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Analysis of Factors Influencing the Effect of Red Blood Cell Suspension Infusion in Children

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Abstract

Objective: The related factors of no improvement of hypoxia and ineffective infusion were analyzed to provide new ideas, clinical observation and evaluation pathway for RBC transfusion in clinical children. **Methods:** Retrospective analysis from January 2020 to December 2020, Guangzhou women and children's medical center hospital in the emergency observation room of 249 children under 1 month to 18 years of blood cell suspension infusion, analyze the clinical effect of red blood cell infusion and children gender, age, fever after transfusion, disease type, delay transfusion. The possible influencing factors were analyzed by logistic regression. **Results:** Invalid transfusion was associated with the type of transfusion product ($P = 0.032$), logistic regression analysis showed that patients infused with washed RBC suspension were 3.231 times more likely to not achieve the expected effect than those infused with RBC suspension ($P = 0.025$). Failure transfusion was associated with the type of transfusion products. In ineffective transfusion was closely related to post-transfusion fever ($P < 0.001$). Logistic regression analysis showed that post transfusion fever was a risk factor for ineffective red blood cell transfusion (OR = 9.026, $P < 0.001$). The improvement of hypoxia after transfusion in children was related to fever, age, sex and transfusion time. Compared with male children, female children are more likely to have no improvement in hypoxia after blood transfusion ($P = 0.031$). Logistic regression analysis showed that fever after transfusion was a risk factor for no improvement of hypoxia (OR = 5.809, $P = 0.001$), and the improvement of hypoxia in adolescent children was 10.744 times higher than that of infants (0 - 3 years old). Late transfusion hypoxia improvement was 4.212 times more likely to achieve no effect than timely transfusion. If ineffective infusion of red blood cells is considered and hypoxia after transfusion is not improved, univariate suggests a close correlation with fever after transfusion ($P = 0.002$), logistic regression analysis showed that fever after transfusion was an independent risk factor

(OR = 7.258, $P = 0.002$). **Conclusion:** There was no correlation between the ineffective transfusion of red blood cells and the type of disease affected in the child. Infusion of red cell suspension has an advantage over the wash red cell infusion. Ineffective RBC transfusion and no improvement in hypoxia after transfusion were closely related to post-transfusion fever, with no difference between children in all age groups. Red blood cell infusion in pediatric clinical treatment activities should pay attention to adolescent children, especially female children to give more attention, and give timely red blood cell infusion as much as possible.

Keywords

Children, Invalid Red Blood Cell Transfusion, No Improvement in Hypoxia, Influencing Factors

1. Introduction

Red blood cell suspension is one of the main components of blood transfusion in children [1], Because of the particularity of blood products, it is necessary to pay attention to post-transfusion evaluation. The evaluation of infusion effect is an important aspect. Compared with adults, the type and frequency of adverse blood transfusion reactions in children are also different. Moreover, for the most common adverse reactions of blood transfusion, the overall prevalence of adverse reactions of blood transfusion in children is higher than that in adults [2]. Some studies have identified malignancy as an independent risk factor for ineffective blood transfusion [3]. In addition, diseases that require multiple mass blood transfusion, such as blood diseases, may reduce the efficacy of red blood cell transfusion due to the production of similar antibodies in the patient, which is a risk factor of ineffective blood transfusion [4]. With the development of medical technology, more and more emergency pediatric patients need red blood cell transfusion, but there is less research on the effect of blood transfusion in children. Blood transfusion is an important part of supporting treatment in the treatment of children's acute and severe diseases. To evaluate the effect of blood transfusion and provide more evidence for clinical rational blood use and evaluation of children's blood transfusion treatment, the research analysis is reported as follows.

2. Materials and Methods

2.1. Study Subjects

From January 2020 to December 2020, 249 pediatric patients, including 156 males and 93 females, were treated by infusion of red blood cell suspension in the pediatric emergency observation room of Guangzhou Women's and children's Medical Center Hospital. Inclusion criteria 1) meet the blood transfusion indication; 2) Children can cooperate with blood transfusion; 3) The family

members of the patients understand the purpose of the study and sign the informed consent form. Exclusion criteria: 1) occult blood loss; 2) Severe dehydration or massive fluid infusion cause blood dilution; 3) There is hemolytic transfusion reaction; 4) Children cannot cooperate with blood transfusion treatment; 5) Newborn; 6) Surgical patients or surgical trauma patients.

