

“To be or not to be”

“Complications Of Neonatal Transfusion”

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Confessions

1. I'm a Neonatologist.
2. I'm here to share my clinical experience

How common is Neonatal transfusion?

- ❖ >90% of ELBW & >60% of VLBW infants receive at least One RBC transfusion during their NICU stay.

Maier RF, Sonntag J, Walka MM, Liu G, Metze BC, Obladen M. Changing practices of red blood cell transfusions in infants with birth weights less than 1000 g. J Pediatr 2000;136:220-4.

- ❖ A 2011 meta-analysis “Restrictive vs Liberal” transfusion regimen:
 - (1) fewer transfusions and lowered donor exposures,
 - (2) no differences in mortality, serious morbidity at discharge,
 - (3) no differences at 18 to 21 months CGA in mortality, major morbidity, and serious neuro-developmental impairment.

Whyte R, Kirpalani H. Low versus high haemoglobin concentration threshold for blood transfusion for preventing morbidity and mortality in very low birth weight infants. Cochrane Database Syst Rev 2011;(11):CD000512.

Journey of “Mini Cooper”

- Preterm infant born at 26+3 weeks
- Mother presents with APH
- At birth very pale, floppy and with HR <60
- Suboptimal response to Resuscitation
- Does this baby need transfusion?

“What did we use for transfusion”

✗ “Delayed Clamping OR Milking” the Cord

☑ “Emergency O-ve” transfusion (15 ml/kg)

Acute Immune-mediated Transfusion Reactions

- Neonates do not produce red blood cell (RBC) antibodies; any antibodies present are of maternal origin. (1)
- Prior to the first transfusion, neonates must be screened for passively transferred RBC antibodies, including ABO antibodies if non-O RBCs are to be given. (2)
- If the initial screen result is negative, no further testing is needed for the first 4 postnatal months.

1. Floss AM, Strauss RG, Goeken N, Knox L. Multiple transfusions fail to provoke antibodies against blood cell antigens in human infants. *Transfusion*. 1986;26:419–422

2. AABB. Standards for Blood Banks and Transfusion Services. 23rd ed. Bethesda, Md: AABB; 2004

Acute Active Immune-mediated Haemolytic Transfusion Reactions

- Mainly when ABO-incompatible blood administered
- Unlike adults: fever, hypotension and flank pain, usually are not identified.
- Neonates may present with: \uparrow plasma free Hb, hemoglobinuria, \uparrow potassium and \downarrow pH.
- Diagnosis: DAT/Coombs test
- Treatment: Supportive
- Prevention: Minimise human errors

Acute Passive Immune-mediated Haemolytic Transfusion Reactions

- Mainly in surgical settings
- Quantity of ABO-incompatible plasma in the supernatant of platelet and RBC transfusions
- Minimise the risk:
“Platelets containing incompatible plasma can be volume reduced and RBC may be washed”

Anaphylactic Reactions

- Preformed IgE antibody against an allergen in the donor plasma.
- RANTES released by stored platelets .
- Severe reactions related to anti-IgA antibodies.
- Treatment: epinephrine, steroids, or both as well as intubation and vasopressors if needed.
- Prevention: washed cellular products.

“Mini Cooper on NICU”

- Uneventful transfer to the unit
- Stable on the ventilator

BUT

- Enthusiastic SHO (first day on NICU) is worried:
“Could this be because of Blood Transfusion?”

Transfusion-related acute lung injury (TRALI)

Two cumulative events:

1. Linked to patient:

underlying sepsis, trauma, hematologic disease, or postsurgical status.

2. Related to transfusion of potential neutrophil primers:

such as inflammatory cytokines, active lipids, or AN/HLA alloantibodies.

Pathogenesis:

Antibodies bind to patient's WBCs → adhere & alter pulmonary capillary endothelium → fluid leak into alveoli.

Transfusion-related acute lung injury (TRALI)

- Although donor HLA antibodies have been implicated in TRALI, most products containing these antibodies do not cause TRALI. (3)
- Blood components from postpartum women commonly contain anti-HLA antibodies reactive with the infant, but there are very few reports of TRALI associated with a maternal-infant transfusion. (4)
- Furthermore, these antibodies are not detectable in every case of TRALI.

3. Toy P, Hollis-Perry KM, Jun J, Nakagawa M. Recipients of blood from a donor with multiple HLA antibodies: a lookback study of transfusion-related acute lung injury. *Transfusion*. 2004; 44:1683–1688

4. Yang X, Ahmed S, Chandrasekaran V. Transfusion-related acute lung injury resulting from designated blood transfusion between mother and child. *Am J Clin Pathol*. 2004;121:590–592

Transfusion-related acute lung injury (TRALI)

Recommended “Diagnostic Criteria”: Acute onset of hypoxemia with bilateral infiltrates on chest radiograph

1. Within 6 hours of a blood transfusion and
2. No evidence of circulatory overload.

Patients who have circulatory overload respond to diuresis, but those who have TRALI do not.

Treatment of TRALI is oxygen support and mechanical ventilation, recovery within 96 hours for most patients.

