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Early Hemodynamic Changes as Predictors of Mortality after Packed Red Blood Cells Transfusion in Critically Ill Children

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Abstract:

Objectives: *to evaluate effects of packed red blood cells (PRBCs) transfusion on some hemodynamic responses and its relation to patient mortality* ***Patients:*** *64 critically ill infants and children were included in the study admitted to in Pediatric Intensive Care Unit (PICU) and required PRBCs transfusion10 mL/kg.*

Methods: *Heart rate (HR), mean arterial blood pressure (MABP), blood hemoglobin (Hb) and hematocrite value (HCT) were measured for conventional hemodynamic(HD) monitoring .Trans-esophageal measurement of stroke volume (SV), cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR) and systemic vascular resistance index (SVRI) before and 2 hours after PRBCs transfusion were also performed.*

Results: *CI at a cut-off value >1.9 had the highest sensitivity while CO, SV and SVR at a cut-off values (>1.5, >12.2 and ≤ 3081 respectively) had the highest specificity for prediction of mortality among patients before start of treatment..CO at a cut-off value ≤ 12.5 and CI at a cut-off value ≤ 14.5 had the highest sensitivity while all parameters had low specificity for prediction of mortality among patients after PRBCs transfusion, while SV, SVR and SVRI were less sensitive (38.46%, 38.46%,53.85% and 40% respectively).*

Conclusions: *CI had the highest sensitivity and CO, SV and SVRI had the highest specificity for prediction of mortality among patients before start of PRBCs transfusion. CO and CI had the highest sensitivity for prediction of mortality among patients after PRBCs transfusion.*

Keywords: *Hemodynamic , Trans-esophageal , PRBCs , Cardiac Index, vascular resistance .*

1. INTRODUCTION

Cardiac output (CO) is the volume of blood that is pumped by the heart around the systemic circulation in one minute. It equals stroke volume (SV) which is the volume pumped out by the heart in one contraction multiplied by heart rate (HR). CO is affected by heart rate, preload and contractility [1,2]

The CardioQ-ODM (Deltex Medical) which is an esophageal Doppler monitor is used in assessing CO and intravascular fluid status through using single-use probe, which is placed in the esophagus via the mouth or nose. Such monitoring helps in assessment of the initial hemodynamic state, judging response to therapy, and ongoing evaluation of changes in hemodynamic state with disease progression is crucial. [3]

RBCs are transfused to increase hemoglobin (Hb) concentration and Oxygen delivery (DO2). However, there are many side effects such as metabolic, hypothermia, infection, iron overload, and graft versus-host disease.[4] Also some studies showed association between RBC transfusions and adverse outcomes such as Multiple Organ Dysfunction Syndrome (MODS) mortality, increased length of stay and duration mechanical ventilation in critically ill patients[5]

2. AIM OF THE STUDY

The purpose of this study was to evaluate the effects of PRBCs transfusion on some hemodynamic responses and its relation to mortality in patients admitted to PICU.

3. PATIENTS AND METHODS

Study sample and design:

This study was conducted in PICU of Pediatric department of Tanta university hospital at Egypt from September 2016 to September 2017 on 68 infants and children; their ages ranged from 2 months to 9 years old.

Inclusion Criteria:

Patients were included in the study if hemoglobin < 7 g/dL and in post-surgical patients and/or the presence of alarming symptoms/signs (chest pain, orthostatic

hypotension, tachycardia unresponsive to fluid resuscitation, congestive heart failure) if hemoglobin is < 8 g/dL. [6]

The study has been approved by the local institutional research ethics committee of Tanta Faculty of Medicine.

Exclusion Criteria:

Patients who have hereditary hematopoietic disorders, congenital heart diseases, Patients treated with diuretics, vasoactive drugs (Dopamine, Dobutamine etc.), nasal injuries, nasal polyps, facial trauma, intra-aortic balloon pumping, carcinoma of the pharynx, larynx or esophagus, aneurysms of the thoracic aorta, necrosis of the esophagus or nasal passage, and coagulopathies were excluded from the study

All patients were subjected to routine laboratory investigation(Hb and Ht value) andconventional and trans-esophageal HD monitoring before and 2 hours after PRBCs.

