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Evaluation of a new restricted transfusion protocol in neonates admitted to the NICU

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Abstract

Background: Although transfusion is a common procedure for treating anemia of prematurity, there is no specific protocol for blood transfusion in premature newborns. So in this study we investigate whether application of a strict protocol has any statistically significant effect on reduction of blood transfusion.

Methods: In this study, first group admitted in NICU during 2005 - 2006 and the second group admitted during 2006 - 2007. Whereas in the first group the blood transfusion performed based on neonatologists' opinion following consultations with a pediatric hematologist, blood transfusion in the second group was based on the Shannon's protocol.

Results: During 2005-2006, out of 206 cases, 71 cases (%34.5) underwent blood infusion. During 2006-2007, out of 211 cases, 56 (%26.5) received blood transfusion based on the Shannon's strict protocol. Although the number of cases decreased, no significant difference was found betweenthe two groups (p= 0.07).

Conculsion: Applying strict criteria alone is not effective in reducing the frequency of transfusion in infants.

Keywords: Blood transfusion, Premature infants, Anemia.

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Introduction

Anemia of prematurity is an exaggeration of the normal physiologic anemia. The following factors play important roles in the development of anemia: (1)

- RBC survival is decreased
- RBC mass and iron stores are decreased
- Rapid growth.
- Physiological consequences of transition from fetus to infancy.
- Recurrent iatrogenic phlebotomies for laboratory test.
- Vitamin E deficiency in small premature infants.

For premature babies therapy is required and folic acids and iron are provided. In rare cases, well-fed premature newborns with good growth may well need therapy. Anemia of prematurity clinically presented with paleness, apnea, and failure in weight gain, decreasing activity, tachycardia, and nutritional difficulties (1).

Even though normal level of Hb, and HCT for mature and premature newborns are determined, no specific guide for blood transfusion is yet unanimously introduced (1, 2).

Several factors need to be taken into account for newborns which is listed as follows:

- The severity of clinical manifestations

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- Hb level

- Presence of another disease (which result in oxygen-transportation difficulty):
  - Pulmonary dysplasia
  - Congenital heart disease
  - Respiratory distress syndrome (1)

In most cases transfusion is a common procedure for treating anemia of prematurity or as a replacement for the blood taken from newborns (2).

Blood transfusion may result in serious side effects such as hemolytic or non-hemolytic allergic reactions. Infections like CMV, HIV, HBV and HCV in addition to electrolytic abnormalities are among other critical side effects (3).

Erythropoietin therapy, limiting phlebotomy for tests, avoiding disproportionate blood transfusions, have reduced the transfusion in newborn weighing less than 1500 grs (4 - 5).

Since there is no specific protocol for blood transfusion in premature newborns (6-8) and subsequently the seriousness of its side effects, the researchers decided to investigate whether application of a strict protocol has any statistically significant effect on reduction of blood transfusion. To do so, the researchers applied a strict protocol in the NICU of Vali-e-Asr hospital for a year and compared the results with those of the previous year in which was decided on the basis of the attendees' judgment.

Methods

This two group comparison study was conducted during 2005- 2007 on consecutive samples of newborns in NICU of Vali-e-Asr hospital. Two groups of newborns were examined, first group admitted in NICU since September 2005 until August 2006 and the second group admitted during September 2006 to August 2007.

Whereas in the first group the blood transfusion took place based on neonatologist's opinion following consultations with a pediatric hematologist, blood transfusion in the second group was based on the Shannon's protocol (5).

Eventually the two groups were compared. It should be said that Vali-e-Asr Hospital is a referral training general hospital with Obstetrics and Gynecology wards, and neonatal intensive care unit patients are inborn newborns hospital.

Excluding Criteria:

- Presence of multiple or a major anomalies based on International Coding of Diseases(ICD10)
- Presence of either hemolytic disease with any causation
- partial/total Exchange during hospitalization
- Death in the first 24 hours of life
- Less than 25 weeks of gestational age
- Birth weight 500grs or less

Information obtained was based on filled questionnaires with the following subheadings: Gestational Age, Gender, Birth weight ,Weight at the time of hospital discharge, Birth Apgar, Newborn diseases (such as Pneumonia, RDS, Sepsis, IVH, BPD, imminent need for surgery, cardiac diseases and DIC), Maternal underlying conditions or diseases, Labor complications and Drugs administered to mother.

Diagnostic criteria for pneumonia and RDS were based on clinical manifestations such as respiratory distress at birth along with paraclinical manifestations including ABG and radiographic signs. Diagnosis of sepsis was based on positive blood culturing together with positive CRP. Furthermore, IVH diagnosis was established by means of brain sonography in third and seventh days of birth. Finally, BPD was diagnosed using (Jobe AH) (11) criteria and cardiac diseases were detected by echocardiography. To achieve a uniform application, all attendees in the NICU ward were justified to use the new strict Blood transfusion protocol.