2.2. Research Method

The influencing factors of red blood cell infusion were evaluated retrospectively. All red blood cell suspensions were provided by Guangzhou central blood station, which met the national requirements for blood quality. All children met the ABO and Rh (d) blood group verification before blood transfusion, and the blood matching by micro column gel test was consistent. ABO and Rh (d) isotype red cell suspensions were infused. The gender, age, clinical diagnosis, hemoglobin value before blood transfusion, blood transfusion time, body temperature, heart rate, respiration, blood oxygen saturation, hemoglobin value and clinical outcome of the children were collected. The fever temperature after blood transfusion was defined as axillary temperature ≥ 37.3˚C. The vital signs after blood transfusion refer to relevant literature, and exceeding the normal range of the corresponding age is defined as rapid respiration/heart rate [5]. Delayed blood transfusion is defined as: the blood transfusion time exceeds 12 hours after the issuance of the blood transfusion application form. The hemoglobin value shall be rechecked within 6 hours to 24 hours after blood transfusion.

2.3. Judgment of Red Blood Cell Infusion Effect

Recheck the blood routine within 24 hours after blood transfusion, and determine whether the hemoglobin rises to the expected value by using the formula for the estimated value of hemoglobin rise (as follows) [6]. If the expected value is not reached, it will be regarded as invalid red blood cell infusion.

Expected value of HB increase (g/L) = [donor hemoglobin (g/L) * input (L) * 90%]/patient weight (kg) * 0.085 (L/kg)

Judgment on improvement of hypoxia after blood transfusion: record the vital signs of the children after blood transfusion. According to the heart rate and respiratory rate standards of the age group, if one of the respiration and heart rate exceeds the standard value, it is judged that the hypoxia has not improved.

Judgment on the overall effect of blood transfusion: after blood transfusion, the anoxia of children has improved, and the hemoglobin value has risen to the expected value. It is considered that the overall blood transfusion is effective.

2.4. Statistical Analysis

Spss22.0 software was used to statistically process the data. The counting data were expressed by frequency and rate (%). The statistical method was x^2 and t-test. $P < 0.05$ means that the difference is statistically significant. The non conditional logistic regression analysis was used to screen the influencing factors of

red blood cell infusion effect and hypoxia change.

3. Result

3.1. General Information

A total of 249 cases of RBC suspension infusion were included in the analysis, including 156 males and 93 females. The age range was 5 (3.9) years. 222 cases (89.2%) were infused with concentrated red blood cell suspension, and 27 cases (10.8%) were infused with washed red blood cell suspension. 163 cases (65.5%) were diagnosed as malignant hematological diseases, the main diseases were leukemia and solid tumors, and 86 cases (34.5%) were non-malignant hematological diseases. The main diseases were hereditary spherocytosis, aplastic anemia, thalassemia, iron deficiency anemia, hemolytic anemia, etc. 209 patients (83.9%) received timely blood transfusion and 40 patients (16.1%) received delayed blood transfusion. The hemoglobin value before blood transfusion was 53.41 ± 9.53 g/l, and that after blood transfusion was 76.76 ± 16.83 g/l.

3.2. Correlation Analysis of Hemoglobin Value after Blood Transfusion

There was no statistical difference in gender, age, weight, malignant disease, hemoglobin value before blood transfusion, fever before blood transfusion and timely blood transfusion between the group whose hemoglobin value after blood transfusion reached the expected value and the group whose hemoglobin value did not reach the expected value. There was statistical difference in the type of red blood cells infused, hemoglobin value after blood transfusion and fever after blood transfusion (Table 1). Single factor analysis was conducted on whether the hemoglobin value after blood transfusion reached the expected value. Logistic regression data analysis was conducted on the factors related to the expected value of red blood cell transfusion in the single factor analysis. The results showed that there was no fever before blood transfusion, but in the patients with fever after blood transfusion, the probability of hemoglobin not reaching the expected effect was 9.026 times higher than that in the patients without fever before and after blood transfusion. The probability of hemoglobin not reaching the expected effect in those who received washed red blood cell suspension was 3.231 times higher than that in those who received washed red blood cell suspension (Table 2).

