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

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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 days 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.

Keywords: blood transfusion, ICU, Restrictive, Liberal.

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 [(1)].

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 [(2)].

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, other studies show that measures of tissue oxygenation either decrease or do not change [(3)].Some studies have identified RBC transfusion as a risk factor for mortality in critical care patients in general [(4)]. However other studies reported that RBC transfusion was associated with a decreased risk of in-hospital death in ICU patients [(5)]. 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 [(6)].

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. Then, 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.

Patients Inclusion and Exclusion criteria:

We included patients who were expected to stay in the intensive care unit more than 24 hours,

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had a hemoglobin concentration of less than 9.0 gm per deciliter after admission to the intensive care unit, and were considered to have euvolemia after initial treatment by attending physicians.

Patients were excluded for any of the following reasons: an age of less than 18 years, active blood loss during the study, pregnancy, brain death or imminent death (within 24 hours), patients with acute heart ischemia and patients with acute neurological insult. According to the inclusion and the exclusion criteria, 50 anemic patients (26 males and 24 females), their ages ranged from 49 to 75 years old were included in this study. Patients were divided into 2 groups: **Group I (Restrictive Transfusion strategy):** consisted of 25 patients (13 males and 12 females). Participants allocated to this group were eligible for blood transfusion when their Hb level is ≤7 g/dl. The objective was to maintain the Hb level between 7.1 - 9 g/dl. **Group II (Liberal Transfusion strategy):** consisted of 25 patients (13 males and 12 females). Participants allocated to this group were eligible for transfusion when their Hb level is ≤9 g/dl. The objective was to maintain the Hb level between 9.1 - 11g/dl.

METHODS

Patients were subjected to:

1- Detailed history taking.
2- Thorough clinical examination.
3- Routine laboratory investigations (complete blood counts, liver and kidney profiles, coagulation profile).
4- To determine the severity of illness and stratify patients according to it, the acute physiology and chronic health evaluation (APACHEII) and multiple-organ-dysfunction (MOD) scores were calculated from data gathered within 24 hours after admission to the intensive care unit.
5- To Measure the number and rates of organ failure the multiple-organ-dysfunction score was calculated during hospital stay.
6- Lactate is measured initially and then after resuscitation and transfusion.
7- Hemoglobin concentrations, the use of red-cell transfusions, medications given, including vasoactive drugs, and the need for mechanical ventilation, dialysis, and surgical intervention were recorded on a daily basis.

Treatment Program

In both groups, hemoglobin level was measured immediately after hospital admission and every 24 hours after that. Units of packed RBCs were transfused to reach the target level of Hb.

The outcome:

The outcomes evaluated in 2 groups were:

1- Mortality rate including ICU mortality and mortality within 60 days.
2- The length of ICU stay.
3- The number of organ failure using Δ **MOD** score.
4- Number of transfused RBCs units.
5- Blood transfusion complications (for example, febrile transfusion reactions, allergic transfusion reaction, transfusion transmitted infections and transfusion-related acute lung injury).
6- Hospital acquired infections.
7- Patients experiencing thrombo-embolic and ischemic events (myocardial ischemia or infarction, cerebrovascular stroke, pulmonary embolism, deep venous thrombosis, and acute renal failure).

Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

<u>The following tests were done:</u>

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:
- Probability (P-value)
  – P-value ≤0.05 was considered significant.
  – P-value ≤0.001 was considered as highly significant.
  – P-value >0.05 was considered insignificant.

RESULTS

This is an observational double armed clinical trial that was conducted on 50 patients admitted to Intensive Care Department in Benha Teaching Hospital with diagnosis of anemia. Patients who had ischemic heart disease, patients with acute blood loss during the study or patients with neurological deficits were excluded from our study. The purpose of this study is to compare the effect of restrictive versus liberal strategies of blood transfusion on mortality and morbidity in critically ill patients. Patients included in this study were divided into 2 groups:

1- Group A: 25 patients receive restrictive blood transfusions.
2- Group B: 25 patients receive liberal blood transfusions**.**

Table (1): Comparison between group A and group B according to demographic data.

	Demographic Data	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	t/x2#	p-value
Age (years)	Mean±SD Range	63.06±7.56 50-76	62.18±7.52 49-75	0.413	0.682
Sex	Male Female	13 (52.0%) 12 (48.0%)	13 (52.0%) 12 (48.0%)	0.000	1.000

This table shows that mean age for restrictive group 63.06 ± 7.56 and for liberal group was 62.18 ± 7.52 years old. No statistically significant difference between groups according to demographic data.

