TRALI, TACO, and other Transfusion Complications

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Evolution of Transfusion Practices

• 1665 - The first Blood transfusions of record take place. Animal experiments conducted by Richard Lower, an Oxford physician started as dog-to-dog experiments and proceeded to animal-to-human over the next two years.

• 1678 - Transfusion from animals to humans, having been tried in many different ways, was deemed to be unsuccessful, and was subsequently outlawed by the Paris Society of Physicians because of reactions, many resulting in death.

• 1795 - In Philadelphia an American physician, Philip Syng Physick, performed the first known human Blood transfusion, although he did not publish the particulars.

• 1867 - English surgeon Joseph Lister utilized antiseptics to control infection during Blood transfusions.

• 1873 to 1880 - Physicians in the United States are documented, during these years, to have transfused milk (from cows and goats) to humans.

• 1884 - Saline infusion replaced milk as a ‘Blood substitute’ due to increased frequency of adverse reaction to milk.

• 1901 - Karl Landsteiner an Austrian physician, and the most important individual in the field of Blood transfusion, documented the first three human Blood groups (based on substances present on the red Blood cells), A, B and O.

• 1902 - A fourth main Blood type, AB was found by A. Decastrello and A. Sturli.

• 1915 - At Mt. Sinai Hospital in New York City, Richard Lewisohn was documented to have used sodium citrate as an anticoagulant which was to, in the future, transform transfusion procedure from one that had to be performed with both the donor and the receiver of the transfusion in the same place at the same time, to basically the Blood banking system in use today.

• 1939 and 1940 - The Rh Blood group system was discovered by Karl Landsteiner, Alex Wiener, Philip Levine and R. E. Stetson and was soon recognized as the cause of the then majority of transfusion reactions. Known as the Rhesus (Rh) system, once this reliable test for this grouping had been established, transfusion reactions became rare. Identification of the Rh factor has stood next to ABO as another important breakthrough in Blood banking.

• 1971 - Hepatitis B surface antigen (HBsAg) testing of donated Blood began in the United States.

• 1979 - A new anticoagulant preservative, CPDA-1, which extends the shelf life of whole Blood and red Blood cells to 35 days, increasing the Blood supply and facilitating resource sharing among Blood banks is introduced.

• 1985 - The first Blood screening test to detect the probable presence of HIV was licensed and implemented by Blood banks in the United States.

• 1987 - Two tests for screening for indirect evidence of hepatitis C were developed and implemented: hepatitis B core antibody (anti-HBc) and the alanine aminotransferase test (ALT).

Global Prevalence

- Number of units of red blood cells (RBC’s) transfused per 1000 citizens:
  - United States: 50 units
  - United Kingdom: 40 units
  - Western Australia: 28 units
  - Denmark: 54 units
  - Europe: 4 – 73 units
Risks vs. Benefits

When to transfuse?

- Blood loss > 10 – 20% of the pt’s EBV
- Hemoglobin < 7 – 8 g/dL
- Hematocrit 21 – 24%

Do we only assess numbers??

- Do not transfuse based on lab values alone.
- Assess comorbidities and surgical procedure.
- Are signs of hypovolemia present?
- Are signs of decreased tissue oxygenation present?

Measures to avoid transfusion

- Attempt to prevent anemia or early recognition and treatment of anemia.
- Correction of anemia and replacement of lost iron stores before an elective surgery.
- Replace lost blood volume with crystalloid or colloid solutions to maintain normovolemia.
- Good anesthetic and surgical management.

Transfusion Approaches

- Trauma – aggressive
- Standard – conservative

- 5 million people die worldwide each year due to trauma.
- Trauma remains a leading cause of death worldwide and 30%–40% of patients with trauma die secondary to hemorrhage.
- Trauma induced coagulopathy
- Lethal triad: coagulopathy, acidosis, hypothermia.
Massive Transfusion Protocol

- Adults - 10 or more units of RBC’s in 24 hour period
- Pediatrics – 1 unit of RBC’s x age in years in 24 period
- Limit crystalloid infusions

Predetermined Ratio Approach

- RBC: plasma: platelets – 1:1:1
- Pediatric ratio unknown
  - more susceptible to hyperkalemia than adults
  - more studies needed
- May decrease occurrence of coagulopathy → decreased blood products transfused

Complications of Transfusion

- Electrolyte disturbances
- Hypothermia
- Coagulopathy
- Hemolytic reaction
- Febrile reaction
- Anaphylactic reaction
- Transfusion Related Acute Lung Injury (TRALI)
- Transfusion Associated Circulatory Overload (TACO)
- Immunosuppression
- Graft vs. Host disease

Common Complications

- Electrolyte disturbances
  - hyperkalemia
  - hypocalcemia
- Coagulopathy
  - dilutional thrombocytopenia
  - lack of coagulation factors
- Hypothermia
  - increased blood loss
  - increased risk of transfusion
  - worsens hyperkalemia, hypocalcemia, and coagulopathy
Electrolyte Disturbances

- Hyperkalemia
- Hypocalcemia

Coagulopathy

- Dilutional thrombocytopenia
- Lack of coagulation factors

Hypothermia

- Increased blood loss
- Increased risk of transfusion
- Worsens hyperkalemia, hypocalcemia, and coagulopathy

Transfusion Reaction Classifications

- Hemolytic
- Non-hemolytic
- Delayed
- Immediate
- Immunological
- Non-immunological

Acute Hemolytic Reaction

- ABO incompatibility
- Intravascular hemolysis
  - occurs through activation of the complement system.
- Severe reaction
  - dependent on amount of volume given
  - reaction can occur with as little as 10-15 mls.
- Mortality rate is 1 in 30 persons