3.3. Correlation Analysis of Whether Hypoxic Symptoms Improve after Blood Transfusion

There was no statistical difference between the improved group and the non improved group in the hemoglobin value before blood transfusion, whether there was fever before blood transfusion, whether there was malignant disease, the type of red blood cells infused, and whether blood transfusion was timely, but there were statistical differences in gender, age, weight, whether blood transfusion

Table 1. Univariate analysis of the group with hemoglobin reaching the expected value and the group without hemoglobin reaching the expected value after blood transfusion.

	Hemoglobin increased to the expected level (n = 93)	Hemoglobin elevation did not reach the expected group (n = 156)	*P*
Gender, number of cases (%)			0.312
male	62 (66.7)	94 (60.3)	
female	31 (33.3)	62 (39.7)	
Age, number of cases (%)			0.461
Less than 3 years old	17 (18.3)	33 (21.2)	
3- 6 years old	30 (32.3)	57 (36.5)	
6 - 12 years old	25 (26.9)	43 (27.6)	
12 - 18 years old	21 (22.6)	23 (14.7)	
Body weight (kg), mean ± SD	21.77 ± 12.12	19.29 ± 10.79	0.095
Hemoglobin value before blood transfusion (g/L), mean ± standard deviation	52.51 ± 9.82	53.96 ± 9.34	0.246
Hemoglobin value after infusion (g/L), mean ± standard deviation	85.8 ± 16.78	71.38 ± 14.42	<0.001
Malignant disease, cases (%)			0.974
Yes	61 (65.6)	102 (65.4)	
No	32 (34.4)	54 (34.6)	
Type of red blood cell suspension infused, number of cases (%)			0.032
Red blood cell suspension	88 (94.6)	134 (85.9)	
Wash red blood cell suspension	5 (5.4)	22 (9.1)	
Whether there is fever before infusion, number of cases (%)			0.647
Yes	18 (19.4)	34 (21.8)	
No	75 (80.6)	122 (78.2)	
Whether blood transfusion is timely, number of cases (%)			0.737
timely	79 (84.9)	130 (83.3)	
delay	14 (15.1)	26 (16.7)	
No fever before blood transfusion, fever after blood transfusion, cases (%)			<0.001
Yes	3 (4.0)	32 (26.2)	
No	72 (96.0)	90 (73.8)	

was timely, temperature after blood transfusion, and hemoglobin value after blood transfusion (Table 3). Univariate analysis was carried out on the improvement of hypoxia symptoms after blood transfusion, and the factors related to the improvement of hypoxia in univariate analysis were analyzed by logistic regression data. The results showed that people who did not have fever before blood transfusion but had fever after blood transfusion were 5.809 times more

Table 2. Logistic regression analysis of hemoglobin not reaching the expected value after blood transfusion.

Variable	b	SE (b)	*P value*	OR	95% confidence interval of OR	
					Upper limit	lower limit
Wash red blood cell suspension	1.173	0.522	0.025	3.231	1.246	10.056
No fever before blood transfusion; fever after blood transfusion	2.200	0.626	<0.001	9.026	3.054	38.743
Fever before blood transfusion	0.444	0.335	0.186	1.559	0.816	3.054

Table 3. Univariate analysis of hypoxia improved group and hypoxia not improved group after blood transfusion.