Sample size of 127 in each group was analyzed with confidence level of %95, power of %80, P_1=0.18 and P_2=0.3 based on a pilot study. Data were analyzed by SPSS 11.5 and by means of relative frequency, mean, chi-square test, T student test.

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In the first group the blood transfusion took place based on neonatologists' opinion, so blood transfusion guide was applied according toneonate's general condition, symptoms and laboratory test.

Shannon's strict Blood transfusion guide was applied as follows: Infant with Hct< 40% if requiring> 35% 0_2 or mean airway pressure≥ 8 cm H20 by CPAP or IMV or cyanotic heart diseases or congestive heart failure or major surgery or needs to transfer to another ward or hospital with mechanical ventilation.

Infant with Hct< 35% if requiring> 35% 0_2 by hood or CPAP or mean airway pressure 6-8 cm H20.

Infant with Hct< 30% if requiring 0_2< 35% by hood or CPAP or if having mean airway pressure< 6 cmH_2o or taking vasopressor or> 9 apneic and bradycardic episodes per 12 h or if requiring 2times bag and mask ventilation per 24hr while on adequate methylxantine therapy or HR>180/min or RR> 80/min sustained for 24h or gaining weight< 10g/d for 4 days on 100 Kcal/kg/d calories intake or having minor surgery.

Infant with Hct< 20% and asymptomatic with reticulocytes< 2% or symptomatic

Results

A total of 206 cases were admitted in NICU during 2005-6 in which 71 cases (%34.5) underwent blood transfusion. During 2006-2007, on the other hand, out of 211 admitted cases, 56 (%26.5) received blood transfusion based on strict protocol. Although the number of cases decreased, no significant difference was found between the two groups. (p= 0.07)

In both groups, there was no significant difference in gestational age, birth weight, and newborns' age in first blood transfusion (Table 1).

Respectively, no significant difference has been found in frequencies of following factors: Severe Apnea, Death occurrence after the first 24 hours of life , Pneumonia, RDS, Sepsis, IVH, BPD, NEC, DIC, PROM, Cardiovascular diseases, Imminent need for surgery, Apgar of 5^{th} min< 6 (Table 2).

With decreasing gestational age and birth weight, counts increased. In both groups, male subjects had higher frequencies, whereas in first group girls and boys had %44 and %56 frequencies, in the second group the frequencies were %31 and %69 respectively. As it can be seen, there was no difference in gender (p= 0.12). The dominant method of delivery was C/S in

Table 1. frequency of neonates in the first and second group based on birth weight, gestational age and first transfusion's age

Group variable		First group	Second group	p
(gr) Birth weight	>1500	32 (51/6%)	47 (66%)	0.46
	1500-1999	12 (19/4%)	9 (12/7%)	
	≥ 2000	18 (27/2%)	15 (12/1%)	
Gestational age (wk)	<30	19 (30/6%)	32 (45/5%)	0.07
	30-35	36 (58/1%)	27 (30/0%)	
	≥ 35	7 (11/3%)	12 (16/9)	
Age of first transfusion (day)	≤ 7	46 (74/2%)	44 (62%)	0.13
	7-14	36 (9/7%)	11 (15/5%)	
	≥ 14	10 (16/1%)	16 (22/5%)	

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Table 2. comparison between two groups based on neonatal problem

Variable value	Group	Number-percent	Total	p
Sever apnea	First	18(25/4%)	71	0/42
	Second	18(29%)	56	
Death after first 24 h	First	21(29/6%)	71	0/46
	Second	22(35/5%)	56	
sepsis	First	31(43/7%)	71	0/69
	Second	23(37/1%)	56	
pneumonia	First	25(32/5%)	71	0/79
	Second	20(23/3%)	56	
Respiratory distress syndrome	First	35(49/3%)	71	0/93
	Second	30(50/0%)	56	
IVH	First	21(30/0%)	70	0/78
	Second	19(32/2%)	56	
BPD	First	5(7/1%)	70	0/59
	Second	3(4/9%)	56	
NEC	First	3(4/2%)	71	0/72
	Second	2(3/2%)	56	
DIC	First	9(12/7%)	71	0/49
	Second	10(16/9%)	56	
PROM	First	20(29/0%)	69	0/23
	Second	24(38/7%)	56	
Cardiovascular disease	First	17(23/9%)	71	0/56
	Second	17(27/4%)	56	
Surgery (Minor,Major)	First	6(8/5%)	71	0/78
	Second	6(9/8%)	56	
5min apgar< 6	First	8(11/9%)	67	0/32
	Second	4(6/8%)	56	

Table 3. Comparison between in two groups based on frequency and volume of transfusion

Variable value	Group	Mean	Number	Std Deviation	Min	Max	Sig (2-tailed)
Numbers of phlebotomy	First	25/86	71	17/28	4	93	0/11
	Second	32/84	56	29/84	3	142	
Volume of phlebotomy during admission(cc)	First	46/30	71	26/57	13	150	0/17
	Second	54/27	56	39/15	13	190	
Mean volume of blood transfusion(cc)	First	18/85	71	7/86	5	40	0/47
	Second	19/79	56	7/40	7	40	
Numbers of transfusion	First	2/94	71	2/85	1	13	0/94
	Second	2/98	56	3/52	1	18	
Mechanical ventilation time(days)	First	11/85	41	14/00	1	70	0/30
	Second	9/1	45	10/40	1	47	
hospitalization time(day)	First	28/68	71	19/24	2	94	0/11
	Second	23/50	62	18/44	1	67	

both group, %66 in the first group and %77 in the second one (p= 0.74).

