Application of exchange transfusion in the treatment of hyperleukocytosis:a retrospective analysis

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Research article

Keywords: pulmonary hypertension, WBC, ET, pulmonary blood flow, exacerbate hypoxemia

Posted Date: March 31st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-366328/v1

Abstract

Background

Few reports have described the application of exchange transfusion in patients with hyperleukocytosis.

Methods

A retrospective clinical analysis of infants with exchange transfusion in the treatment of hyperleukocytosis was performed.

Results

A total of 13 patients were enrolled in the study.7 patients survived and 6 died after exchange transfusion.The incidence of pulmonary hypertension, heart failure, pertussis encephalopathy, Increased C-reactive protein, and increased PCT in the survival group were lower than those in the death group,The incidence of received Gamma globulin and received steroids were higher than those in the death group.The highest WBC count in the survival group was 74.15 ± 19.68*10^9/L, and in the death group patients was 86.29 ± 23.51*10^9/L.There were not significant differences two groups(P = 0.332). Decrease rate of WBC after the first ET in the survival group was significantly higher than that of the death group (P 0.05). In the survival group, there were 5 patients (71.42%) which decrease rate of WBC after the first ET more than 50%, and the remaining 2 patients (28.58%) all exceeded 45%.In contrast, there was 1 patient which decrease rate of WBC exceeded 45% ,no patient exceed 50%. All patients with Decrease rate of WBC after the first ET exceed 50% survived. In the death group, there were 4 patients (66.67%) which N/L exceeded 1, 3patients (50%) which N/L exceeded 2. In the survival group, only 3 patients (42.85%) which N/L exceeded 1, but there was no patient which N/L exceed 2.

Conclusion

Exchange transfusion is an effective method to reduce WBC count. Patient with Decrease rate of WBC after the first ET exceed 50% were easier to survive. Patients with hyperleukocytoemia which N/L exceeding 2 predict death.

Background

Pertussis is a highly contagious respiratory illness. Increased peripheral WBC count is a common clinical manifestation in children with pertussis, especially hyperleukocytosis was an independent predictor of death[1].Fatal cases had significantly higher peak WBC counts was more likely to have a WBC count ≥ 30 000 cells/μL[2];Children with WBC greater than 50,000 × 109/L had nearly a ten times higher risk of death[3]. And WBC count > 100_109/L] is strongly predicts mortality in cases of severe pertussis[4]Research indicates that elevated WBC counts are associated with increased mortality risk. Hyperleukocytosis ultimately compromise pulmonary blood flow, exacerbate hypoxemia, and create a vicious cycle of refractory pulmonary hypertension[5–6]. Early leukopenia therapy has an important effect on severe pertussis complicated with hyperleukocytosis[7–8]Leukocyte reduction measures include ET, leukocyte apheresis, etc. Leukocyte apheresis requires high requirements and may have serious adverse reactions[9],ET may be preferable to leukocyte apheresis because it can remove PT and reduce the WBC count[2]. At present, there are scattered studies that have reported that ET is beneficial to improve the survival rate of patient[2, 4].It

indicate that ET may be an effective method in severe hyperleukocytosis. ET has been widely used in hyperleukocytosis treatment, but there is no unified understanding of the effect and standard use of ET in patients with pertussis. Cherry suggested exchange blood transfusion and monitoring criteria for infants with pertussis who are ≤ 60 days of age[10].But it has not been widely accepted and used clinically. Based on previous reports and research, our hospital has formulated the ET standard for children with pertussis and hyperleukocytosis. According to this standard, there were 13 patients with hyperleukocytoemia received ET treatment. We wanted to analysis the clinical data of 13 patients with hyperleukocytoemia, and the role of exchange transfusion.

Methods

Patients

A total of 13 patients under 1 year old who were diagnosed with pertussis from January 2018 to October 2019 at the Children's Hospital of ChongQing Medical University were enrolled in this study. All patients received exchange transfusion treatment.The diagnosis of pertussis was based on clinical findings and confirmed by PCR. Clinical data and laboratory data were collected and analyzed.

This study was approved by the Ethics Committee of Children's Hospital of ChongQing Medical University. Exchange transfusion criteria for infants with pertussis:1. Who are ≤ 1 year of age 2. Total WBC count ≥ 50,000/mm3 with ≥ 15,000/mm3 lymphocytes;2. Persistent tachycardia;3. Early symptoms of dyspnea, respiratory failure, continuous mechanical ventilation.