	Hypoxia improvement group (n = 209)	Hypoxia not improved group (n = 40)	*P*
Sex, number of cases (%)			0.031
male	137 (65.6)	19 (47.5)	
female	72 (34.4)	21 (52.5)	
Age, number of cases (%)			<0.001
Less than 3 years old	46 (22.0)	4 (10.0)	
3 - 6 years old	78 (37.3)	9 (22.5)	
6 - 12 years old	60 (28.7)	8 (20.0)	
12 - 18 years old	25 (12.0)	19 (47.5)	
Body weight (kg), mean ± SD	19.19 ± 11.06	25.56 ± 11.45	0.001
Hemoglobin value before blood transfusion (g/L), mean ± standard deviation	53.80 ± 9.56	51.40 ± 9.20	0.145
Hemoglobin value after infusion (g/L), mean ± standard deviation	79.03 ± 16.03	64.9 ± 16.09	<0.001
Malignant disease, cases (%)			0.51
Yes	135 (64.6)	28 (70.0)	
No	74 (35.4)	12 (30.0)	
Type of red blood cell suspension infused, number of cases (%)			0.356
Red blood cell suspension	188 (90.0)	34 (85.0)	
Wash red blood cell suspension	21 (10.0)	6 (15.0)	
Whether there is fever before infusion, number of cases (%)			0.261
Yes	41 (19.6)	11 (27.5)	
No	168 (80.4)	29 (72.5)	
Whether blood transfusion is timely, number of cases (%)			0.009
timely	181 (86.6)	28 (70.0)	
delay	28 (13.4)	12 (30.0)	
No fever before blood transfusion, fever after blood transfusion, cases (%)			0.011
Yes	25 (14.9)	10 (34.5)	
No	143 (85.1)	19 (65.5)	

likely than those who did not have fever before and after blood transfusion to improve their hypoxia, and the probability that the improvement of hypoxia in adolescent children was 10.744 times that of infants (0 - 3 years old), The probability that the hypoxia improvement of delayed blood transfusion did not reach the effect was 4.212 times higher than that of timely blood transfusion (Table 4).

3.4. Correlation Analysis of the Overall Effect of Blood Transfusion

The overall effect of blood transfusion: there was no statistical difference between the ineffective group and the effective group in gender, age, weight, whether blood was transfused in time, hemoglobin value before blood transfusion, total time of blood transfusion, type of blood transfusion products, whether there was fever before admission, benign and malignant diseases, and whether there was fever after blood transfusion (Table 5). Logistic regression data analysis was carried out for the factors related to the overall effect in the single factor analysis. The results of variable screening by the regression method were as follows: for those who did not have fever before blood transfusion, but had fever after blood transfusion, the overall probability of ineffectiveness was 7.258 times higher than those who did not have fever before and after blood transfusion. Patients who received washed red blood cell suspension were 2.607 times more likely to be ineffective than those who received ordinary red blood cell suspension (Table 6).

4. Discussion

The evaluation of the effect of red blood cell infusion includes clinical evaluation and laboratory evaluation. Generally, the index of ineffective red blood cell infusion is the laboratory evaluation index, which refers to whether the hemoglobin value reaches the expectation after infusion. However, the laboratory evaluation index has certain limitations, that is, the hemoglobin value after blood transfusion may be slightly lower than the expected value, the laboratory evaluation is invalid, but the clinical symptoms are improved, that is, the clinical evaluation is effective. Therefore, we will evaluate clinical evaluation and laboratory evaluation at

Table 4. Logistic regression analysis of no improvement in hypoxia after blood transfusion.

Variable	b	SE (b)	*P value*	OR	95% confidence interval of OR	
					Upper limit	lower limit
No fever before blood transfusion; fever after blood transfusion	1.759	0.536	0.001	5.809	2.032	16.962
Fever before blood transfusion	0.572	0.484	0.237	1.772	0.670	4.542
(3 - 6) preschool children	−0.047	0.655	0.943	0.954	0.275	3.831
(6 - 12) school age children	0.197	0.671	0.769	1.218	0.338	5.004
(12 - 18) adolescence	2.374	0.642	0.000	10.744	3.331	43.245
Delayed transfusion	1.438	0.500	0.004	4.212	1.581	11.422

Table 5. Single factor analysis of the group with improved total effect after blood transfusion.