Table (2): Comparison between group A and group B according to 1ry diagnosis.

1ry Diagnosis	Group A: Restrictive (N=25)	Group B: Liberal (N=25)
1ry peritonitis	0 (0.0%)	1 (4.0%)
Acute DVT	1 (4.0%)	1 (4.0%)
Acute Hepatitis	1 (4.0%)	0 (0.0%)
Acute kidney Injury	5 (20.0%)	4 (16.0%)
Cellulitis	2 (8.0%)	2 (8.0%)
COPD exacerbation	1 (4.0%)	1 (4.0%)
Deccompensated Liver Failure	0 (0.0%)	1 (4.0%)
Diabetic Ketoacidosis	2 (8.0%)	2 (8.0%)
Hepatic Encephalothy	4 (16.0%)	4 (16.0%)
Hypoglycemia	1 (4.0%)	0 (0.0%)
Hypovolemic Shock	1 (4.0%)	1 (4.0%)
Pneumonia	4 (16.0%)	4 (16.0%)
Pulmonary embolism	1 (4.0%)	1 (4.0%)
Sepsis	3 (12.0%)	2 (8.0%)
Severe ashtma	1 (4.0%)	1 (4.0%)
Urinary Tract Infection	1 (4.0%)	1 (4.0%)

Table (2) shows that there were different presentations of critically ill patients admitted to the intensive care with relative matching between both groups.

Table (3): Comparison between group A and group B according to APACHE II score.

APACHE II Score	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	t-test	p-value
Mean ± SD	21.48 ± 4.93	22.16 ± 4.81	0.494	0.624
Range	14-29	14-30		

This table shows no statistically significant difference between groups according to APACHE II score.

Table (4): Comparison between group A and group B according to Organ Failure (Δ MODS score).

Organ Failure (Δ MODS score)	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	t-test	p-value
At admission Mean ± SD Range	5.76±2.01 3-11	5.68 ± 2.01 3-10	0.020	0.889
Adjusted score Mean ± SD Range	5.80 ± 8.22 0-24	7.40 ± 8.79 1-24	2.442	0.039
Change from base-line score Mean ± SD Range	0.04 ± 6.92 -5_16	1.72 ± 7.61 -4_19	3.667	0.018

This table shows statistically significant difference between groups according to adjusted score and change from baseline score.

Table (5): Comparison between group A and group B according to no. of transfused RBCs units, Hb and average Hb.

	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	t-test	p-value
No. of Transfused RBCs units				
Mean ± SD	1.96 ± 1.31	4.40 ± 1.08	51.800	<0.001
Range	0-5	3-7		
Hb at admission				
Mean ± SD	6.43 ± 0.98	6.38 ± 0.89	0.028	0.869
Range	4.7-8.5	4.6-8		
Average Hb				
Mean ± SD	7.79 ± 0.33	9.73 ± 0.41	337.221	<0.001
Range	7.2-8.5	9-10.5		

This table shows highly statistically significant difference between groups according to no. of transfused RBCs units and average Hb.

Table (6): Comparison between group A and group B according to mortality

Mortality	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	t-test	p-value
Mortality during ICU stay				
No	21 (84.0%)	20 (80.0%)	0.136	0.713
Yes	4 (16.0%)	5 (20.0%)		
Mortality within 60 ds				
No	19 (76.0%)	18 (72.0%)	0.104	0.747
Yes	6 (24.0%)	7 (28.0%)		

Table (6) shows that 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.

Table (7): Comparison between group A and group B according to interventions during ICU stay.

Interventions during ICU stay	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	x2	p-value
Dialysis				
No	21 (84.0%)	25 (80.0%)	0.090	0.765
Yes	4 (16.0%)	5 (20.0%)		
Vasoactive Drugs				
No	19 (76.0%)	18 (72.0%)	0.104	0.747
Yes	6 (24.0%)	7 (28.0%)		
Mechanical Ventilation				
No	19 (76.0%)	20 (80.0%)	0.026	0.873
Yes	6 (24.0%)	5 (20.0%)		

This table shows no statistically significant difference between groups according to interventions (dialysis, vasoactive drugs and mechanical ventilation) during ICU stay.

