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ORIGINAL ARTICLE

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Transfusion of red blood cells as risk predictor for nosocomial infections in pediatric intensive care units

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ABSTRACT

Background: Transfusion of red blood cells (RBCs) is a common intervention in Pediatric Intensive Care Units (PICU) due to anemia occurring in over one-third of children hospitalized there.

Objectives: To establish the relation between transfusion of RBCs and nosocomial infections in PICU and evaluate its impact on absolute lymphocytic count.

Patients and methods: A case-control study carried out on 200 critically ill children admitted to PICU, of which one hundred received blood transfusion and one hundred did not. All patients underwent history taking and clinical examination.

Results: A statistically significant higher prevalence of mechanical ventilation, central venous catheterization, PRISM score and longer PICU length of stay were observed in the transfused group compared with the non-transfused group ($P < 0.001$). Nosocomial infections were present in 62% patients in the transfused group and in 32% patients in the non-transfused group ($P < 0.05$), including nosocomial pneumonia, bacteremia, and urinary tract infection. Mechanical ventilation, presence of central venous catheter, number and age of transfused RBCs were risk predictors for nosocomial infections. Lymphopenia was evident in the transfused group.

Conclusion: Nosocomial infections are related with red blood cells transfusion in patients hospitalized in PICU. Mechanical ventilation, presence of central venous catheter, number and age of transfused RBCs, and lymphopenia were risk predictors for nosocomial infections.

Key words: RBCs transfusion, nosocomial infections, pediatric intensive care units, mechanical ventilation, central venous catheter.

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Introduction

Anemia is a common problem in critically ill children admitted to pediatric intensive care units (PICU) due to the underlying causes and severity of the disease, malnutrition, and hemodilution [1]. Up to 50% of children who are admitted to PICU receive red blood cells (RBCs) transfusion [2].

Indications for blood transfusion in adults and children are similar, but hemoglobin threshold, transfusion infusion rates and volume in relation to the body weight are not well established in children [1].

RBCs transfusion are given to patients with low hemoglobin concentration and in some conditions that require increased oxygen supply to relieve tissue hypoxia, but this hypothetical benefit of RBCs transfusions have not been unequivocally demonstrated [3].

Blood transfusions may be safer today than were a decade ago because of changes in blood preparation, not only in terms of viral transmission but also in transfusion-related immunosuppression. Some of negative immunosuppressive effects of transfusions can be reduced by leukoreduction [4].

Blood transports oxygen and nutrients throughout the body, connects organs, heals wounds, and protects from dangerous infections [5].

Blood donation is giving the gift of life as one unit may benefit different patients in different places and time.

The blood transfusion today is safer than ever, with more screening protocols and safety measures; however transfusion of blood still may cause fatal complications [6]. Therefore, in the current research, we aimed to establish the relation between transfusion of RBCs and nosocomial infections in PICU.

Patients and methods

Patient's selection

The present study was conducted on two hundred critically ill children admitted to PICU of Menoufia University Hospital, Egypt between 01.01.2016 and 01.012017. One hundred patients received RBCs transfusion and the other one hundred did not. All parents of children included in the study gave their written consent. The study was approved by the Menoufia University Ethics Committees. The inclusion criterion was age from 1 month to ≤ 18 years for any child admitted to the PICU. The exclusion criteria included diagnosis of infection < 48 hours before the admission or within the first 48 hours after admission to the PICU, patients with transplanted organs, patients with primary immune deficiencies or treatment with chemotherapy within the previous.

Bloodstream infection, pneumonia, and urinary tract infections were our primary measures and considered post-transfusion if they occurred ≤ 14 days after transfusion. Pneumonia was diagnosed based on positive bacterial cultures of tracheal specimen and/or new evidence of infiltrations by chest X-ray, or in the absence of a new infiltration pneumonia was diagnosed clinically by a combination of rales, hypoxia, and elevated leukocytes in the tracheal smear, leukocytosis, and/or ventilation abnormalities. Urinary tract infections were diagnosed based on positive bacterial cultures, with colony counts ≥ 1000 CFU/mL or cm^3), while bacteriemia was diagnosed based on positive blood cultures. All patients were observed for length of stay and mortality risk scoring during their PICU stays which were the secondary outcome measures.