“Mini Cooper on NICU”

- Still stable on the ventilator

BUT

- Contentious Nurse In-charge chased blood results is worried:

“Hb is still only 80 g/dl and baby has already received
15 ml/kg of Blood Transfusion on CDS”

Transfusion Associated Circulatory Overload (TACO)

- Neonates are at increased risk of fluid overload from transfusions.
- In the absence of blood loss, care should be taken to ensure that, volumes infused do not exceed 20 mL/kg.
- Massive transfusions or Exchange transfusions increase risk of metabolic complications

Metabolic Complications Of Massive/Exchange Transfusion

- Hypocalcemia

Citrate binds calcium → Myocardial depression → Prolonged QT
(Cardiac & Ionised calcium monitoring)

- Hyperkalemia

Rapid infusion of Stored RBC through small-gauge needle <24 G
(Rate 3-5 ml/kg/hr)

- Hypoglycemia

Especially if other sources of glucose discontinued during transfusion and use of CPDA-1 RBCs rather than additive RBCs

- Hypothermia

Associated with hypoglycemia, apnea and arrhythmia → cardiac arrest
(Prevented by using a monitored blood warming system with alarms)

“Mini Cooper on NICU”

- Still stable on the ventilator

BUT

- Experienced Registrar is worried:
“Transfusion Associated Necrotising
Enterocolitis”

Transfusion Associated Necrotising Enterocolitis (TANEC)

- Anemia ($Hct < 25$) → hypoxic or immunologic gut injury → blood transfusion → trigger NEC additional changes in viscosity, inflammation, perfusion to gut.
- Stored RBCs – reduced deformability, increased adhesion and aggregation, prothrombotic effects and lead to impaired blood flow, vasoconstriction and thrombus formation.
- Immunologic injury to intestine – similar to TRALI

Transfusion Associated Necrotising Enterocolitis (TANEC)

- Unclear whether is pathogenetic or a epiphenomenal marker.
- Infants with TANEC were more premature, had lower birth weight, likely to have PDA, or receive ventilatory support
- Overall quality of the evidence is low to very low: inconsistency among the studies, the lack of a consistent definition, and heterogeneity amongst the patient groups (5-13)

5. Hay S, Zupancic JA, Flannery DD, et al. Should we believe in transfusion-associated enterocolitis? Applying a GRADE to the literature. *Semin Perinatol* 2017; 41:80.
6. Christensen RD, Lambert DK, Henry E, et al. Is "transfusion-associated necrotizing enterocolitis" an authentic pathogenic entity? *Transfusion* 2010; 50:1106.
7. Josephson CD, Wesolowski A, Bao G, et al. Do red cell transfusions increase the risk of necrotizing enterocolitis in premature infants? *J Pediatr* 2010; 157:972.
8. Blau J, Calo JM, Dozor D, et al. Transfusion-related acute gut injury: necrotizing enterocolitis in very low birth weight neonates after packed red blood cell transfusion. *J Pediatr* 2011; 158:403.
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10. Singh R, Visintainer PF, Frantz ID 3rd, et al. Association of necrotizing enterocolitis with anemia and packed red blood cell transfusions in preterm infants. *J Perinatol* 2011; 31:176.
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12. Mohamed A, Shah PS. Transfusion associated necrotizing enterocolitis: a meta-analysis of observational data. *Pediatrics* 2012; 129:529.
13. Stritzke AI, Smyth J, Synnes A, et al. Transfusion-associated necrotising enterocolitis in neonates. *Arch Dis Child Fetal Neonatal Ed* 2013; 98:F10.
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“Mini Cooper on NICU”

- Still stable on the ventilator

AND

- Parents arrived & updated on clinical progress
- They are relieved

BUT

wish for Mini to have a:

“Designated or Directed Donation”

“Blood Donation Screening”

- First time donor: 17-65 year, >50 kg, 125 g/dl
- Questionnaire: health, lifestyle, travel history, medical history and medication
- Specialist Questionnaire: screen for vCJD.
- Screening for Infectious Agents:
 1. Mandatory tests: Hepatitis B/C, HIV/HTLV & syphilis.
 2. Additional tests (performed special circumstances): CMV, Malaria, WNV & T Cruze

Limitations: “Current Screening Programme”

- Testing limited to only “few” infectious agents
- “Parasites & Prions” only based on questionnaire
- “Window period” donations
- Limited & variable use of “Pathogen Inactivation”

Risks: “Designated or Directed Donation”

- Designated donations are not safer than volunteer community donors.
- Designated donors have a higher prevalence of positive tests for hepatitis B and C attributed to a different demographic composition of the directed versus non-directed donor populations.
- Directed donors may be more reluctant to admit to deferrable risks during the donor interview.

Own Concerns: “Associations”

1. Broncho-pulmonary Dysplasia
 2. Intra-ventricular haemorrhage
 3. Retinopathy of Prematurity
 4. Neuro-Developmental Outcomes
- ❖ The causal relationship is still not clear and little is known of the underlying patho-physiology of this relationship.

Own Concerns: “TA-GVHD”

- Immunosuppressed recipient unable to recognise transfused immunocompetent T-lymphocytes
- Highest risk in extreme pre-terms receiving:
 - 1) Intra-uterine or Exchange transfusion
 - 2) Designated or directed transfusion.
- Late manifestation & increased morbidity/mortality
- Pre-transfusion irradiation:
 - ↓ shelf life ↑ potassium concentration ↔ risk of TT-CMV

Own Concerns: “Human Factors”

- Need & Complications associated with placement and use of Intra Venous Catheters
- Identification errors (of patients, blood samples and blood components) by hospital staff are the root cause of “most wrong blood into patient” incidents, including ABO-incompatible transfusions.

Conclusion

1. The safest blood transfusion is always the “one not administered”.
2. When a transfusion is needed, it is important for all stakeholders to be aware of its potential “acute and delayed adverse effects”
3. Adverse consequences may be minimized through “early recognition and prompt therapeutic intervention”.

“Questions?”

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