Indian Journal of
CRITICAL CARE MEDICINE

C O N T E N T S

A prospective cohort study on anemia and blood transfusion in critically ill patients

Naveen Manchal, S. Jayaram

Abstract

Background: The management of anemia and blood transfusion practices in the ICU have been a subject of controversy. **Aims:** The aims of this study were 1) To assess the prevalence of anemia and study the association of blood transfusion and mortality in critically ill patients. 2) To compare restrictive transfusion policy (Hb < 7 g/dl) and liberal transfusion policy. (Hb < 10 g/dl). **Settings and Design:** A matched cohort study was performed in a tertiary care teaching hospital. **Materials and Methods:** To study the association between blood transfusions and mortality, control patients were those who never received blood during ICU stay. They were selected according to the following matching criteria: Age ($\pm$ 5 years), sex, APACHE II score ($\pm$ 5 points), history of cardiac or renal disease and clinical diagnosis. **Statistical Analysis Used:** The Chi-square test. **Results:** The incidence of anemia is high in critically ill patients. Anemic patients had a longer duration of stay in the ICU. There is an association between blood transfusion and higher mortality in critically ill patients. A restrictive transfusion policy was associated with lesser mortality. **Conclusions:** Anemia is associated with increased morbidity reflected by the increased duration of stay in the ICU. Blood transfusion is associated with increased mortality and a restrictive transfusion policy is associated with increased survival.

Key words: Anemia, blood transfusion, critically ill, mortality

Introduction

As the entire practice of medicine has evolved in the past few decades, so have transfusion practices. Two decades ago, a hematocrit between 0.20 and 0.25 was considered an urgent indication for transfusion, but at the turn of this century, maintaining a hematocrit at this level is considered to be "best- practice medicine".[1]

Nearly two thirds of patients admitted to an ICU have hemoglobin levels of 10 g/dl or lower.[1] Although intraoperative blood loss and gastro intestinal hemorrhage contribute to these statistics and are a frequent reason for administering transfusions, only 40% of transfusions administered were because of acute blood loss.

Although anemia is apparently tolerated in most patients, particularly those who are young /relatively healthy, the ICU population must be thought of differently. Anemia in the ICU may be due to acute blood loss, phlebotomy or to the presence of inflammatory disease. The risks of blood transfusions are many. Nonetheless, hemoglobin levels at or above 10 g/dl may be important for oxygen delivery to vital organs, especially in critically ill patients with increased oxygen demands.[1] The appropriate transfusion trigger for critically ill patients in this setting remains unknown.[6,8,16-17]

This study aims to assess the prevalence of anemia in critically ill patients and studies the association of blood transfusion and mortality in critically ill patients. It also

From:
Department of Medicine, J. J. Group of Hospitals, Mumbai - 400 008, India

Correspondence:
Dr. Naveen Manchal, No. 278, 5th Main, 5th Cross, Micokgnss Layout, Arekere, Bangalore - 76, Karnataka, India. E-mail: drsoda79@yahoo.com

Free full text available from www.ijccm.org

compares restrictive transfusion policy (Hb < 7 g/dl) and liberal transfusion policy (Hb < 10 g/dl).

Materials and Methods

A total of 100 patients were included in the study. A matched cohort study was performed. The complete blood count was done every week and patients were followed for 21 days or till death/ transfer from the ICU. The following standards were used for case identification:- Hb less than 12 g/dl (males). Hb less than 10 g/dl (females) [any single episode during ICU stay].

Inclusion criteria

All patients admitted in the intensive care unit during the study period in the age group of 15-65 years.

Exclusion criteria

1. Patients with a known hematological disorder
2. Hematological malignancies
3. Patients on chemotherapy
4. HIV positive patients

Matching and selection of control patients

To study the association between blood transfusions and mortality, control patients were those who never received blood during ICU stay. They were selected according to the following matching criteria:

- Age (±5 years)
- Sex
- APACHE II score on first day of ICU admission (± 5 points)
- History of cardiac disease (ischemic heart disease, congestive heart failure)
- History of renal disease (acute or chronic renal failure)
- Clinical diagnosis
- The Chi-square test was used for statistical significance and P<0.05 was considered significant at 95% confidence interval.

Results

The study cohort of 100 patients had an average APACHE score of 16.2. The overall mortality was 46% and the age-wise distribution of mortality was as shown in Table 1.

