Original Article

A one year anticipated blood transfusion requirements among patients with acute leukemia undergoing chemotherapy in the National Center of Hematology in Baghdad

Alaa Fadhil Alwan, Nidal Kareem Alrahal[1], Maha Abdul-Jabbar Alnuaimi[2]

Abstract:

BACKGROUND: Acute leukemia is considered one of the most diseases that required frequent blood transfusion. Despite that blood transfusion is one of the main parts in the supportive management of acute leukemia patients, still, there are few data showing the exact requirements in regard to blood components for those patients.

OBJECTIVES: The aims of this study were to review the predicted amount of blood transfusions needed for a patient with acute leukemia under a regimen of chemotherapy and to verify the transfusion frequency practices, according to the types of acute leukemia, levels of treatment, prognosis, and other demographic factors.

MATERIALS AND METHODS: A prospective cohort study conducted at the National Center of Hematology/Mustansiriyah University from January 2013 to January 2015. Thirty newly diagnosed patients were enrolled in this study. The inclusion criteria included newly diagnosed acute leukemia whether lymphoid or myeloid except acute promyelocytic leukemia (M3) patients who were excluded. All patients subjected to detailed history and routine hematological investigations. They were followed up and assessed during induction and consolidation phases for both disease entities.

RESULTS: Thirty patients were included in this study; 20 were male and 10 were female. The mean age was 31.4 years, ranging from 15 to 66 years. There were 15 cases of AML and 15 cases for ALL. The number of transfused units was found to be higher and statistically significant in those below 40 years of age, male patients and in patients with complete remission, while it was not significant for type of disease.

CONCLUSION: This study provides information to estimate the anticipated requirements for blood transfusion for those patients in regard to different factors which can be considered as guideline for these tertiary centers for accurate assessment of transfusion requirements and to direct resources for better outcome.

Keywords:
Acute leukemia, blood transfusion, requirement

Departments of Clinical Hematology and [1]Laboratory Department, Apheresis Unit, The National Center of Hematology, Mustansiriyah University, [2]Department of Community Medicine, Mustansiriyah University College of Medicine, Baghdad, Iraq

Address for correspondence:
Dr. Alaa Fadhil Alwan, Department of Clinical Hematology, The National Center of Hematology, Mustansiriyah University, Baghdad, Iraq.
E-mail: ala_sh73@yahoo.com

Introduction

It was proposed that most of the patients with malignancies will need blood transfusion at one stage of treatment or follow-up because of associated anemia-related malignancy.[1] In solid cancer, the malignant cells usually not invade bone marrow; therefore, most of the patients may need only a few blood transfusions during designated chemotherapy course. In solid cancer, the malignant cells usually not

invade bone marrow; therefore, most of the patients may need only a few blood transfusions during designated chemotherapy course , this is In contrast to patients with hematological malignancies, especially acute leukemias, in which bone marrow involvement by leukemic cells will prevent normal hematopoiesis, which in turn cause significant cytopenias that require red cell transfusion and platelet transfusion. In fit patients, after induction, chemotherapy phase is usually followed by high-dose chemotherapy to consolidate the remission status, and the effects of this therapy will add more to an already dysfunctional marrow.[2] The mechanism by which chemotherapy leads to anemia is by direct impairment of hematopoiesis, including synthesis of erythropoiesis in bone marrow. Malignant and normal stem cells are affected similarly by the chemotherapeutic agents, and it takes period of time for regeneration to occur in marrow after eradicating of malignant cells. Consequently, patients with acute leukemia are commonly affected by both their disease status and its protocol used in treatment, resulting in general requirements for both blood and platelet transfusions.[3]

The clinical presentation and prognosis of cases of acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) varies in patients depending on the molecular and cytogenetic features of the clone, not only the disease-associated characters are important as prognostic factors, but also patient-related characters such as age and pre- or coexisting illnesses (comorbidity) are of importance.[4-7] AML patients usually presented with critically compromised bone marrow function; in addition, intensive cytotoxic protocols further suppress their immunity, leading to infectious complications with frequent organ dysfunction or multi-organ failure which necessitate intensive supportive therapy to save their lives.[4] Mortality rate in patients with AML admitted to intensive care units might reach to 80%–90%.[8]

