SOMATO PUBLICATIONS

Annals of Stem Cell Research

Research Article

Clinical Study on Part Factors Affecting the Effect of Platelet Transfusion during Hematopoietic Stem Cell Transplantation

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Received: 15 March 2019; **Accepted:** 09 April 2019; **Published:** 10 April 2019

Citation of this article: Chen, B., Yang, J. (2019) Clinical Study on Part Factors Affecting the Effect of Platelet Transfusion during Hematopoietic Stem Cell Transplantation. Ann Stem Cell Res, 2(1): 023-028.

ABSTRACT

Objective: At present, patients with hematopoietic stem cell transplantation (HSCT) are gradually increasing due to hematological diseases. However, there are no further studies on the factors affecting the effect of platelet transfusion during HSCT. This study analyzed the possible factors that affect the platelet transfusion efficiency.

Methods: The clinical data of patients with HSCT were collected from the Department of Hematology, Zhongda Hospital Affiliated to Southeast University from March 2015 to March 2018. According to the inclusion and exclusion criteria, a retrospective statistical analysis on the factors affecting the infusion effect was taken in all patients from +1 d to the day that the peripheral blood granulocyte count was more than 0.5×10^9/L after transplantation. The factors are including gender, age, types of disease, whether initial treatment, platelet inventory days in the effective period, types of transplantation, duration of disease and transfusion times. Furthermore, non-conditional logistic regression analysis was performed on the mentioned factors with statistical significance.

Results: A total of 52 patients, 299 platelet transfusions were included in this study. The patients involve 28 men and 24 women, and there were 233 effective infusion and 66 invalid infusion. After chi-square test, the effects of gender, age, disease types, whether initial treatment, transplantation types, duration of disease and transfusion times on platelet transfusion were statistically significant ($P<0.05$), while platelet inventory days within the validity period had no statistically significant effect on platelet transfusion ($P\geq0.05$). Furthermore, the results of non-conditional logistic regression analysis showed that gender, disease type and whether initial treatment had a statistically significant impact on the effect of platelet transfusion ($P<0.05$).

Conclusion: There are many factors related to poor platelet transfusion during HSCT, in which the gender, disease types and whether initial treatments are the main influencing factors.

Keywords: Hematological cancer; Hematopoietic stem cell transplantation; Platelets; Transfusion effects; Clinical trials; Statistical analysis

Introduction

In the recent year, cancer has become the first killer to human's health and life, including hematological cancer. Hematopoietic Stem Cell Transplantation (HSCT) is an effective treatment for hematological cancer patients. After myeloablative preconditioning, the bone marrow of patients receiving HSCT keep empty state for a certain period of time, and the hematopoietic function has not been reconstructed [1]. During this process, the number of platelets in patients is extremely low and the risk of bleeding is greatly increased.

When the platelet count less than $0.5*10^9$/L, intracranial hemorrhage is likely to occur. At this time, treatment and prevention transfusion is often an important link during the HSCT [2,3]. Some clinical doctors believe that platelet transfusion is the most effective treatment and prevention of bleeding caused by thrombocytopenia or functional defects [4,5]. However, with the increasing number of platelet transfusion in the clinic, platelet transfusion refractoriness (PTR) often occurs in patients. At the same time, the supply of platelet is still relatively tight and expensive. Based on the above, the indications and effects of platelet transfusion have received increasing attention.

This study collected data and conducted retrospective analysis to analyze the factors affecting the effect of platelet transfusion during HSCT. In order to provides relevant theoretical basis and guidance for platelet transfusion during transplantation in patients with clinical hematological diseases.

Methods

We collected 52 patients who underwent HSCT in Department of Hematology, Zhongda Hospital Affiliated to Southeast University from March 2015 to March 2018. The time of preservation and the number of platelets are subject to the data provided by Jiangsu or Nanjing Blood Station. Inclusion criteria included clear diagnosis, and undergoing HSCT in the laminar flow ward in Department of Hematology, Zhongda Hospital Affiliated to Southeast University during the study period. Any of the following conditions occurring within 24 hours of platelet transfusion (8:00 to 8:00 of next day) was not included in the study: (1) temperature >38; (2) nose bleeding, gastrointestinal bleeding and other bleeding manifestations; (3) the occurrence of super-acute graft-versus-host (GVHD) disease; (4) hepatic vein occlusion; (5) complicated with cardiac, liver, kidney and other serious organ lesions. A retrospective statistical analysis on the factors affecting the effect of infusion was taken in all patients from +1 d to the day that the peripheral blood granulocyte count was more than $0.5*10^9$/L after transplantation.