Table (8): Comparison between group A and group B according to complications.

Complications	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	x2	p-value
Total Complications	8 (32.0%)	12 (48.0%)	1.333	0.248
Transfusion Complications	3 (12%)	7 (28%)	4.400	0.623
Acute hemolysis	0 (0.0%)	1 (4.0%)		
Allergy	1 (4.0%)	1 (4.0%)		
Anaphylaxis	0 (0.0%)	1 (4.0%)		
Fever	2 (8.0%)	2 (8.0%)		
Fever, Allergy	0 (0.0%)	1 (4.0%)		
TRALI	0 (0.0%)	1 (4.0%)		
Hospital Acquired Infection	3 (12%)	6 (24%)	4.553	0.473
Catheter related infection	1 (4.0%)	1 (4.0%)		
Gastroenteritis	0 (0.0%)	2 (8.0%)		
Pneumonia	1 (4.0%)	1 (4.0%)		
Urinary tract infection	1 (4.0%)	2 (8.0%)		
Other Complications	2 (8%)	3 (12%)	2.356	0.502
Encephalopathy	1 (4.0%)	0 (0.0%)		
Ileus	0 (0.0%)	1 (4.0%)		
Pulmonary edema	1 (4.0%)	2 (8.0%)		

This table shows that higher complications in group B relative to group A with no statistically significant difference between groups according to complications.

Table (9): Comparison between group A and group B according to ICU stay.

ICU stay	Group A: Restrictive (N=25)	Group B: Liberal (N=25)	t-test	p-value
ICU stay with death			2.072	0.156
Mean ± SD	6.80 ± 2.31	7.72 ± 2.21		
Range	4-12	3-12		
ICU stay without death			3.747	0.060
Mean ± SD	6.67 ± 2.06	7.95 ± 2.19		
Range	4-12	5-12		

This table shows longer stay in ICU in group B but without statistical significant difference between groups according to ICU stay.

DISCUSSION

Anemia is common in critically ill patients admitted to the intensive care unit (ICU) and is associated with a poorer outcome. However, red blood cell (RBC) transfusion can have complications and its availability is limited. Hence, one has to find a balance between the risks of anemia and the risks of transfusion [7].

Restrictive versus liberal blood transfusion during the last 30 years has many debates and a large body of clinical evidence was generated, resulting in the publication of many guidelines for RBC transfusion in different settings. A common theme of these guidelines is the need to balance the benefit of treating anemia with the desire to avoid unnecessary transfusion, with its associated costs and potential harms [8,9,10,11].

The series of recommendations by the AABB regarding the RBC transfusion threshold have their principal origin in the large published clinical trials (seven trials each being Level 1, >400 patients) that have demonstrated the relative safety of a restrictive transfusion strategy (Hb transfusion threshold <7 g/dl) in specific clinical settings in adult cohorts [12,13,14,15].

Anemia has long been associated with adverse patient outcomes. With respect to correlative data, anemia in older people has been well documented as being an independent risk factor for increased mortality, functional dependence, impaired cognition, re-admission to hospital, and falls [16].

Restrictive transfusion practices are associated with equivalent or improved patient outcomes. Given the high costs of allogeneic blood transfusions, their very selective efficacy and their side effects, an enhanced blood management in intensive care medicine is mandatory [17].

The challenge remains to elucidate at what risk–benefit point the treatment of anemia with transfusion will be associated with net improvement in functional capacity and outcome. The large prospective restrictive versus liberal transfusion studies evaluated selected populations over a short period of time, typically ICU or hospital lengths of stay, the main focus was on complications with no assessment of ultimate functional outcome or rate of recovery [18].

These hypothesis-driven trials have proposed that restrictive RBC transfusion strategies are as safe as, or perhaps safer than, liberal transfusion practices. To evaluate the primary hypotheses proposed in these trials, explicit potential adverse effects of RBC transfusion were also evaluated, aiming to demonstrate that guideline compliance would lead to a reduction in a number of transfusion-related adverse effects, of which the most commonly cited include hospital-acquired infection, transfusion reaction(severe and mild incompatibility), transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury, and immunomodulation, all of which could lead to an increase in patient morbidity and mortality [19].

