneumonia, mediastinitis, and sepsis was lower in patients undergoing restrictive blood transfusion than in patients undergoing liberal blood transfusion (11.8% and 16.9%, respectively). No difference was reported between the two groups in terms of hemorrhage, cardiac events, and total mortality. Consequently, applying restrictive RBC transfusion strategies in the ICU has the potential to reduce the incidence of health care-associated infections (17). Studies examining the mean transfusion volumes given to patients reported that 2 to 4.3 units of RBC transfusion were given per transfusion (18,19). In the literature review, it is observed that a higher volume of RBC transfusion is performed. This difference may be due to the patient population, intensive care practice, and guideline recommendations that have changed since the publication date.

It was reported that two-thirds of the patients had a hemoglobin concentration of <12 g/dL during the ICU stay, and 97% became anemic by the eighth day of hospitalization (5,20). In our study, the mean transfusion time of the patients who had received transfusion was found to be 4.1 ± 6.4 days. It was reported that the incidence of anemia may increase when patients stay longer in the ICU as a result of taking blood daily for examination and blood loss due to various reasons (7,8). The length of ICU stay (16 ± 23 days) of patients who had received transfusion was longer than the other group (4.9 ± 5.5 days). As shown in other studies, the rate of transfusion was found to be related to the prolonged length of ICU stay (21). In the study conducted by Vincent et al. (10) and in another multicenter study of 1136 patients, disease severity scores such as SAPS II, APACHE (Acute Physiology and Chronic Health Evaluation) II, and SOFA (Sequential Organ Failure Assessment) were reported to be higher in transfused patients (5).In our study, the SAPS II score and ICU mortality were found to be higher in patients who had received transfusion (p<0.001). Furthermore, patients needed more life-support treatments such as mechanical ventilation and vasopressor support during ICU stay.

Our study has several limitations. Firstly, this is a retrospective study conducted with a limited number of patients in a single center. Secondly, complications such as transfusion-related allergic reactions that may affect mortality and length of ICU stay, circulatory system overload, and transfusion-related acute lung injury were not included in the data collection.

Conclusion

This study shows that one-fifth of our ICU patients underwent RBC transfusion during the ICU stay. The patients who had received transfusion had higher disease severity scores and lower hemoglobin levels on the day of ICU admission. The patients who had received transfusion had a longer length of ICU stay and higher mortality rates.

AUTHOR CONTRIBUTIONS:

Concept: AG; **Design:** KG; **Supervision:** KG; **Data Collection and/or Processing:** KG; **Analysis and/or Interpretation**: AG; **Literature Search:** AG; **Writing Manuscript**: KG; **Critical Review:** AG.

Ethics Committee Approval: Kutahya University of Health Sciences Ethics Review Board 2019/06-4

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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