Protocol of blood transfusion:

PRBCs were chosen after ABO, Rh and cross matching done. It was warmed before transfusion by blood warmer using infusion pump with at a rate of <10 mL/kg/hour in absence of heart failure. Rate was ~ 2 mL/kg/hour in the presence of cardiac failure.[7]

On enrollment in the study, scoring systems for patients were done Pediatric Risk for Mortality (PRISM) III scoring immediately on admission [8] and Sequential Organ Failure Assessment (SOFA) scoring 48 hours after admission.[9]

Hemodynamic monitoring of stroke volume, cardiac output, cardiac index, systemic vascular resistance and systemic vascular resistance index by Deltex the CardioQTM Transesophageal Doppler. CardioQTM Product code. (9015-7103); Deltex medical.[10]

Insertion of the probe:

Water-based lubricant applied liberally to probe tip and lower part of probe and insert into esophagus. For oral placement, probe advanced until incisors are at the second depth marker at starting after first month or more than 3 kilograms. When the CardioQ signal located the volume knob adjusted as required. Probe depth adjusted to locate the descending aortic signal and then rotated to optimize the signal. [10]

4. STATISTICAL ANALYSIS

The collected data were organized, tabulated and statistically analyzed using SPSS version 19 (Statistical Package for Social Studies) created by IBM, Illinois, Chicago, USA. For numerical values the range mean and standard deviations were calculated. [11]

The differences between two mean values before and after therapy were tested using paired student's t test. Testing of mean differences between survivors and survivors was done using Mann-Whitney test (Z) due to small sample size in each category. For categorical variable the number and percentage were calculated. The level of significant was adopted at $p<0.05$. A receiver operating characteristic (ROC) curve: used to illustrate the diagnostic properties of a test on a numerical scale. [11]

5. RESULTS

Table (1) showed demographic and clinical characteristics of the studied subjects. 68patents with mean age 27.35± (34.96) months were included. Patients with Bronchopneumonia complicated with respiratory failure represented the commonest diagnosis, 34 (50%) of the studied group.

Table 1: *Demographic and clinical characteristics of the studied subjects*

Characteristics	
Age (month):	
Mean±(SD)	27.35±(15.9)
Gender (M/F)ratio:	15/19
Diagnosis	Number (%)
Admission diagnosis: no (%)	
Bronchopneumonia complicated with	34(50)
respiratory failure	6(8.82)
Status epileptics	6(8.82)
Encephalitis	
Werdnig Hoffmann Syndrome	4(5.88)
GuillainBarre syndrome	4(5.88)
Congenital myopathy on MV	4(5.88)
Intraventricular hemorrhage with aspiration	4(5.88)
pneumonia	2(2.94)
Refsum disease on MV	2(2.94)
Rheumatic heart disease complicated with	2(2.94)
Infective endocarditis and cerebral infarction	
Myocarditis,Dilatedcardiomyopathy	

M/F, male/female; MV, mechanical ventilation; PICU, pediatric intensive care unit.

Table (2) showed conventional HD mointering parameters (heart rate and mean arterial blood pressure (MABP) before and after PRBCs transfusions. There was non significant changes in group II (after transfusion) compared with group I (before transfusion).

Table (2): *Comparison of heart rate (bpm) and MABP (mmHg) before and after PRBCs transfusion*

Heart rate (bpm)	**Group I**	**Group II**
Mean±SD	136.62±22.30	135.35±23.11
t	0.513	
p	0.611	
MABP (mmHg)	**Group I**	**Group II**
Mean±SD	72.54±19.16	74.18±17.60
t	0.990	
p	0.329	

gm/dL: Gram per Deciliter.

Table (3) showed blood hemoglobin and blood hematocrite before and after PRBCs transfusions. There was significant increase in group II (after transfusion) compared with group I (before transfusion).

Table (3): *Comparison of blood hemoglobin (gm/dL) and hematochrite value before and after PRBCs transfusion*

Blood hemoglobin (gm/dL)	Group I	**Group II**
Mean± SD	7.37±1.08	10.03**±**0.86
t	8.231	
p	0.001*	
HCT (%)	Group I	Group II
Mean±SD	27.08±3.93	34.76**±**3.96
t	6.105	
p	0.001*	

Table (4) showed changes in stroke volume (SV), cardiac output (CO), cardiac index (CI) and systemic vascular resistance (SVR) before and after PRBCs transfusions. There were no significant changes in the studied parameters when compared before and after PRBCs transfusion.