ABO Compatibility
Signs & Symptoms

- Fever
- Chills
- Hypotension
- Tachycardia
- Nausea
- Lumbar and substernal pain
- Hemoglobinuria
- Dyspnea
- Oozing in the surgical field
- Skin flushing
- Death

Treatment

- Immediate cessation of the transfusion
- Liberal administration of isotonic fluids
- Sodium bicarbonate
- Osmotic diuretics
- FFP
- Platelets
Delayed Hemolytic Reaction

- Caused by antibodies to non-D antigens of the Rh system
- Occurs after a subsequent RBC transfusion
- Extravascular hemolysis
- Generally a mild reaction
- 2-21 days after transfusion

Signs & Symptoms

- Malaise
- Jaundice
- Fever
- Hemoglobinuria
- No increase in hematocrit
- Decreased hemoglobin
- Increased serum unconjugated bilirubin

Tests and Treatment

- Test: Direct Coombs test
- Treatment: primarily supportive

Non-hemolytic Transfusion Reactions

Febrile Reaction

- Most common of reactions
- Symptoms
  - Increased temperature
  - Chills
- Treatment is symptomatic
  - slow transfusion rate
  - antipyretics
  - subsequent transfusions with leukocyte poor PRBC’s

Anaphylactic Reaction

- Due to an Immunoglobulin A deficiency.
- Autoantibodies develop against IgA.
- Requires only several milliliters of transfused blood for a severe reaction to occur.
**Signs & Symptoms**

- Hypotension
- Bronchospasm
- Dyspnea
- Loss of consciousness
- Respiratory arrest
- Shock

**Treatment**

- Immediate cessation of the transfusion
- IV fluids
- Epinephrine

**TRALI**

TRALI was the leading cause of transfusion related fatalities in years 2005-2009.

British Journal of Anesthesia:

TRALI is the most common cause of major morbidity and death after transfusion.

United States Food and Drug Administration. (2009). Fatalities reported to FDA following blood collection and transfusion.


- Due to an interaction between transfused blood products and the recipients WBC’s.
- WBC’s aggregate in the pulmonary microvasculature → congestion → noncardiogenic pulmonary edema.

**Signs & Symptoms**

- Pulmonary edema in the absence of cardiac deficiencies.
- Dyspnea
- Marked hypoxemia
- Fever
- Hypotension
- Chest X-Ray typical of Acute Respiratory Distress Syndrome
- Death
Treatment

- Immediate cessation of transfusion
- IV fluids
- Support of vital signs and respiratory system
- Diuretics are not indicated

TACO

- Presenting symptoms indistinguishable from TRALI
  - tachycardia
  - dyspnea
  - tachypnea
  - pulmonary edema
  - jugular vein distension
  - hypertension
  - hypotension
- Cardiogenic pathogenesis of pulmonary edema.

Susceptibility

Patients:
- decreased cardiac reserve
- Pneumonia
- anemia
- coronary heart disease

Procedures:
- pneumonectomy
- multiple lobectomy

Prevention

- Susceptible patients:
  - Transfuse slowly, not to exceed 1ml/kg/hr
  - Administer a pre-transfusion diuretic
  - Monitor central venous pressure
  - Place in a semi-Fowler’s position

TRALI or TACO??

- Brain Natriuretic Peptide (BNP) can be used to differentiate between TACO and TRALI.
  - BNP will be elevated in TACO
  - Post-transfusion to pre-transfusion ratio of 1:5 is diagnostic.
- anti-HLA or anti-HNA present in plasma suggestive of TRALI diagnosis.
**Blood Transfusion Imunosuppression**

- Decreased cell mediated immunity
  - Decreased macrophages
  - Altered T-cell ratios
  - Decreased concentration of cytokines
- Reduced non-killer cell activity

**Graft vs. host disease**

- Occurs 10-12 days post transfusion
- Rare, but usually fatal
- Supportive care
- No specific treatments
- Most common in already immunocompromised patients

**GVHD signs and symptoms**

- Maculopapular skin rash and desquamation
- Fever
- Diarrhea
- Hepatitis
- Pancytopenia

**Global Blood Safety and Availability**

- 65% of all blood donations are made in developed countries, home to just 25% of the world’s population.
- In 73 countries, donation rates are still less than 1% of the population (the minimum needed to meet basic needs in a country). Of these, 71 are either developing or transitional countries.
- 42 countries collected less than 25% of their blood supplies from voluntary unpaid blood donors, which is the safest source.
- 31 countries still reported collecting paid donations in 2007, more than 1 million donations in total.
- 41 countries were not able to screen all blood donations for one or more of the following transfusion-transmissible infections (TTIs)—HIV, hepatitis B, hepatitis C and syphilis.

**Imunosuppression**

**Risks Associated With Blood Transfusion**

- Risk of death
- Risk of transplant rejection
- Suppression of T-cell activity
- Suppression of B-cell activity
- Risk of transmission of transfusion-transmissible infections
  - Incidence of graft-versus-host disease
  - Carrageen proliferation in blood lymphocyte cultures
  - Natural killer cell activity
  - Helper T-cell function
  - Leukocyte function

**Tranexamic Acid**

- Antifibrinolytic agent
- Alternative to blood transfusion?
Cell Salvage

• Used to decrease the need for allogenic blood transfusion and associated complications.
• Three phases:
  – Collection
  – Washing
  – Re-infusion
• Salvaged RBC hematocrit ~ 50 – 80%
• Transfuse within 6 hours

Risks of Cell Salvage

• Coagulopathy
• Obstetrics
• Enteric content contamination
• Sickle-cell disease