Government of Newfoundland and Labrador

Department of Health and Community Services
Provincial Blood Coordinating Program

INVESTIGATION OF ADVERSE TRANSFUSION REACTIONS	NLBCP-006

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Overview

All adverse reactions shall be immediately reported to the Transfusion Medicine (TM) Laboratory. The TM Laboratory shall investigate all reports of serious adverse reactions to determine the probable cause. The investigation shall include appropriate laboratory tests.

Policy

1. The TM Laboratory shall investigate all reports of adverse reactions. The investigation shall determine the probable cause and shall include appropriate laboratory tests.
2. An investigation is conducted if a preliminary inquiry indicates that the root cause of the adverse reaction is attributable to an activity carried out by the facility. Any establishment which has received implicated blood component or product must be notified.
3. All adverse reactions shall be documented.
4. Donor units and recipient blood cultures shall be sent to the Microbiology/Bacteriology Laboratory whenever there is investigation of suspected transfusion transmitted bacterial contamination.
   4.1. It is not necessary to send empty donor unit bags to Microbiology/Bacteriology Laboratory for culture.
5. The following procedures and tests shall be performed **as soon as possible** to rule out an Acute Hemolytic Transfusion Reaction:
   5.1. Clerical check;
   5.2. Visual inspection of post-transfusion specimen for hemolysis;
   5.3. Direct Antiglobulin Test, post-transfusion specimen;
   5.4. Regrouping of recipient's pre- and post-transfusion specimens, implicated blood component unit and other units transfused within 6 hours of the reaction (if available).
6. The anti-human globulin (AHG) reagent used for a Direct Antiglobulin Test shall contain antibodies to IgG and the C3 component of complement (polyspecific AHG).
7. The following tests shall be performed on pre and post transfusion samples, if pre-transfusion samples are available:
   7.1. Direct Antiglobulin Test on pre-transfusion specimen (if not performed during pre-transfusion testing) if post–transfusion specimen is positive;
   7.2. Repeat Indirect Antiglobulin Test (Antibody Screen) on recipient's pre- and post-transfusion specimens;
   7.3. AHG crossmatch of implicated unit and other units transfused within six hours of the reaction (if available) using recipient's pre- and post-transfusion specimens.
   7.4. Gram stain and culture of implicated unit(s) if required;

7.5. Blood cultures (from recipient prior to antibiotic therapy) if required;
7.6. Urinalysis; and
7.7. Additional testing as requested by physician.

8. Transfusion reactions due to plasma protein products are documented on an adverse events form and forwarded to the TM Laboratory.
9. Transfusion reactions with suspected hemolysis due to IVIG require the following tests to be performed on the post-transfusion sample:
   9.1. ABO/RH testing;
   9.2. Indirect antiglobulin test (IAT);
   9.3. Direct antiglobulin test (DAT);
   9.4. Elution (if required). When testing the eluate ensure reagent A_1 cells and B cells are included. This will identify passively acquired anti-A1 or anti-B as IVIG may contain blood group antibodies which cause a positive (DAT) and hemolysis; and
   9.5. Additional testing as requested by physician.
10. The TM Laboratory shall report to Health Canada within 15 days of learning of a serious and/or unexpected adverse reaction which is attributable to the quality and/or safety of a blood component and related to a Health Canada-regulated activity carried out by the TM Laboratory.
11. When a transfusion fatality or other serious, unexpected adverse event occurs that is suspected to be related to an attribute of a donor or a donor unit, the collecting facility shall be notified immediately, within 24 hours, and subsequently in writing.

Guidelines

1. Serological investigation is not required if the only sign/symptom is a mild rash less than 2/3 of the body surface area, pruritus, urticaria, or flushing **UNLESS** ordered by the attending physician.
2. Pink or red discoloration in the post-transfusion specimen but not in the pre-transfusion specimen is suggestive of intravascular red cell destruction and release of free hemoglobin.
3. If post-transfusion specimen is not collected until 5-7 hours after an acute hemolytic episode, hemoglobin degradation products, especially bilirubin, may cause a yellow or brown discoloration of the plasma. Bilirubin may begin to rise as early as one hour post reaction, peak at 5-7 hours, and disappear within 24 hours if liver function is normal.
4. If transfused incompatible red cells have been coated with antibody and not immediately destroyed, the post-transfusion reaction DAT will likely be positive, frequently with a mixed field agglutination pattern. If there is a delay in collection of the post reaction specimen and the transfused cells have been rapidly destroyed, the DAT may be negative.

5. Examination should be performed on the centrifuged supernatant fluid of a freshly collected urine specimen. In acute hemolytic transfusion reactions, free hemoglobin released from damaged cells can cross the renal glomeruli and enter the urine. If previously intact red cells in a specimen undergo in-vitro hemolysis during transportation or storage, misleading free hemoglobin may be present.
6. If blood in the administration tubing and/or the donor unit is hemolyzed, a faulty infusion device or the addition of an incompatible solution may be suspected. For example, 5% dextrose in water will hemolyze red cells.
7. If the blood in the administration tubing is clotted, the use of an incompatible solution may be suspected. For example calcium containing intravenous fluids such as lactated Ringer's solution can cause clots to form in blood.
8. Platelets, due to their storage temperature, are the most common blood component implicated in suspected bacterial contamination reactions.
9. Initiation of treatment for suspected bacterial contamination should be based on the patient's clinical presentation as a delay in treatment may result in severe morbidity or death.

