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Prophylactic platelet transfusion threshold during therapy for adult acute myeloid leukemia: 10,000/µL versus 20,000/µL

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Abstract

Background and Objective. **The threshold for prophylactic platelet transfusions has been classically established at 20,000/µL. In 48 patients with *de novo* acute myeloblastic leukemia (AML) we analyzed the effect of reducing the threshold for prophylactic platelet transfusion from 20,000/µL (group A) to 10,000/µL (group B) after induction and consolidation chemotherapy.**

Design and Methods. **Forty-eight adult patients with *de novo* AML diagnosed in a single institution in a nine year period were enrolled in the study. Between January 1989 and December 1993 the patients received prophylactic platelet transfusions when their platelet count was below 20,000/µL (group A), and from January 1994 to March 1998 prophylactic platelet transfusions were indicated below 10,000/µL or between 10,000/µL and 20,000/µL if there was any consumption factor.**

Results. **The mean number (SD) of platelet transfusions during induction was 8.4 (5.3) in group A and 8.5 (5.5) in group B; and during consolidation 4.7 (3.4) in group A and 4.6 (3.8) in group B (p=n.s.). Excluding the cases with consumption factors from the analysis, group B patients required 34% fewer transfusions during induction and 15.5% fewer during consolidation (p=0.04). There were no differences between groups regarding major bleeding episodes.**

Interpretation and Conclusions. **Our data show that the threshold for prophylactic platelet transfusion can be safely set at 10,000 µL during induction and consolidation chemotherapy for adult patients with *de novo* AML.**

Key words: prophylactic platelet transfusion, acute myeloid leukemia, threshold, induction, consolidation, consumption factors

Platelet transfusions are often used prophylactically to prevent bleeding in patients with thrombocytopenia induced by chemotherapy. The first studies on thrombocytopenia in patients with acute leukemia suggested a substantial increase in hemorrhagic episodes at platelet counts lower than 20,000/µL.[1] With the development of aggressive chemotherapeutic regimens the threshold for prophylactic platelet transfusion was established at 20,000/µL.[2,3] Recent studies indicate that a lower platelet count can be set for prophylactic transfusions without an increase in the hemorrhagic risk.[4,5]

We have reviewed and evaluated the results of our prophylactic platelet transfusional policy in a series of 48 adult (age >15 yr) patients with *de novo* acute myeloblastic leukemia (AML) (except acute promyelocytic leukemia) between January 1989 and March 1998 during induction and consolidation chemotherapy with special emphasis on the comparison of the thresholds of 20,000/µL and 10,000/µL.

Materials and Methods

The prophylactic platelet transfusions of 48 adult (age >15 yr) patients with *de novo* AML diagnosed in a single institution and included in a protocol of intensive chemotherapy between January 1989 and March 1998 were analyzed. Patients with promyelocytic leukemia were excluded from the analysis. All the patients received one or two cycles of remission-induction chemotherapy: idarubicin (10 mg/m^2 days 1, 3, and 5) or daunorubicin (an IV bolus of 60 mg/m^2, days 1, 2 and 3), cytarabine (an intravenous bolus of 25 mg/m^2 followed by a continuous IV infusion of 100 mg/m^2 from day 1 to day 7, and etoposide (100 mg/m^2 from day 1 to day 5). Those patients who were in first complete remission (n=38) received two consecutive chemotherapy regimens for consolidation: a) mitoxantrone 10 mg/m^2, IV for 3 days plus cytarabine 1.2 g/m^2, IV every 12 hours for 4 days; b) amsacrine 100 mg/m^2, IV for 3 days plus cytarabine 1.2 g/m^2 IV every 12 hours for 2 or 4 days.[6]

Between January 1989 and December 1993, patients with AML received prophylactic platelet transfusions when their platelet count was below 20,000/µL (group A), and from January 1994 to March 1998 prophylactic platelet transfusions were indicated in patients with AML if the platelet count was lower than 10,000/µL or between 10,000/µL and 20,000/µL if there was any factor of increased platelet consumption (fever, active infection or coagulopathy) (group B). Except for this change in the platelet transfusion policy, there were no other modifications in the management of the AML patients (i.e. red cell

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transfusion criteria, prophylaxis and treatment of infections). The platelet count was performed daily from a sample of blood collected in a tube with EDTA and processed in an automatized cell counter (Technicon H.2 system, Bayer®, Barcelona, Spain). In all cases transfused platelets were from random donors and had been processed to reduce the number of leukocytes.

The following data were evaluated for each record: age, sex, leukemia subtype (FAB classification),[7] daily platelet count in the morning, presence of platelet consumption factors such as fever, active infection or coagulopathy, significant bleeding episodes (WHO scale), number of platelet transfusions (from random donors in all cases, at a dose of one unit every 10 kg b. w.) and number of packed red cell concentrates transfused.

Table 1. Comparison of patient characteristics and prophylactic platelet support between the two groups (A: platelet count threshold 20,000/μL; B: threshold 10,000/μL).

