Outcome of Restrictive versus Liberal Blood Transfusion Strategies in Intensive Care Unit Admitted Patients

Thesis

Submitted for the Partial Fulfillment of Master Degree in Intensive Care

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2018

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgments

First and forever, thanks to **Allah**, Almighty for giving me the strength and faith to complete my thesis and for everything else.

I would like to express my deepest gratitude and appreciation to **Prof. Omar Mohamed Taha ElSafty,** Professor of Anesthesia and Intensive Care,, Faculty of Medicine, Ain Shams University, who initiated and designed the subject of this thesis, for his kindness, over available, fatherly attitude and untiring supervision, helpful criticism and support during the whole work.

My extreme thanks and gratefulness to **Dr. Heba Abdelazim Labib Ahmed,** Assistant Professor of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, I'm much grateful for her patience and strict supervision and revision of this work.

I would like also to thank **Dr. Mohamed Mohamed Kamal Abdallah,** Lecturer of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, for the efforts and times he has devoted to accomplish this work. His valuable advice helped me a lot to pass many difficulties.

Last but not least, I would like to thank all members of my family, specially my **Parents** and my **Wife**, for their care and support.

Yahia Mohamad Yahia

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List of Abbreviations

Abbrev.	Full-term
AABB	: American Association of Blood Banks
ACS	: Acute coronary syndrome
AIDS	: Acquired immunodeficiency state
ALI	: Acute lung injury
APACHE	: Acute Physiology and Chronic Health Evaluation
ARDS	: Acute respiratory distress syndrome
ARISE	: Australasian Resuscitation In Sepsis Evaluation
BCL-XL	: B-cell lymphoma-extra large
BFU-E	: Burst forming unit erythroid
BiPAP	: Bilevel positive airway pressure
BM	: Bone marrow
Bmp4	: Bone morphogenetic protein 4
CABG	: Coronary artery bypass grafting
CFU-E	: Colony forming unit erythroid
CKD	: Chronic kidney disease
COPD	: Chronic obstructive pulmonary disease
CPAP	: Continuous positive airway pressure
CVP	: Central venous pressure
DAT	: Direct antiglobulin test
DHTRs	: Delayed hemolytic transfusion reactions
DIC	: Disseminated intravascular coagulation

DO2 : Oxygen delivery
EGDT : Early goal-directed therapy
EPO : Erythropoietin
FASL : FAS ligand
FNHTRs : FEBRILE NONHEMOLYTIC REACTIONS
G6PD : Glucose-6-phosphate dehydrogenase
GR : Glucocorticoid receptor
GVHD : Graft-versus-host disease
Hb : Hemoglobin
HCT : Hematocrit
HGB : Hemoglobin
Hif-2α : Hypoxia inducible factor 2 α
HIFs : Hypoxia inducible transcription factors
HR : Heart rate
ICU : Intensive care unit
IL : Interleukin
JAK2 : Janus kinase 2
LDH : Lactate dehydrogenase
MACCE : Major cardiovascular and cerebrovascular adverse events
MCHC : Mean corpuscular hemoglobin concentration
MCV : Mean corpuscular volume
MI : Myocardial infarction
PLT : Platelets
PPARalpha : Peroxisome proliferator-activated receptor alpha
PRBC : Packed red blood cells

ProCESS	: Protocol-based Care for Early Septic Shock
RBC	: Red blood cell
RCM	: Red blood cell mass
RDW	: Red cell volume distribution width
ScvO2	: Central venous oxygenation saturation
SD	: Standard deviation
STAT5	: Signal transducer and activator of transcription 5
PI3K-AKT	: Phosphatidylinositol-3-Kinase and Protein Kinase B
TACO	: Transfusion associated cariac overload
TBI	: Traumatic brain injury
TNF	: Tumor necrosis factor
TRACS	: Transfusion Requirements After Cardiac Surgery
TRALI	: Transfusion-related acute lung injury
TRICC	: Transfusion requirement in critical care Trial
TRISS	: Transfusion Requirements In Septic Shock
WB	: Whole blood
WBC	: White blood cell
WHO	: World Health Organization

