Sultanate of Oman

Ministry of Health

Directorate General of Khoula Hospital

Department of Neonate Intensive Care Unit

Institution Name: Directorate General Khoula Hospital

Document Title: Guideline for Blood Transfusion in Neonate Intensive Care Unit

Approval Process

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Location of original copy: Document Owner

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Acronyms:

ACOG	American College of Obstetrics and Gynecology
BP	Blood pressure
CHD	Congenital heart disease
CMV	Cytomegalovirus
COVID	Coronavirus Disease
CPAP	Continuous positive airways pressure
CPD – A1	Citrate, phosphate, Dextrose, Adenine
DCT	Direct Coombs Test
DGKH	Directorate General Khoula Hospital
DIC	Disseminated Intravascular Coagulopathy
ECMO	Extracorporeal Membrane Oxygenation
ET	Endotracheal
FFP	Fresh Frozen Plasma
FiO2	Fraction of Inspired Oxygen in 1 second
FNAIT	Fetal Neonatal Allo Immune Thrombocytopenia
FNHTR	Febrile non-hemolytic transfusion reactions
GALD	Gestational Alloimmune Liver Disease
Hb	Heart rate
Hct	Hematocrit
HDN	Hemorrhagic Disease of the Newborn
HIV	Human Immunodeficiency Viruses

HR	Heart rate
ICH	Intracranial Hemorrhage
INR	International Normalized Ratio
ITP	Immune Thrombocytopenia
IVH	Intraventricular Hemorrhage
IVIG	Intravenous Immune Globulin
KG	Kilogram
MAP	Mean Airway Pressure
MDP	Multiple Donors Platelets
NEC	Necrotizing Enterocolitis
NICU	Neonatal Intensive Care Unit
NNF	National Neonatology Forum
PC	Platelet Concentrate
PPV	Positive Pressure Ventilation
PRBC	Packed Red Blood Cells
PTP	Post Transfusion Purpura
PT	Prothrombin Time
aPTT	Activated Partial Thromboplastin Time
RR	Respiratory rate
SAGM	Saline-Adenine-Glucose-Mannitol)
SDP	Single Donor Platelet
TACO	Transfusion Associated Circulatory Overload
TRALI	Transfusion Related Acute Lung Injury
TSB	Total Serum Bilirubin

Guidelines of Blood Transfusion in Neonate Intensive Care Unit

1. Introduction

Blood and blood products provide unique and life-saving therapeutic benefits to patients.

It is well known that errors in blood transfusion practices can lead to serious consequences for the recipient in terms of morbidity and mortality. Sick neonates frequently receive transfusion of different blood components: packed red blood cells (PRBCs), platelet concentrates (PC), plasma and immunoglobulin. Their judicious use is of upmost important, and present guidelines will be helpful in this direction.

2. Scope

These guidelines apply to all healthcare professionals involved administration of blood and blood products in Neonatal Intensive Care Unit (NICU).

3. Purpose

The guidelines provide a standardized approach to transfusion so the potential for errors is minimized and the administration of safe and efficacious blood products in the health care setting is maximized.

4. Definitions

4.1 Neonate - For the purposes of transfusion medicine, a neonate is defined as an infant under four months of age.

4.2 Fresh blood – Any blood after donation, less than 24 hours is considered as fresh blood. After 24 hours of storage, it has few viable platelets or granulocytes and decrease factors of factors V and VIII levels.

4.3 Massive blood loss - defined as either 80 ml/kg in 24 hrs, 40 ml/kg in 3 hrs or 2 to 3 ml/kg/mt

4.4 Major haemorrhage or bleeding include:

4.4.1 Intracranial haemorrhage (leading to neurosurgical intervention or radiologic imaging showing midline shift)

4.4.2 Intraventricular haemorrhage filling 50% or more of the cerebral ventricle, IVH ≥ grade 3.

4.4.3 Pulmonary haemorrhage (fresh bleeding through an endotracheal tube with increased Ventilatory requirements),

4.4.4. Frank rectal bleeding,

4.5 Severe bleeding includes fatal bleeding, life-threatening bleeding associated with shock, or bleeding requiring fluid boluses or red-cell transfusion.

