ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 12 | December - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

FREQUENT BLOOD SAMPLING LEADS TO SIGNIFICANT IATROGENIC BLOOD LOSS IN VERY LOW BIRTH WEIGHT BABIES

Pediatric Medicine

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ABSTRACT

INTRODUCTION: Newborns receiving intensive care require frequent determination of hematologic status, blood chemistry and arterial gas analysis. Anemia of prematurity (AoP) is common in preterm very low birth weight babies (<1.5 kg body weight).Nearly all extremely preterm infants develop AoP and up to 90% require atleast one red blood cell transfusion during their NICU stay. However, anotherim[ortant cause for AoP seems to be related to iatrogenic blood loss due to frequent laboratory investigations. Recently, several small studies reported that newborns especially preterm VLBW infants may lose more than half of their blood volume due to cumulative laboratory blood sampling in the first weeks after birth.

OBJECTIVES: To determine the total amount of blood sampled in VLBW new-borns during the stay in the neonatal unit (SNCU& NICU). The number and total amount of blood transfused in VLBW new-borns during the stay. The relationship between blood loss due to blood sampling and blood transfusion in VLBW.

MATERIALS AND METHODS: A prospective observational study is being planned to perform in all VLBW new-borns admitted in the neonatal unit of a tertiary care centre in eastern India. This study will be conducted for 6 months in all VLBW. Subjects will be subdivided into 1000gm (500gm to 999gm) and >- 1000gm- < 1500gm. Each group will be subdivided into critically ill or not. Babies with RDS requiring surfactant and/or ventilator treatment, birth asphyxia with HIE and/or in whom infection is strongly suspected or verified by blood investigation and culture will be considered as critically ill. Those babies with duration of stay more than 5 days will be considered for the study.

RESULTS: Our study showed that total of 214 babies (both VLBW, ELBW) admitted from 1/11/2019 to 30/4/2020.Among these, 130 babies admitted in the SNCU for more than 5 days. Out of this, 86 babies were eligible in the study satisfying all inclusion criteria. Baseline characteristics are mentioned in table 1.Table 2 presents the comorbidities like respiratory distress, birth asphyxia, sepsis. The total iatrogenic blood loss was 3ml (0.90- 11.89). The average blood loss was 3.4 ml/kg.

CONCLUSION: From our study we found that sampling related blood loss is higher among lower birth weight babies. As birth weight decreases, sampling related blood loss increases and further need for transfusion increase.

KEYWORDS

Very Low Birth Weight Babies, Frequent Blood Sampling, Iatrogenic Blood Loss

INTRODUCTION

Newborns receiving intensive care require frequent determination of hematologic status, blood chemistry and arterial gas analysis. Anemia of prematurity (AoP) is common in preterm very low birth weight babies (<1.5 kg body weight).Nearly all extremely preterm infants develop AoP and up to 90% require atleast one red blood cell transfusion during their NICU stay[1,2]. However,anotherim[ortant cause for AoP seems to be related to iatrogenic blood loss due to frequent laboratory investigations[3]. Recently, several small studies reported that newborns especially preterm VLBW infants may lose more than half of their blood volume due to cumulative laboratory blood sampling in the first weeks after birth [4-6]. After significant phlebotomy loss, they fail to increase erythropoietin production. Not surprisingly, a direct correlation was found between the volume of phlebotomy blood loss and volume of RBC transfusions, emphasizing the necessity of reducing blood loss in order to reduce the need of transfusions [7]. Importantly, transfusions of blood products are increasingly being reported to be associated with an increased risk of inflammatory responses, neonatal morbidity, and mortality [1]. Reducing iatrogenic blood loss in VLBW newborns could therefore not only reduce the need for transfusions but simultaneously reduce the associated risk of mortality and morbidity [8].

Neonatal blood sampling and related issues are not well researched in Indian/ Asian context. So hereby we are planning to study the blood loss due to neonatal blood sampling and transfusion requirement in our set up to address the issues.

OBJECTIVES

1) To determine the total amount of blood sampled in VLBW new-borns during the stay in the neonatal unit (SNCU& NICU).
2) To determine the number and total amount of blood transfused in VLBW new-borns during the stay.
3) To evaluate the relationship between blood loss due to blood sampling and blood transfusion in VLBW.