	Total effect improvement group (n = 83)	Group with no improvement in overall effect (n = 166)	*P*
Sex, number of cases (%)			0.266
male	56 (67.5)	100 (60.2)	
female	27 (32.5)	66 (39.8)	
Age, number of cases (%)			0.909
Less than 3 years old	16 (19.3)	34 (20.5)	
3 - 6 years old	27 (32.5)	60 (36.1)	
6 - 12 years old	24 (28.9)	44 (26.5)	
12 - 18 years old	16 (19.3)	28 (16.9)	
Body weight (kg), mean ± SD	21.22 ± 11.99	19.71 ± 11.01	0.323
Hemoglobin value before blood transfusion (g/L), mean ± standard deviation	52.77 ± 9.73	53.73 ± 9.44	0.453
Hemoglobin value after infusion (g/L), mean ± standard deviation	86.98 ± 16.53	71.66 ± 14.53	<0.001
Malignant disease, cases (%)			0.509
Yes	52 (62.7)	111 (66.9)	
No	31 (37.3)	55 (33.1)	
Type of red blood cell suspension infused, number of cases (%)			0.084
Red blood cell suspension	78 (94.0)	144 (86.7)	
Wash red blood cell suspension	5 (6.0)	22 (13.3)	
Whether there is fever before infusion, number of cases (%)			0.659
Yes	16 (19.3)	36 (21.7)	
No	67 (80.7)	130 (78.3)	
Whether blood transfusion is timely, number of cases (%)			0.625
timely	71 (85.5)	138 (83.1)	
delay	12 (14.5)	28 (16.9)	
No fever before blood transfusion, fever after blood transfusion, cases (%)			<0.001
Yes	64 (95.5)	98 (75.4)	
No	3 (4.5)	32 (24.6)	

Table 6. Logistic regression analysis of no improvement in the total effect after blood transfusion.

Variable	b	SE (b)	*P value*	OR	95% confidence interval of OR	
					Upper limit	lower limit
Wash red blood cell suspension	0.958	0.522	0.066	2.607	1.005	8.113
No fever before blood transfusion; fever after blood transfusion	1.982	0.626	0.002	7.258	2.454	31.157
Fever before blood transfusion	0.408	0.343	0.234	1.504	0.778	3.007

the same time, and make a more comprehensive analysis of the evaluation of the effect of red blood cell infusion.

In this study, it was found that the hemoglobin did not reach the expected value after blood transfusion had no statistical significance with gender, age of children, whether blood transfusion was timely or not, and whether malignant disease was present. Some studies have reported that the main reason for ineffective infusion of red blood cells is immune factors, including changes in molecules on the surface of red blood cells, changes in the content of metabolites, and the influence of immune substances in the recipients [7]. The red blood cells of children with multiple blood transfusions have more complement C3 receptors [8], a variety of immune related substances, and a variety of irregular antibodies [9], which are considered as independent risk factors for ineffective blood transfusion in patients with malignant diseases. Malignant and non malignant blood related diseases accounted for 96.8% of the patients in this group, and most of these children had a history of multiple blood transfusions. In this study, there was no significant difference between the groups of malignant and non malignant diseases in terms of whether hemoglobin rose to the expected value and whether hypoxia improved after blood transfusion ($P > 0.05$), indicating that children with blood related diseases do not need to pay too much attention to the distinction between benign and malignant diseases in blood transfusion. It should be noted that in this study, the time to detect whether there is invalid blood transfusion is collected within 24 hours after blood transfusion, and some reports suggest that tumor patients may have delayed hemolytic reaction leading to invalid blood transfusion [10]. Although the incidence of delayed hemolytic reaction is low, it has been reported that the incidence is 0.01% [11]. However, there is no statistical data on the incidence in specific populations. Therefore, for blood related diseases requiring repeated blood transfusion, it is necessary to monitor the hemolysis index and the presence of red blood cell isotype antibodies.

We found that some children would have fever reaction after blood transfusion. In order to exclude the interference of fever before blood transfusion, we collected the data of children without fever before blood transfusion and carried out logistic regression analysis. It showed that fever after blood transfusion was a risk factor for hemoglobin not reaching the expected effect (OR = 9.026, 95% CI: 3.054 - 38.74, $P < 0.001$). Some studies have shown that the fever reaction may lead to the ineffective or poor effect of red blood cell infusion. The reason may be related to the activation of the immune system of the body. The heat source (IL-6/IL-1/TNF, etc.) will be generated at the time of fever, which will activate the phagocytic system of mononuclear macrophages in the body, resulting in the elimination of red blood cells and shortening the life of red blood cells. It may also be related to the high metabolic state of the body [12]. Most of the post-transfusion fever reported in the literature is based on the febrile non-hemolytic blood transfusion reaction among the adverse reactions of blood transfusion, and the body temperature within 4 hours after the cessation of blood transfusion