4.6. Minor haemorrhage or bleeding include:

4.6.1. Pseudo menstruation

4.6.2. Minimal ET bleed without increase in ventilator requirements

4.6.3. Mild bleeding caused by necrotizing enterocolitis (NEC))

4.6.4. Brown colour gastric aspirates

4.6.5 Petechiae, puncture site oozing

5. Significant coagulopathies in Neonates:

5.1. Neonate reference range of common coagulation tests see **Appendix 1**

5.2. CPD A1 (Citrate, phosphate, Dextrose, Adenine) is preservative added to increase shelf life of blood or PRBC from 21 days to 35 days.

5.3. SAGM (saline-adenine-glucose-mannitol) Mannitol is a free radical scavenger and membrane stabilizer, and thus provides nutrients for longer storage. Mannitol increases the shelf life of blood and PRBC from 21 days to 42 days.

6. Guidelines:

6.1. Blood or its components are transfused as following:

6.1.1. Whole blood:

A. One unit = 450 ml donor's blood + 63 ml anticoagulant preservative

B. CPDA-1 whole blood should be used in newborn.

6.1.2. Indications:

A. Acute hypovolemia e.g., surgical blood loss,

B. Massive blood transfusions.

C. Exchange transfusion (plasma reduced whole blood should be used in newborns).

D. After cardiopulmonary bypass.

6.1.3. Dose: 10 to 15 ml / kg (Determined by clinical situation (e.g., correction of tachycardia).

6.1.4. Exchange Transfusion – Choice of blood

A. Ideally, for both ABO & Rh incompatibility, O Rh negative red blood cells + AB Rh negative plasma should be used. However, it is not always available.

B. ABO incompatibility: O with low titer of anti A and anti B, Rh compatible. It should be cross matched with infants as well as mother's blood.

C. Rh incompatibility ABO compatible, Rh negative blood. It should be cross matched with infants as well as mother's blood.

6.2.4 Blood should be plasma reduced and irradiated

6.2.5 It should be as fresh as possible, but < 5 days old

6.1.5. Transfusion threshold of PRBC'S for neonates:

A. Criteria for transfusion of PRBC'S for neonates

B. Anemia in first 24 hours defined in preterm as Hb < 12 g/dL (Hct 36 %) & in term as Hb < 10 g/dL (Hct 30 %)

C. Hct < 30 % with FiO2 < 35 %:

i. MAP <6 cmH2O by CPAP or mechanical ventilation

ii. Significant apneas while on adequate methylxanthine treatment (> 9 apneic episodes/12 hours or >2/day severe apnoeas needing PPV)

iii. HR>180/min or RR>80/min sustained for 24 hours

iv Weight gain of <10 g/day for 4 days on 100 kcal/kg/day

v. Having Surgery

D. Hct < 35 % with FiO2 > 35 % on CPAP or mechanical ventilation with mean airway pressure ≥ 6 - 8 cm of H2O

C. Hct less than 45% in a neonate with cyanotic CHD or ECMO

D. Acute blood loss ≥ 10% of blood volume

E. Late anemia with ≤ Hb 7 g/dl (Hct < 20 %) with low reticulocyte count (< 2 %) asymptomatic

F. Symptomatic anemia (Lethargy, tachycardia, tachypnea, poor feeding, apnoea).

6.1.6. PRBCs threshold according to age of the child see **Appendix 2**

A. Volume to be transfused 10 to 15 ml / kg to be given over 4 hrs.

B. Furosemide 1 mg / Kg can be considered at beginning or during mid-transfusion (especially in the first week of life). Routine use of furosemide should be avoided.

C. Type of blood Rh compatible O group cross matched with the baby can be given safely. For example, in Rh positive baby, O Rh positive cross matched with baby can be given. Otherwise, if baby's and mother's blood group is same, baby's blood group can be given. Once transfusion is given, it is wise to use the same group of blood for repeated transfusions during hospital stay.

D. CPDA-1 blood should be preferably used. If CPDA-1 is not available, SAGM PRBC'S can be used for packed cell transfusion.

E. It is not necessary to use "fresher (< 7 days old) packed red blood cells" for the PRBC transfusion. (Strong recommendation, High quality evidence)

6.2. Fresh frozen plasma (FFP):

6.2.1. Indications:

A. Bleeding patients with multiple coagulation factor deficiencies secondary to:

i. Liver disease.

ii. Disseminated intravascular coagulation.

iii. Haemorrhagic disease of new-born.

iv. Dilutional coagulopathy resulting from massive blood replacement (Exchange transfusion).

B. Congenital factor deficiencies for which there is no coagulation concentrate available, such as deficiencies of Factor V or XI.