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Abstract

Background: Anemia is a very common disease in critically ill patients. Approximately 29% of patients have lower than normal hemoglobin levels when admitted to an ICU, and about 95% develop anemia within 3 days of admission. **Aim of the Work:** The purpose of this study was to evaluate the effects of restrictive and liberal red blood cell transfusion strategies on mortality and morbidity in critically ill patients. And as a result, recommend the more beneficial and the less deleterious strategy for critically ill patients. **Patients and Methods:** This clinical interventional study was carried out at Intensive Care Unit, Benha Teaching Hospital, Egypt, during a period from July 2017 to November 2017. This study was approved by Ethical Committee of Faculty of Medicine, Ain Shams University, including the informed consents which were obtained from either the patient or the closest family member. **Results:** Mortality rates in ICU were 16 % and 20% in group A and B respectively, 24% and 28% within 60 ds respectively. There were lower mortality rates with group A but with no statistically significant difference between groups according to mortality during ICU Stay and Mortality within 60 days. **Conclusion:** Comparison between the effect of restrictive and liberal strategies of blood transfusion on mortality and morbidity in critically ill patients showed no significant differences. Restrictive strategy is at least as effective to liberal strategy in critically ill patients. Blood transfusion may be hazardous and cost-effective. **Recommendations:** Anemia is associated with adverse clinical outcomes. However, randomized clinical trials are required to establish if transfusion is beneficial or harmful in anemic patients. A restrictive transfusion strategy should be recommended within the well-studied patient populations and clinical conditions, and the clinicians must continue to use their experience and bedside clinical judgment to advocate the best management for their patients.

Key words: blood transfusion, ICU

Introduction

The World Health Organization (WHO) defines anemia as hemoglobin (Hb) less than 13 gm/dl in men and 12 gm/dl in women. It is known that anemia is very common in critically ill patients; 65% of critically ill patients have Hb level < 12 gm/dl at time of admission to the ICU and a mean admission Hb level of 11.3 gm/dl ***(Corwin et al, 2004).***

As a result of this, 14.7 to 33% of patients admitted to ICUs are transfused with RBCs during their stay and 90% of transfusions are administered to non-bleeding patients with a mean of 5 units of RBC per transfused patient. The mean pre-transfusion Hb level in ICU patients is reported to be around 7.7-8.2 gm/dl ***(Westbrook et al, 2010).***

Anemia may result in insufficient oxygen delivery (DO_2) to vital organs and tissues if DO_2 drops below a critical DO_2. While clinical studies suggest that increasing hemoglobin level via transfusion increases DO_2, studies also show that measures of tissue oxygenation either decrease or do not change ***(Casutt et al, 2011)***.

Some studies have identified RBC transfusion as a risk factor for mortality in critical care patients in general ***(Leal-Noval et al, 2013).*** However other studies reported that RBC transfusion was associated with a decreased risk of in-hospital death in ICU patients ***(Park et al, 2012).***

This makes it is essential to specify an appropriate risk/benefit ratio for the transfusion. This is because it is also not permissible to subject the patient to an intervention whose effectiveness has not been documented in terms of reduced mortality or morbidity ***(Perkins and Busch, 2013).***

Aim of the Work

The purpose of this study is to evaluate the effects of restrictive and liberal red blood cell transfusion strategies on mortality and morbidity in critically ill patients. And as a result, recommend the more beneficial and the less deleterious strategy for critically ill patients.

Chapter 1
Erythropoiesis

Erythropoiesis is a dynamic multistep process where erythroid progenitors differentiate to produce mature enucleated RBC. Hematopoietic stem cells, residing in the bone marrow (BM) niche, generate committed erythroid progenitors, which can be further functionally defined in colony assays in vitro ***(Eaves, 2015).***

The early stage burst forming unit erythroid (BFU-E) generate large erythroid colonies and progress to late stage colony forming unit erythroid (CFU-E), characterized by smaller erythroid colonies. This process occurs with a concomitant decrease in proliferative capacity and increase in erythropoietin (EPO) sensitivity, noted by the appearance of erythropoietin receptors (EPOR) on the cell surface ***(Tsiftsoglou et al, 2009).*** As erythropoiesis progresses, morphologically recognizable precursors emerge by successive mitoses ***(Migliaccio, 2010).***

The earliest recognizable erythroblast is the proerythroblast, which undergoes cytoplasmic maturation and nuclear changes to generate basophilic, polychromatophilic and orthrochromatic erythroblasts. Finally, the latter extrude their nuclei to become reticulocytes and, ultimately, mature RBC, which circulate in the blood stream until senescence. Maturation of erythroblasts is marked by progressive