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Quality and Safety in Transfusion Therapy through Haemovigilance

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Contents

Foreward

National Blood Transfusion Service (NBTS), with a vision to be a unique model for the world, is a nationally coordinated network comprising of 83 blood banks. The system has been strengthened island wide with the establishment of Cluster Management System to ensure the fair distribution on man power, material, technology & monitoring to all the blood banks in the country.

The establishment of Hospital Transfusion Committees (HTC) in almost all hospitals with blood bank facilities is one activity done under the above policy. The NBTS together with the HTCs will fulfill the mission of ensuring the quality, safety, adequacy and the cost effectiveness of the blood and blood products. An important component in achieving this aim is Haemovigilance, where the entire process of transfusion is carefully monitored and the untoward effects are either minimized or prevented.

The National Haemovigilance Unit of Sri Lanka was established on the 4th May 2009 and since then it has been actively collecting data on transfusion related reactions, processing them, investigating and implementing corrective actions. This publication will act as a guide for the clinicians to diagnose, treat and report all adverse reactions observed in recipients of blood and blood products.

Dr. Ananda Gunasekara
Director,
National Blood Transfusion Service.

Introduction

Transfusion of blood and blood products is an essential part of healthcare. Decision to transfuse blood or blood product must be taken after carefully weighing the benefits against the risks that could lead to severe morbidity or even mortality.

Many of these risks are preventable; therefore every effort must be taken to evade such events. Correctly used blood and blood products provide numerous clinical benefits and will even save lives.

The provision of safe transfusion therapy has therefore become a basic requirement of advanced medical care.

Haemovigilance is an integral part of modern day transfusion practice and is a tool to improve the quality of the transfusion chain. The word 'haemovigilance' was coined in France in 1991. It is derived from the Greek word 'haema'= blood and the Latin word 'vigilans'= watchful. In other words it simply means "Traceability" or being able to trace each individual unit of blood, blood component or blood product from the donor to it's final destination, whether this is a patient, manufacturer or disposal.

The Haemovigilance unit of Sri Lanka was established on the 4th of May 2009 at the National Blood Centre with the aim of actively monitoring the untoward effects in the transfusion process, and to take corrective/ preventive actions. This will help to minimize the repetition of such events. The ultimate goal will be to improve the safety of blood transfusion.

All hospitals in Sri Lanka report any form of untoward effect that occurs during the transfusion process to the Haemovigilance unit. These reports are compiled to a final report. This Haemovigilance report will be used for future decision and policy amendments and as a training guide. It will also be used as a key tool to raise awareness among clinicians regarding transfusion reactions and to gain knowledge on how to minimize them.

1. Clinical Transfusion Practice

1.1 Appropriate use of blood

Appropriate transfusion is defined as the transfusion of safe blood products to manage clinical conditions with a significant risk of morbidity and mortality that cannot be prevented or managed effectively by other means. Appropriate use of blood reduces the potential risks of blood transfusion.

Adequate documentation of the transfusion process as well as its outcome is needed wherever transfusion therapy is practiced. Local policies and procedures that reflect the best national and international transfusion practices should be available.

Local policies and procedures should include guidance on:

- Informed consent.
- Request of blood products.
- Collection of blood samples for pre transfusion testing.
- Collection of blood products from the hospital blood bank or other sites.
- Delivery of blood products to where the transfusion is to be given.
- Administration of blood products.
- Care and monitoring of patients receiving a transfusion.
- Documentation of transfusion.
- Management and reporting of adverse events.
- Staff responsibilities and the training required for these procedures.
- Management of donor with positive results for TTI.

1.2 Prescribing Blood Products

Prescribing blood products is normally the responsibility of a clinician and he/she should ensure that transfusion therapy is given only when clearly indicated and that the patient is appropriately monitored during the transfusion procedure.

1.3 Consideration while prescribing blood:

- What improvement in the patient's condition am I aiming to achieve?

- Can I minimize the blood loss to reduce the patient's need for transfusion?
- Are there any other treatment modalities that I should consider before giving blood?
- Are there any specific clinical or laboratory indications for transfusion?
- What are the risks of transmitting infectious agents through the available blood products?
- Do the benefits of transfusion outweigh the risks to this particular patient?
- Have I recorded my decision to transfuse and the reasons for transfusion on the patient's chart?
- Will a trained person monitor this patient and respond immediately if any acute transfusion reactions occur?
- Will I use a blood transfusion for myself or my dear one in this condition?

1.4 Informed Consent to Receive a Transfusion

This requires that patients be provided with information and an explanation of the purpose for which blood products are being prescribed and that they consent to transfusion. Although most patients will be prepared to give consent for a transfusion after receiving appropriate information, some will seek detailed reasons for the transfusion, information on the risks involved and the alternatives available.