C. Purpura fulminant secondary to severe homozygous deficiency of protein C or protein S Protein C concentrates is sometimes available. However, for protein S deficiency, FFP is only solution since factor concentrate not available.

D. Neonates with significant coagulopathy who must undergo invasive procedures

6.2.2. Conditions where Fresh frozen plasma (FFP) not indicated:

Emphasis should be in the face of clinically significant bleeding rather than prophylactic use in association with abnormalities of standard coagulation tests.

A. **The following are not considered as indications:**

i. FFP should not be used as a source of protein for nutritionally deficient patients
ii. as a volume expander
iii. FFP should not be used to restore a prolonged international normalized ratio (INR).
iv. Prolonged PT and aPTT are seen in premature infants.
v. for prevention of IVH
vi. Prophylactic fresh frozen plasma transfusion (FFP) is not recommended in non-bleeding neonates receiving therapeutic hypothermia and having deranged coagulation parameters. Coagulation studies are not validated at 33.5ºC, and will give high reading of PT and aPTT & INR.
vii. For reconstitution of PRBC for an exchange transfusion.

6.2.3. Dose: 10 TO 15 ML / KG to be given over 1 hour.

6.2.4. Can be repeated at 8 to 12 hours interval if required.

6.2.5. It increases the level of plasma coagulation factors by 20 % immediately after infusion.

6.2.6. ABO compatible with recipient should be used.

6.2.7. AB type FFP is compatible with red blood cells of all recipients.

6.3. Cryoprecipitate:

6.3.1. Cryoprecipitate are precipitated proteins of plasma, rich in factor VIII, Fibrinogen, von Willebrand's factor and coagulation factor XIII.

6.3.2. ABO compatible with the patient should be used

6.3.3. **Dose:** 5 to 10 ml / kg

6.3.4. It should be given over 30 to 60 minutes

6.3.5. **Indications: (If specific factors concentrate is not available)**

A. von Willebrand's disease

B. Congenital/ acquired deficiency of fibrinogen

C. Hemophilia A

D. Congenital deficiency of factor XIII

E. Actively bleeding patient when Fibrinogen level is less than 100 mg/dL as in DIC or massive blood replacement.

6.4. Platelets:

6.4.1. Thrombocytopenia is the most common haemostatic abnormality in sick neonate.

6.4.2. Platelet transfusions are indicated for the support of selected neonates with clinically significant quantitative or qualitative platelet disorders.

6.4.3. Guidelines for platelet transfusion in the neonate acknowledge the lack of evidence on which to make recommendations and aim for a safe approach.

6.4.4. Experience from allo-immune thrombocytopenia indicates that in a well term neonate, the risk of significant hemorrhage as a result of thrombocytopenia is unlikely at counts above 25×10^9/L

6.4.5. Early thrombocytopenia has a consistent pattern with nadir around day 4 and recovery of platelets number by day 7 to 10 of life.

6.4.6. **Indications:** Recommended threshold of platelets transfusion in neonates see **appendix 3.**

6.4.7. **Amount of transfusion** - 10 to 15 ml / kg.

6.4.8. Transfusion on higher side is preferable so as to raise the platelet count sufficiently and to avoid repeated platelet transfusions.

6.4.9. **Rate of transfusion: -** Transfuse as soon as possible and should be completed in about 20 minutes in term babies & 30 minutes in preterm babies.

6.4.10. After one hour of platelet transfusion, platelet count can evaluate its survival in circulation.

6.4.11. Choice of Platelets **see appendix 4.**

6.4.12. Ideally same blood group platelets should be used for transfusion.

6.4.13. Only ABO type specific is taken into consideration in newborns. Rh system is not considered while transfusing platelets, because neonates do not mount immunological response (sensitization to Rh type does not occur).

6.4.14. If same group of platelets is not available, if possible, use SDP (single donor platelets), because it contains less plasma compared to MDP (multiple donors' platelets or pooled platelets) or apheresis platelets.

6.4.15. Avoid transfusion of group O platelets in AB group of patients, unless situations are critical and other choice is not available. Ideally if O group is being given to other groups and especially to AB blood group, high and low anti A & anti B antibodies titers, should have been done, and high antibodies titers should be avoided.

6.4.16. In newborns and especially extremely low birth weight babies, blood volume and plasma volume is less, the impact of incompatible platelets is going to be more.

