Predictive Value of Transfusion Frequency for Adverse Outcomes in Extremely/Very Low Birth Weight Infants: A Retrospective Cohort Study Postprint

Authors: I' m sorry, but the input you provided ("方小红") appears to be a proper name and does not contain any paragraph tags (…) or academic content to translate according to your specific instructions. Please provide the text within the required structural format for translation., Chun Xu, Dali Huang, Liping Xu, Liping Xu

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Abstract

Abstract

Background: Red blood cell transfusion (RBCT) is common within the first 28 days of life for very/extremely low birth weight infants (VLBWI/ELBWI). Current controversy focuses on the choice of transfusion threshold strategies, with a lack of in-depth discussion regarding transfusion frequency and adjustment for disease severity.

Objective: This study aims to investigate the relationship between the frequency of blood transfusion within the first 28 days of life and adverse outcomes (severe complications and in-hospital mortality) in VLBWI/ELBWI.

Methods: Data from 408 VLBWI/ELBWI admitted to the Neonatal Intensive Care Unit of Zhangzhou Affiliated Hospital of Fujian Medical University from 2018 to 2020 were retrospectively analyzed. Based on RBCT status, the 408 infants were divided into a transfusion group (303 cases) and a non-transfusion group (105 cases). Clinical characteristics and adverse outcomes [occurrence of at least one complication, including retinopathy of prematurity (ROP) > stage 2, moderate-to-severe bronchopulmonary dysplasia (BPD), or in-hospital death] were compared between the two groups. Spearman rank correlation analysis was used to explore the relationship between gestational age (GA), birth weight (BW), comorbidities (delivery room intubation, mechanical ventilation > 5 days, proven sepsis, periventricular-intraventricular hemorrhage grades 3–4), and the number of transfusions. Multivariate Logistic regression models were used to

evaluate the association between GA, BW, comorbidities, transfusion frequency, and the occurrence of adverse outcomes in VLBWI/ELBWI.

Results: Among the 408 infants, 256 (62.7%) were male and 152 (37.3%) were female, with a mean GA of (29.8 ± 2.1) weeks and a mean BW of $(1,205 \pm 248)$ g. Of these, 303 infants (74.3%) received RBCT within the first 28 days of life. Statistically significant differences ($P < 0.05$) were observed between the transfusion and non-transfusion groups in terms of GA, BW, 5-minute Apgar score, small for gestational age (SGA), delivery room intubation, mechanical ventilation > 5 days, proven sepsis, periventricular-intraventricular hemorrhage grades 3–4, ROP > stage 2, moderate-to-severe BPD, and in-hospital mortality. Correlation analysis showed that GA and BW were negatively correlated with transfusion frequency ($r_s = -0.544, P < 0.001$; $r_s = -0.541, P < 0.001$), while comorbidities were positively correlated with transfusion frequency ($r_s = 0.385, P < 0.001$). Multivariate Logistic regression analysis revealed that GA $\geq$ 30 weeks (OR = 0.482, 95% CI = 0.281–0.827, $P = 0.008$) and BW $\geq 1,250$ g (OR = 0.447, 95% CI = 0.261–0.765, $P = 0.003$) were protective factors against adverse outcomes in VLBWI/ELBWI. Comorbidities (OR = 1.868, 95% CI = 1.138–3.066, $P = 0.013$) and transfusion frequency $\geq$ 3 times (OR = 3.275, 95% CI = 1.707–6.275, $P < 0.001$) were identified as risk factors for adverse outcomes in VLBWI/ELBWI.

Conclusion: Receiving RBCT within the first 28 days of life is common among VLBWI/ELBWI (74.3%). GA < 30 weeks, BW < 1,250 g, presence of comorbidities, and transfusion frequency $\geq$ 3 times may be independent risk factors for severe complications and in-hospital mortality. It is recommended to use "transfusion frequency $\geq$ 3 times within 28 days" as a high-risk early warning sign for VLBWI/ELBWI, and to intensify complication monitoring for infants receiving $\geq$ 3 transfusions to improve prognosis.

Full Text

Predictive Value of Red Blood Cell Transfusion Frequency for Adverse Outcomes in Very and Extremely Low Birth Weight Infants: A Retrospective Cohort Study

Fang Xiaohong, Xu Chun, Huang Dali, Xu Liping*

Abstract

Background: Very low birth weight infants and extremely low birth weight infants (VLBWI/ELBWI) commonly require red blood cell transfusion (RBCT) within the first 28 days of life. Current academic controversy centers on the selection of transfusion threshold strategies, while in-depth discussions regarding transfusion frequency and adjustments for disease severity remain insufficient.