Some patients may refuse transfusion for personal or religious reasons, for example members of the Jehovah's Witnesses faith. Some of these patients may be prepared to accept plasma fractions or other alternatives.

The seeking of informed consent, together with the reasons for the transfusion, should be recorded in the case notes of the patient. The prescribing physician should understand that the patient has the right to clarify any queries that he or she may have.

1.5 Requesting Blood Products

The blood and blood products should be requested by sending a duly filled request form to the blood bank. Only the medical officers can place the orders. The request form must:

- Contain the correct identification details of the patient.
- Provide details of any previous transfusion or obstetric history.
- State the reason for transfusion.
- Mention the blood product and the quantity required.
- Have the phlebotomists name and signature.
- Have the name and signature of the medical officer who ordered the blood products.
- Contain the urgency of the transfusion.

Blood is dispensed only against a fully completed request form received from the hospital medical officer. This will ensure,

- the right product is made available to the right patient at the right time.
- in providing suitably matched compatible blood for patients.

Patients who cannot be reliably identified at the time of admission must be given an identification band with a unique number. This number must be used to identify this patient when requesting blood and blood products.

1.6 Collecting blood samples for pre transfusion testing

The following principles must be observed when collecting blood samples for pre transfusion testing.

- At the time of drawing blood samples the patient must be positively identified. If the patient is conscious and rational, ask the patient to state their name and age/date of birth. If patient is unconscious or irrational alternative identification procedure is necessary. Eg: identification by a close relative and checking the identification band with a unique number.
- Check this information against the patient's B.H.T and details on the request form.

- Collect 5-7 ml blood sample into a leak proof bottle.
- Label the sample, hand written with the following details.
    - Name with initials
    - B.H.T. number
    - Age of the patient/DOB
    - Ward. (hospital)
    - Date and time sample collected

1.7 Important note

Sample labeling:

- Sample bottle must be labeled at the bed side of the patient, at the time the blood is collected by the person who obtained the sample.(after collecting the blood and before leaving the bedside)
- Never delegate sample labeling to a third party.
- Do not label the sample bottles before the sample is obtained. This is an international standard requirement to prevent patient's blood being put into a wrong bottle.

1.8 Time Limits for Infusion after removing from Storage

It is important that blood components are transfused as soon as possible following issue from the blood bank so that the required efficacy of the component is achieved and bacterial proliferation is avoided.

Red Cells

- A red cell unit must be transfused within 30 minutes after being issued from the blood bank.
- If transfusion cannot be started within 30 minutes the unit should be returned without delay to a monitored blood refrigerator for controlled storage.
- Non-medical reasons for delay in starting a blood transfusion should be avoided.
- Transfusion of red cells should be completed within four hours of removal from a blood refrigerator or a validated transport container.
- Red cells must be stored in a refrigerator that is manufactured for the purpose of storing red cell components, has permanent temperature

monitoring and is validated for this purpose. They must not be stored in a ward refrigerator, domestic refrigerator or a refrigerator intended for vaccine storage.

Transfusion should be started as soon as Platelets, Fresh Frozen Plasma, Stored Plasma and Cryoprecipitate are received from the blood bank.

2. Administration and Observation of Transfusion

2.1 Before starting the transfusion check the following

- Patient's name and BHT number on compatibility report and label.
- Donor unit number on compatibility report, label and blood pack.
- Blood group of unit and patient's blood group.
- Expiry date of blood pack.
- Physical check of the pack- Eg: Haemolysis, clots, leaks, etc.

2.2 Starting the transfusion

The size of cannula chosen should depend on the size of the vein and the speed at which the blood is to be transfused.

- Transfusion should be started only after medical officer's 'written orders'.
- Transfusions should be given in clinical areas where patients can be observed by the clinical staff.
- Transfusion should be started only if clinical or nursing staff can observe the patient right throughout.
- Reconfirm patient identification information by a second individual to prevent any human error.
- Hands should be washed before starting a transfusion.
- Before starting the transfusions make sure that there are no air bubbles in the line and the drip chamber is not more than half full.

- Check the patient's pulse, blood pressure, temperature and respiratory rate prior to initiation of the transfusion and record on the patient's records (BHT).
- Initiate the transfusion slowly(1-2 ml/min)
- Record the date and time at which the blood transfusion was started.
- Signature of the person who has started the transfusion is mandatory.
- Visual observation of the patient is often the best way of assessing patients during transfusion. They should be monitored carefully for potential complications of transfusion.
- Check the pulse rate, blood pressure and temperature 15 minutes after the start of each component transfusion. If no reactions increase the rate. For rapid infusions more frequent observations may be required.
- Many serious reactions are apparent within 30 minutes after starting the transfusion of blood and close observation during this period is essential.
- Monitor pulse, blood pressure, temperature again after one hour and at the end.

