Clinical efficacy of platelet transfusion therapy in patients with leukemia and analysis of risk factors for ineffective transfusion

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Abstract. Clinical efficacy of platelet transfusion therapy in patients with leukemia was investigated to analyze risk factors for ineffective transfusion. A total of 105 cases of patients with leukemia admitted to The First Affiliated Hospital of Bengbu Medical College from August 2016 to November 2018 were selected as research subjects. A total of 49 patients received transfusion of apheresis platelet suspension, and were group A. Fifty-six patients who received mixed multi-person platelet suspension were group B. The percentage plate recovery (PPR) and corrected count increment (CCI), interleukin-11 (IL-11) and soluble glycoprotein 130 (sgp130) levels were compared between the two groups, and the correlation of PPR and CCI with serum IL-11 and sgp130 levels was analyzed. Multivariate logistic regression was used to analyze the independent risk factors affecting ineffective transfusion in patients with leukemia. After transfusion, PPR and CCI in both groups were significantly higher than those before transfusion (P<0.05). IL-11 was significantly increased in both groups after transfusion, and sgp130 was significantly decreased in the two groups after transfusion (P<0.05). Serum IL-11 level in leukemia patients was positively correlated with PPR and CCI (r=0.7693, P<0.001), (r=0.7760, P<0.001), and serum sgp130 level in leukemia patients was negatively correlated with PPR and CCI (r=-0.7086, P<0.001), (r=-0.7733, P<0.001). There were differences between the effective group and the ineffective group in transfusion frequency, fever, infection and splenomegaly (P<0.05). Fever (OR, 0.382; 95% CI, 0.183-0.972) and infection (OR, 0.367; 95% CI, 0.140-0.956) were independent risk factors for ineffective transfusion. In conclusion, apheresis platelet or mixed multi-person platelet suspension transfusion can significantly improve the disorder of platelet count in patients with leukemia, and improve the clinical efficacy. Fever and infection are independent risk factors leading to ineffective transfusion.

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Introduction

Leukemia is a malignant clonal disease of the heterogeneous hematopoietic system, and its pathogenesis originates from the disordered differentiation process of hematopoietic stem cells (1). Leukemia is divided into lymphocytic leukemia and myeloid leukemia, mainly characterized by malignant proliferation of lymphoid and myeloid hematopoietic stem cells (2). The main manifestation of the body is the disorder in differentiation and apoptosis of hematopoietic stem cells. Primary and immature leukemia cells accumulate in the body after malignant proliferation, affecting normal hematopoietic function, and abnormal cells will be spread to numerous tissues and organs throughout the body fluid. Hence, patients with clinical leukemia often have anemia, hemorrhage, infection and extramedullary infiltration (3-5). The main cause of hemorrhage is the destruction of platelets caused by bone marrow hematopoietic dysfunction and chemotherapy drug injury, leading to a large number of platelet reduction and death of patients when serious hemorrhage cannot be timely controlled (6). Some literature has reported that the average life cycle of leukemia patients is short, and the treatment is difficult. It is necessary to control the disease development through timely treatment. In recent years, chemotherapy is still the main treatment method for leukemia patients. Although the remission rate of leukemia has been significantly improved, the clinical efficacy is not ideal. There are problems such as increased complications, high recurrence rate and reduced immunity of patients, and the problem of thrombocytopenia has not been fundamentally solved (7,8).

In order to prevent death caused by excessive blood loss in patients with leukemia, platelet decline can be prevented from the perspective of controlling the normal operation of blood in the body. In this case, patients can be treated with platelet transfusion repeatedly. Moreover, with the progress of medical technology, platelet transfusion therapy is gradually getting mature in the treatment of leukemia patients, but this way does not have a significant effect on all patients. The incidence of ineffective platelet transfusion continues to rise, and even leads to death in severe cases. These problems remain difficult for clinical researchers and executive physicians (9).