Measures

Basic information of all patients including gender, age, types of disease, duration of disease, whether initial treatment, types of transplantation, platelet inventory time(less than 24 hours counted 1 day) and platelet transfusion times were collected. Besides, the number of peripheral blood platelet count before and after per infusion was involved.

The effect after infusion was evaluated using corrected count increment (CCI). CCI was calculated within 1 hour or 24 hours after platelet transfusion and the formula as follows: CCI = (platelet count after infusion - platelet count before infusion) *body surface area / total number of platelets infused. It is generally considered to be a valid infusion when the CCI value higher than $10*10^9$/L. However, in the actual clinical data collection process, the platelet count can't be accurate to exact platelet count. Therefore, we adopted adjusted data during analysis with the adjusted corrected count increment (aCCI). The calculation formula is as follows: aCCI= (platelet count after infusion - platelet count before infusion) *body surface area / number of platelets infused bags. Based on the platelet count of $2.5*10^{11}$ per bag, the aCCI value <5 is approximately equivalent to the ineffective infusion standard value of CCI value $<2.5*10^9$/L.

Statistical methods

The data of patients were established into a database, and statistical analysis was performed using computer software SPSS (version 21, SPSS Inc., Chicago, IL). The chi-square test was used to compare the infusion effects between different groups according to gender, age, disease types, whether initial treatment, duration of disease, types of transplantation, platelet inventory time during the effective period, and transfusion times. In addition, unconditional logistic multivariate analysis was performed on all the factors mentioned above. All data were analyzed by bilateral statistical test. The P value <0.05 was considered to be statistically significant.

Results

Basic clinical characteristics of patients

A total of 52 patients, 299 platelet transfusions were enrolled in this clinical trial. According to gender, age, types of disease, duration of disease, whether initial treatment, types of transplantation, platelet inventory time(less than 24 hours counted 1 day) and platelet transfusion times, all the patients included in the study were divided into different groups (Table 1).

The effect of gender on the platelet transfusion

The grouping by gender is as follows. After chi-square test, the difference between the two groups was statistically significant (P<0.05) (Table 2).

The effect of age on the platelet transfusion

The grouping by age is as follows. After chi-square test, the difference between the three groups was statistically significant (P<0.05). Furthermore, chi-square test was performed between ≤18 years group and 19~59 years group, ≥60 years group respectively. The results showed that there was statistically significant difference between ≤18 years group and 19~59 years group (P<0.05), and there was no statistically significant difference between ≤18 years group and ≥60 years group (P≥0.05) (Table 3).

The effect of disease types on the platelet transfusion

The grouping by disease types is as follows. After chi-square test, the difference in platelet transfusion between the six groups was statistically significant (P<0.05). Furthermore, chi-square test was performed between ALL group and ML group, AML group, MM group, AA group and MDS group, respectively. The difference between AA group, MDS group and ALL group was statistically significant respectively (P<0.05). The difference between ML group, AML group, MM group and ALL group was not statistically significant respectively (P≥0.05) (Table 4).

The effect of treatment timing on the platelet transfusion

The grouping by disease types is as follows. After chi-square test, the difference between the two group was statistically significant (P<0.05) (Table 5).

The effect of transplantation types on the platelet transfusion

The grouping by disease types is as follows. After chi-square test, the difference between the three groups was statistically significant (P<0.05). Furthermore, chi-square test was performed between allo-HSCT group and syn-HSCT group, auto-HSCT group respectively.

The results showed that there was statistically significant difference between allo-HSCT group and syn-HSCT group (P<0.05), and there was no statistically significant difference between allo-HSCT group and auto-HSCT group (P≥0.05) (Table 6).

The effect of duration on the platelet transfusion

The grouping by disease types is as follows. After chi-square test, the difference between the three groups was statistically significant (P<0.05). Furthermore, chi-square test was performed between ≤6 months group and 6months~1year group, >1year group respectively.