2.3 Rate of transfusion

The appropriate rate of transfusion may vary significantly according to the clinical circumstances:

- During the first 15 minutes transfuse at a slow rate- approximately 25-50 ml of blood.
- If there is no reaction increase the rate depending on the recipient's haemodynamic status.
- All red blood cell transfusions must be completed within 4 hrs. Transfusion can be completed within 2 hrs in a haemodynamically stable patient. However for a haemodynamically unstable patient it should take up to 4 hrs.
- Patients who are actively bleeding and/or are in hypovolaemic shock will require blood products to be transfused as rapidly as possible.
- Patients with cardiac failure are at risk of circulatory overload and it will be necessary to transfuse slowly and cautiously with frequent monitoring. Concomitant use of diuretics should also be considered.

- For plasma derivatives the product insert provides guidance on specific protocols regarding the administration of the product.

Advice must be sought from the doctor treating the patient if there is any doubt regarding the transfusion process.

2.4 Completing the transfusion

- At the end of the transfusion record the time in BHT.
- The empty bag should be discarded according to the hospital policy for disposing clinical waste
- The blood transfusion compatibility report should be attached to the patient's notes.
- After completing the transfusion observe the patient for ½ - 1 hour.
- Monitor for post transfusion effects as per component transfused and patient.

2.5 Blood Administration Sets and Filters

All blood components, including platelets and plasma, must be infused using transfusion sets with inbuilt filters. Standard filters have a pore size of 170- 200 μ .This helps to remove clots, cellular debris and undesirable particles. Microaggregate filters are not indicated.

Blood administration sets must be used in accordance with the manufacturer's instructions.

- Administration sets may be primed with normal saline or the component being transfused. Dextrose or lactated Ringer's solution should not be used.
- One set may normally be used for transfusing one red cell unit. In the case of a massive transfusion, the set can be used continuously for transfusion of 2 units.
- Each administration set should only be used for 4 hours to minimize the bacterial contamination. The set should be replaced when the filter becomes clogged.
- Transfusing platelets through a giving set previously used to administer red cells is not recommended.

- Administration sets should be flushed with normal saline before and after platelet transfusion if the same set is to be subsequently used for the transfusion of red cells or FFP.
- No drugs should be administered through this line.
- Use of leucocyte filters will help in providing leucodepleted blood.

2.6 Warming of Blood Products

Blood should only be warmed using a specifically designed commercial device (blood warmers) with a visible thermometer and audible warning. Blood and blood components must not be warmed using improvisations such as immersing the pack in hot water, keeping under a hot water tap or keeping on a sterilizer.

Clinical indications for the use of blood warmers:

- Large volumes transfused rapidly, for example > 50 ml/kg/hr in adults and > 15 ml/kg/hr in children.
- Neonatal exchange transfusions.
- Transfusions for patients with clinically significant cold reactive antibodies ('cold agglutinins').

2.7 Infusion Pumps

Electronic infusion pumps may damage blood cells and should not be used for the administration of red cells unless they have been verified as safe to use for this purpose according to the manufacturer's instructions.

2.8 Documentation of Transfusion

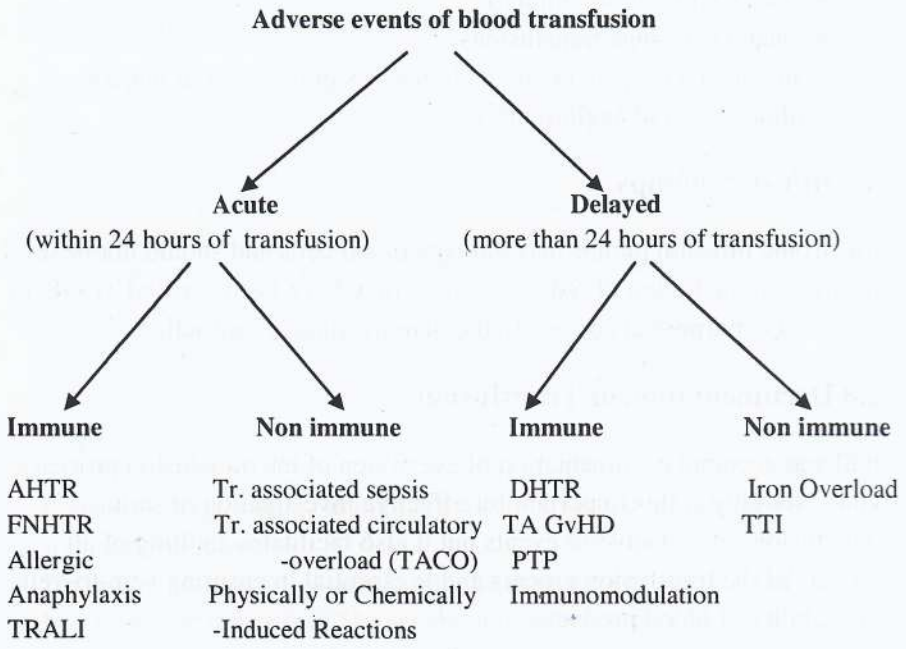
Full and accurate documentation of every step of the transfusion process is vital. Not only is this important for effective investigation of serious transfusion-related adverse events but it also facilitates auditing of all aspects of the transfusion process and is essential in ensuring vein-to-vein traceability of blood products.

