

Blood Cross-Matching

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ABSTRACT

Blood cross-matching is very essential in any major surgery. Essentially, it is a test that is performed prior to transfusing blood to determine if the donor's blood is compatible with the recipient's blood. The process approximately takes one hour, and it should be performed at least three days prior to transfusion so that it is ready to be transfused for the surgical patient if required.

Strict guidelines should be followed where blood is to be collected, delivered to the lab, and thorough and precise tests should be carried out to produce necessary blood for the recipient patient.

Human errors should be eliminated as they can lead to acute and severe complications. Any infectious diseases should also be eliminated prior to transfusing blood to the recipient.

INTRODUCTION

Blood cross-matching is defined as a procedure to exclude incompatibility between donor and recipient and may include serological tests or electronic cross-matching. In the United Kingdom, the blood donation is voluntary, with only 4% of eligible population regularly donating blood (1). Two million units of red blood cells are used for transfusion every year in the United Kingdom.

The non-utilization of cross-matched blood is an expensive waste of scarce resources (2). The Maximum Surgical Blood Order Schedule (MSBOS) has been advocated as a means of improving the efficiency of using blood for transfusion and is currently extensively used in elective surgical practice (3,4). It is a table of elective surgical procedures which lists the recommended units of blood to be cross-matched on the basis of retrospective analysis of blood usage of the individual surgical procedures (5). Blood is ordered for patients scheduled for an operation according to a locally agreed tariff (expected blood usage). This practice still involves unnecessary cross-matching and consequently over-ordering of blood (6). The British Committee for Standards in Hematology (BCSH) guidelines included pre-transfusion testing, also known as compatibility testing, to ensure quality and safety in blood transfusion (7,8).

There are four stages involved in compatibility testing (7,8):

1. Transfusion history of the patient,
2. ABO and Rh grouping,
3. Antibody screening of both donor and recipient blood,
4. Cross-match

Over the last two decades, the importance of each stage has changed. There has been a shift in focus from the serologic crossmatch to the antibody screen. Blood typing and cross-matching are used by doctors and healthcare workers in appropriate setting to ensure that the right patient is getting the right blood (7,8).

Blood Groups

There are four types of blood groups. O, A, B, and AB. Blood typing test is used to find out the blood group. The presence of certain type of antigens on the red blood cells determines the patient's blood type. Antigens themselves are specific proteins that cause the production of antibodies by the individual's immune system. The process of cross-matching detects major and minor antigens. The ABO is the most important blood group because of the production of antibodies in patients who do not have the right antigens. Wrong red cells by the donor are identified as a foreign body and result in severe transfusion haemolytic reaction. Extremely strict criteria and regulations are applied to reduce the transfer of infection from the donor blood. The screening of blood is done for human immunodeficiency viruses 1 and 2, hepatitis B and hepatitis

C, human T-cell viruses 1 and 2, malaria and West Nile virus. Blood type is inherited. It means that people are born with a particular type of blood type, as they are born with certain types of eye color. The table below gives ABO blood distribution. The table shows, you can see that blood type O is the most common type [12].

ABO Blood Group	Rh (D) Type	% of population with this group
O+	Pos	37%
O-	Neg	7%
Total Blood type O		44%
A+	Pos	35%
A-	Neg	7%
Total Blood type A		42%
B+	Pos	8%
B-	Neg	2%
Total Blood type B		10%
AB+	Pos	3%
AB-	Neg	1%
Total Blood type AB		4%
Total	Pos	83%
Total	Neg	17%

Blood type results are confirmed by mixing anti serum with the blood. If the blood cells agglutinate when mixed with anti-A serum, the blood type is A. If the cells agglutinate when mixed with anti-B serum, the blood type is B. If the blood cells agglutinate when mixed with both serums, then the blood type is AB. Lastly, if the blood does not agglutinate when either serum is added, then the blood type is O. Individuals with blood type O have anti A and anti B antibodies. Individuals with blood type B have anti-A antibodies and individuals with blood type A have anti-B antibodies. An, whereas individual has type A blood, if the blood clumps when only B cells are added. Individuals will have type B blood, if the blood clumps when only the A cells are added. If the blood clumps in both cases, then individual has type O blood and if the individual's blood does not clump when both types of bloods are added, then he has blood type AB [11].