It was well known that the fundamental reason of morbidity moreover the mortality of the cancer patient is myelosuppression that frequently induced as a result of cancer itself in addition to its treatment.[9-11] Consequently, blood transfusion is a crucial employment in almost all patients with cancer together with acute leukemia, as an essential compassionate concern policy for enhancing clinical outcomes and even patient's survival as well as quality of life by prevailing over the life-threatening complications of acute leukemia and the treatment all at once.[12]

Thus, reversing the blood-transfusion numbers from the starting point of chemotherapy to the end of regimen has a critical importance in health planning at the level of institutions and even at the level of patient decision. Particularly, the information about the quantity of

blood-transfusion requirements for these patients are scarcely available overseas and regrettably none locally.[13]

The aims of this study were to review the predicted amount of units of blood transfusions needed for a patient with acute leukemia under a regimen of chemotherapy and to verify the transfusion frequency practices, according to the types of acute leukemia, levels of treatment, prognosis, and other demographic factors.

The limitation of this study is that the transfusion decision was not standardized but depended on the medical judgment of the treating physician and this may represent a possible source of bias.

Materials and Methods

Setting and study design
A prospective cohort study conducted at the National Center of Hematology/Mustansiriyah University in Baghdad from January 2013 to January 2015. This study was approved by the Institutional Review Board at National Center of Hematology. All patients signed an informed consent before enrollment in the study and for their data to be obtained in accordance with the Declaration of Helsinki.

Inclusion and exclusion criteria
The criteria for inclusion included all newly diagnosed acute leukemia patients (AML except acute promyelocytic leukemia and ALL) and patients more than 15 years of age admitted to the inpatient ward undergoing chemotherapy according to protocol regimens for AML 3 + 7 protocol for induction followed by three cycles of Midac protocol for consolidation. UKALL 12 was used for patients with ALL. The hemoglobin target of 8 g/dl was used as triggering point for transfusion.

The exclusion criteria included previous diagnosis of acute leukemia, relapse or refractory acute leukemia, associated severe comorbidities such as acute coronary syndrome (as defined by active chest pain, dynamic electrocardiogram changes, and troponin >2.5), and known active blood loss with hemodynamic instability.

Thirty sequential patients were enrolled in this study; all of them were newly diagnosed acute leukemia; the diagnosis was based on complete blood picture with bone marrow aspirate and confirmed by flow cytometry.

All patients received induction chemotherapy followed by consolidation according to protocol used. The blood components for those patients were all prepared according to institutional standard procedure from our blood bank. All red blood cell (RBC) units were given to patients after cross-match and compatibility test done.

Statistical analysis

Patients' data were tabulated and processed using the Statistical Package for the Social Sciences SPSS 20.0.0 (Chicago, IL, USA) for windows. Qualitative data are expressed as frequency and percentage and quantitative data as mean and median. Chi-square test and *t*-test were used to identify the association between two factors.

Results

Thirty patients were included in this study; 20 were male and 10 were female. The mean age ± standard deviation was 31.4 ± 15.17 years, age range from 15 to 66 years. There were 15 cases of AML and 15 cases for ALL. Baseline data are summarized in Table 1.
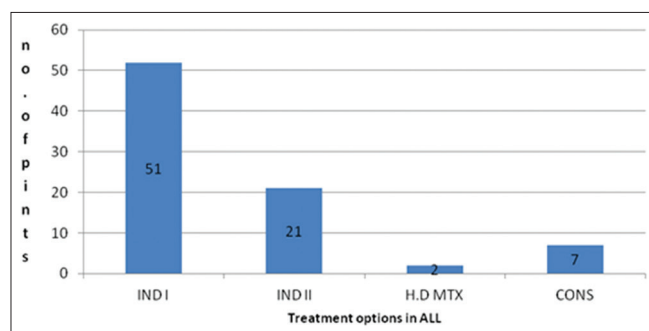
The number of transfused units was found to be higher and statistically significant $P < 0.001$ in those below 40 years of age, male patients and in patients with complete remission, while it was not significant for type of disease.