3. Adverse Events of Blood Transfusion

Transfusing Blood and Blood products can both benefit and harm the patient. Good clinical practice depends on the correct judgment that the benefits of a transfusion to a patient are justifiable in comparison to the risks.

Blood transfusion has become steadily safer over the years with modern technology being advocated to detect transfusion transmitted infections and the use of better donor selection procedures.

Although the infectious hazards of transfusions have steadily declined over the years, misidentifications and non infectious hazards still account for a significant proportion of the reported transfusion related adverse events.



3.1 Acute Haemolytic Transfusion Reaction (AHTR)

A haemolytic transfusion reaction is the occurrence of lysis or accelerated clearance of red cells in transfusion recipients. This occurs due to incompatible red cells reacting with the patient's Anti A/Anti B antibodies and causing acute severe clinical reactions. This can also occur following transfusion of plasma rich components such as platelets that have high titres of Anti A or Anti B.

Clinical features

- Symptoms- Chills, Flushing, Chest pain, Back pain, Pain at infusion site, Nausea, Vomiting, Abdominal discomfort, Dyspnoea
- Signs – Increase in temperature, Tachycardia, Pallor, Hypotension, Haemoglobinuria, Anuria, Oliguria
- Unconscious patients- Uncontrollable Hypotension, Haemoglobinuria, Oozing from wound or puncture sites due to Disseminated Intravascular Coagulation (DIC).

Laboratory evidence

- Haemoglobinemia
- Haemoglobinuria
- No rise or inadequate rise in hemoglobin following transfusion.
- Positive Direct Antiglobulin Test(DAT)
- Increased Indirect bilirubin

Clerical errors such as collecting the sample from the wrong recipient, mislabeling the recipient's pre-transfusion sample at collection or failing to identify the intended recipient before transfusion are the usual causes rather than the laboratory errors. Therefore, to investigate suspected AHTR, one of the first tests is a recheck of the sample and patient's identification. Early recognition and management of an immune AHTR is crucial in minimizing or preventing associated morbidity and mortality.

Complications

Renal failure develops in up to 36% of patients as a result of acute tubular necrosis. Disseminated Intravascular coagulation develops in up to 10% of patients.

Management

- Stop the transfusion immediately and start supportive treatment.
- Maintain a good IV access.
- Monitor vital signs and urine output.
- Normal saline infusion- to maintain the urine output more than 1 ml/kg/h in adults for at least 24 to 48 hours.
- If urine output low: Frusemide 40 -80 mg IV (1 to 2 mg/kg in children) given to induce diuresis. This dose can be repeated.
- If no diuretic response within 2 to 3 hours: restrict further fluid and diuretic therapy.
- If hypotension develops: Consider inotrope support.
- If shock occurs: low dose of Dopamine and seek urgent critical care/ admit to ICU.
- If anuria develops: dialysis or haemofiltration.
- Repeat coagulation screening and biochemistry 2-4 hourly.
- If renal failure and/or DIC develop: medical consultation necessary.
- If DIC develops with associated impaired coagulation: Blood components (Platelets, Fresh Frozen Plasma and cryoprecipitate) may be necessary.

Prevention

AHTR due to clerical errors can be prevented through careful identification of the patient, correct sample collection and labeling. All intended recipients must be positively identified and blood samples drawn for pre-transfusion testing should be correctly labeled. Two persons should always verify the identification of the recipient and the blood component prior to transfusion.

In the future, computerized systems will be used to verify the patient, samples collected for pre-transfusion testing and the unit of the blood or blood components.