6.4.17. Risk of mismatched repeated platelets transfusion is even higher and leads to platelets refractoriness & less platelet recovery.

6.5. Intravenous Immune Globulin Uses in the Fetus and Neonate (IVIG):

6.5.1. Indications: see **appendix 5.**

6.5.2. IVIG **rate calculation** (Increase the infusion rate gradually if well tolerated)

A. 0.5 mL/kg/h for first 30 minutes, then

B. 1 mL/kg/h for second 30 minutes, then

C. 2 mL/kg/h for third 30 minutes, then

D. The remaining should be given on a maximum rate of 4 mL/kg/h (For patients with renal dysfunction or at risk of renal dysfunction, Maximum rate is 2 mL/kg/h)

6.5.3. Continuous monitoring during and after the infusion is recommended.

6.5.4. The following vitals should be monitored:

A. 10.5.1. HR, BP, Respiration, Temperature, & Oxygen Saturation.

B. 10.5.2. Prior to the start of infusion.

C. 10.5.3. After 15 minutes of IVIG initiation.

D. 10.5.4. Prior to each rate increase.

E. 10.5.5. Once maximum rate is achieved.

F. 10.5.6. Within 60 minutes of completion of the infusion.

6.6. Hazards/Complications of Blood Products Transfusions:

6.6.1. The following should be observed for:

6.6.2. Transfusion-related circulatory overload (TACO).

6.6.3. Febrile non-haemolytic transfusion reactions (FNHTR).

6.6.4. Severe allergic reactions (Anaphylactoid reactions or anaphylaxis).

6.6.5. Minor allergic reactions (Urticaria).

6.6.6. Transfusion associated infections HIV, Hepatitis (B, C), syphilis, Transfusion-transmitted – CMV.

6.6.7. Post-transfusion Purpura (PTP).

6.6.8. Transfusion-related Acute Lung Injury (TRALI).

6.6.9. Transfusion-associated graft versus host disease.

6.6.10. Complications of massive transfusion: (Hypothermia, Coagulopathy, Hypocalcaemia, Hypomagnesaemia, Citrate toxicity, Lactic acidosis, Hyperkalemia, Hypoglycemia).

6.7. How to prevent complication of blood transfusions:

6.7.1. Immuno-sensitization can be avoided by use of leucocyte depletion filter.

6.7.2. CMV risk can be reduced by use of CMV negative blood or use of leucocyte depletion filter.

6.7.3. Graft versus host disease can be prevented by irradiation (2500 rads).

6.7.4. Use of multiple pediatric transfer packs (satellite bags) allows Infant to receive multiple transfusions in times of need from the same bag (donor)

7. Responsibilities:

7.1. Head of Pediatrics shall:

7.1.1. Ensure that all doctors are aware of Guidelines of Blood Transfusion in Neonate Intensive Care Unit.

7.1.2. Ensure that this guideline is updated as per guideline of DGKH.

7.2. Pediatrician shall:

7.2.1. Identify the babies who need blood products.

7.2.2. Explain to parents about need of the blood products.

7.2.3. Administer blood products according to this policy.

7.2.4. If any complications occur, discontinue transfusion immediately, to be notified to blood bank immediately.

8. Document History and Version Control

Document History and Version Control			
Version	**Description of Amendment**	**Author**	**Review Date**
01	Initial Release	Dr. Satish Bhandari	2017
02			
03			
04			
05			
Written by	**Reviewed by**	**Approved by**	
Dr. Satish Bhandari			

14. References:

Title of book/ journal/ articles/ Website	Author	Year of publication	Page
Use of Blood Components in Newborns, Clinical Practice Guidelines.	NNF India	2020	99-124
Intravenous Immune Globulin uses in the Fetus and Neonate: A Review Antibodies	Basel	2020	
BC PBCO Intravenous Immune Globulin (IVIG) Utilization Management Program Guidelines	BC Womens Hospital Health Centre, UK	2014	
Randomized Trial of Platelet-Transfusion Thresholds in Neonates	N Engl J Med	2019	242-251
Blood Component Transfusion in a Tertiary Care Hospital	J Pediatr.	2020	339–344
Neonatal Transfusion Recommendations at RCH, Melbourne,Australia	https://www.rch.org.au		
Effects of ABO Matching of Platelet Transfusions in Critically Ill Children	Pediatr Crit Care Medicine	2019	
Neonatal and pediatric platelet transfusions: Current concepts and controversies	Curr Opin Hematol	2019	
Recent advances in transfusions in neonates/ infants. F1000Research, 7, F1000 Faculty Rev-609.	Goel, R., & Josephson, C. D.	2018	
Transfusion practices in Neonates	Korean J Pediatr	2018	
Neonatal Plasma Transfusion: An Evidence-Based Review :	Transfusion Medicine Reviews	2016	
Neonatal Thrombocytopenia and Platelet Transfusion	Robert Carr a Anne M. Kelly b Lorna M. Williamson	2015	