The purpose of this study is to compare the effect of restrictive versus liberal strategies of blood transfusion on mortality and morbidity in critically ill patients. Our findings showed that the mean age for restrictive group 63.06 ± 7.56 and for liberal group was 62.18 ± 7.52 years old. No statistically significant difference between groups according to demographic data. There were different presentations of critically ill patient in intensive care with relative matching between both groups. Higher mean ages in our study was in line with several studies. In the TRICC study, the critically ill patient had a mean age of 58 years old, ≥55 years old in critically ill patients and elective surgery [14,20], ≥65 years old in hip fracture patients, and ≥70 years old in elective hip and knee replacement patients (a high-risk subgroup) [21].

Our findings showed that mortality rates in ICU were 4(16 %) and 5(20%) in group A (Restrictive) and B (Liberal) respectively, 6(24%) and 7(28%) within 60 days 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. This difference may be due to variable presentation of cases in both groups and late stage diseases in group B. This goes with several studies that showed no differences in mortality between restrictive and liberal blood transfusions as follows; **Hébert and co-investigators** of the landmark [11] Transfusion Requirements in Critical Care (TRICC) trial acknowledged at the trial’s end that there was no difference between liberal and restrictive cohorts in the only primary outcome measure of all-cause 30-days mortality. The critically ill patient had a mean age of 58 years old. The mortality rate during hospitalization was lower in the restrictive transfusion group [22].

A multicenter study from the Scandinavian countries; Transfusion Requirements in Septic Shock (TRISS) study, in which 998 patients were enrolled, the restrictive transfusion policy did not harm the septic shock patients. The number of day's alive, ischemic events, and severe adverse reactions to blood were similar in the two groups. In the TRISS study, all participants who fulfilled the inclusion criteria had septic shock before the randomization [15].

A restrictive RBC transfusion strategy generally appears to be safe in critically ill patients with cardiovascular diseases, though there may be an exception in patients with severe ischemic heart disease [14].

One large single-center RCT in elective cardiac surgery patients; Transfusion Requirements After Cardiac Surgery (TRACS) study showed similar rates of mortality between patients with restrictive and liberal transfusion strategies [23].

A Cochrane meta-analysis published in 2012, which included 6264 patients in 19 trials in the settings of surgery, including cardiac surgery, critical care, trauma and acute hemorrhage. It was found that the use of restrictive transfusion strategy led to 39% fewer patients receiving transfusion and a decrease in the total number of transfusions compared to liberal strategy. The two strategies produced similar 30-day mortality rates. There was decrease in in-hospital mortality with the restrictive strategy [24].

The early goal-directed therapy (EGDT) study was a single-center RCT in patient with severe sepsis and septic shock [25]. Transfusion of RBC’s to a hematocrit of 30% was one of the interventions used on the EGDT arm to raise the central venous oxygenation saturation ($ScvO_2$)>70%. Patients in the EGDT group received more RBC transfusions and had an improved mortality compared to those patients receiving standard resuscitation measures for severe sepsis and septic shock. These results have not been confirmed by two recent multicenter

RCT's [Protocol-based Care for Early Septic Shock (ProCESS) Investigators et al. and Australasian Resuscitation In Sepsis Evaluation (ARISE) Investigators et al.]. In both studies, no mortality benefit was observed in patients assigned to EGDT [(26)].

On the other hand **Walsh *et al.*** [(27)] observed an absolute mortality difference over 6 months of 18% in favor of the restrictive strategy, which approached statistically significant despite the small sample size in patients with higher risk of death than in previous studies.

Also, **Park *et al.*** [(28)] in an observational study, found a lower risk of in-hospital death in transfused patients with severe sepsis and septic shock. However, in recently published TRISS Trial, patients with septic shock and managed in an ICU setting, a transfusion threshold of 7g/dL compared with 9g/dL resulted in significant difference in the primary outcome -death by 90 days [(29)].

In 7,552 perioperative patients (17 RCTs), **Fominskiy *et al.*** [(30)] found that a liberal blood transfusion strategy improved survival in acute anemia. The perioperative settings causing anemia were hip fracture surgery, cardiac surgery, abdominal cancer surgery, elective hip and knee replacement, spinal fusion with instrumentation and postpartum hemorrhage.

The current findings showed that higher complications in group B relative to group A with no statistically significant difference between groups according to complications. Our findings were in agreement with several studies that reported many complications without significant difference between restricted or liberal transfusions.