It has been reported that interleukin-11 (IL-11) is a kind of cytokine that plays a multipotent role in various cells including macrophages and T cells, mainly promoting the production of megakaryocytes and platelets, anti-inflammatory and other functions (10). At present, it is known that the intracellular signaling chain of IL-11 is mainly gp130, which exists in the body in two modes: humoral and model (11). Therefore, this study investigated how to improve the efficacy of platelet transfusion therapy and reduce the risk factors of ineffective transfusion, so as to achieve the goal of radical treatment of leukemia patients.

Materials and methods

General data. A total of 105 leukemia patients admitted to The First Affiliated Hospital of Bengbu Medical College from August 2016 to November 2018 were selected as research subjects. Among them, 49 cases of patients received transfusion of apheresis platelet suspension, and were group A. Fifty-six cases of patients received mixed multi-person platelet suspension, and were group B. The study was approved by the Ethics Committee of The First Affiliated Hospital of Bengbu Medical College (Bengbu, China). Signed informed consents were obtained from the patients and/or the guardians.

Inclusion and exclusion criteria. Inclusion criteria were as follows: Patients who were diagnosed with leukemia by pathological features and met the Diagnostic Criteria for Leukemia (12). Patients who met all platelet transfusion indexes (13). The exclusion criteria were as follows: Patients with incomplete clinical data. Patients with other organ solid lesion. Patients with hepatic and renal insufficiency. Patients with transfusion history before transfusion. Patients with cognitive impairment or communication disorder. The patients and their families agreed to participate in the experiment and signed informed consents.

Experimental materials. Platelets were from the downtown blood station, and each pocket of platelets was treated as one quantity (10 units, 200-250 ml). The average number of platelets in each pocket was $2.5x10^{11}$, red blood cell count $<8.0x10^{11}$, and white blood cell count $<5.0x10^{11}$. IL-11 antibody was from Shanghai Hushi medicine technology Co., Ltd. Soluble glycoprotein 130 (sgp130) antibody was from Shanghai Kanglang Biotechnology Co., Ltd. ELISA chromogenic reagent was purchased from Beijing Biotss Biotechnology Co., Ltd. and the microplate reader was from Jinan Olabo Scientific Instrument Co., Ltd.

Test methods

Platelet transfusion method. The patients received platelet prophylactic transfusion. Blood typing of patients was checked and recorded, and blood matching was performed before transfusion. Transfusion was conducted strictly in accordance with the ABO homologous blood transfusion standard. During transfusion, patients tolerance was observed to timely adjust the speed of transfusion. The standard amount of adult transfusion was one curative dose of platelet suspension (10 units, 200-250 ml). Dexamethasone (5 mg) intravenous injection was used to prevent adverse reactions during transfusion, and the transfusion was completed within 30 min on average. Furthermore, platelet transfusion was required to be finished 48 h after collection.

Detection methods of serum IL-11 and sgp130 levels. After two consecutive full platelet transfusions, test solution (100 μl) of serum samples of the two groups was added to 96-well plates. The standard wells and blank wells were set, incubated at 37˚C for 120 min, and then 400 ml washing solution was added for washing three times. IL-11 (6 ml) goat anti-human antibody were added, incubated at 37˚C for 120 min, and washed three times. Chromogenic agent (150 μl) were added, developed at 37˚C for 30 min. A total of 50 μl was taken out and mixed, and placed at 500 nm wavelength to measure and record the average optical density value of each well. Detection of sgp130 level was also performed in strict accordance with the ELISA kit instructions and the above operations.

Observational indexes. i) Percentage plate recovery (PPR) and corrected count increment (CCI) were compared between patients in the two groups before and after platelet transfusion. ii) Serum IL-11 and sgp130 levels were compared between patients in the two groups before and after platelet transfusion. iii) Correlation of PPR and CCI with IL-11 and sgp130 levels in leukemia patients after transfusion treatment was analyzed. iv) Patients were divided into an effective group and an ineffective group in accordance with clinical efficacy of patients, and logistic regression was used to analyze the related risk factors of ineffective transfusion of the patients.