Coagulation indices in very preterm infants from cord blood and postnatal samples:	Journal of Thrombosis and Haemostasis	**2015**	
Neonatal thrombocytopenia: causes and management.	BMJ JOURNAL		
Interpretation of clotting test in neonate	Sanchita Pal,	2015	
Blood components transfusion : AIIMS Protocols in Neonatology	AIIMS Protocols	2019	
Blood Transfusion Clinical Practical Manual, Neonatal Transfusion Guidelines.	London Health Sciences Centre	2019	
Intravenous Immunoglobulin IVIG For newborn use only.	NMF Consensus Group	2018	
Intravenous Immunoglobulin Guideline	The Royal Children's Hospital Melbourne	2018	
Clinical Transfusion: International society of blood transfusion.	International Society on Blood Transfusion	2018	

Appendixes 1:

Gestational age	< 28 weeks	28 – 34 weeks	30 – 36 weeks	Term neonates
PT 95th centile (s)	> 21	> 21	> 16	> 16
aPTT 95th centile (s)	> 64	> 57	> 55	> 55
Fibrinogen 5 th centile, mg/Dl	71	87	225	150
INR abnormal if.	> 2	2	1.6	1.6

Appendixes 2:

Postnatal week	No respiratory support (gms/ dL)	Respiratory support of any kind (gms/ dL)
1	10 – 12	11 – 13
2	8.5 – 11	10 -12.5
≥ 3	7 – 10	8.5 – 11

Appendixes 3:

Platelet count (mm3)	Indication for platelet transfusion
< 25,000	Neonates with no bleeding (including neonates with Neonatal Alloimmune Thrombocytopenia (NAIT) with no bleeding and no family history of ICH)
< 50,000	Neonates with bleeding, current coagulopathy, before surgery, or infants with NAIT if previously affected sibling with intracranial haemorrhage

< 100,000	Neonates with major bleeding or requiring major surgery (e.g., neurosurgery)

Appendixes 4:

Blood group of the baby	Platelet type **First choice**	Platelet type **Second choice**	Platelet type **Third choice**	Platelet type **Last choice**
A	A	AB	B	O
B	B	AB	A	O
AB	AB	B	A	O

O	O	B	A	AB

Appendixes 5:

Suggested Clinical Indications of IVIG Use in Fetuses & Neonates

	Clinical Indications	IVIG Dose
1	Immune hemolytic disease of the new-born (HDN)	0.5 to 1 gm/ kg
2	Fetal Alloimmune Thrombocytopenia (FNAIT)	0.5 gm/kg*, 1gm/kg **
3	Neonatal Alloimmune Thrombocytopenia (NAIT)	1 gm/kg x 2 days
4	Neonatal immune - mediated thrombocytopenia (ITP)	1 gm/ kg
5	Neonatal Enterovirus infection	2 gm/kg
6	Neonatal Parvovirus infection	1 gm/kg x every 3 weeks x 8 months
7	COVID -19 related neonatal disease	2 gm/kg
8	Gestational Alloimmune Liver disease (GALD)	1 gm/kg weekly from 18 wks till delivery
9	Primary Immune deficiency	0.4 – 0.5 gms/kg monthly (IgG level 500 to 800 mg /dL for life)
10	Neonatal Lupus	1 gm/kg
11	Neonatal Myasthenia gravis	2 gm/kg
12	Neonatal Kawasaki disease	2 gm/kg

No siblings with ICH (standard risk) *, a previous sibling with ICH (high risk) **Recommended by ACOG

Routine IVIG use in alloimmune hemolytic disease of the new-born should not be recommended. However, its targeted use for selected neonates with immune mediated Haemolytic Disease of the New-born (DCT +) in whom the TSB is rising despite intensive phototherapy for 4 hours or the TSB level is within 2 to 3 mg/dL (34-51 umol/L) of the exchange level, is more likely to benefit than harm and remains prudent.