1. Out of 100 patients 68 were found to be anemic during the study period. The mean Hb level was 9.76 g/dl. The predominant peripheral smear picture

Table 1: Age wise distribution of mortality

Age (years)	Number of deaths
15-24	6
25-34	8
35-44	11
45-54	12
55-64	9
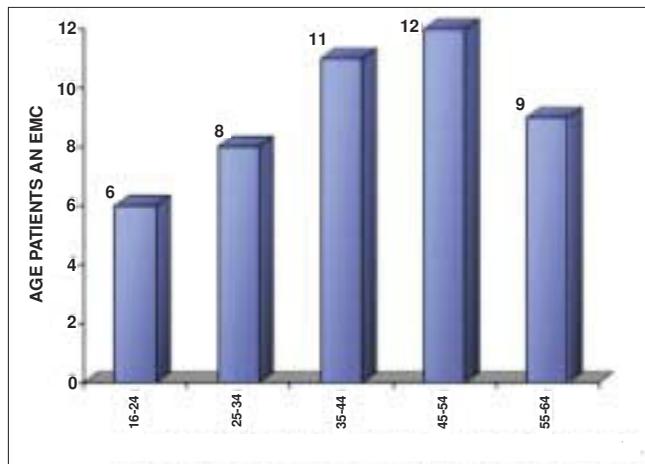
Bar diagram showing age-wise distribution of mortality

Table 2: The predominant peripheral smear picture was microcytic hypochromic
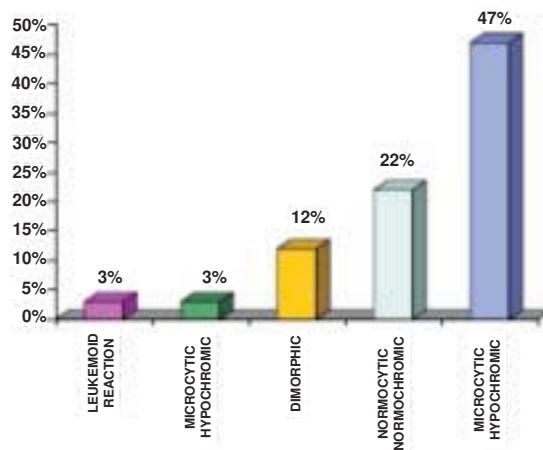
was of microcytic hypochromic type. The others were normocytic normochromic with 3% showing a leukemoid reaction [Table 2].

2. Sepsis[4] was the commonest clinical setting associated with anemia. The others being gastrointestinal bleed, chronic renal failure and postoperative blood loss [Table 3].

3. Out of the 100 patients studied, 38 patients were given blood transfusion and matching control patients were identified for 36 patients. The mortality in the

transfusion group was 58.33% when compared to 25.0% in the non transfusion group (*P* 0.005). The attributable mortality was 33.33% with a relative risk of 2.33 [Table 4].

4. The mortality rate in those transfused at Hb< 7 g/l was 10% when compared to 70% mortality rate in those transfused at Hb<10 g/l (*P* 0.005) [Table 5]

5. The duration of stay in the ICU was doubled in anemic patients [Table 6].

Discussion

The study shows that nearly two-thirds of patients admitted to an ICU have Hb levels less than 10 g/l. Anemia may be caused by decreased production of RBCs, nutritional deficiencies, inadequate endogenous erythropoetin production, renal failure and diagnostic blood sampling.[7,14,15,18,22]

Table 3: Causes of anemia identified in the study

Aetiology	No. of patients
Gl. Bleed	8
CRF	9
Sepsis	33
Blood loss due to internal hemorrhage, post operative etc.	9
Protozoal infections (malaria, leptospirosis)	8

Table 4: Association between blood transfusion and mortality

	No. of deaths	No. of survivors
Total number transfused	21	15
Number of patients not transfused	9	27

Pie diagram showing mortality in transfused and non transfused groups

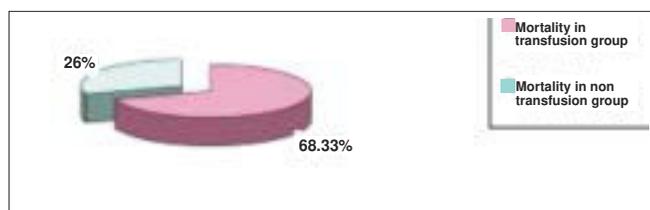**Table 5: The results comparing two strategies of blood transfusion are as follows: out of the 21 patients transfused, matching controls were found for 10**

	Restrictive transfusion (Trigger <7 g/L)	Liberal transfusion (Trigger <10 g/L)
Mortality	10.0%	70.0% (*P* 0.005)

Table 6: Duration of ICU stay

|	Anemia	Normal Hb
Average duration of stay in ICU (days)	8.72	4.10

As anemia progresses in otherwise healthy persons, compensatory mechanisms are recruited and a certain degree of anemia may be tolerated. These mechanisms may not operate efficiently or at all in critically ill patients. Under various preconditions anemia may be associated with increased mortality of the critically ill. The same is true with blood transfusion.[13,19]

The complications of blood transfusions include volume overload, febrile reactions and fatal hemolytic reactions which may all contribute to increased mortality.[5,9-11,20,21] The anemia and blood transfusions study included 3534 patients from 146 Western European ICUs. Both ICU and overall mortality rates were significantly higher in patients who had *vs* who had not received a transfusion (ICU rates: 18.5% vs 10.1% respectively; *P*<0.001).[2]

The concept of optimal Hb concentration has been challenged. Wilkerson and colleagues using a paralyzed, anesthetized, normovolemic anemic primate model, noted that compensatory mechanism for low Hb concentration did not occur until the Hb concentration fell below 7 g/dl.[14]