Statistical Analysis

Statistical analyses were performed using SPSS software version 25. Descriptive analyses for nonnormally distributed data are presented using the median (interquartile range); comparisons between two groups were calculated using the Mann-Whitney test and multigroup comparisons were conducted using the Kruskal-Wallis rank test. Count data are expressed as the rate (%), and the difference between groups was calculated using the chi-square test. Receiver operating characteristic curve (ROC) analyses and sensitivity and specificity values were calculated by using Med Calc version 14. A P value < 0.05 was considered statistically significant.

Results

1. Study Population

During the study period, 13 patients were enrolled in this study. All patients had B pertussis DNA detected by PCR in nasopharyngeal secretions or in sputum. The clinical data of the study patients are shown in Table 1.

6 patients died after exchange transfusion (death group), and 7 patients survived after exchange transfusion (survival group). There were 3 females (42.85%) in the survival group and 5 females (83.33%) in the death group. 8 patients which age of onset within 90 days and 5 patients over 90 days. The incidence of pulmonary hypertension, heart failure, Pertussis encephalopathy, increased CRP, and increased PCT in the survival group were lower than those in the death group, and the use of hormones and gamma globulin were higher than those in the death group.

2. Peripheral blood cells and changes after exchange transfusion

The peripheral blood cell examination was perfected in 13 patients. The peripheral blood cells and changes after exchange transfusion of the study patients are shown in Table 2.The highest WBC count in the survival group was

74.15±19.68*10^9/L, and in the death group patients was 86.29±23.51*10^9/L.There were not significant differences two groups(P=0.332).In the death group, there were 4 patients (66.67%) which N/L exceeded 1, 3patients (50%)which N/L exceeded 2. In the survival group, only 3 patients (42.85%) which N/L exceeded 1, but there was no patient which N/L exceed 2.Decrease rate of WBC after the first ET in the survival group was significantly higher than that of the death group (P<0.05).

3. The process and complications

10 patients received 1 exchange transfusion treatment, 3 patients received 2 exchange transfusion treatments. The process and complications of the study patients are shown in Table3. Complications occurred in 4 patients with exchange transfusion. there was 1 patient in the survival group which showed convulsions; there were 3 patients in the death group which showed convulsions(1patiten) and Cardiac arrest (2 patients).In the survival group, there were 5 patients (71.42%) which decrease rate of WBC after the first ET more than 50%, and the remaining 2 patients (28.58%) all exceeded 45%.In contrast,there was 1 patient which decrease rate of WBC exceeded 45% ,no patient exceed 50%. All patients with Decrease rate of WBC after the first ET exceed 50% survived.

Discussion

Hyperleukocytosis as a risk factor for death of pertussis patients has been confirmed in many previous studies[1–3]。 Early effective leukocyte-reducing treatment can reduce patient mortality and improve patient prognosis[7].From now, many studies have focused on the application of exchange transfusion therapy in hyperleukocytosis. But there is no unified understanding of the effect and standard use of ET in patients with pertussis. Some scholars believe that it should be considered based on pulse, respiratory rate, total number of WBC and ascent speed, and the early incidence of pneumonia[11].In our study, exchange transfusion criteria for infants with pertussis:1. Who are ≤ 1 year of age 2. Total WBC count ≥ 50,000/mm3 with ≥ 15,000/mm3 lymphocytes;2. Persistent tachycardia;3. Early symptoms of dyspnea, respiratory failure, continuous mechanical ventilation. When considering transfusion therapy, we refer to respiration, heart rate, early pneumonia and WBC count.And we also refer to the age of onset, continuous mechanical ventilation, lymphocytes count. Tian et al. summarized the 56 patients with hyperleukocytosis from 2004 to 2017, with a survival rate of 68% (38/56) [4].In our study, 7 cases survived, and the survival rate was 53.8% (7/13).TOur study is slightly lower than previous studies.