Regarding gender, male patients received 127 pints of blood (66.7%) while female patients received 43 pints of blood (33.3%), $P < 0.001$. There were no statistical differences between type of leukemia and blood-transfusion numbers, $P = 0.539$, while when considered the outcome of treatment, the study found that complete remission and relapse status have higher percent of blood-transfusion requirement 50% and 40%, respectively, in comparison to partial remission $P = 0.001$ as shown in Table 2.

The total number of blood-transfusion requirements in each type of leukemia according to treatment protocol was detailed in Figure 1 for ALL and Figure 2 for AML.

Discussion

The current practice in most tertiary center uses hemoglobin target of 8 g/dl for the purpose of transfusion for patients with acute leukemia. However, there is little information about transfusion requirements for those patients who underwent chemotherapy for induction or consolidation.[2]

Supportive measures with blood transfusion are considered integral to patient care in leukemia setting, and substantial amounts of blood may be required per patient during their treatment. Understanding the transfusion requirements of patients with acute leukemia is crucial for planning health-care systems and national bank strategies, including providing blood products and reinforcement of blood donation.

In this study, the mean age for all patients recruited was 31.4 years which consider younger when compared to other western studies; on the other hand, male patients constituted 66.7%, and male-to-female ratio was 2:1, which was higher than a study by Dawson *et al*.[13] These

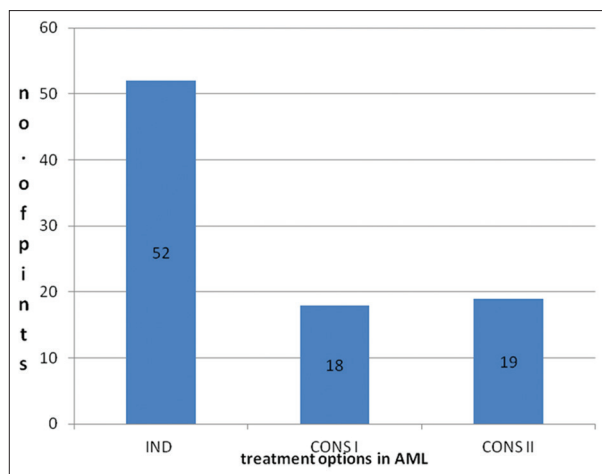**Table 1: Characteristics of the study sample, with the number of blood pints given for each character**

Variables	*n*=30	Percentage	Number of units
Age			
<40	23	76.7	128
40-60	6	20	37
>60	1	3.3	5
Sex			
Male	20	66.7	127
Female	10	33.3	43
Disease class			
ALL	15	50	81
AML	15	50	89
Prognosis*			
CR (AML + ALL)	15 (8+7)	50	66
PR (AML + ALL)	3 (2+1)	10	11
RE (ALM + ALL)	12 (6+6)	40	93

*CR=Complete remission, PR=Partial remission, RE=Relapse. ALL=Acute lymphoblastic leukemia, AML=Acute myeloid leukemia

Table 2: Number of blood-transfusion units needed according to the sample characteristics

Variables	Number of units	Mean
Age		
<40	128	χ^2=143.728, P=<0.001 (S)
40-60	37	
>60	5	
Sex		
Male	127	χ^2=41.506, P=<0.001 (S)
Female	43	
Disease class		
ALL	81	χ^2=0.376, P=0.539 (NS)
AML	89	
Prognosis		
CR	66	χ^2=61.637, P=<0.001 (S)
PR	11	
RE	93	

CR=Complete remission, PR=Partial remission, RE=Relapse, ALL=Acute lymphoblastic leukemia, AML=Acute myeloid leukemia, S=Significant, NS=Not significant

Figure 1: Number of blood-transfusion units versus phases of treatment in acute lymphoblastic leukemia patients in UKALL 12

Figure 2: Number of blood-transfusion pints versus types of treatment in acute myeloid leukemia patients

differences in demographic characteristics may be due to small sample size in this study and that young age group forms the majority in Iraqi population.