The study by Hebert *et al.*,[12] showed that a restrictive transfusion policy (Hb < 7 g/dl) had better overall outcomes than when the transfusion trigger was more liberal (Hb <10 g/dl).[3] The decision to transfuse or not must be taken after weighing up the potential consequences of anemia against blood transfusion associated risks. Every single patient's ability to compensate for anemia is different. The question of whether a potential transfusion is capable of affecting the clinical outcome of a given patient is related to the question whether tissue hypoxia is in in fact prevailing at a certain Hb concentration.
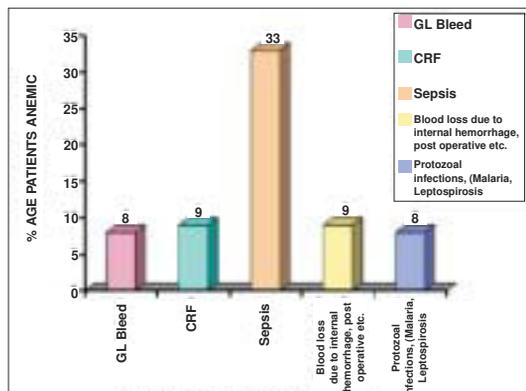
Clinical settings associated with anemia

Acknowledgement

References

1. Pearl RG, Pohlman A. Understanding and managing anemia in critically ill patients. Crit Care Nurse Dec 2002;Suppl:1-14.

2. Vincent JL, Baron JF, Reinhart K, Gattinoni L, Thijs L, Webb A, *et al.* Anemia and blood transfusion in critically ill patients. JAMA 2002;288:1499-507.

3. Hebert PC, Well G, Martin C, Tweeddale M, Marshall J, Blajchman M, *et al.* Variation in red cell transfusion practice in the intensive care unit: A multicentre cohort study. Crit Care 1999;3:57-63.

4. American College of Chest physicians/Society of Critical Care Medicine Consensus Committee: Definitions for sepsis and organ failures and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992;20:864-74.

5. Carson JL, Duff A, Poses RM, Berlin JA, Spence RK, Trout R, *et al.* effect of anemia and cardiovascular disease on surgical mortality and morbidity. Lancet 1996;348:1055-60.

6. Carson JL, Hill S, Carless P, Hebert P, Henry D. Transfusion triggers: A systematic review of the literature. Transfus Med Rev 2002;16:187-99.

7. Warrel DA, Lox TM, Firth JD, Benz EJ Jr. Oxford text of medicine 4th ed. 2003. p. 1219-27.

8. Drews RE. Critical issues in hematology: Anemia, thrombocytopenia, coagulopathy, and blood product transfusions in critically ill patients. Clin Chest Med 2003;24:607-22.

9. Edna TH, Bjerkeset T. Association between blood transfusion and infection in injured patients. J Trauma 1992;33:659-61.

10. Stephan F, Montblanc Jd, Cheffi A, Bonnet F. Thrombocytopenia in critically ill surgical patients: A case-control study evaluating attributable mortality and transfusion requirements. Crit Care 1999;3:151-8.

11. Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine: First of two parts-blood transfusion. N Engl J Med 1999;340:438-47.

12. Herbert PC, Well G, Tweeddale M, Martin C, Marshall J, Pham B, *et al.* Does transfusion practice affect mortality in critically ill patients? Am J Respir Crit Care Med 1997;155:1618-23.

13. Jesse B Hay, Gregory A Schmidt, Laurence DH Wood. Principles of critical care 1992. p. 1807-17.

14. Civetta JM, Taylar RW, Kirby RR. Transfusion therapy. Crit Care 1996;vol 3rd Edition:639-52.

15. Kasper, Braunwald, Fauci, Hauser, Longo, Jameson. Transfusion biology and therapy. Harrison's principles of internal medicine. 16th ed. 2005. p. 662-7.

16. Practice guidelines for blood component therapy: A report by the American Society of Anesthesiologists task force on blood component therapy. Anesthesiology 1996;84:732-47.

17. Schroder ML. Principles and practice of transfusion medicine. *In*: Wintrobe's Clinical Hematology. Lee GR, Foerster J, Lukens J, *et al*, editors. Williams and Wilkin: Baltimore; 1998. p. 817-74.

18. Shoemaker, Ayers, Grenvik, Holbrook, Thompson: Textbook of critical care. p. 903-18.

19. Evans TW,(2001) Hemodynamic and metabolic therapy in critically ill patients,NEJM 345:1368-77.

20. Thurer RL. Blood transfusion in cardiac surgery. Can J Anesth 2001;48:S6-12.

21. Vamvakas ES, Moore SB, Cabanela M. Blood Transfusion and septic complications after hip replacement surgery. Transfusion 1995;35:150-6.

22. Wallace EL, Churchill WH, Surgenor DM, Cho GS, McGurk S. Collection and transfusion of blood components in the United States, 1994. Transfusion 1998;38:625-36.