Statistical analysis. SPSS 19.0 statistical software (Beijing Qingsi technology Co., Ltd.) was used for statistical analysis of the experimental data. Enumeration data were qualified by Chi-square test. Measurement data were expressed as mean ± standard deviation. t-test was used for comparison between the two groups, and paired t-test was used between the two groups before and after transfusion. Pearson's was used for correlation analysis and Multivariate logistic regression to analyze the risk factors affecting the ineffective transfusion of leukemia patients. GraphPad Prism 8 was employed to draw the illustrations, and $P<0.05$ was considered statistically significant.

Results

Comparison of general data. There were no significant differences between the two groups in sex, age, disease course, anemia, infection and fever ($P>0.05$) (Table I).

Comparison of PPR and CCI of patients between the two groups before and after platelet transfusion. There were no significant differences in PPR and CCI between the two groups before transfusion ($P>0.05$). There were no significant differences in PPR between group A (17.34±1.82) and group B (17.39±1.83) after transfusion, and no significant differences in CCI between group A (12.32±2.09) and group B (12.36±2.07) after transfusion ($P>0.05$). However, the factors in both groups were significantly higher than those before transfusion, with statistically significant differences ($P<0.05$) (Fig. 1).

Table I. Comparison of general data of patients in the two groups.

Factors	Group A (n=49)	Group B (n=56)	t/χ^2 value	P-value
Sex (n)			0.006	0.938
Male	24 (48.98)	27 (48.21)		
Female	25 (51.02)	29 (51.79)		
Age (years)	57.35±5.45	57.83±5.62	0.443	0.659
Disease course (month)	11.43±2.45	11.51±2.47	0.166	0.868
Anemia (n)			0.207	0.650
With	18 (36.73)	23 (41.07)		
Without	31 (63.27)	33 (58.93)		
Hemorrhage (n)			0.223	0.637
With	12 (24.49)	16 (28.57)		
Without	37 (75.51)	40 (71.43)		
Infection (n)			0.094	0.760
With	11 (22.45)	14 (25.00)		
Without	38 (77.55)	42 (75.00)		
Fever (n)			0.016	0.898
With	10 (20.41)	12 (21.43)		
Without	39 (79.59)	44 (78.57)		
Skeletal arthralgia (n)			0.371	0.543
With	9 (18.37)	13 (23.21)		
Without	40 (81.63)	43 (76.79)		

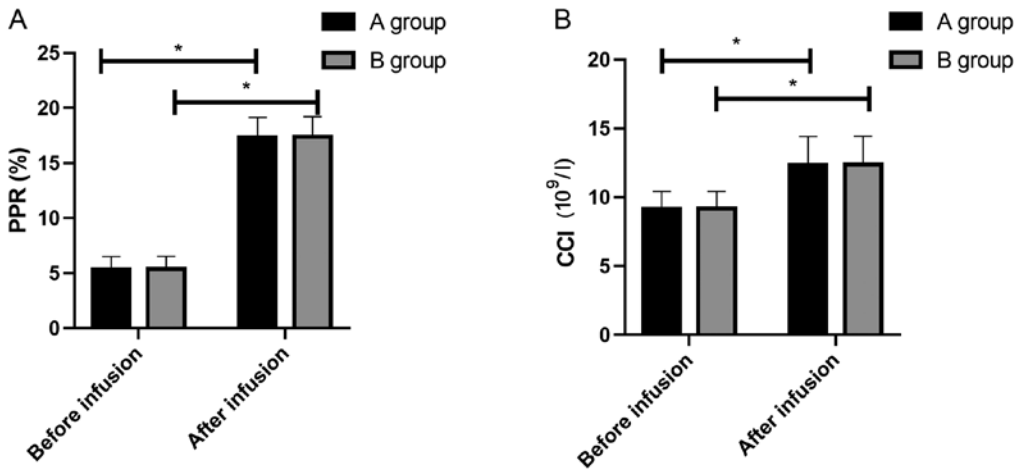

Figure 1. Comparison of PPR and CCI between the two groups before and after platelet transfusion. (A) PPR of patients in the two groups after transfusion was significantly higher than that before transfusion, but there were no significant differences between the two groups. (B) CCI of patients in the two groups after transfusion was significantly higher than that before transfusion, but there were no significant differences between the two groups. *P<0.05. PPR, percentage plate recovery; CCI, corrected count increment.