The incidence of pulmonary hypertension, heart failure, pertussis encephalopathy, Increased C-reactive protein, and increased PCT in the survival group were lower than those in the death group,The incidence of received Gamma globulin and received steroids were higher than those in the death group.We know that pulmonary hypertension, heart failure, and pertussis encephalopathy are risk factors for severe pertussis and death. However, it is not clear whether the use of hormones and gamma globulin has a clear meaning. Some scholars found that after 3 days of intravenous injection of pertussis immunoglobulin in children with pertussis, the white blood cell count was significantly reduced, the spastic cough was reduced, and the tachycardia improved[12].But currently there is no pertussis immunoglobulin in our hospital。After using gamma globulin, we found that the use rate of gamma globulin in the survival group was 71.42%, which was significantly higher than 16.67% in the death group, suggesting that gamma globulin use may also improve the prognosis of children. Hormones are used more in pertussis。Kathleen Winter et al[2] found that steroid hormones were used in fatal cases more than non-fatal cases, suggesting that steroid hormones may be a risk factor for death from pertussis。James D. Cherry et al [10] also believe that steroid hormones should not be used in patients with pertussis. However, the use rate of hormones in the survival group was higher than that in the death group in this study, suggesting that hormones may be meaningful for disease

improvement. However, this study has a small sample size compared with previous studies, and the death of patients is related to many factors. Hormones play a role in the final prognosis of patients. It may be inaccurate and needs further discussion

The change in the level of WBC is an intuitive indicator that reflects the effect of exchange transfusion. Analyzing the level of WBC counts and the rate of WBC decline in the two groups of patient, The WBC counts of the two groups decreased significantly after exchange transfusion, but there was no significant difference in two groups(P = 0.636). It suggesting that exchange transfusion can effectively reduce the level of WBC.

Decrease rate of WBC after the first ET in the survival group was significantly higher than that of the death group (P□0.05). In the survival group, there were 5 patients (71.42%) which decrease rate of WBC after the first ET more than 50%, and the remaining 2 patients (28.58%) all exceeded 45%.In contrast, there was 1 patient which decrease rate of WBC exceeded 45% ,no patient exceed 50%. All patients with Decrease rate of WBC after the first ET exceed 50% survived. It shows that Decrease rate of WBC after the first ET may have a certain effect on the prognosis of death.

The patient's blood exchange volume was 87.99 ± 17.36ml/kg, there was no significant difference between the two groups (P = 0.918). However, in the death group, only 3 (50%) patients had a blood exchange volume of more than 80ml/kg for the first time of ET; In the survival group, 6 patients(85.71%), it indicating that blood exchange volume may also have an impact on the prognosis of the disease At the same time, we also recommend that the first exchange blood volume should exceed 80ml/kg.

N/L ratio is an easily available biomarker that may help predict the severity of the disease in children with pertussis. Clinical studies have shown that the proportion of lymphocytes in ordinary children with whooping cough is mainly increased, but in children with severe pertussis, the ratio of neutrophils to lymphocytes may be inverted. In patients with benign pertussis with leukocytosis, within 48 hours of admission, The median N/L were 0.33 and 0.39. In contrast, the median N/L of children with malignant pertussis within 48 hours of admission were 1.1 and 1.6, respectively[13]. In the death group, there were 4 patients (66.67%) which N/L exceeded 1, 3patients (50%)which N/L exceeded 2. In the survival group, only 3 patients (42.85%) which N/L exceeded 1, but there was no patient which N/L exceed 2. It indicate patients with hyperleukocytoemia which N/L exceeding 2 predict death.

Complications during or after transfusion are important factors affecting patient prognosis. In our study, complications occurred in 4 patients with exchange transfusion. There was 1 patient in the survival group which showed convulsions; there were 3 patients in the death group which showed convulsions(1patient) and Cardiac arrest (2 patients). It is suggested that the occurrence of complications may be a poor prognosis, especially the occurrence of cardiac arrest. At the same time, we found that patients with complications are mainly those with more than 100*10^9/L white blood cells. There were 3 patients with the highest white blood cell exceeding 100*10^9/L, all of which had complications during or after exchange transfusion, while only 1 case had complications in patients with white blood cell lower than 100*10^9/L. It suggests that white blood cells are significantly increased, especially patients with higher than 100*10^9/L are very prone to complications.

Conclusion

Taken together, exchange transfusion is an effective method to reduce WBC count. Patient with Decrease rate of WBC after the first ET exceed 50% were easier to survive. Patients with hyperleukocytoemia which N/L exceeding 2 predict death. Blood exchange volume of more than 80ml/kg for the first time of ET may have an impact on the prognosis of the disease.

Abbreviations

WBC: White blood cell; ET: exchange transfusion; CRP: C-reactive protein; PCT: procalcitonin; ALT: alanine aminotransferase.

Declarations

Acknowledgments

We thank all patients involved in the study.

Authors' contributions

Dr. Wu XY and Dr. Xu HM contributed to data collection and writing; Dr. Gan C. contributed to the conception and design of the work. All authors contributed to the acquisition, analysis and interpretation of data.