Table (4): *Comparison of Stroke Volume, Cardiac Output (L/min) , of Cardiac Index and Vascular Resistance before and after PRBCs Transfusion*

SV (mL)	**Group I**	**Group II**
Mean±SD	9.23±8.98	9.52±6.03
t	0.433	
p	0.667	
CO(L/min)	**Group I**	**Group II**
Mean±SD	1.21±0.832.0	1.23±1.13
t	0.108	
p	0.915	
CI (L/min/m2)	**Group I**	**Group II**
Mean±SD	2.45±1.29	2.74±1.1
t	1.804	
p	0.080	
SVR (dyn.s/cm5)	**Group I**	**Group II**
Mean±SD	6068.07±3843.72	5357.40±2922.27
t	1.919	
P	0.064	

Table (5): *ROC Curve for CO, CI, SV, SVR and SVRI before treatment to predict mortality*

	AUC	**P**	**Cut off**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**95% CI**	
								LL	**UL**
CO	0.590	0.112	>1.5	38.46	100.0	100.0	72.41	0.371	0.809
CI	0.670	0.099	>1.9	100.0	57.14	59.09	100.0	0.483	0.585
SV	0.650	0.146	>12.2	38.46	100.0	100.0	72.41	0.447	0.854
SVR	0.755	0.014*	≤3081	53.85	100.0	100.0	77.78	0.566	0.944
SVRI	0.610	0.288	≤2636	40.0	57.14	18.18	80.0	0.406	0.814

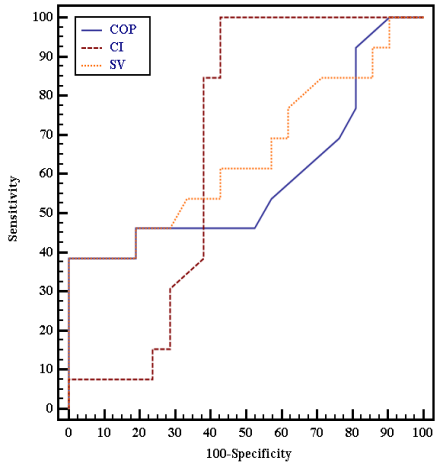

Figure (1): *Optimum diagnostic cut-off values derived from the receiver operating characteristics curves (ROC) for prediction of mortality before PRBCs transfusion*

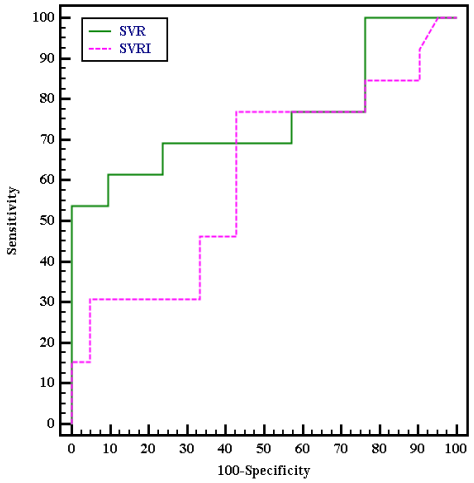

Figure (2): *Optimum diagnostic cut-off values derived from the receiver operating characteristics curves (ROC) for prediction of mortality after PRBCs transfusion*

Table (5) and figure (1) show that CO at a cut-off value ≤12.5 and CI at a cut-off value ≤14.5 had the highest sensitivity (100% for each) for prediction of mortality among patients after PRBCs transfusion, while SV, SVR and SVRI were less sensitive (38.46%, 38.46%,53.85% and 40% respectively). All parameters had low

specificity for prediction of mortality among patients **after** PRBCs transfusion. AUC for ROC curve of CI, SV and SVR was significant for prediction of mortality in patients after PRBCs transfusion (p<0.05%), while that for CO and SVRI was non significant (p>0.05%).