Comparison of IL-11 and sgp130 of patients between the two groups before and after platelet transfusion. There were no significant differences in IL-11 and spg130 between the two groups before transfusion (P>0.05). There were no significant differences in IL-11 between group A (66.14±2.08) and group B (65.98±9.76) after transfusion, and no differences in spg130 between group A (414.32±39.09) and group B (415.36±38.94) after transfusion (P>0.05). The factors in both groups were significantly higher than those before transfusion, with statistically significant differences (P<0.05) (Fig. 2).

Correlation analysis of PPR and CCI with serum IL-11 and sgp130 levels in leukemia patients. Pearson's correlation analysis showed that PPR in leukemia patients was positively correlated with serum IL-11 level (r=0.7693, P<0.001), CCI in leukemia patients was positively correlated with serum IL-11 level (r=0.7760, P<0.001), PPR in leukemia patients was negatively correlated with serum sgp130 level (r=-0.7086, P<0.001), and CCI in leukemia patients was negatively correlated with serum sgp130 level (r=-0.7733, P<0.001) (Fig. 3).

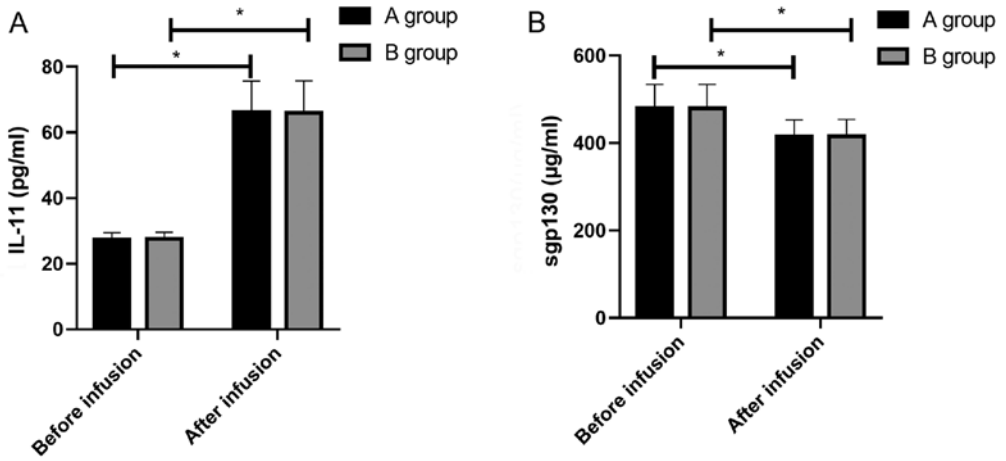

Figure 2. Comparison of serum IL-11 and sgp130 levels between the two groups before and after platelet transfusion. (A) IL-11 level of patients in the two groups after transfusion was significantly higher than that before transfusion, but there were no significant differences between the two groups. (B) sgp130 level of patients in the two groups after transfusion was significantly lower than that before transfusion, but there were no significant differences between the two groups. *P<0.05. IL-11, interleukin-11; sgp130, soluble glycoprotein 130.