3.2 Febrile Non Haemolytic Transfusion Reaction (FNHTR)

FNHTR is defined as occurrence of one or both of

- Fever ($\geq 1^0$C from pre transfusion temperature) associated with transfusion, for which no other cause is identifiable.
- Chills/rigors

FNHTR is relatively innocuous in itself, but it is important to differentiate it from more serious complications of transfusion particularly AHTR and Transfusion associated sepsis. FNHTR are the most common type of transfusion reaction reported to the Transfusion Service. Severe rigors and temperature elevation $>2^0$C may imply bacterial sepsis.

Cause

- FNHTR have been attributed to the transfusion of white cells present in red cell transfusion and cytokines in platelet transfusion.
- Occurs more frequently in patients who have been pregnant or multi transfused

Clinical features

- Fever with or without chills, flushing, tachycardia

Management

Most febrile reactions are mild; only a rise in temperature is seen without severe symptoms.

- Stopping the transfusion temporarily.
- Maintain an IV line with N. saline.
- Give antipyretics (Paracetamol 1g orally is preferred over Asprin)
- Rule out an acute hemolytic or septic reaction-by initiating a transfusion reaction work-up.
- Clerical check: to determine whether the right unit is given to right patient.
- Send a blood sample from the patient and from the pack to the blood bank: to investigate for an AHTR.
- If no further symptoms and investigations are normal: Restart the transfusion under close observation.

Prevention

The best way to prevent severe febrile reactions is to use pre storage leukocyte reduced blood components. Washed red cells can be given if FNHTR continues to occur in spite of giving leukocyte reduced products.

If a patient is continuously having febrile reactions even for leukocyte reduced blood components, it may be necessary to pre-medicate them with antipyretics such as Paracetamol. But pre-medication with antipyretics may mask the early signs and symptoms of an acute hemolytic reaction or septic reaction.

3.3 Allergic Reaction

Mucocutaneus signs and symptoms occurring during or after transfusion. These reactions are commonly associated with transfusion of components with plasma. Eg: Platelets, FFP.

Clinical features

- Reactions are usually mild.
- Itching, urticaria, rash, flushing, allergic dyspnoea (stridor, cyanosis, wheezing) localized angioedema.

Management:

- Stop the transfusion.
- Give an antihistamine to ease discomfort: Chlopheniramine (4mg orally or 10mg IV) depending on severity.
- Monitor the patient carefully because urticaria could be the first sign of a more serious allergic reaction.
- If the only symptom is skin rash or hives and if there is no progression of symptoms after 30 minutes of treatment: resume the transfusion under close observation for recurrence of symptoms.

Prevention

In a patient with a history of repeated allergic transfusion reactions, premedication with oral or parenteral antihistamine (Chlorpheniramine 4mg)

may be given just before the transfusion or at the start of transfusion. If reactions continue, washed red cells should be considered. Corticosteroids (Hydrocortisone) are indicated only in severe, repetitive cases.

In all cases, even if the transfusion is restarted, a transfusion reaction form should be filled out and sent to the blood bank with other samples for evaluation. If a patient suffers a severe allergic reaction, consult the Transfusion Physician before administering additional blood products.

3.4 Anaphylactic Reaction

These are rare but life threatening complications of transfusion. In addition to mucocutaneus symptoms there is respiratory and/or cardiovascular involvement.
Anaphylaxis may occasionally be associated with antibodies against IgA in patients with absence or extremely low levels of IgA in their plasma.

Clinical features

- Laryngeal symptoms- Tightness in throat, dysphagia, dysphonia, hoarseness, stridor,
- Pulmonary symptoms- Dyspnoea, Cough, bronchospasm, respiratory distress
- Cardiovascular symptoms- hypotension, shock, loss of consciousness

Anaphylactic reactions can be associated with almost any type of blood component and are life-threatening

Management:

- Stop the transfusion immediately and do not be restarted.
- Maintain a good IV access with N. saline.
- Monitor the patient carefully.
- Maintain blood pressure and volume with N. saline infusions.
- Airway management and supportive care is very important.
- Give 0.2 to 0.5 ml of 1:1000 Epinephrine subcutaneously or IM. (Children: 0.01 mg/kg, with a maximum dose of 0.3 ml subcutaneously). This dose can be repeated as necessary.

- In extreme emergencies: Give 0.05 to 0.2 ml of 1:1000 solution diluted to 1:10,000 is given IV slowly.
- If bronchospasm occurs: Give Aminophylline (6mg/kg) infusion with an antihistamine (Chlorpheniramine 10mg IV). May need a corticosteroid (IV Dexamethasone or IV Hydrocortisone)
- If hypoxia develops: Give oxygen by nasal catheter or mask. Endotracheal intubation may be necessary.