Methodology

A complete history taking and physical examination were performed for all included children. Severity score was calculated, namely Pediatric Risk of Mortality (PRISM) [7], whichc was automatically calculated from the website: http://www.sfar.org/scores2/prism2.php within 24 hours from admission. Inserting age of the patient in months in the specified window led to the automatic calculation of the predicted death rate. The laboratory work-up comprised arterial blood gas analysis, complete blood count, C-reactive protein, serum electrolytes, hepatic and renal function tests, and blood cultures. The radiological work-up including chest X-rays, computed tomography of the central nervous system, and other laboratory or radiological investigations were performed when needed.

Statistical analysis

IBM SPSS software version 20.0 (SPSS, Inc., Chicago, IL, USA) was used for analysis of data. Descriptive analysis was perfomed using percentages, mean and standard deviation. Analytical analysis used were t-test, Pearson correlation analysis, and logistic regression. The diagnostic power of the lymphocyte was evaluated by the receiver operating characteristic curve. P values < 0.05 were considered statistically significant.

Results

Out of 200 patients, 100 patients received blood transfusion (48 were males and 52 were females, with mean age 25.1 ± 18.2 months) while the other 100 patients did not (58 were males, 42 were females, with mean age 37.3 ± 19.7 months) (Table 1).

A statistically significant higher prevalence of mechanical ventilation, central venous catheterization, PRISM score, and longer PICU length of stay was observed in the transfused group compared with the non-transfused group ($P < 0.001$). Also, there was a statistically significant difference regarding increased mortality rate in the transfused group compared with the non-transfused group ($P < 0.05$) (Table 1).

The respiratory disorders represented the most common cause of admission to PICU in both groups (32%) (Table 2). Nosocomial infections were diagnosed in 62% patients in the transfused group and in 32% patients in the non-transfused group ($P < 0.05$), including nosocomial pneumonia, bacteriemia, and urinary tract infection (22%, 20%, 5% respectively) (Table 3).

According to the logistic regression analysis the number of transfusions, mechanical ventilation, central venous catheterization, and age of RBCs were predictors of nosocomial infections (Table 4).

Lymphopenia was more evident in the transfused group than the non-transfused group. ROC curve showed a sensitivity of 78% and specificity of 65%, the cut off level of the absolute lymphocytic count was 1.20, and the area under the curve was 61 (Table 5, Table 6, Figure1).

Discussion

Anemia is a common condition in critically ill patients that results in frequent transfusion of RBCs. Approximately 95% of patients who require the intensive care unit stay of 3 days or longer are anemic, with almost 50% prevalence of decreased blood oxygenation which can increase the rates of organ failure and morbidity [8].

Table 1. Demographic data and clinical parameters of the studied groups

		Patients groups				Total		t- test	P value
		RBCs transfusion		No RBCs transfusion					
Age (months)		25.1 ± 18.2		37.3 ± 19.7		31.2 ± 19.7		2.1	< 0.05
Sex	♂	48	48%	58	58%	106	53%	$X^2 = 3.2$	> 0.05
	♀	52	52%	42	42%	94	47%		
MV		74	74.0%	44	44%	118	59.0%	9.30	< 0.001
CVC		92	92.0%	56	56%	148	74.0%	16.84	< 0.001
PICU stay		27.5 ± 7.9		18.1 ± 2.5		22.8 ± 8.6		6.5	< 0.001
Surgery*		8	8.0%	4	4.0%	12	6.0%	$X^2 = 0.71$	> 0.05
PRISM Score		25.6 ± 8.2		18.8 ± 4.2		24.5 ± 7.5		5.2	< 0.001
Mortality (N / %)	+ve	64	64%	82	82%	146	73%	4.1**	< 0.05
	-ve	36	36%	18	18%	54	27%		

MV: Mechanical Ventilation; CVC: Central venous catheter;* exposure to surgical procedures;** Fisher's Exact Test

Table 2. Comparison between the studied groups as regards causes of admission.

Causes of admission	Patients groups				Total		*Chi 2*	*P* value
RBCs transfusion	No RBCs transfusion							
Respiratory	28	28.0%	36	36.0%	64	32.0%	12.34	<0.05
CNS	18	18.0%	24	24.0%	42	21%		
Hematological	16	16.0%	4	4.0%	20	10%		
Cardiac	16	16.0%	20	20.0%	36	18%		
Metabolic	8	8.0%	4	4.0%	12	6%		
Gastrointestinal	6	6.0%	8	8.0%	14	7%		
Surgery	8	8.0%	4	4.0%	12	6%		

Table 3. Comparison between the studied groups as regards causes of nosocomial infections.