Procedure

1. Collect **post-transfusion specimens, as required:**
   - 1.1. Ethylenediaminetetraacetic acid (EDTA) specimen;
   - 1.2. Urine;
   - 1.3. Specimens for other tests which may be requested by physician;
   - 1.4. A minimum of one set of blood cultures (aerobic and anaerobic bottles) should be collected if there is a combination of symptoms which include fever, tachycardia, hypotension, chills, rigors, nausea, vomiting, diarrhea, dyspnea, oliguria, other signs of shock or a high suspicion of bacterial contamination without sign/symptom presentation.
   - 1.5. Obtain post-transfusion reaction specimens, facility adverse transfusion reaction reporting form, blood unit with compatibility tag attached, administration set and attached IV solutions, if available. In certain circumstances, such as a suspected delayed hemolytic transfusion reaction, the physician or designate may request additional donor unit testing.
2. **Perform a clerical check:**
   - 2.1. Check compatibility tag attached to donor unit for errors. Ensure the blood types of the recipient and donor unit are compatible and that the correct tag is attached to the correct donor unit.

2.2. Ensure that the recipient's name and unique identification number on the pre-transfusion specimen, requisition and worksheet match exactly with the name and unique identification number on the compatibility tag.

2.3. **If a clerical error is discovered:**

2.3.1. Notify Transfusion Medicine Supervisor or designate, and the attending physician or designate;

2.3.2. Initiate a search of records to determine if other patients are at risk due to error; and

2.3.3. Review the recipient's transfusion history (if available) for previous adverse transfusion reaction.

3. **Confirm proper labeling of the post-transfusion sample.** The label on the post-transfusion specimen(s) must include recipient's name, unique identification number, the date/time of collection and the identity of the phlebotomist**.** Ensure the recipient's name and unique identification number on the post transfusion specimen(s) matches that on the adverse transfusion reaction reporting form.

4. **Perform a visual check for hemolysis.** Centrifuge post-transfusion blood specimen and visually compare the color of the plasma to pre-transfusion specimen for evidence of hemolysis/icterus. If hemolysis is observed in post-transfusion specimen, a second specimen should be obtained to confirm the hemolysis in the first specimen was not due to improper collection technique.

5. **Perform Direct Antiglobulin Test (DAT) on post-transfusion EDTA specimen.** If DAT on post-transfusion specimen is positive, test specimen using monospecific IgG and C3 reagents. If DAT is positive due to IgG and/or C3, perform elution.

6. **Perform ABO/ Rh typing on pre and post-transfusion specimens**. If post-transfusion ABO/ Rh typing differs from the pre-transfusion ABO/Rh typing, notify Transfusion Medicine Supervisor or designate and the attending physician or designate. Initiate appropriate search to determine if another patient may be at risk.

7. **Perform ABO/ Rh typing on donor unit(s).** Notify blood supplier if discrepancy detected.

8. **Perform DAT on pre-transfusion specimen if not performed during pre-transfusion testing.** If DAT on pre-transfusion specimen is positive, test specimen using monospecific IgG and C3 reagents. If DAT is positive due to IgG and/or C3 and the recipient has been transfused or pregnant within the past three months or the recipient's transfusion history is unknown, perform elution.

9. **Perform an Indirect Antiglobulin Test (IAT) on pre and post-transfusion specimens using original pre-transfusion method.**

9.1. If the post-transfusion IAT is positive, perform an antibody identification;

9.2. If the pre-transfusion IAT is positive, perform an antibody identification; and

9.3. If an antibody is identified, phenotype the transfused units for the corresponding antigen.

10. **Perform an Anti-Human Globulin (AHG) crossmatch on donor unit(s) using pre and post-transfusion specimens.** The AHG crossmatch method must be used for transfusion reaction investigation regardless of original method, i.e. immediate spin, computer crossmatch, or AHG crossmatch.

11. If indicated, following completion of the investigation, forward the transfusion reaction donor unit, administration set(s) and attached IV solutions, if any, to the Microbiology/Bacteriology Laboratory for culture. If transport to the Microbiology/Bacteriology Laboratory is delayed, refrigerate the donor unit, administration set, and attached IV solutions, if any.

12. Enter results of the transfusion reaction investigation into the LIS as per facility policy.

13. Notify the attending physician/designate or nurse with results of serological investigation.

14. Document details of date, time and the name of the person notified.

Materials

1. Blood component unit which was implicated in adverse transfusion reaction, with the compatibility tag attached, the administration set (without needle) and the IV solutions (if any).
2. Pre-transfusion specimen.
3. Post-transfusion reaction blood specimens (EDTA specimen, blood cultures, specimens for other tests requested by physician, correctly labelled.)
4. First voided urine post adverse transfusion reaction, correctly labelled.
5. Blood banking reagents required for testing of specimens.
6. Facility adverse transfusion reaction reporting form or occurrence form (computer or paper).

Quality Control

1. All reagents are used and controlled according to the manufacturer's written instructions.
2. All reagent antisera and red cells are controlled each day of use.
3. All anti-sera must be visually inspected for contamination such as discoloration, cloudiness, turbidity and/or particulate matter.
4. All reagent red cells must be visually inspected for hemolysis.

Key Words

Adverse, transfusion, reaction

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