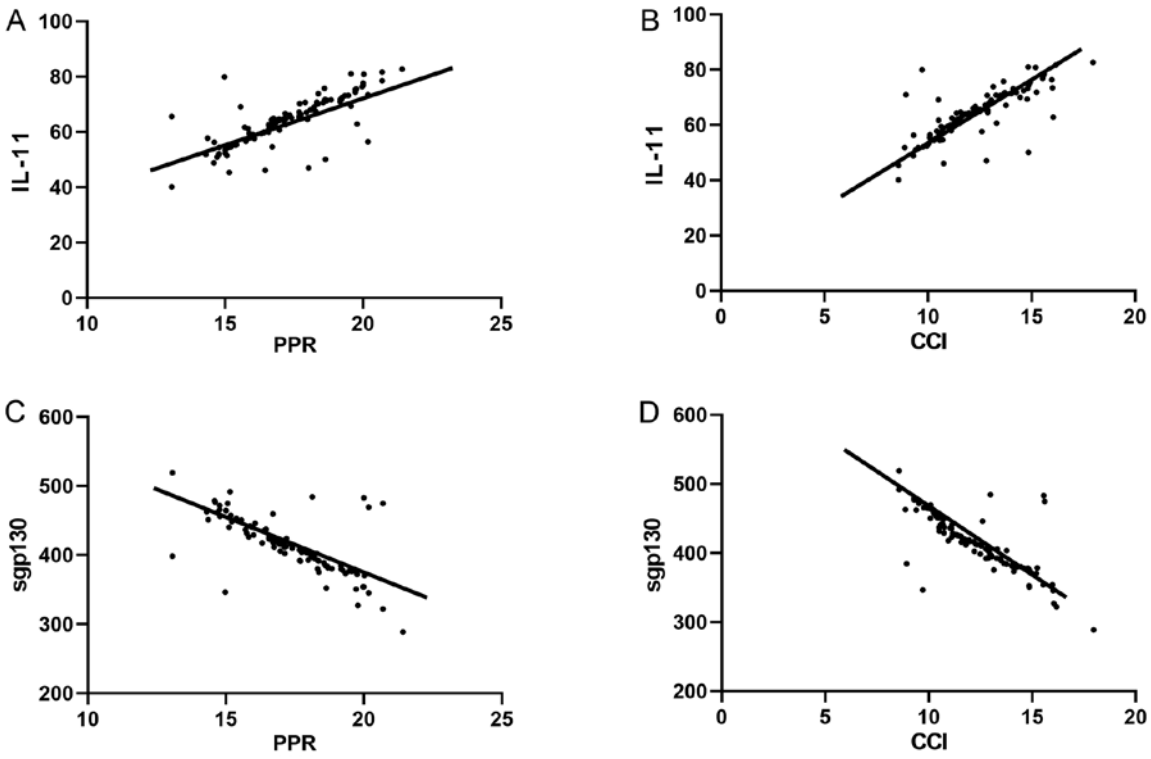

Figure 3. Correlation analysis of PPR and CCI with serum IL-11 and sgp130 levels in leukemia patients. (A) Pearson's correlation analysis showed that PPR in leukemia patients was positively correlated with serum IL-11 level (r=0.7693, P<0.001). (B) Pearson's correlation analysis showed that CCI in leukemia patients was positively correlated with serum IL-11 level (r=0.7760, P<0.001). (C) Pearson's correlation analysis showed that PPR in leukemia patients was negatively correlated with serum sgp130 level (r=-0.7086, P<0.001). (D) Pearson's correlation analysis showed that CCI in leukemia patients was negatively correlated with serum sgp130 level (r=-0.7733, P<0.001). PPR, percentage plate recovery; CCI, corrected count increment; IL-11, interleukin-11; sgp130, soluble glycoprotein 130.

Univariate analysis of ineffective transfusion of patients. Patients were divided into an effective treatment group (n=83) and an ineffective group (n=22) according to the clinical efficacy. The clinical data of patients in both the effective group and ineffective group were collected for univariate analysis. There were no significant differences in age, sex, antibiotic use, or blood sampling method (P>0.05), but there were differences in number of transfusion, fever, infection, hemorrhage, and splenomegaly (P<0.05) (Table II).

Multivariate analysis of treatment. Indicators with differences in univariate analysis were included in the assignments (Table III). Multivariate logistic regression analysis was performed, the results showed that transfusion frequency, hemorrhage and splenomegaly were not related risk factors for ineffective transfusion, while fever (OR, 0.382; 95% CI, 0.183-0.972) and infection (OR, 0.367; 95% CI, 0.140-0.956) were related risk factors for ineffective transfusion (Table IV).

Table II. Univariate analysis.