MATERIALS AND METHODS

A prospective observational study is being planned to perform in all VLBW new-borns admitted in the neonatal unit of a tertiary care centre in eastern India. This study will be conducted for 6 months in all VLBW. Subjects will be subdivided into 1000gm (500gm to 999gm) and >- 1000gm- < 1500gm. Each group will be subdivided into critically ill or not. Babies with RDS requiring surfactant and/or ventilator treatment, birth asphyxia with HIE and/or in whom infection is strongly suspected or verified by blood investigation and culture will be considered as critically ill. Those babies with duration of stay more than 5 days will be considered for the study. Based on the duration of stay it will be further divided into <15 days, >15 days. Babies with surgical disorders, congenital anomalies, those babies who took admission in the SNCU after the first day of life will be excluded. Those babies whose parents who do not give consent will be excluded. All details regarding the weight, gestational age, diagnosis, comorbid illness will be recorded in a predesigned proforma. All the details regarding blood sampling will be included.

Neonatal blood sampling related details in VLBW new-borns will be recorded in detail (birth weight (g), present weight(g), gestational age (weeks), mode of delivery, gender of the baby, inborn/out-born, any associated illness, receiving any intensive care support or not ,type of blood investigation ,type of collection container, date and time of phlebotomy, whether one or more collection containers being filled at the time of phlebotomy, location (i.e., NICU or SNCU).

Blood transfusion related details will be recorded in details (frequency, amount, pretransfusion and post transfusion haemoglobin). The criteria for RBC transfusions used in the SNCU are based on BCSH guideline (British Committee for Standards in Haematology).

The study will be blinded to the doctors ordering the analysis, but not to the technicians performing the samples. SNCU Medical officers, post

graduate trainees, residents, lab technician who are posted in the neonatal unit are trained beforehand under the guidance of the faculty posted in the department.

The hub of 24-gauge needle will be removed and the shaft of the needle will be used for blood sampling. Then the shaft of the needle will be introduced into the vein. Marked containers, 1ml syringes will be used for collecting samples. Less than 1ml blood is to be quantified with the use of micropipette.

A protocol will be used to determine the exact amount of blood needed for each specific laboratory test depending on the laboratory analysers. The amount of blood lost on cotton, bedding, and intravenous tubing will be kept minimum and will not be considered.

RESULTS

Our study showed that total of 214 babies (both VLBW, ELBW) admitted from 1/11/2019 to 30/4/2020.Among these,130 babies admitted in the SNCU for more than 5 days. Out of this, 86 babies were eligible in the study satisfying all inclusion criteria. Baseline characteristics are mentioned in table 1.Table 2 presents the comorbidities like respiratory distress, birth asphyxia, sepsis. The total iatrogenic blood loss was 3ml (0.90- 11.89). The average blood loss was 3.4 ml/kg.

We found comparision of blood loss as per duration of stay is depicted in Table 5. Statistically significant difference in the total amount of blood loss exists between 2 groups(ie one with duration of stay < 15 days and >-15 days). Median blood in those babies with duration of stay <15 days is around 2.72. Median blood loss in those babies with duration of stay >15 days is around 5.52. As the duration of stay increases statistically significant loss of blood is documented in this study.

In our study showed total amount of blood loss is compared with respect to birthweight is depicted in table no 6. Median amount of blood lost from babies with birth weight <1000gm is 4.38ml whereas those with birth weight >=1000gm is 3ml. As birth weight increases blood loss decreases.

We found that correlation between birth weight in relation to amount of blood loss and number of transfusion is depicted in table . Blood loss is higher in lower weight babies compared to bigger babies. Similarly transfusion requirement is higher in those with lower weight. Similarly as duration of stay increases transfusion requirement also increases.

DISCUSSION

Several findings which can be deducted from this prospective observational study. The cumulative iatrogenic blood loss is higher in those babies with lower birth weight babies compared to those with higher birth weight. As the duration of stay increases amount of iatrogenic blood loss increase. As the duration of stay increase requirement for blood transfusion increase.

Similar to other study cumulative iatrogenic blood loss in lower birth infants is higher compared to higher birth weight babies. The cumulative iatrogenic blood loss in extreme preterm infants in the first 28 days of life is high and is approximately 24 ml/kg, which equals to almost a third of the total blood volume [3]. The average cumulative iatrogenic blood loss in our study is 3.4ml/Kg. In our study both ELBW and VLBW babies are considered. This significant difference in reported total blood loss can be due to various reasons, including variation in the study subjects (considered both ELBW,VLBW), in particular, the gestational age at birth.

The mean blood loss due to sampling in Madsen study was 13.6ml/kg. Most of the studies showed blood loss due to diagnostic sampling was higher range As the blood loss increases, number of transfusions also increases. Similar to other studies, the cumulative iatrogenic blood loss is directly associated to the volume of RBC transfusions, suggesting that iatrogenic blood loss is the one of the main cause of AOP (Anemia Of Prematurity) and RBC transfusions.