	Patients groups				Total		*Chi 2*	P- value
	RBCs transfusion (N = 100)		No RBCs transfusion (N = 100)					
Nosocomial infections	62	62%	32	32%	94	47		
Blood stream infection	24	24%	16	16%	40	20%	5.2	<0.05
UTI	6	6%	4	4%	10	5%		
Nosocomial Pneumonia	32	32%	12	12%	44	22%		

A significant difference in the mean age of the included patients which were 25.1 ± 18.2 months in the transfused group versus 37.3 ± 19.7 months in the non-transfused group may be explained by the vulnerability of this age group to life-threatening diseases.

The overall length of stay in PICU was 22. 8 ± 8.6 days (27.5 ± 7.9 days in the transfused patients versus 18.1 ± 2.5 days in the non-transfused patients) due to a large number of patients subjected to mechanical ventilation for longer periods. Choudhury et al. found that nosocomial infections are related with longer hospital stay and more common performance of invasive procedures [9]. El-Nawawy stated that the length of stay in PICU reflects the severity of the disease and health status, PICU quality and performance [10]. Aglu et al. mentioned that the length of stay in intensive care unit can be directly affected by the type and severity of illnesses [11]. Gomez et al. found that the prolonged hospitalization is a vital risk factor for infection in intensive care units [12].

Table 4. Logistic Regression analysis to determine predictors for risk of nosocomial infections.

	B	Wald	Sig.	Odds ratio	95% C.I. for Odds ratio	
					Lower	Upper
Age	-0.048-	0.203	0.652	0.953	0.775	1.173
sex(Males)	-1.963-	3.326	0.068	0.140	0.017	1.158
Lengthof stay	-0.022-	0.175	0.676	0.978	0.881	1.086
Increasing RBC transfusions	1.310	3.756	0.043	3.707	0.193	71.084
Mechanical ventilation	-2.700-	3.965	0.046	0.067	0.005	0.958
Central venous catheterization	0.463	3.064	0.048	1.589	0.045	56.643
Exposure to surgery	2.221	1.369	0.242	9.221	0.223	381.211
Age of RBCs in days	0.187	4.307	0.038	1.205	1.010	1.438

Table 5. Comparison between the studied groups as regards Absolute Lymphocytic count.

	RBCs Transfusion	No RBCs Transfusion	t.test	P.value
Absolute Lymphocytic count	1.76 ± 0.64	2.2 ± 1.01	2.4	<0.05

Table 6. ROC curve and AUC of absolute lymphocytic count for the prediction of nosocomial infection.

Area	SE	P	95% Confidence Interval		Cut off value	Sensitivity	Specificity
			Lower Bound	Upper Bound			
0.61	0.083	0.059	0.348	0.673	1.20	78%	65%

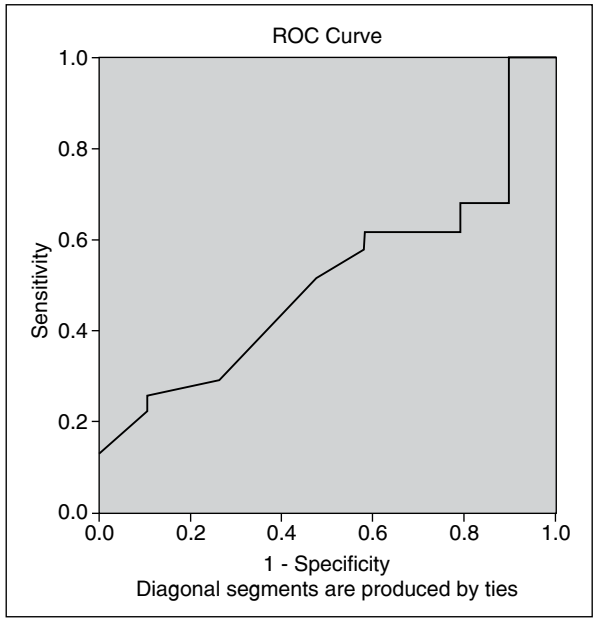

Figure 1. ROC curve and AUC of absolute lymphocytic count for prediction of nosocomial infection.