Table 1: Basic clinical characteristics of patients.

characteristics	Transfusion times (n)		Proportion (%)	
	Valid	Invalid	Valid	Invalid
Gender				
Male	114	50	69.5	30.5
Female	119	16	88.1	11.9
Age				
≤18 (years)	141	27	83.9	16.1
19~59 (years)	86	35	71.1	28.9
≥60 (years)	6	4	60.0	40.0
Disease types				
ALL	97	4	96.0	4.0
ML	42	5	89.4	10.6
AML	40	7	85.1	14.9
MM	34	10	77.3	22.7
AA	10	24	29.4	70.6
MDS	10	16	38.5	61.5
Treatment timing				
Initial	218	46	82.6	17.4
Relapsed	15	20	42.9	57.1
Transplantation types				
allo-HSCT	98	39	71.5	28.5
syn-HSCT	102	20	83.6	16.4
auto-HSCT	33	7	82.5	17.5
Duration				
≤6 months	86	15	85.1	14.9
6 months ~1year	53	11	82.8	17.2
>1year	94	40	70.1	29.9
Platelet inventory time				
1 (d)	153	37	80.5	19.5
2 (d)	71	27	72.4	27.6
3 (d)	9	2	81.8	18.2
Transfusion times				
6	97	17	85.1	14.9
7	63	20	75.9	24.1
8	58	19	75.3	24.7
10	15	8	65.2	34.8
15	0	2	0.0	100.0

Table 2: The effect of gender on the platelet transfusion [n(%)].

Group	Valid	Invalid	*x*2	P value
Male	114 (69.5)	50 (30.5)	14.950	0.000
Female	119 (88.1)	16 (11.9)		

Table 3: The effect of age on the platelet transfusion [n(%)].

Group	Valid	Invalid	*x*2	P value
≤18 years	141 (83.1)	27 (16.9)		
19~59 years	86 (71.1)	35 (28.9)	6.897	0.009*
≥60 years	6 (60.0)	4 (40.0)	3.757	0.053*

* representing compared to ≤18 years group

Table 4: The effect of disease types on the platelet transfusion [n(%)].©

Group	Valid	Invalid	*x*2	P value
ALL	97 (96.0)	4 (4.0)		
ML	42 (89.4)	5 (10.6)	2.504	0.114*
AML	40 (85.1)	7 (14.9)	4.097	0.043*
MM	34 (77.3)	10 (22.7)	10.317	0.001*
AA	10 (29.4)	24 (70.6)	68.692	0.000*
MDS	10 (38.5)	16 (61.5)	47.417	0.000*

* representing compared to ALL group

Table 5: The effect of treatment timing on the platelet transfusion [n(%)].

Group	Valid	Invalid	Results	
			*x*2	P value
Initial	218 (82.6)	46 (17.4)	28.342	0.000
relapsed	15 (42.9)	20 (57.1)		

Table 6: The effect of transplantation types on the platelet transfusion [n(%)].

Group	Valid	Invalid	*x*2	P value
allo-HSCT	98 (71.5)	39 (28.5)		
syn-HSCT	102 (83.6)	20 (16.4)	5.348	0.021*
auto-HSCT	33 (82.5)	7 (17.5)	1.936	0.219*

*representing compared to allo-HSCT group

The results showed that there was no statistically significant difference between ≤6 months group and 6months~1year group (P≥0.05), and there was statistically significant difference between ≤6 months group and >1year group (P<0.05) (Table 7).

The effect of platelet inventory time on the platelet transfusion

The grouping by platelet inventory time is as follows. After chi-square test, the difference between the three groups was not statistically significant (P≥0.05). Furthermore, chi-square test was performed between 1d group and 2d group, 3d group respectively. The results showed that there was no statistically significant difference between 1 d group and 2 d group, 3 d group respectively (P≥0.05) (Table 8).

The effect of platelet transfusion times on the platelet transfusion

The grouping by platelet transfusion times is as follows. After chi-

square test, the difference between the five groups was statistically significant (P<0.05). Furthermore, chi-square test was performed between 6 times group and 7 times group, 8 times group, 10 times group, 15 times group respectively. The results showed that there was no statistically significant difference between 6 times group and 7 times group, 8 times group, 10 times group respectively (P≥0.05), and there was statistically significant difference between 6 times group and 15 times group (P<0.05) (Table 9).

