Blood transfusion requirements for patients undergoing chemotherapy for acute myeloid leukemia how much is enough?

Although essential in the management of AML, there is little information quantitating transfusion requirements for these patients. We evaluated 111 consecutive adults treated for AML, showing that approximately 150 blood donors are required to adequately cater for a single patient's complete therapy with little variation for age, prognostic group or intensity of treatment.

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Over the last 30 years, chemotherapy regimens and supportive care have been extensively evaluated and significant advances made in the management of acute myeloid leukaemia (AML).[1] However, there is little information about transfusion requirements for these patients.[1] Transfusion support is integral to patient care and substantial amounts of blood may be required per patient. Special needs, including HLA-matched platelets and CMV-seronegative components, can place high demands on limited resources. Understanding the transfusion requirements of these patients is crucial for planning health care strategies, including blood product provision and donor recruitment. Between November 2000 and June 2006, 158 consecutive adult patients with newly diagnosed AML presented to our institution. Of these, 111 patients received combination chemotherapy with curative intent and were evaluated for transfusion requirement. Patients with acute promyelocytic leukemia or receiving palliative care alone were excluded. Blood component requirements up to day 35 following induction and two further courses of consolidation therapy were assessed. Median follow up for the cohort was 405 days. Patient characteristics are summarized in Table 1. Chemotherapy regimens were based on published data by the Australasian Leukemia and Lymphoma Group.[2,3] These included *lower dose*, *standard dose* and *high dose* cytarabine based therapy (LDAC, SDAC and HDAC) and Fludarabine, Cytarabine and G-CSF (FLAG). The choice of chemotherapy regimen was at the discretion of the treating physician. However, where possible, patients aged < 60 years were to receive two courses of HDAC in their treatment course. Blood components were supplied by the Australian Red Cross Blood Service according to defined specifications.[4] All patients received irradiated and leucodepleted (leucocyte count $<1\times10^6$/unit of red cells [RBC] or platelets) cellular components. CMV-seronegative patients received cellular components from CMV-seronegative donors wherever possible. Transfusion thresholds were consistent with current Australian guidelines.[5] All analyses were conducted using SAS version 8.2 (SAS Institute Cary, NC, USA). Comparisons between groups were made using χ^2 tests for proportions, *t*-tests for normally distributed data, and Wilcoxon rank sum tests for all others. Differences between induction and consolidation courses were determined using paired *t*-tests and Wilcoxon sign rank tests. A two-sided *p*-value of 0.05 was considered statistically significant. All patients receiving chemotherapy required transfusion. Twenty-four percent of the study population were CMV-seronegative at the time of diagnosis and all of these patients remained CMV-seronegative following the completion of therapy. The median RBC, platelets and ancillary product (plasma and albumin) requirement was higher during induction therapy compared to either course of consolidation (Figure 1). For patients receiving two courses of con-

Table 1. Patients characteristics.

Variable	*Number (%)*
Sex	
Male	55 (50%)
Female	56 (50%)
Age (years)	58 (range 17-74)
WHO Classification[6]	
AML-RGA	8
AML-M0	4
AML-M1	11
AML-M2	20
AML-M3	excluded
AML-M4	14
AML-M5	9
AML-M6	7
AML-M7	2
AML-MLD	24
AML-TR	8
AML-AL	4
Cytogenetic risk	
Good	8 (7%)
Standard	61 (55%)
Poor	35 (32%)
Unknown	7 (6%)
CR post induction	
Yes	72 (65%)
No	32 (29%)
Unknown	7 (6%)

RGA: recurrent genetic abnormalities; MLD: multilineage dysplasia; TR: therapy-related; AL: ambiguous lineage. Cytogenetic risk groups were defined according to previously established criteria.[1] CR: complete remission was defined as < 5% myeloblasts on bone marrow aspirate cytology and no evidence of residual leukemia following assessment with flow cytometry and if applicable conventional cytogenetics, FISH and RT-PCR.

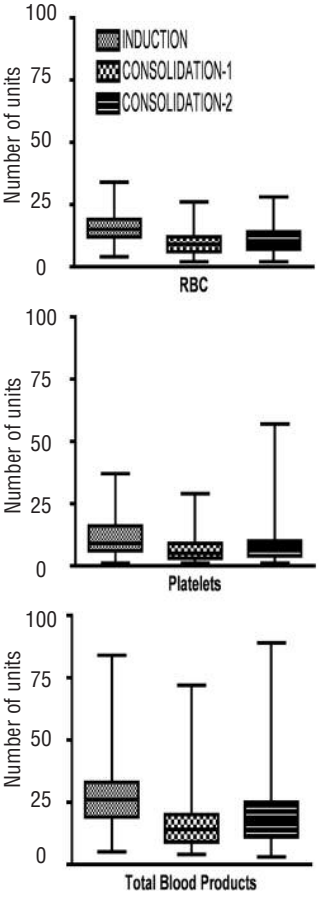

Figure 1. Transfusion requirements for the cohort. Box and whiskers chart demonstrating the transfusion requirements for red blood cells (RBC), platelets and total blood products (which includes RBC, platelets, plasma and albumin) during induction and both consolidation courses. The mean number of RBC, platelets and total blood products required was greatest during induction therapy. Requirements during consolidation-2 were marginally greater than those during consolidation-1.