As regard Infection risk during transfusion, our findings goes with several studies. Taylor et al [(31)] in a retrospective study of 1711 patients demonstrated that transfused patients were six times more likely to develop a nosocomial infection than non-transfused patients.

Claridge *et al.* [(32)] demonstrated in a prospective study of 1593 trauma patients that 33.6% of transfused patients developed infection versus 7.6% patients who did not receive transfusions.

Ali *et al.* [(33)] in a prospective, single-center study of 234 patients demonstrated that PRBC was not associated with increased risk of infection in postoperative cardiac surgery patients.

As regard risk of Transfusion-Related Acute Lung Injury (TRALI). The TRICC trial showed a significant increase in cardiac and pulmonary complications and a trend toward increased mortality in the liberal transfusion group during patients intensive care stay. In subgroup analysis, younger (age <55 years old) or less critically ill (APACHE II scores < 20) patients randomized to a liberal strategy had a statistically significant increase in mortality [(11)].

A cohort analysis within the CRIT study found blood transfusion to be independently associated with development of acute respiratory distress syndrome (ARDS) [(35)].

As regard transfusion impact on cardiac disease. TRICC trial demonstrated that patient in the liberal transfusion arm (i.e., those transfused at threshold hemoglobin of 9 g/dL versus 7 g/dL for the restrictive group) had a higher incidence of MI [(11)]. Subsequently, a subgroup analysis of patients from the TRICC trial with heart disease failed to demonstrate any significant mortality outcomes between groups [(22)].

Cooper *et al.* [(36)] reported that liberal RBC transfusion practices have not been readily associated with increased rates of transfusion-related complications. There has been no overall greater mortality risk or significant increases in the rates of multisystem organ dysfunction, nosocomial infection, acute kidney injury, coagulopathy, immune disorder, acute respiratory distress syndrome or pneumonia, or ischemic complications such as myocardial infarction or stroke in review of primary outcome data [(37)].

TRICC trial reported 10 hemolytic complications in each arm, however, it did not specify which of them were associated with RBC transfusion [(12)]***;*** while on TRISS trial only acute hemolysis associated with RBC transfusion in the liberal group were reported [(15)].

Holst *et al*. [(38)] carried out a similar study and added the RCT data published in the last 3 years to examine whether the evidence of the previous meta-analyses still supporting a restrictive strategy without harming the patient. The analysis now including 9,813 patients (31 RCTs) confirmed the findings of Carson et al. [(12)].

Rohde *et al.* [(39)] found that serious infections were related to a liberal policy in pooled data from 7,593 patients (18 RCTs). However, health care-associated infections such as pneumonia, mediastinitis, wound infection, and sepsis were not linked to a liberal strategy.

In 2014, **Salpeter *et al*.** [(40)] studied 2,364 patients (3 RCTs) and pooled the results from patients with critical illness with the results from the bleeding patients and found that a restrictive strategy (Hb threshold 7 g/dL) reduced cardiac events, re-bleeding, and 30-day mortality. No difference in infection risk was found in the disparate populations.

Fernandes *et al.* [(41)] evaluated hemodynamics and oxygen usage induced by hemoglobin infusion in critically ill septic patients and documented that an increase in hemoglobin did not improve the global or regional oxygen use in anemic septic patients.

The heart may be particularly prone to adverse consequences of anemia, because the myocardium consumes 60% to 75% of all O2 delivered to the coronary circulation [(42)]. Such a high extraction ratio is unique to the coronary circulation. During anemic states (Hb<10 g/dL), systemic oxygen delivery is maintained via initial increases in stroke volume and then heart rate, which led to early subendocardial ischemia when coronary sinus oxygen supply is diminished [(43)].

Several studies have suggested that blood transfusions are associated with adverse outcomes and high costs. Reduction of complications related to blood transfusion could speed the postoperative rehabilitation of patients and avoid the huge medical expenses. The study of **Corwin *et al*.** [(1)] demonstrated that there were no significant differences in terms of mortality, and the incidence rates of pneumonia, wound infection, myocardial infarction, and congestive heart failure between the restrictive and liberal transfusion thresholds for RBC transfusion, suggesting that restrictive transfusion strategies could potentially reduce the number of transfusions and relieve the economic burden of using liberal transfusion strategies, without increasing the risk of adverse events [(1,44)].