Prevention:

Patients with a history of anaphylactic reactions or IgA deficiency with anti-IgA antibody should receive only washed red blood cells. If plasma or platelets is needed, it must be obtained from a known IgA deficient donor.

3.5 Transfusion Related Acute Lung Injury (TRALI)

TRALI is characterized by acute respiratory distress and non cardiogenic pulmonary oedema developing during or within 6 hours of transfusion. It is often the donor plasma that contains antibodies against the patient's leucocytes. Transfusion-related acute lung injury (TRALI) is indistinguishable from adult respiratory distress syndrome (ARDS).

Clinical features

- Presentation within 4-6 hrs of transfusion
- Acute respiratory distress and non cardiogenic pulmonary oedema
- Hypoxia, Hypotension, fever
- Chest X ray shows bilateral pulmonary infiltrate
- Normal CVP

Management

- Stop the transfusion immediately.
- Prompt and vigorous supportive therapy is essential.
  - Administration of oxygen administration
  - Intubation and mechanical ventilation if necessary.

(General supportive therapy started very early, leads to recovery without long-lasting sequale.)

- Corticosteroids are often used, but their effectiveness has not been proven.
- Diuretics: not effective.

Prevention

Patients who develop TRALI are unlikely to have another reaction because it is most often donor specific. If TRALI is diagnosed, the blood bank should be notified. The implicated donor should be identified and should be permanently deferred from future donations.

When any blood component is required for these patients, discuss with the Transfusion Physician to select safe blood products.

3.6 Transfusion Associated Circulatory Overload (TACO)

This can occur when too much fluid is transfused or when the transfusion is too rapid, especially to patients with poor cardiac reserve. Fluid overload can lead to systemic and pulmonary venous engorgement. As a result, they develop heart failure and acute pulmonary edema.

Clinical features

- Respiratory distress
- Tachycardia
- Increased blood pressure within 12 hours of completion of the transfusion.
- Diagnosis is typically supported by signs of cardiogenic pulmonary oedema in the chest X-ray along with a positive fluid balance and/or a known compromised cardiac status.

Management

- At the first sign, place the patient in a sitting position and stop the transfusion.
- If symptoms progress: treat with oxygen and IV diuretic (Frusemide 20 to 40 mg IV)
- If acute heart failure occurs: standard medical treatment should be initiated immediately.

Prevention

Avoid transfusion of whole blood and unnecessary fluids for the patients with poor cardiac reserve. Concentrated components such as red cell concentrates should be transfused slowly over a period not exceeding 4 hours. If the recipient cannot tolerate the transfusion for 4 hours, the blood bank can split a unit into divided doses. Diuretics can also be given prior to transfusion or in mid transfusion but should not be added to the blood bag.

3.7 Transfusion Associated Sepsis

The recipient has evidence of infection post transfusion, and there is no evidence of an alternative source of infection. Sources of bacteria in blood components includes contamination from skin organisms of the donor at the phlebotomy site due to ineffective skin disinfection, transient bacteremia in donors and rarely contamination during handling and processing of components.
Bacterial contamination is more likely in components stored at room temperature such as platelets.

Clinical features

- fever (temperature rise from baseline of ≥1.5°C)
- rigors
- nausea / vomiting
- diarrhea
- tachycardia (≥120 beats per minute or change from baseline of ≥40 beats per minute)
- hypotension or hypertension (fall /rise in systolic blood pressure of ≥30 mm Hg)
- haemolysis
- shock
- multiple organ failure during or immediately after the transfusion

Management

- Stop the transfusion immediately.

- Inform the patient's physician immediately.
- Start broad spectrum IV antibiotics active against gram positive negative and anaerobic bacteria provided the patient is not already on IV antibiotics.
- Examine the implicated component for the presence of bacteria by gross examination and a microscopically.
- The component and the patient's blood: cultur for aerobic and anaerobic bacteria using sensitive blood culture system.

Prevention

Sterility should be maintained in all procedures of collection, handling, and storage of blood components. Blood components should be inspected prior to transfusion for any abnormal color, opacity, hemolysis or clots. Suspected units should not be issued for transfusion. The blood bag should be spiked using aseptic technique with a new transfusion set.

Transfusions should be started as soon as the units are available (at least within 30 minutes) and the transfusion completed within 4 hours. If the transfusion cannot be started within 30 minutes the unit should be promptly returned to the Blood Bank for proper storage. The transfusion set should not be used for more than 4 hours.

3.8 Physically or Chemically Induced Transfusion Reactions (PCITR)

Physically or Chemically Induced Transfusion Reactions are a heterogeneous group of transfusion reactions include mechanical or physical RBC damage, hypothermia, Citrate toxicity, Hyperkalemia or Hypokalemia and Air embolism.