Objective: This study aimed to explore the relationship between the frequency

of RBCT within 28 days after birth and adverse outcomes (severe complications and in-hospital mortality) in VLBWI/ELBWI.

Methods: A retrospective analysis was conducted on data from 408 VLBWI/ELBWI admitted to the Neonatal Intensive Care Unit (NICU) of Zhangzhou Hospital, Affiliated to Fujian Medical University, between 2018 and 2020. Based on their RBCT status, the 408 infants were divided into a transfusion group ($n = 303$) and a non-transfusion group ($n = 105$). Clinical characteristics and adverse outcomes—defined as the occurrence of at least one complication including retinopathy of prematurity (ROP) > stage 2, moderate-to-severe bronchopulmonary dysplasia (BPD), or in-hospital death—were compared between the two groups. Spearman rank correlation analysis was used to investigate the relationships between gestational age (GA), birth weight (BW), comorbidities (intubation in the delivery room, mechanical ventilation > 5 days, proven sepsis, and periventricular-intraventricular hemorrhage [PV-IVH] grades 3–4), and the frequency of transfusion. Multivariate logistic regression models were employed to evaluate the associations between GA, BW, comorbidities, transfusion frequency, and the occurrence of adverse outcomes.

Results: Among the 408 infants, 256 were male (62.7%) and 152 were female (37.3%), with a mean GA of (29.8 ± 2.1) weeks and a mean BW of $(1,205 \pm 248)$ g. A total of 303 infants (74.3%) received RBCT within 28 days of birth. Statistically significant differences were observed between the transfusion and non-transfusion groups regarding GA, BW, 5-minute Apgar score, small for gestational age (SGA) status, delivery room intubation, mechanical ventilation > 5 days, proven sepsis, PV-IVH grades 3–4, ROP > stage 2, moderate-to-severe BPD, and in-hospital mortality ($P < 0.05$). Correlation analysis showed that GA and BW were negatively correlated with transfusion frequency ($r_s = -0.544, P < 0.001$; $r_s = -0.541, P < 0.001$), while comorbidities were positively correlated with transfusion frequency ($r_s = 0.385, P < 0.001$). Multivariate logistic regression analysis indicated that GA $\geq$ 30 weeks (OR = 0.482, 95% CI = 0.281–0.827, $P = 0.008$) and BW $\geq 1,250$ g (OR = 0.447, 95% CI = 0.261–0.765, $P = 0.003$) were protective factors against adverse outcomes. Conversely, the presence of comorbidities (OR = 1.868, 95% CI = 1.138–3.066, $P = 0.013$) and a transfusion frequency $\geq$ 3 times (OR = 3.275, 95% CI = 1.707–6.275, $P < 0.001$) were independent risk factors for adverse outcomes in VLBWI/ELBWI.

Conclusion: RBCT within the first 28 days of life is prevalent among VLBWI/ELBWI (74.3%). GA < 30 weeks, BW < 1,250 g, the presence of comorbidities, and a transfusion frequency $\geq$ 3 times are potential independent risk factors for severe complications and in-hospital mortality. It is recommended that "transfusion frequency $\geq$ 3 times within 28 days" be used as a high-risk early warning marker. Infants receiving $\geq$ 3 transfusions should undergo intensive monitoring for complications to improve clinical prognosis.

Keywords: Very low birth weight infants; Extremely low birth weight infants; Red blood cell transfusion; Transfusion frequency; Adverse outcomes

1. Introduction

Very low birth weight infants (VLBWI, BW < 1,500 g) and extremely low birth weight infants (ELBWI, BW < 1,000 g) represent a highly vulnerable population in the neonatal intensive care unit (NICU). Due to the extreme immaturity of their organs, both groups frequently face severe challenges from iatrogenic anemia. Statistics indicate that up to 90% of VLBWI require red blood cell transfusion (RBCT) [**?**]. The pathophysiological mechanisms of neonatal anemia are complex, involving factors such as a low erythropoietin response, frequent iatrogenic blood loss, and insufficient nutritional reserves.

Although RBCT is a core clinical intervention for maintaining tissue oxygen supply, its potential risks have drawn increasing attention. Recent studies suggest associations with serious complications, including necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), and periventricular-intraventricular hemorrhage (PIVH) [**?**]. However, existing evidence remains contradictory regarding transfusion thresholds [**?**]. Notably, previous research has focused primarily on threshold selection, with less exploration of the dose-response relationship between transfusion frequency and adverse outcomes. High-frequency transfusion may amplify pathological effects through cumulative inflammatory damage and oxidative stress. This study aims to define the intensity of RBCT requirements and verify whether high-frequency transfusion is independent of disease severity.