In the present study, the predicted death rate for all included patients was 25.65% estimated with the PRISM score. The overall mortality rate was 27% which was significantly higher in the transfused patients (36%) compared with the non-transfused patients (18%). White et al. stated that 98% had PRISM scores less than 10%. The overwhelming majority of the patients in his study were the low-risk category of illness severity on admission into PICU [13]. Omar et al. documented a higher mortality rate in transfused patients compared to non-transfused ones (28.6% versus 12.4%, $P = 0.012$) [14]. Kneyber et al. stated that transfusion of RBCs in critically ill children is independently related with increasing of mortality [15]. Lee et al. mentioned that the mortality rate reflects the quality of ICU. The mortality rate can be strongly affected by the severity of diseases, comorbidities and demographics [16].

In the current study, respiratory diseases were the main cause for admission to PICU (32%) followed by central nervous system causes (21%) and cardiac causes (18%). Respiratory causes were the main causes of admission due to the rapid spread of infection by droplet infection [17]. Seasonal distribution of respiratory diseases, as most of the cases, are concentrated in winter [18]. Pollack et al. stated that respiratory diseases are the main reasons for admission to PICU (33.55%), followed by cardiovascular conditions (24.1%), then neurologic diseases (20.1%) [19]. Lee et al. found that the most common diagnostic category was a cardiovascular disorders (38.80%), followed by

hemato-oncological diseases (21.20%) and respiratory disease (19.30%) [16].

Nosocomial infections represented 62% in the transfused group compared to 32% in the non-transfused group ($P < 0.05$). The patients in the intensive care units are frequently exposed to infections, these infections being variable depending on the country, hospital and medical unit [20]. Rogers et al. showed that allogeneic blood transfusion was associated with an increased risk of infection at multiple sites [21]. Omar et al. noticed that among the 113 non-transfused patients, 12 had a nosocomial infection, while among 49 patients who received atransfusion, 23 developed an infection. This evidences a significantly higher proportion of infection in this group (46.9% versus 10.6%, $P < 0.0001$) [14]. Engele et al. found no relation between transfusion of RBCs and nosocomial infection [22].

Nosocomial infections are associated with mortality up to 50%. Rapid detection, effective therapy and good prevention are the important therapeutic means for the nosocomial infections [23].

The age of RBCs transfused as well as the increasing numbers of RBCs transfusion were risk factors for nosocomial infections in the present study.

Transfusion of RBCs stored for more than 14 days is a risk for bacterial infection after trauma, irrespective of using prophylactic antibiotics [24]. Corwin et al. reported that the average age of allogeneic packed RBCs administered to an ICU patients is 21 days, and did not find any relation between the age of blood transfused and the incidence of nosocomial infections, because the subset of patients transfused with fresh blood in their study was very small [25].

Joao et al. stated that transfusions of blood are related with nosocomial infections, and correspond with the number of transfusion units [26].

Moreover, lymphopenia was more evident in the transfused group than the non-transfused group. ROC curve showed a sensitivity of 78% and specificity of 65%, with the cut off level of the absolute lymphocytic count 1.20, and the area under the curve 0.61 to predict nosocomial infections. A decrease in the absolute lymphocyte count results in impairment of the adaptive immune system. Low absolute lymphocyte counts are more important predictors of bacteremia than markers used in patients admitted to intensive care units, and persisting lymphopenia or a non-significant increase at day 3 is related with developing nosocomial infection and increasing 28-day mortality [27].

The association between RBCs transfusions and nosocomial infections can be explained by mechanisms such as immune suppression including induction of T cell suppression and reduced natural killer T cell activity [14]. A reduced production of interleukin-2 and an increased production of prostaglandin E2, with a decrease in CD4 T helper cells and positive interleukin-2 receptor in helper cells. However, a recent interest in immune modulatory effects and lesions caused by relation to storage of transfused RBCs is documented [28]. White et al. found that ALC measured post-transfusion, are significantly lower than ALC in non-transfused patients, whereas white blood cell is unchanged [13]. Felmet et al. found that there is no significant difference in lymphocyte counts in critical patients except multiple organ failure, even over the course of weeks [29]. Vamvakas and Blajchman suggested many possible mechanisms for the relation between transfusions of RBCs and invasive bacterial infections, with one of these mechanisms being inhibition of lymphocyte proliferation [30].

Conclusion

Transfusion of RBCs is related with increased risk for nosocomial infections. Invasive procedures such as mechanical ventilation and central venous catheterization along with increasing number of RBC transfusions, advanced age of RBCs and lymphopenia were predictors of increased risk of nosocomial infections.

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