Restrictive transfusion practices are associated with equivalent or improved patient outcomes, given the high costs of allogeneic blood transfusions. The primary benefit of administering blood is the support of oxygen supply as transported by the Hb and delivered to the cells. The hazards of administering blood are far more extensive. Infective risks are potential due to blood borne viruses, bacteria, parasites, and prions. Immunologic risks include hemolytic reactions, immunosuppression, transfusion-related acute lung injury, mis-transfusion, and allo-immunization. There are ample published data reflecting the risks and benefits of liberal versus restrictive transfusion strategies in perioperative medicine. However, there is a universal lack of agreement among clinicians in perioperative medicine when it concerns the decision to transfuse blood products or not [(45)].

The current findings showed that interventions by dialysis and vasoactive drugs were higher in group (B), but mechanical ventilations were lower in group (B) with no statistically significant difference between both groups during ICU stay. Our findings were in agreement with several studies that reported many complications without significant difference between restricted or liberal transfusions. In recently published TRISSTrial, patients with septic shock, no differences were found in percentage of days alive without vasopressor/inotropic support mechanical ventilation and renal replacement therapy; and approximately 50% less blood was administered in the restrictive strategy [(14)]. Additional analysis of the data (n = 713) found that there was no advantage with liberal over restrictive transfusion strategy in weaning patients from mechanical ventilation [(14)]. Fernandes et al. [(41)], who reviewed Hb level and hemodynamic and oxygen use effect in 15 critically ill septic patients on mechanical ventilation and with Hb less than 10 g/dL. Fernandes et al. reported no improvement in global or regional oxygen use in anemic septic patients by increasing Hb. In addition, **Silverman and Tuma** [(46)] compared efficacy of dobutamine infusion and RBC transfusion. Their findings suggest that dobutamine is more effective than RBC transfusion in increasing oxygen delivery to tissue. **Holst *et al.*** [(14)] reported that the use of life support at days 5, 14, and 28 was similar in the two intervention groups; as were the percentages of days alive without vasopressor or inotropic therapy, without mechanical ventilation, and without renal-replacement therapy and the percentage of days alive and out of the hospital.

The incidence of renal failure with dialysis in our findings was similar in the restrictive and liberal groups. In consistent with (TRICS III) trial, that reported no difference between liberal and restrictive groups as regard renal replacement therapy [(47)]. Also, **Hajjar *et al.*** [(48)] randomly assigned 502 consecutive patients who underwent cardiac surgery with cardiopulmonary bypass to a liberal or restrictive transfusion strategy (to maintain hematocrit at 30 or 24 percent respectively) throughout surgery and the postoperative period (Transfusion Requirements after Cardiac Surgery; TRACS). Incidence of acute renal injury requiring dialysis or hemofiltration had no difference in this composite endpoint between the groups (10 percent liberal versus 11 percent restrictive).

In our findings, longer stay in ICU in group B but without statistical significant difference between groups according to ICU stay. Our finding goes with the CRIT study ("Anemia and blood transfusion in the critically ill-current clinical practice in the United States"). This study evaluated 4892 ICU patients in 213 US hospitals and observed that the number of RBC transfusions was an independent predictor of length of ICU stay, overall hospital length of stay. In addition, the association with mortality was particularly pronounced when more than 2 RBC units were transfused [(1)]. In 2002, **Vincent *et al*.** [(49)] published a prospective observational study (Anemia and Blood Transfusion in Critically Ill Patients ABC) evaluating the blood sampling, hemoglobin levels, and transfusion rates in 146 Western European ICUs. They concluded that receipt of a blood transfusion increased a patients odds of dying and increased patients length of stay in the ICU.

Limitations

Our results may be decreased due to heterogeneity caused to the inclusion of patients with different pathology, and the different time analysis of the intervention. Moreover, a small number of patients, single center study and small event rates.

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

1- Anemia is associated with adverse clinical outcomes. However, randomized clinical trials are required to establish if transfusion is beneficial or harmful in anemic patients.

2- All patients should be assessed clinically when transfusion is considered. If the patient is stable, transfusion may not be needed even when the hemoglobin level is low. Hospital-wide patient blood management programs may be helpful in guiding transfusion practices and reducing unnecessary transfusions, but they should not supersede clinical judgment.

3- 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.

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