	GROUP A (27 patients)	*GROUP B (21 patients)*
Age (yr)		
Median	50	48
Range	(16-72)	(16-70)
AML FAB subtype		
M0	3	4
M1	1	1
M2	3	4
M4	7	8
M5	11	3
M6	2	1
INDUCTION	36 cycles	31 cycles
Platelet transfusions		
Mean (SD)	8.4 (5.3)†	8.6 (5.5)†
Median	8	8
Range	2-8	2-24
Platelet transfusions without consumption factors		
Mean (SD)	4.1 (4.2)‡	2.7 (1.8)‡
Median	3	2
Range	0-24	0-7
*Major bleeding episodes**	11	13
CONSOLIDATION	39 cycles	23 cycles
Platelet transfusions		
Mean (SD)	4.7 (3.4)†	4.6 (3.8)†
Median	3	3
Range	(1-16)	(1-15)
Platelet transfusions without consumption factors		
Mean (SD)	2.6 (1.9)‡	2.2 (1.8)‡
Median	2	2
Range	0-10	0-8
*Major bleeding episodes**	4	5

*AML: Acute myeloblastic leukemia; FAB: French-American-British. *WHO grade ≥ 2; †p<0.001 (analysis of variance), comparison of total number of platelet transfusions between induction and consolidation; ‡p=0.04 (analysis of variance), comparison of platelet transfusions without consumption factors between groups A and B patients.*

A descripitive study of all variables was performed. Differences in quantitative variables between groups were compared by the Wilcoxon rank-sum test (Mann-Whitney test) and differences in qualitative variables by the χ^2 test. Analyses of variance were performed to compare simultaneously platelet transfusions in induction and consolidation; and platelet transfusions without consumption factors between groups A and B.

Results

Thirty-six cycles of pancytopenia after induction chemotherapy were evaluated in 27 patients in group A and 31 in 21 patients in group B. Thirty-nine episodes of pancytopenia after consolidation chemotherapy were evaluable in 20 patients in group A, and 23 in 18 patients in group B. The characteristics of both groups are listed in Table 1. There were no differences in either the patients' characteristics or features of AML or the number of packed red cells transfused between groups A and B.

In group A the median number of platelet transfusions after induction was 8, identical to that of group B. In group A the median number of platelet transfusions after consolidation was 3 (range 1-16) and the mean 4.7±3.4 (SD), while in group B the median was 3 (range 1-15) and the mean 4.6±3.8 SD). We did not find any difference in the number of platelet transfusions between the groups either during induction or during consolidation when the overall number of transfusions was considered. However, when we analyzed only those transfusions performed in the absence of consumption factors, there was a reduction of 34% during induction and 15.5% during consolidation in group B patients (p=0.04). In group A there were 23 patients (32 cycles) who received transfusions without comsumption factors during induction and 20 (37 cycles) during consolidation; in group B there were 16 (27 cycles) during induction and 18 (20 cycles) during consolidation. The total number of platelet transfusions performed without concomitant presence of consumption factors was 150 in induction and 101 in consolidation for group A; and 83 in induction and 50 in consolidation for group B. In addition, considering both groups, the total number of platelet transfusions during consolidation was significantly lower than that given during induction (p<0.001).

Major bleeding events (WHO grade ≥ 2) occurred in 11 cases of group A (30%) and in 13 (42%) of group B after induction, and in 4 cases (10%) of group A and in 5 cases of group B (21%) after consolidation chemotherapy (p=n.s.). There were no deaths secondary to major bleeding in either group.

Discussion

Prophylactic platelet transfusion is currently a matter of controversy. The wide availability of platelets for transfusion has led to their excessive use with a

consequent increase in health costs in addition to increased risk of virus transmission.[8,9] For these reasons several studies have been carried out in an attempt to establish a restrictive threshold for prophylactic platelet transfusion.[4,10,11] In difference to other studies which included patients with a variety of hematologic diseases in different treatment phases, we analyzed the effect of reducing this threshold in two groups of patients with the same hematologic disease (*de novo* AML). Furthermore, the patients and AML characteristics of the two groups were comparable, and there were no changes in the management of the patients throughout the study. We did not find a decrease in the number of platelet concentrates transfused in group B patients, possibly because marked thrombocytopenia is usually associated with severe neutropenia with fever or infection, which lead to an increase in platelet consumption. In fact, when we analyzed the number of platelet transfusions given in the absence of any consumption factor, there was a decrease in the number of platelet concentrates transfused in group B patients during induction (34%), as well as during consolidation (15%) (p=0.04). In addition, other authors have reported that the number of days on which the patients have platelet counts below 10,000/μL or below 20,000/μL are not significantly different.[12] The number of platelet transfusions during consolidation was significantly lower than during induction (p<0.001), perhaps because of the normal platelet counts at the onset of consolidation phase. As in other studies[4,11,13] no significant differences were found in the number and severity of bleeding episodes between the groups and no patient in either group died due to hemorrhage.

Although this study was carried out retrospectively, we think that our results are valuable because only *de novo* AML patients treated with the same induction and consolidation therapy were included. Our results complete those given by others,[4,11,13] because, to our knowledge, there are no published studies including the analysis of prophylactic platelet transfusion during consolidation chemotherapy. In our series, similarly to that referred by other authors,[4,11,13] no differences were found in the number of major bleeding episodes regardless of the threshold platelet count. As a consequence, our data also support the concept that patients undergoing myelotoxic chemotherapy for AML could safely receive prophylactic platelet transfusions at a threshold of 10,000/μL during induction, as well as consolidation treatment. Further evaluations with an even lower threshold platelet level (e.g. 5,000/μL) would be useful to establish the real platelet count required for prophylactic transfusion.

Contributions and Acknowledgments

JTN and JMR formulated the design of the study and wrote the paper. JTN, JAH and JMS collected the data and made the data base. JTN and AO performed the statistical analysis. MP was the responsible for platelet support. JTN, JAH, JMR, JMS, FM and EF were responsible for the patients' diagnosis and clinical management.

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Disclosures

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