Number of phlebotomy in the first group was 25/86, in the second group was 32/84 and volume of phlebotomy in first one was 46/30 ^{cc}, in the second was 54/27^{cc} which shows no significant difference (p= 0.11, p= 0.17). The average blood volume taken from the newborns for tests was shown in Table 3.

The prevalence of ventilator used for the two groups was as follows: in first group 41 out of 71 cases (%57.7), and in the second group 43 out of 63 cases used ventilator (%70.5) which shows no significant difference (p= 0.12).

Discussion

Using Shannon strict protocol did not show any significant difference which is in contrast with Shannon study where the number of blood infusions reduced from first phase (1.9±2) to second phase (1.4±1.6), p= 0.01. (5)

Whereas in Shannon study newborns under age of 37 weeks, with less than 1500 grams weight and in the first 28 days of their lives were examined, in our study there were cases with 70 days of hospitalization and they underwent several phlebotomies which naturally arose the need for more blood infusion. As it can be inferred, since most of the subjects in our study were

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less than 1500 grams and under age of 35 weeks, number of blood infusions may have shown an increase. And from this aspect our study showed the same results as other studies (3-8). Moreover it is established that newborns need far more blood transfusion in the first week of their lives which is as same as Hale Oren and Shwarz studies (3-8).

The average blood volume taken from the newborns for tests was not significantly different in the two groups but it was reported higher in the second group which is exactly in contrast with the Shannon study. Therefore it can be inferred that the amount of blood taken from newborns plays an important role in exaggeration anemia of prematurity resulting in an increased need for blood transfusion. And as long as this major factor is not reduced, the decrease in counts will not be tangible.

As our study's result confirms, need for ventilation in the two groups was %70.5 and %57.7 respectively. In Shannon (5), ventilation need in first phase was %68 whereas in the second phase it was %75. Therefore, we can assert that there is a link between need for transfusion and ventilator application. In other words, the more we use ventilator, the higher will be our need for transfusion. This is the same as Shwarz. (8) The two groups were similar in terms of the diseases which necessitated blood transfusion.

In Joseine study (9), which uses the Shannon protocol as a guide in blood infusion, newborns under age of 37 weeks and 1500 grams of weight in the first 28 days of their lives were examined. Two phases (as same as Shannon's and ours) were established. No significant decrease in terms of counts in preterm newborns was recognized. In Josiene study the average blood volume taken from the newborns was 47.2±18.6 in the first phase and 46.9±18 in the second phase, which is less than our study (p= 0.9).

In another study Paul asserts that the following factors affect need: birth weight, gestational age, hospitalization period, ventilation application period, IVH, presence of other diseases, number of blood taken during hospitalization, which is more or less similar to our study (10).

Finally, given that in our study the number of patients who received blood transfusion declined from 71 to 56, which in itself was not significant, but bearing in mind the risks of even this small reduction is extremely important.

In Chen study conducted randomly in 2006 on hospitalized newborns placed in two strict protocol and non-strict protocol groups, it was revealed that there was no significant difference in the two groups in RDS, IVH, BPD and PROM frequency. At the end, this study suggested that using strict criteria can be applied to decrease volume and thus reduce the incidence of chronic lung diseases in very low birth weight neonates (12). Shen' s suggests the possible benefits from liberal-transfusion for clinical recovery in very low birth weight infants. Even though, the restrictive transfusion does not decrease the number of transfusions (13).

Conclusion

Consequently we can conclude that applying strict criteria alone is not effective in reducing the frequency of transfusion in infants. Trying to reduce the frequency of blood sampling during the neonatal hospitalization could reduce counts in infants. Therefore we should apply stricter criteria in taking blood from newborns. However taking into account the dangers of blood transfusions, even if it is not considered a significantly meaningful difference, the reduction of blood recipients in our study is particularly important. Although the most important reason for restricted transfusion is decreasing of side effects especially ROP , BPD, NEC but by applying stricter criteria, along with making efforts to reduce the frequency of blood sampling we can decrease infants' blood transfusions. Also using new methods such as measuring hemoglobin via micro sampling would be so accommodating. We suggest other studies to

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be conducted to reduce the volume of blood taken in newborns. Nonetheless in all blood banking texts, there is a phrase that \" There is no strict protocol for blood transfusion and blood transfusions protocol is under physician decision\"

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