Overall multivariable analysis of factors influencing transfusion

Unconditional logistic multivariate regression analysis was performed on all factors included in the study. The results showed that gender, disease type, and whether or not the initial treatment had a significant effect on platelet transfusion (P<0.05). Among them, the platelet transfusion effect of female patients is worse than that of male patients; the patients with disease types including ML, AML MM and AA have better platelet transfusion effect than ALL patients, and the effect of platelet transfusion in patients with MDS is not as good as that of ALL patients; the effect of platelet transfusion in newly diagnosed patients is better than relapsed patients. There was no significant difference in the effect of age, type of transplantation, duration of disease, platelet inventory days and platelet transfusion times on platelet transfusion (P≥0.05) (Table 10).

In summary, we reached the following conclusions: (1) the effect of platelet transfusion in female patients is better than that of male patients; (2) the type of disease including ML, AML MM and AA patients with platelet transfusion is better than ALL patients, and MDS patients with platelet transfusion effect is not as good as ALL patients; (3) the initial patients with platelet transfusion is better than relapse patients; (4) age, types of transplant, duration of disease, platelet inventory time during the effective period, and platelet transfusion times had no significant effect on platelet transfusion.

Table 7: The effect of duration on the platelet transfusion [n(%)].

Group	Valid	Invalid	*x2*	P value
≤6 months	86 (85.1)	15 (14.9)		
6months~1year	53 (82.8)	11 (17.2)	0.161	0.688*
>1year	94 (70.1)	40 (29.9)	7.228	0.007*

* representing compared to ≤6 months group

Table 8: The effect of platelet inventory times on the platelet transfusion [n(%)].

Group	Valid	Invalid	*x2*	P value
1 d	153 (80.5)	37 (19.5)		
2 d	71 (72.4)	27 (27.6)	0.000	1.000*
3 d	9 (81.8)	2 (18.2)	0.000	1.000*

* representing compared to 1 d group

Table 9: The effect of platelet transfusion times on the platelet transfusion [n(%)].

Group	Valid	Invalid	*x2*	P value
6 times	97 (85.1)	17 (14.9)		
7 times	63 (75.9)	20 (24.1)	2.656	0.103*
8 times	58 (75.3)	19 (24.7)	2.864	0.091*
10 times	15 (65.2)	8 (34.8)	3.821	0.051*
15 times	0 (0.0)	2 (100.0)	5.106	0.024*

* representing compared to 6 times group.

Table 10: Unconditional logistic multivariate regression analysis of factors influencing transfusion.

Variable	OR	95% CI	P value
Gender	2.784	1.268~6.112	0.011
Age			0.118
Age (1)	0.557	0.085~3.643	0.541
Age (2)	1.370	0.205~9.142	0.745
Disease types			0.000
Disease type (1)	0.036	0.008~0.154	0.000
Disease type (2)	0.123	0.031~0.496	0.003
Disease type (3)	0.103	0.028~0.374	0.001
Disease type (4)	0.131	0.038~0.454	0.001
Disease type (5)	1.450	0.430~4.889	0.549
Treatment timing	0.154	0.054~0.439	0.000
Transplantation types			0.141
Transplantation type (1)	3.796	1.005~14.338	0.049
Transplantation type (2)	2.739	0.704~10.652	0.146
Duration			0.067
Duration (1)	0.456	0.190~1.093	0.078
Duration (2)			0.292
Platelet inventory time	1.826	0.595~5.603	0.343
Platelet inventory time (1)	0.261	0.527~5.836	0.962
Platelet inventory time (2)	0.957	0.161~5.684	0.143
Transfusion times	0.000	0.000~	0.674
Transfusion time (1)	0.000	0.000~	0.999
Transfusion time (2)	0.000	0.000~	0.999
Transfusion time (3)	0.000	0.000~	0.999
Transfusion time (4)			0.999

Note: 1, 2, 3 and 4 represent the reference code that generates dummy variables with the first variable in each group as the reference.