is more than 38˚C, at the same time, it is more than 1˚C higher than that before blood transfusion, or the patient has chills, and there are no other factors to explain it [13]. The difference is that the fever after blood transfusion in this study is defined as the body temperature greater than 37.3˚C, and the statistical results show that the fever after blood transfusion may affect the blood transfusion effect. Therefore, we think that whatever degree of fever should be paid attention to. The occurrence of non-hemolytic febrile blood transfusion reaction is mainly caused by white blood cells mixed in the input red blood cell suspension, which causes alloimmune reaction and releases heat source after the white blood cells are destroyed. Transfusion of leukocyte depleted suspension can reduce non-hemolytic febrile transfusion reaction [14]. Will it be more advantageous to wash red blood cells? In this study, when analyzing the factors of effective blood transfusion, it was found that the infusion of red blood cell suspension was more advantageous than the infusion of washed red blood cells. Logistic regression analysis showed that the probability of hemoglobin not reaching the expected effect in the recipients of washed red blood cell suspension was 3.231 times higher than that in the recipients of washed red blood cell suspension (P = 0.025). The reason may be that there is partial hemolysis during the preparation of washed red blood cells, and the national standard stipulates that the recovery rate of red blood cells is less than 0.8% and 70% - 90% [15]. Resulting in poor effect of infusion of washed red blood cells compared with infusion of red blood cell suspension. Therefore, when choosing the blood type, we should choose the appropriate type according to the disease condition and purpose. It is necessary to infuse and wash red blood cells, and an appropriate dose should be used.

In addition, this study found that post-transfusion fever was associated with no improvement in post-transfusion hypoxia (P = 0.006). Logistic regression analysis also showed that children with fever after blood transfusion were 5.809 times more likely to have no effect on the improvement of hypoxia than normal people. If the ineffective infusion of red blood cells is considered at the same time and the hypoxia does not improve after the infusion of red blood cells, the single factor suggests that it is closely related to post-transfusion fever (P = 0.002). Logistic regression analysis shows that post-transfusion fever is an independent risk factor (OR = 7.258, P = 0.002). In addition to the association with abnormal body temperature after blood transfusion, univariate analysis was also associated with the gender, age group and whether or not the child received blood transfusion in time ($P < 0.05$), and had no statistical significance with whether the child had malignant or non-malignant diseases (P = 0.51).

5. Limitation of the Study

At present, there are few studies to evaluate the improvement of hypoxia symptoms and the overall effect of red blood cell suspension infusion. This study comprehensively discusses the evaluation indicators of the effect of red blood cell suspension infusion. This study still has some limitations. This study is a re-

trospective study, and there may be selection bias; And the sample size is small, and there are many factors affecting the blood transfusion effect, which may affect the results. To better evaluate the efficacy of red blood cell infusion, further large sample studies are still needed.

6. Conclusions

There was no correlation between the ineffective transfusion of red blood cells and the type of disease affected in the child. Infusion of red cell suspension has an advantage over the wash red cell infusion. Ineffective RBC transfusion and no improvement in hypoxia after transfusion were closely related to post-transfusion fever, with no difference between children in all age groups. Red blood cell infusion in pediatric clinical treatment activities should pay attention to adolescent children, especially female children to give more attention, and give timely red blood cell infusion as much as possible.

Searching the literature on the evaluation of the effect of red blood cell infusion, it was found that the main evaluation index was the change of hemoglobin value after infusion, but there were few studies on the improvement of symptoms and the evaluation of the overall effect after blood transfusion. In our study, we found that the main factors affecting the overall effect evaluation after blood transfusion were the infusion of washed red blood cells and fever. Clinically, we need to pay attention to children whose temperature exceeds 37.3˚C after blood transfusion. Their hemoglobin does not reach the expected value and their anoxia does not improve more often. At the same time, we found that the influencing factors of hemoglobin not reaching the expected value after blood transfusion and symptoms not improving after blood transfusion are not the same. Whether symptoms improve after blood transfusion is particularly important for clinical work, so clinicians need to pay more attention to the factors that improve symptoms.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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