In VLBW and ELBW it is needed to keep the number of samples and amount of blood sampled are reduced to an absolute minimum. Blood loss related to sampling is very much important among ELBW patient group because even small volumes of blood loss are large relative to an ELBW infant's body weight and blood volume.

However, one of the important causes of AoP seems to be related to iatrogenic blood loss due to frequent laboratory investigations.

Iatrogenic blood loss should be kept minimum by protocols should be followed strictly regarding the amount of blood that is needed for every specific test and bedside point-of-care testing with the lowest volumes needed.

A periodical review of their procedures should be followed. A continuous registration of all iatrogenic blood losses in every individual infant should be maintained. General awareness of this fact may indeed have diminished blood losses further.

Use of bedside or in-line laboratory analysers can be considered to reduce blood sampling related losses. Blood sampling related loss in the first week of life can be minimised by obtaining initial blood tests from the umbilical cord at delivery RBC transfusions has its own disadvantages in ELBW infants. Transfusing adult blood to an extremely low birth weight might potentially dilute important foetal factors during an essential stage of development. Extremely preterm infant blood contains factors specific for foetal development, predominantly foetal haemoglobin On day 1, blood sampling related loss can be reduced by sampling blood cultures from the placenta instead of from the neonate.

To reduce there requirement for RBC transfusions, a strict transfusion protocol should be followed and adequate training should be given to staff regarding neonatal care and blood analysis. Other methods to reduce PRBC transfusions in the neonatal period could include delayed cord clamping at delivery Other options available for reducing blood sampling related blood loss include technologic advancements like more reproducible and better capillary blood-sampling containers, and use of in-line point-of-care monitors in which little to no blood is required.

Most important factor is individual phlebotomists, nurses, and other members of the care team should be aware of this sensitive issues to reduce unnecessary blood loss, e.g., ordering only essential blood tests, exercising the greatest care in the smallest infants, may also help. Proper education regarding this will reduce unnecessary blood loss to a great extent.

CONCLUSION

From our study we found that sampling related blood loss is higher among lower birth weight babies. As birth weight decreases, sampling related blood loss increases and further need for transfusion increase.

Table 1: Baseline characteristics and Results of cumulative iatrogenic blood loss, RBC transfusions, duration of hospital stay and outcome

N=86		
	Frequency	Percentage
Gestational age		
Extremely preterm (<28 weeks)	5	5.8%
Very preterm(28-31 weeks)	29	33.7%
Moderate preterm(32-33 weeks)	26	30.2%
Late preterm (34-36 weeks)	22	25.6%
Term(>-37weeks)	4	4.7%
Gender		
Male	37	43%
Female	49	57%
Mode of delivery		
LSCS	13	15.1%
Normal delivery	73	84.9%
Inborn/ outborn		
Inborn	54	62.8
Outborn	32	37.2%
VLBW/ ELBW		
ELBW	16	18.6%
VLBW	70	81.4%
Total stay		
<15 days	44	51.2%
>15 days	42	48.8%
Need for RBC transfusion		
Yes	9	10.5%
No	77	89.5%

No. of transfusion		
3	1	1.2%
2	2	2.3%
1	6	7%
0	77	89.5%
Outcome		
Discharged	75	87.2%
Expired	11	12.8%

Table 2: Co Morbidities

	Yes		No	
	Frequency	**Percentage**	**Frequency**	**Percentage**
RDS	28	32.6%	58	67.4%
BA	3	3.5%	83	96.5%
Sepsis	26	30.2%	60	69.8%
Others	2	2.3%	84	97.7%

Table 3: Total Iatrogenic Blood Loss In ml

Minimum	Maximum	Median
0.90	11.89	3.0

Table 4: Comparison Of Blood Loss As Per Duration Of Stay Using Mann Whitney U Test

	N	Median	P Value
<15 Days	44	2.72	<0.0001
≥15 Days	42	5.52	

Table 5: Comparison Of Blood Loss As Per Birth Weight Using Mann Whitney U Test

	N	Median	P Value
<1000	16	4.38	0.037
≥1000	70	3.0	

Table 6: Correlation Of Iatrogenic Loss With Transfusion Requirement

	Correlation coefficient	P value
Birth weight with no.of tranfusion	-0.332**	0.002
Total Stay with no. of transfusion	0.470**	<0.0001
Total loss with no. of transfusion	0.401**	<0.0001
Birth weight with total stay	-0.378**	<0.0001
Birthweight with total loss	-0.477**	<0.0001

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