Blood Components

In the UK all blood components are filtered to remove white cells. Blood can be split into different components. Whole blood is very rarely used now days.

Red Cells

Red blood cells or erythrocytes are the most common type. The blood sample has very few white cells and no platelets. The sample is good for up to 14 days and can be stored in suitable conditions to be used for up to 42 days.

Platelets

Platelets in the United Kingdom come from a single donor or from whole donated blood. The platelets suspended in plasma may be stored for up to 4 days. They need to be continually agitated at 22 degrees Celsius to preserve their function. Rhesus compatibility is a must for ladies with childbearing age and children. children to ensure that newborn baby is prevented from hemolytic disease.

Fresh Frozen Plasma

Fresh frozen plasma is produced from whole donated blood, or plasmapheresis. All clotting factors, antibodies and albumin are kept in 150ml bags. Fresh frozen plasma must be used immediately and it must have ABO compatibility. 10-15ml/kg is the normal starting dose [12].

Rhesus System

Rhesus system is one of the thirty-five human blood group systems. This system is genetically the most complex of all blood systems. It involves 45 different antigens on the surface of red cells that are controlled by two closely linked genes on chromosome 1. Rhesus monkeys were initially used to make antiserum for blood typing samples. Hence, the name of the system is named after the rhesus monkey. Serious medical complications can occur due to the Rhesus factor, such as the Abo factors. The major complication does not usually occur after transfusion, but mostly between a mother and her developing fetus. Mother-fetus incompatibility occurs when the fetus is rhesus positive, and the mother is rhesus negative. Fetal red blood cells can be destroyed by the maternal antibodies, which can cross the placenta. The risk increases with each pregnancy. The leading cause of potentially fatal blood-related problems of the newborn is still the rhesus blood type incompatibility. Mother-fetus incompatibility of rhesus type occurs when rhesus negative mother and rhesus positive father give birth to a child. Anti-rhesus positive antibodies may be produced in an individual with rhesus negative as a result of receiving a mismatched blood transfusion. The result of this procedure is that there is likely to be the production of the antibodies throughout life. Hence, it is important to check and investigate for the rhesus blood group type [14-16].

Transfusion

There are various methods for ensuring the availability of blood for elective surgery.

Group and save

group and save involves determining the patient's blood group using the ABO system and screening serum for the presence of antibodies to antigens that can cause severe transfusion reactions. Group and save, group and hold, screen and hold, group and screen, type and screen and group and hold are all the whole blood sample, normally taken into an EDTA tube, which is hand written with four points of reference. It is then transported to the lab, where ABO, Rh (D) type and antibody screening is performed (indirect antiglobulin test, IAT). The antibody

screen involves incubating the patient's serum with pooled Red Blood Cells (RBCs) containing all common RBC antigens. If the antibody screen is negative, the patient can safely have any ABO- & Rh-compatible blood 'off the shelf'. If it were positive, the responsible antibody is identified, and a conventional cross-match is performed [17-18]. The reason for taking a group and save at pre-assessment is that the pros and cons of blood transfusion can be discussed in depth with the patient and informed consent can be obtained. This can be carried out in a calm environment for the patient and the clinician. It also gives time to the lab to identify antibodies before the surgical procedure and organize suitable and compatible blood. The lab may require further information and testing, and this can be carried out without distress. The lab can hold at least one group for the patient in case of any emergency. Depending on the procedure to be carried out, one may require the need for group and save PAC [19]. There may be a need for a blood product due to an underlying condition or as a prevention measure for example prophylactic anti-D. The patient should always have a group and save taken once identified into the at-risk group. The lab's main concerns are antibody status, the validity of the sample, the number of units to be cross-matched, the amount of blood available and WBIT's. (Wrong Blood in Tube). BCSH guidelines state that the sample is valid for 72 hours if the patient is pregnant or transfused in the last three months [20]. The sample is valid for up to 7 days if do not fall in the above cases and the plasma can be used for three months, if frozen. In most hospitals, the current blood product guides states that pre-operative group and save products are used only for antibody screen. Upon admission, if blood is required for theatre, a further group and save sample is required [21,22]. Group and save is processed in a nonurgent manner, and the group is recorded in the patients history. The status of antibody is recorded, and if results are negative, they can be issued it electronically [23-25]. But if the results are negative, then one should investigate, and the details are given to transfusion department to order antigen negative units [26-27].