Physical damage to RBC:

- Excessive warming
- Erroneous Freezing
- Intravascular lysis by Hypertonic or Hypotonic solutions.

Mechanical damage:

- Trauma from extracorporeal devices

- Infusion under pressure through small- bore needles.

Clinical features

Many of the clinical signs and symptoms of PCITR are non specific. Common signs and symptoms are Facial numbness, generalized numbness, muscle twitching, chills, arrhythmias, altered respiration, nausea, vomiting and anxiety.

Management

The management is directed at correcting the underlying cause of the signs and symptoms.

Prevention

Precautionary measures are the best strategies to avoid PCITR.

3.9 Other Acute Adverse Reactions of Unknown Pathophysiology

3.9.1 Transfusion Associated Dyspnoea (TAD)

Respiratory distress within 24 hours of transfusion that do not meet the criteria of TRALI, TACO or allergic reaction and is not explained by the patient's underlying condition.

3.9.2 Acute Pain Transfusion Reaction (APTR)

APTR have recently been described and are characterized by abrupt onset of severe pain in the trunk and proximal extremities shortly after discontinuation. The cause is unknown.

3.10 Delayed Hemolytic Transfusion Reaction (DHTR)

Delayed Hemolytic Transfusion Reactions are due to secondary immune response following re exposure to a given red cell antigen. A few days after transfusion there is a rapid increase in the antibody concentration, resulting

in destruction of transfused red cells. Primary exposure can be a previous blood transfusion, transplant or a pregnancy.

Clinical features

Signs and symptoms usually appear 5-10 days post transfusion.

- Fever
- Failure of Haemoglobin to rise
- Jaundice
- Haemoglobinurea (rare)
- Hypotension and Renal failure (rare)

Laboratory evidence

- Evidence of extra vascular haemolysis
- Presence of alloantibodies in post transfusion sample

Management

- Treatment is rarely necessary.
- Monitor the urine output and renal function should be monitored.

Prevention:

Responsible red cell allo antibody should be identified and red cell units negative for the corresponding antigen should be transfused in future.

The interval between the sampling and the transfusion is important in repeatedly transfused patients to detect newly developing antibodies. Following table can be used to collect the samples for pre transfusion testing.

Patient transfused within	Sample to be taken not more than
3 – 14 days	24 h before transfusion
15 – 28 days	72 h before transfusion
29 days to 3 months	1 week before transfusion

When RBC allo antibodies are identified, an antibody card should be issued by the transfusion service with the details of the allo antibody and the patient should be advised to provide this information when hospitalized for blood transfusions. Transfusion service or the hospital blood bank should be notified immediately when a patient with previously identified antibodies requires blood.

All patients who need blood transfusions should be questioned regarding previous transfusions, transplant and pregnancies and this information should be noted in blood transfusion request forms.

3.11 Transfusion Associated Graft vs Host Disease(TA-GvHD)

Transfusion associated Graft vs Host Disease (TA-GvHD) is highly fatal and is usually caused by the engraftment of immunocompetent lymphocytes in an immunosuppressed recipient. It can also occur when transfusing cellular blood components to those with shared haplotypes (1st degree relatives).

Blood components implicated in TA-GvHD are Whole blood, Packed red cells, Platelet concentrate and Buffy coat (cellular blood products).

Patients at risk:

- All immunocompromised patients
- All newborn and premature babies
- Recipients of cellular blood components from family members
- Recipients of HLA matched blood components

Clinical features

Clinical features appear 1-2 weeks after transfusion.

- Fever
- erythematous skin rash
- Diarrhoea
- Deranged liver functions with or without Jaundice.
- Pancytopenia

Management

There is no effective treatment of TA-GVHD and the mortality rate is extremely high.

A number of drugs have been used in acute GVHD such as Cyclosporine, Methotrexate and Steroids but the role of these drugs is uncertain.

Prevention

TA-GVHD can be prevented by gamma irradiation (25 Gy) of cellular blood components including red blood cells, platelets, and granulocytes before transfusing to susceptible recipients.

Fresh frozen plasma and cryoprecipitate do not need to be irradiated. Leukocyte reduction by filtration does not prevent graft versus host disease.

At risk patients should be given a card indicating that irradiated blood components should be transfused.

3.12 Post Transfusion Purpura (PTP)

Post Transfusion Purpura is an acute episode of severe Thrombocytopenia occurring about a week after a blood transfusion. PTP typically occur in middle aged or elderly women, although it can rarely affect males. It usually affect Human Platelet Antigen(HPA)-1a negative women who have previously been alloimmunized by pregnancy.