2. Methods

2.1 Study Population A total of 408 VLBWI and ELBWI admitted to the NICU of Zhangzhou Affiliated Hospital of Fujian Medical University between 2018 and 2020 were retrospectively selected. Inclusion criteria were: (1) hospital stay > 28 days; (2) GA < 37 weeks and BW < 1,500 g. Exclusion criteria included: (1) postnatal age > 48 h at admission; (2) fetomaternal hemorrhage or twin-to-twin transfusion syndrome; (3) major congenital structural anomalies or metabolic diseases; (4) complex congenital heart disease; and (5) multiple pregnancies.

2.2 Data Collection and Definitions Baseline data included GA, BW, sex, SGA status, Apgar scores, and delivery room intubation. Clinical parameters included RBCT status within the first 28 days (frequency, age at transfusion, volume, and pre-transfusion Hb/Hct levels), confirmed sepsis, and PIVH grades 3–4. Adverse outcomes were defined as the occurrence of at least one of the following: ROP > stage 2, moderate-to-severe BPD, or in-hospital mortality. Diagnostic criteria followed the 5th edition of *Practical Neonatology* [**?**].

2.3 Statistical Analysis Data analysis was performed using SPSS 21.0. Quantitative data are expressed as mean ± standard deviation ($\bar{x} \pm s$) or

median and interquartile range ($M(P_{25}, P_{75})$). Categorical data are expressed as frequencies and percentages. Spearman rank correlation was used to explore relationships between GA, BW, comorbidities, and transfusion frequency. Multivariable logistic regression models (Model 1 and Model 2) were utilized to assess independent risk factors. Statistical significance was defined as $P < 0.05$.

3. Results

3.1 Baseline Characteristics The cohort had a mean GA of 29.8 ± 2.1 weeks and a mean BW of $1,205 \pm 248$ g. Among the 408 infants, 303 (74.3%) received RBCT. Statistically significant differences were observed between the transfusion and non-transfusion groups regarding GA, BW, 5-minute Apgar score, SGA status, delivery room intubation, mechanical ventilation > 5 days, sepsis, and PIVH Grade 3–4 (Table 1).

3.2 Transfusion Characteristics In the group with BW < 1,250 g, the frequency of transfusions was significantly higher than in the BW $\geq 1,250$ g group (2.4 ± 1.6 vs $1.0 \pm 0.9, P < 0.001$). The median age at first transfusion was 10 (7, 15) days. For infants receiving ≥ 3 transfusions, the median cumulative dose was 52.5 (45.0, 60.0) mL/kg.

3.3 Correlation and Regression Analysis Spearman analysis showed GA and BW were negatively correlated with transfusion frequency ($r_s = -0.544$ and -0.541, $P < 0.001$), while comorbidities were positively correlated ($r_s = 0.385, P < 0.001$).

Multivariate logistic regression (Model 2) showed that GA ≥ 30 weeks (OR = 0.482) and BW $\geq 1,250$ g (OR = 0.447) were protective factors. Conversely, the presence of comorbidities (OR = 1.868, $P = 0.013$) and a transfusion frequency ≥ 3 times (OR = 3.275, $P < 0.001$) were independent risk factors for adverse outcomes (Table 4).

4. Discussion

This study confirms that RBCT is prevalent among VLBWI/ELBWI (74.3%). Lower GA and BW are associated with higher transfusion needs, likely due to diminished erythropoietin response and increased iatrogenic blood loss.

Our findings indicate that receiving ≥ 3 transfusions significantly increases the risk of severe ROP and BPD. Mechanistically, adult hemoglobin in transfused cells has a lower oxygen affinity than fetal hemoglobin, potentially causing hyperoxic exposure and retinal neovascularization [**?**]. Furthermore, free iron overload from frequent transfusions can catalyze oxidative damage, exacerbating lung and retinal injury [**?**].

The study also found that ≥ 3 transfusions are associated with increased in-hospital mortality. Even after adjusting for disease severity (comorbidities), the

frequency of transfusion remained an independent predictor. This suggests that cumulative exposure to transfusion-related immunomodulation and oxidative stress contributes to poor prognosis independently of the infant' s initial clinical state.

5. Conclusion

Transfusion frequency ≥ 3 times within the first 28 days of life is an independent risk factor for severe complications and mortality in VLBWI and ELBWI. We recommend using this frequency as a high-risk early warning marker. For infants reaching this threshold, intensified monitoring and restrictive transfusion strategies should be prioritized to improve clinical outcomes.

References

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