Clinicopathologic features	Effective group (n=83)	Ineffective group (n=22)	χ^2 value	P-value
Age (years)			0.108	0.742
<57	41 (49.40)	10 (45.45)		
≥57	42 (50.60)	12 (54.55)		
Sex (n)			0.023	0.880
Male	40 (48.19)	11 (50.00)		
Female	43 (51.81)	11 (50.00)		
Transfusion frequency (n)			12.373	0.006
1	36 (43.37)	3 (13.64)		
2-5	24 (28.92)	5 (22.73)		
6-9	14 (16.87)	6 (27.27)		
≥10	9 (10.84)	8 (36.36)		
Fever (n)			6.693	0.010
With	13 (15.66)	9 (40.91)		
Without	70 (84.34)	13 (59.09)		
Hemorrhage (n)			7.748	0.005
With	17 (20.48)	11 (50.00)		
Without	66 (79.52)	11 (50.00)		
Splenomegaly (n)			4.220	0.040
With	11 (13.25)	7 (31.82)		
Without	72 (86.75)	15 (68.18)		
Infection (n)			19.101	<0.001
With	12 (14.46)	13 (59.09)		
Without	71 (85.54)	9 (40.91)		
Antibiotic use (number)			0.315	0.575
With	25 (30.12)	8 (36.36)		
Without	58 (69.88)	14 (63.64)		
Blood sampling methods			0.016	0.898
Apheresis platelet	39 (46.99)	10 (45.45)		
Mixed multi-person platelet	44 (53.01)	12 (54.55)		
Anemia (number)			0.041	0.841
With	32 (38.55)	9 (40.91)		
Without	51 (61.45)	13 (59.09)		
Bone pain			0.053	0.818
With	17 (20.48)	5 (22.73)		
Without	66 (79.52)	17 (77.27)		

Discussion

The process of infiltration of leukemia cells in patients with leukemia in extramedullary and extramedullary lymphocytes includes leukemia cells spilling from the bone marrow and lymphocytes to the peripheral blood, and migrating to the tissues and organs suitable for their growth. It involves complex pathological process such as leukocyte chemotaxis, adhesion, migration and degradation of vascular endothelial cells (14-16). In addition, some studies have shown that both the abnormal function and the decrease in the number of platelets in patients with leukemia would have secondary onset to the hemorrhage of the patient's body (17). Platelet is the most influential clotting factor in the human body, which can significantly improve the condition of hemorrhage caused by platelet dysfunction or decreased platelet transfusion in patients with blood diseases, and is an effective treatment method (18).

Table III. Assignments.

Factors	Assignment
Transfusion frequency (n)	One time=0, 2-5 times=1, 6-9 times=2, ≥10 times=3
Fever	With=1, without=0
Hemorrhage	With=1, without=0
Splenomegaly	With=1, without=0
Infection	With=1, without=0
Transfusion	Effective=1, ineffective=0

Table IV. Multivariate analysis.

Factors	B	SE	Wals	Sig.	Exp (B)	95% CI Of Exp (B)	
						Lower limit	Upper limit
Transfusion frequency	0.423	0.297	2.047	0.157	1.526	0.867	2.724
Fever	-0.997	0.396	4.623	0.039	0.382	0.183	0.972
Hemorrhage	0.372	0.284	1.783	0.185	1.460	0.841	2.589
Splenomegaly	-1.118	0.604	3.458	0.067	0.324	0.148	0.957
Infection	-0.994	0.487	4.245	0.037	0.367	0.140	0.956

B, constant term; SE, standard deviation; Wals, Chi-square value; sig, P-value; Exp (B), odds ratio; 95% CI of Exp (B), 95% confidence interval of odds ratio.

IL-11 can bind to IL-11Ra, a binding chain of cell-surface specific receptor-ligand, and then connect to gp130 (a signaling chain), to activate the biological function of IL-11 and mediate inflammatory response (19). sgp130 is a receptor and signal transmitter shared by IL-11 and leukemia suppressor factors. sgp130 is one of the soluble proteins in various forms and is related to the prognosis of leukemia (20). This study mainly investigated the changes in platelet count and the expression of IL-11 and sgp130 in patients with leukemia after platelet transfusion, and analyzed their correlation, to explore the influencing factors of ineffective platelet transfusion.