Blood components implicated in causing PTP are Whole blood, Red cell concentrates and platelet concentrates.

Clinical features

Rapid onset and severe thrombocytopenia and bleeding about 5-12 days after transfusion.
Platelet count fall from normal to $<10X10^9/L$ within 12-24 hours.

- Wide spread purpura
- Bleeding from mucus membranes, Gastro intestinal and urinary tract.

Treatment

- This condition is generally self limiting and untreated patients recover in approximately two weeks.
- Most patients with PTP are treated with corticosteroids (Prednisolone 2mg/kg or an equivalent alternative preparation) but there is little evidence of the efficacy of this treatment.
- Infusion of high-dose Intravenous Immunoglobulin (IVIG) 2 g/kg administered in divided doses for 2-5 days is the current treatment of choice.
- Plasma exchange is effective in some patients.
- Platelet transfusions are usually ineffective, but may have to be given in large doses to control severe bleeding in the acute phase.

Prevention

The patient should be given a card to indicate that he/she had PTP and "special" blood is required.
All transfusions of red cells and platelets should be obtained from donors negative for the relevant HPA antigen.

3.13 Iron overload

Iron overload is a well known consequence of chronic red cell transfusion therapy in transfusion dependent patients. The body has no mechanism for excreting excess iron, and regular transfusions inevitably leads to accumulation of iron. The organs mainly affects are the skin, endocrine glands, liver and heart.

Clinical features

- Skin pigmentation
- Diabetes mellitus
- Development delay in children
- Cirrhosis
- Heart failure
- Arrhythmias

Management

Treatment with iron Chelators such as Desferrioxamine.

Parenteral Desferrioxamine should be initiated early in the course of chronic transfusion therapy. Current practice is to start Desferrioxamine when serum ferritin values reach 1000 mg/l or when 10-20 transfusions have been given. Newer oral iron chelators (Deferiprone) are also available.

4. Reporting a Transfusion Reaction

In the event of a transfusion reaction the staff should notify the Transfusion Service as soon as possible.
If an especially severe reaction has occurred, a phone call to the on call Transfusion Physician might assist the clinical team in managing the patient.

The following should be sent to the blood bank

- Accurately completed "Transfusion Reaction Notification Form"
- Implicated blood /component unit with attached infusion set
- Post transfusion blood sample (10 cc clotted sample & 2 cc EDTA sample)

All adverse reaction following a transfusion of blood or a blood product should be investigated by the respective blood bank

Once the laboratory evaluation is completed, the blood bank physician will review the case, provide a final diagnosis, and issue recommendations.

In addition all "Near Miss" events should be notified. A near miss is any error or omission which if undetected could have resulted in the determination of a wrong group, issue, collection or administration of an incorrect, inappropriate or unsuitable component or product but which was recognized before the transfusion took place.

If an adverse event currently unknown or unrecognized, is seen it should be reported under "other types of reaction".

All reactions should be reported to the Haemovigilance unit by the blood bank irrespective of the outcome of the patient.

For all serious adverse events fully completed Adverse Events Notification Form should be submitted to the National Haemovigilance Unit within 7days. 'In case of mild reaction or near miss event it should be submitted at the end of the month.

List of serious adverse events

- Acute Haemolytic Transfusion Reaction
- Incorrect blood transfusion even there is no symptoms and signs.
- Delayed Haemolytic transfusion reactions
- Anaphylaxis
- Transfusion Related Acute Lung Injury
- Transfusion Associated Graft vs Host Disease
- Post Transfusion Purpura
- Transfusion Associated Circulatory Overload
- Transfusion Associated Sepsis
- Transfusion Transmitted Infections

The information received at the Haemovigilance unit is strictly confidential. It will not be possible to identify any patient, staff member or hospital from the Haemovigilance report released by the Haemovigilance unit.

Abbreviations

AHTR- Acute Haemolytic Transfusion Reaction

APTR- Acute Pain Transfusion Reaction

ARDS- Adult Respiratory Distress Syndrome

CVP- Central Venus Pressure

DHTR- Delayed Haemolytic Transfusion Reaction

DIC- Disseminated Intravascular Coagulation

FNHTR- Febrile Non Haemolytic Transfusion Reaction

HTC- Hospital Transfusion Committee

PCITR- Physically or Chemically Induced Transfusion Reactions

PTP- Post Transfusion Purpura

TACO- Transfusion Associated Circulatory Overload

TAD- Transfusion Associated Dyspnoea

TA-GvHD- Transfusion Associated Circulatory Overload

TRALI- Transfusion Related Acute Lung Injury

TTI- Transfusion Transmitted Infections

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