Table (6): *Diagnostic values of the studied hemodynamic parameters for prediction of mortality after PRBCs transfusion*

	AUC	P	Cutoff	Sensitivity	Specificity	PPV	NPV	95% CI	
								LL	UL
CO	0.665	0.111	≤12.5	100.0	38.0	50.0	100.0	0.484	0.846
CI	0.780	0.007*	≤14.5	100.0	52.52	56.52	100.0	0.628	0.933
SV	0.744*	0.018*	≤16.87	92.38	52.38	54.55	91.67	0.574	0.933
SVR	0.740*	0.020*	>1.5	84.62	66.67	61.11	87.50	0.561	0.919
SVRI	0.667	0.107	>0	76.92	66.67	58.82	82.35	0.464	0.869

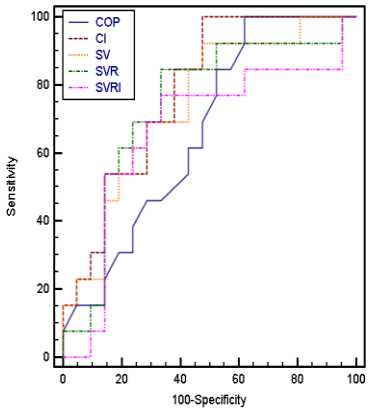

Figure (3): *ROC curve for percent change of hemodynamic parameters to predict mortality*

6. DISCUSSION

The use of RBC transfusion varies widely among physicians; it is not clear that PRBCs transfusion improves patientwith high rates of potentially unnecessary transfusions. [12] Several researches stated that routine RBC transfusion in critically ill patients is associated with excess harm, including the development of nosocomial infection and death. [13]

The present study showed non significant changes in HR and MABP when comparing after with before PRBCs transfusion. This may be explained by that the amount of blood transfused was one unit (10 mL/kg) and that is not enough change the hemodynamic state. This was in accordance with ***Kanmaz et al.,***[14] In contrast to our results, Stute et al., [18], Gramm et al.,[19] and Bernd Saugelet al.,[15] found that PRBCs transfusion caused a significant reduction in HR after compared with before PRBCs transfusion. This was explained by that HR before transfusion was increased in response to anemia as compensatory mechanism to improved oxygenation which would change with repeated PRBCs transfusion rather than single one.

In the current study, there was a significant increase in the hemoglobin concentration and hematocrite value. This could be explained by that the dose was enough to increase both significantly.

The present study showed non significant changes in SV after compared with before PRBCs transfusion. This was in accordance with Kanmaz et al., [14], Bernd Saugelet al., [15]

The present study showed non significant increase in CO when comparing after transfusion with before transfusion. This was in contrast with Kanmazet al.,[14] and Bernd Saugelet al., [15]who found that a decrease CO after compared with before PRBCs transfusion. This may be explained by that they included septic patients in their studies in whom a hyperdynamic hemodynamic state (with high CO) also that the amount transfused here was only 10 ml /kg.

The present study showed non significant changes in CI after compared with before PRBCs transfusion. This was in accordance with Gramm et al., [19]

This may be explained by that CI is closely related to the CO as it is calculated by dividing CO on BSA.[19]

The present study showed non significant changes in SVR and SVRI after compared with before PRBCs transfusion. This was in accordance with Standlet al.,[20], and Andreaset al.,[21] In contrast to these results, Bernd Saugel et al., [15] found an increase in SVR and SVRI after compared with before PRBCs transfusion. They explained this by the fact that SVR, SVRI calculation depends on MABP, CVP, CO and CI. There was inverse relationship between CO, CI and SVR, SVRI

7. CONCLUSIONS

From the current study we can conclude that the use of 10mL/kg PRBCs transfusion showed significant increase in Hb and HCT, while there were no significant changes in other studied variables (HR, MABP, SV, CO, CI, SVR and SVRI).

CI had the highest sensitivity (100%) and CO, SV and SVRI had the highest specificity (100% for each) for prediction of mortality among patients before start of PRBCs transfusion. CO and CI had the highest sensitivity (100% for each) for prediction of mortality among patients after PRBCs transfusion.

Thus Transesophageal monitoring of vital signs and cardiac functions in PICU for observing the effects of PRBCs transfusion on hemodynamics should be done at regular intervals following transfusion and on wider scale of patients to abolish the effect of pathophysiology of the underlying disease on the results of the study.

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