Discussion

So far, platelet transfusion has become one of the most important supportive treatments in the treatment of patients with solid tumor/hematological diseases in the clinic [6]. Platelet counts after platelet transfusion in patients with solid tumor/hematological diseases vary greatly based on factors such as short survival time of platelets *in vivo* and factors affecting platelet transfusion in patients. However, clinical indications for platelet transfusion and platelet transfusion effects are unsatisfactory. At the same time, platelet resources are scarcer than red blood cells, relatively. The time of *in vitro* preservation activity after collection is shorter and the storage cost is higher. Clinically, there is often no platelet availability or platelet residual failure. Therefore, it is necessary to research the factors affecting the effect of platelet transfusion, so as to provide a certain reference for clinical platelet transfusion decision.

In this study, patients undergoing HSCT in the period of bone marrow emptying were involved. On the one hand, the frequency of platelet transfusion was significantly higher in this stage than that in

ordinary patients. On the other hand, the bone marrow of patients at this stage was emptied and the effect of their own bone marrow function can be minimized.

In the study, the effect of gender on platelet transfusion was statistically different, and female infusion was superior to male. Slichter, et al. [7] showed that men are one of the factors that reduce the effect of infusion, which is the same as the results of this study. The single factor chi-square test found that the effect of age on platelet transfusion was statistically different, while the multivariate unconditional logistic regression analysis was contrary. The results of Slichter, et al. [7] suggested that factors associated with patient-improved infusion effects include splenectomy and patient age. However, Guangzeng Wan [8] found that the effect of age on platelet transfusion was not statistically significant ($P \geq 0.05$) by retrospective analysis of factors affecting platelet transfusion. Our study showed that the effect of age on the platelet transfusion effect had completely different results, which may be related to the size of the sample. The specific reasons need further investigation. The results of this study showed that the effect of disease types on platelet transfusion was statistically significant. ML, AML MM and AA patients had better platelet transfusion effect than ALL patients, while MDS patients showed worse effect than ALL patients. Carral, et al. [9] have shown that compared with ML and MM patients, MDS patients' recovery of hematopoietic function was delayed, which suggesting that residual leukemia in patients may also lead to delayed transplantation. The results of this study are consistent with this conclusion. This may be due to the difference in the number of patients with different diseases and the choice of transplantation type. In addition, patients repeatedly infused platelets before transplantation, and more anti-platelet antibodies in the body may also cause the above results [10]. According to the single factor chi-square test results of this study, the effects of different transplantation types on platelet transfusion were statistically significant, while the multivariate unconditional logistic regression analysis showed no statistical difference. Chuancang Zhang [11] and his colleague found that in children with hematological diseases, the effect of transfusion of platelets between different transplantation types was statistically significant ($P<0.05$). The authors analyzed the possible reason for the fact was that patients with better platelet transfusions were more likely to choose auto-HSCT, while patients with poorer disease types were more likely to choose cord blood stem cell transplantation, which reduced transplanted cells survival rate to some extent. The results of this study, in contrast, may be related to the difference in the number of patients with different transplant types. The results of this study showed that there was a statistically significant difference in platelet transfusion between patients with different disease durations. Jaime-Pérez JC, et al. [12] found that the longer the course of the disease, the worse the platelet transfusion effect, the same as the results of this study. Analysis of the reasons, patients with long duration may often receive more platelet transfusions, resulting in ineffective platelet transfusion. There was no statistically significant difference in the effect of platelet inventory time on platelet transfusion during platelet validity. Chuancang Zhang, et al. [11] found that in children with hematological diseases, the effect of platelet inventory days on platelet transfusion was not statistically significant. In this study, the single factor chi-square test results showed that the effect of platelet transfusion times on platelet transfusion was statistically different, while the multivariate unconditional logistic regression analysis showed no statistical difference, suggesting that the number of platelet transfusions was not the predictor of the platelet transfusions effect. Yang Liu, et al. [13] found that the more the times of platelet transfusion in the same patient, the worse the effect of platelet transfusion and the increased probability of PTR. The possible reason was that data was from the same research center. The sample size of the different infusion groups was quite different, and a larger sample analysis was needed. The influencing factors and sample size in this study are limited. A larger sample size study to further improve the evaluation of platelet transfusion effects and more research needs to be further developed.

Acknowledgement

This work was supported by the [Key Medical Projects of Jiangsu Province #1] under Grant [number BL2014078] and [Key Medical of Jiangsu Province #2] under Grant [number ZDXKB2016020].

Conflict-of-interest statement

The authors report no conflicts of interest in this work.

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