Funding

This paper was not funded.

Availability of data and materials

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

Ethical Approval statement

This study was approved by the Ethics Committee of Children's Hospital of ChongQing Medical University.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1. Patients Data

Group	Overall（n=13）	Survival(n=7)	Death(n=6)
Gender（male,n,%）	8（61.53%）	3（42.85%）	5（83.33%）
Age of onset（d）			
（90（n,%）	8（61.53%）	4（57.14%）	4（66.67%）
≥90（n,%）	5（38.47%）	2（28.57%）	3（50.00%）
Any DTaP（n,%）	4（30.76%）	2（28.57%）	2（33.33%）
Days from onset to admission[$M(P_{25}, P_{75})$, d]	6（3，15）	7（3，15）	5（3，15）
Hospital length of stay[$M(P_{25}, P_{75})$, d]	13（2，64）	27（10，64）	3(0,25)
Pulmonary hypertension（n,%）	5（38.47%）	2（28.57%）	3（50.00%）
Heart faliure（n,%）	8（61.53%）	3（42.85%）	5（83.33%）
Respiratory failure（n,%）	13（100.00%）	7（100.00%）	6（100.00%）
Pertussis encephalopathy（n,%）	6（46.15%）	3（42.85%）	3（50.00%）
Increased C-reactive protein（n,%）	9（69.23%）	3（42.85%）	6（100.00%）
Increased procalcitonin（n,%）	5（38.47%）	2（28.57%）	3（50.00%）
Received Gamma globulin（n,%）	6（46.15%）	5（71.42%）	1（16.67%）
Received steroids（n,%）	4（30.76%）	3（42.85%）	1（16.67%）

Table2 Peripheral blood cells and changes

	overall（n=13）	survival(n=7)	death(n=6)	p-value
Highest WBC count（*10^9/L）	78.05±21.57	74.15±19.68	86.29±23.51	0.332
WBC＜70	4（30.76%）	3（42.85%）	1（16.67%）	
WBC≥70	9（69.23%）	4（57.14%）	5（83.33%）	
Neutrophil to lymphocyte ratio（N/L）				
N/L＜1	6（46.15%）	4（57.14%）	2（33.33%）	
2≥N/L≥1	4（30.78%）	3（42.85%）	1（16.67%）	
N/L＞2	3（23.07%）	0（0）	3（50.0%）	
Days to highest WBC count, median (IQR)	11.18±3.87	10.71±3.99	10.17±4.26	0.815
Highest PLT count（*10^9/L）	790.27±201.09	788.71±232.5	789.5±129.7	0.994
Highest lymphocyte count（*10^9/L）	37.80±17.18	35.49±13.76	34.81±22.3	0.948
Days from onset to receive ET（d）	10.69±4.15	11±4.16	10.33±4.5	0.787
Decline of WBC after the first ET（*10^9/L）	37.50±10.20	37±8.61	33.61±11.81	0.636
Decrease rate of WBC after the first ET（%）	48.74±9.05	52.45±4.93	39.32±2.33	0.001

Table 3 Exchange transfusion related information

Patient	Time of ET	Replacement volume (ml/kg)	Duration of the exchange process (min)	complications	WBC count before ET (*10^9/L)	WBC count after ET (*10^9/L)	Decrease rate of WBC(%)	ending
1	1	76.92	100	No	87.8	55.56	36.72	Death
2	1	122.45	120	Cardiac arrest	107.86	-	-	Death
3	1	87.5	140	No	116.04	66.83	42.4	Death
	2	100	180	Cardiac arrest	85.91	-	-	
4	1	100	120	No	83.21	50.74	39.02	Death
	2	100	75	No	50.74	27.1	46.59	
5	1	75	85	Convulsion	70.44	-	-	Death
6	1	62.5	180	No	52.39	31.88	39.14	Death
7	1	66.67	75	No	59.95	30.76	48.69	survival
8	1	82.35	120	No	59.95	29	51.62	survival
9	1	90.91	120	No	51.06	23.98	53.03	survival
10	1	84.5	100	No	80.43	37.11	53.86	survival
11	1	95.07	180	Convulsion	107.25	58.29	45.65	survival
	2	98.59	120	No	80.3	35.5	55.79	
12	1	80	80	No	56.44	21.71	61.53	survival
13	1	120	130	No	84.93	40.12	52.76	survival