When we compare blood-transfusion requirements according to different variables used, the study found that patients below 40 years old have higher percent of blood transfusion 76.7%, male patients received more blood pints than females, and patients with relapsed disease required more blood transfusion than those in partial remission or complete remission; these results agree with other studies which found that the total number of packed RBC units used was greatest during induction therapy, and there was little variation for patient age and intensity of treatment. This suggests that the most important predictor for transfusion requirements may be the presence of a significant burden of disease.

All patients with acute lymphoblastic leukemia receiving chemotherapy required transfusion. The median blood-transfusion requirement was higher during induction therapy compared to other treatment phases [Figure 1]. Moreover, the same thing applied for patients with AML in which all patients required blood transfusion during induction phase in comparison to consolidation [Figure 2]; this is similar to other studies which found that the number of RBC units required to support a leukemia patient through induction therapy has been reported in wide ranges from 30 to 60 units during the first 2 months of therapy but has been decreasing over time likely due to increased attention to transfusion burdens.[2,13]

Conclusion

This study provides information to estimate the anticipated requirements for blood transfusion for those patients in regard to different factors which can be considered as guideline for these tertiary centers for accurate assessment of transfusion requirements and to direct resources for better outcome.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Spivak JL, Gascón P, Ludwig H. Anemia management in oncology and hematology. Oncologist 2009;14 Suppl 1:43-56.
2. DeZern AE, Williams K, Zahurak M, Hand W, Stephens RS, King KE, *et al.* Red blood cell transfusion triggers in acute leukemia: A randomized pilot study. Transfusion 2016;56:1750-7.
3. Cannas G, Fattoum J, Raba M, Dolange H, Barday G, François M, *et al.* Transfusion dependency at diagnosis and transfusion intensity during initial chemotherapy are associated with poorer outcomes in adult acute myeloid leukemia. Ann Hematol 2015;94:1797-806.
4. Stone RM, O'Donnell MR, Sekeres MA. Acute myeloid leukemia. Hematology Am Soc Hematol Educ Program 2004:98-117.
5. Vellenga E, Griffin JD. The biology of acute myeloblastic leukemia. Semin Oncol 1987;14:365-71.
6. van de Loosdrecht AA. The dendritic cell: The piano player in orchestrating the immune response in leukemia. Leuk Lymphoma 2007;48:217-8.
7. Dombret H, Raffoux E, Gardin C. New insights in the management of elderly patients with acute myeloid leukemia. Curr Opin Oncol 2009;21:589-93.
8. Schellongowski P, Staudinger T, Kundi M, Laczika K, Locker GJ, Bojic A, *et al.* Prognostic factors for Intensive Care Unit admission, intensive care outcome, and post-intensive care survival in patients with de novo acute myeloid leukemia: A single center experience. Haematologica 2011;96:231-7.
9. Cannas G, Thomas X. Supportive care in patients with acute leukaemia: Historical perspectives. Blood Transfus 2015;13:205-20.
10. Alkayed K, Al Hmood A, Madanat F. Prognostic effect of blood transfusion in children with acute lymphoblastic leukemia. Blood Res 2013;48:133-8.
11. Friedman BA, Burns TL, Schork MA. A study of blood utilization by diagnosis, month of transfusion, and geographic region of the United States. Transfusion 1979;19:511-25.
12. Blumberg N, Heal JM, Liesveld JL, Phillips GL, Rowe JM. Platelet transfusion and survival in adults with acute leukemia. Leukemia 2008;22:631-5.
13. Dawson MA, Avery S, McQuilten ZK, Bailey MJ, Shortt J, Polizzotto MN, *et al.* Blood transfusion requirements for patients undergoing chemotherapy for acute myeloid leukemia how much is enough? Haematologica 2007;92:996-7.