PPR and CCI were studied in two groups of patients and it was found that PPR and CCI in both groups were significantly higher after transfusion than before transfusion. This indicated that the platelet count in the two groups was effectively increased after different blood sampling methods. Some studies have shown that the disorder of the body's internal environment and the production and release of platelet antibodies in patients with leukemia would affect the maturation of platelets and cause damage to them, leading to a decrease in the number of platelets in patients (21). Platelet transfusion therapy can enhance the intracellular platelet density of patients through matching of blood after transfusion, to prevent the deterioration of patients' condition caused by hemorrhage (22). In clinical practice, CCI, PPR and patients' hemorrhage status were used as the criteria to assess the efficacy of platelet transfusion (23). It is concluded that platelet transfusion can effectively control the hemorrhage rate of leukemia patients, and different blood sampling methods have little effect on the transfusion treatment. This study on IL-11 and sgp130 levels showed that IL-11 levels increased while sgp130 levels decreased in the two groups after transfusion, but there were no significant differences in IL-11 and sgp130 levels between group A and group B after transfusion. Previous studies have shown that (24,25) membrane gp130 is involved in mediating the platelet production, inflammatory response and other biological activities of IL-6 family cytokines. sgp130, as a negative regulator, blocks their biological effects and is involved in immune response, hemopoiesis, inflammation, endocrine and nervous system functions. The literature is consistent with our results to some extent. The anti-inflammatory mechanism of the body is stimulated by the increase in the number of platelets, and the same target causes the IL-11 level to rise and the gp130 level to decrease under the inflammatory action. Pearson's correlation analysis was conducted to further study the relationship of IL-11 and sgp130 with changes of platelet number after platelet transfusion in leukemia patients. The results showed that serum IL-11 level in leukemia patients was positively correlated with PPR and CCI, while serum sgp130 level in leukemia patients was negatively correlated with PPR and CCI. It further indicates that with the treatment of platelet transfusion, the number of platelets in the body can be effectively increased, which has a good effect on improving the inflammatory response and hemopoiesis in the body. Previous literature (26) have reported that the failure of long-term platelet transfusion therapy in clinical practice is particularly prominent, and the clinical efficacy on hemorrhage of patients with blood diseases is poor, and the related factors causing ineffective transfusion have become difficult points and concerns of the academic community. Univariate analysis in this study showed that there were differences in transfusion frequency, fever, infection and splenomegaly between the effective group and ineffective group. From the perspective of efficacy, the treatment success rate decreased with the increase of transfusion times. However, the results of multivariate logistic regression analysis in this study showed that transfusion frequency was not considered as a risk factor for ineffective transfusion, it was speculated that the transfusion of platelet samples and the interval time between transfusions in this study might have influenced the results. Previous studies (27) have shown that with the increase of transfusion times, platelet antibodies will develop in patients, hindering the efficacy of platelet transfusion. The results may be different from the effect of transfusion on the number of transfusion in patients with different physical conditions. Splenomegaly and hemorrhage will cause platelet consumption and loss, affecting the efficacy of platelet transfusion (28,29). In the results of multivariate logistic regression analysis of this study, however, the above two factors were not considered as risk factors for ineffective transfusion. It was analyzed that this was a confounding factor as well as transfusion frequency, which may be related to the fact that the pathological manifestations of patients with splenomegaly were not significant and the cause of hemorrhage was not leukemic immune system damage. Multivariate logistic regression analysis showed that fever and infection were independent risk factors leading to

ineffective transfusion. Previous literature (30) have indicated that platelet of patients with hematological system diseases and fever exposure to recessive antigen would absorb antibody, which may lead to accelerated circulation in patients. When circulation is performed to the reticuloendothelial system, platelet survival time is shortened and depletion is increased, affecting the effectiveness of platelet transfusion.

In conclusion, platelet transfusion can significantly increase the number of platelets after treatment and improve the hemorrhage of patients with leukemia. In this study, it was found that infection and fever were the influencing factors affecting the efficacy of transfusion. Patients should be transfused after the basic clinical inflammatory symptoms are controlled and the causes of ineffective transfusion should be identified and solved timely.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

LC and ZG conceived and designed the study. LC, HZ, BG and ZG were responsible for the collection, analysis and interpretation of the data. HZ drafted the manuscript. BG revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of The First Affiliated Hospital of Bengbu Medical College (Bengbu, China). Signed informed consents were obtained from the patients and/or the guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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