Table 2. Transfusion requirements in subgroups.

Variable	*RBC-I*	*RBC-C1*	*RBC-C2*	*PLT-I*	*PLT-C1*	*PLT-C2*	*TOT-I*	*TOT-C1*	*TOT-C2*
Entire cohort	16(111)	9 (72)	10 (51)	12 (111)	7 (72)	9 (51)	30 (111)	17 (72)	20 (51)
Age<40	15 (22)	12 (18)	14 (10)	12 (22)	10 (18)	9 (10)	28 (22)	22 (18)	24 (10)
Age 40-60	16 (38)	9 (24)	11 (20)	12 (38)	8 (24)	10 (20)	29 (38)	19 (24)	22 (20)
Age >60	16 (51)	8 (30)	8 (21)	12 (51)	5 (30)	7 (21)	30 (51)	13 (30)	15 (21)
*LDAC	11 (4)	7 (5)	9 (3)	7 (4)	4 (5)	5 (3)	18 (4)	12 (5)	14 (3)
*SDAC	16 (94)	11 (25)	7 (21)	12 (94)	9 (25)	6 (21)	30 (94)	20 (25)	14 (21)
*HDAC	14 (13)	11 (39)	13 (27)	14 (13)	9 (39)	11 (27)	30 (13)	20 (39)	24 (27)
Good cytogenetics	17 (8)	10 (8)	11 (8)	13 (8)	5 (8)	9 (8)	32 (8)	15 (8)	21 (8)
Standard cytogenetics	15 (61)	9 (38)	10 (34)	12 (61)	7 (38)	5 (34)	29 (61)	16 (38)	11 (34)
Poor cytogenetics	17 (35)	11 (17)	9 (9)	11 (35)	9 (17)	2 (9)	30 (35)	22 (17)	15 (9)
CR post-induction	15 (72)	NA	NA	11 (72)	NA	NA	28 (72)	NA	NA
No CR post-induction	16 (32)	NA	NA	12 (32)	NA	NA	29 (32)	NA	NA

*The mean number of RBC units, platelet doses (each dose contains a minimum of 2 x 10^{11} platelets per dose and may be derived from 4-5 individual donations or a single apheresis unit) and total products required to support patients in the cohort through induction and both courses of consolidation therapy. Transfusion requirements were not statistically different between any demographic subgroup. The mean requirements are listed for each category with the number of patients in the cohort recorded in brackets. RBC: red cell units; PLT- platelet doses; TOT: total blood products required including RBC, platelets, plasma and albumin; I: induction chemotherapy; C1: first course of consolidation chemotherapy; C2: second course of consolidation chemotherapy .*Three patients received FLAG chemotherapy as first consolidation therapy.*

solidation, blood component requirements were slightly greater during the second cycle. Patient sex, age, AML subtype or cytogenetic risk did not significantly affect transfusion requirements. In addition, requirements for transfusion support were independent of the intensity of chemotherapy delivered (Table 2). The observed difference in transfusion requirements was not accounted for by differences in blood counts before starting induction or either consolidation therapy (*data not shown*). The mean total number of blood components required to support a patient through induction, first and second consolidation chemotherapy was 30, 17 and 20 units respectively (Table 2). HLA-matched apheresis platelets were required by 4 patients and washed RBC were necessary for 1 patient with suspected allergic reactions. Ninety-two percent of platelet doses used were derived from pools of 4-5 donations. Therefore as many as 66, 38 and 47 donations would be required to support a single patient through induction, first and second consolidation chemotherapies respectively, totaling approximately 150 donations over the entire course of therapy. This series documents the transfusion requirements of a representative cohort receiving curative therapy for AML using established transfusion thresholds. All patients required transfusion support, emphasizing how essential this is for AML management. The number of blood components used was greatest during induction therapy and there was little variation for patient age, prognostic category or intensity of treatment delivered. This suggests that the most important predictor for transfusion requirements may be the presence of a significant burden of disease. Substantial numbers of donors are needed to provide the transfusion requirements for a single patient, particularly since most platelet doses transfused in Australia are pooled from several donors. A shift to increased use of apheresis platelets would reduce the number of donors required to provide adequate platelet support and also reduce donor exposure for this multiply transfused population. Accurate assessment of transfusion requirements of this group is essential for planning therapy and directing resources. This is especially important since the vast majority of centres treating AML are tertiary referral hospitals with competing demands on their blood inventory, such as trauma and intensive care services. This study provides information to guide blood centres and hospitals in maintaining adequate inventories based upon anticipated transfusion needs of these complex patients.

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