Cross-match

This is defined as a procedure to exclude incompatibility between donor and recipient and may include serological tests or electronic cross-matching. It refers to the tests that are performed pre-transfusion so as to determine the compatibility of the donor's blood for that intended individual. Blood bank staffs is responsible for providing serologically compatible blood within appropriate time frame. There is a requirement to know the actual blood group and the antibody status. Cross-matching is performed to see any abnormal adverse reactions with the patient's blood when mixed with the samples of the donor in the lab. Number of units of blood is cross-matched if patient needs blood for transfusion. A thumb rule is to order 1 unit of blood to raise the hemoglobin by 1 g/dl in a patient who is not bleeding [28-29].

Cases are discussed in detail with the surgeon and the anesthetist for patients requiring surgery, who will calculate the pre-operative hemoglobin and the likely loss of blood during surgery and patient's tolerance for anemia. It takes 40 minutes or more to crossmatch the patient's blood. The blood is mixed in the lab with some commercially available antibodies against blood types A and

B. If the blood cells stick together to each other, meaning that they agglutinate, it means that the blood has reacted with one or more of the antibodies. Serious adverse effects of blood transfusion do occur sometimes because of human error, despite scientific and technical advances in blood group immunology to make the transfusion of blood a safe procedure. The main reason for cross-matching is to eliminate the transfusion of incompatible cells. The best available way to detect antibodies in the patient serum that might destroy transfused red cells and cause hemolytic transfusion reactions is to test the recipient's serum with donor cells, for this a major cross-match is required. Cross-matching has a number of limitations. A compatible cross-match does not guarantee normal survival of the transfused red blood cells. It does not prevent immunization of the recipient. Also it does not detect unexpected red blood cell antibodies in the recipient serum. Moreover, it does not prevent delayed hemolysis due to an anamnestic antibody response to antigens against which the patient has previous but undetectable immunization. Furthermore, it does not detect all ABO grouping errors in donor or recipient patients. The patients' blood sample has to be less than 72 hours old for testing so that it represents the clear and current immunologic status of the patient [30-32].

The cross-match is incubated at 37-degree celsius to detect agglutinating antibodies. After incubating and washing, anti globulin serum is employed to detect antibodies attached to cells without causing agglutination. Additional solutions such as albumin polymerized albumin, or low ionic salt solutions are frequently added to increase the sensitivity of the cross-match or to reduce the incubation time. An antibody screen is also performed. This antibody screen is important in detecting weak antibodies which may only react with the homozygous screen cells or to detect antibodies present on the reagent screen cells but not on the donor cells. The electronic term cross-matching refers to the blood without direct serological cross-matching, for example, the mixing of patient's plasma with donor red cells. Safety is ensured by computer controls in the transfusion laboratory. The purpose of electronic cross-matching is to respond quickly to blood requests and to reduce the wasting of blood amount that is allocated and to reduce the laboratory workload. This process requires a valid group and saves or cross-match blood sample which is up to date and complies with the local rules and regulations of the hospital and institute's blood transfusion regulations. Also there are no clinically significant antibodies [33]. Individual patients who do not have a current blood sample in the laboratory are not eligible. Other patients who are not eligible are patients with clinically significant antibodies and someone requiring bone marrow and stem cell transplants [35-38].

Complications of Transfusion

Wrong blood in tube

There are a number of incidences causing the wrong blood to end up in the wrong tube. The following are a number of causes of WBIT.

Pre-Labeling of tubes

- i. Failure to identify the patient correctly. This could be due to administration error or patient error.
- ii. Failure to label at the bedside. Labelling not done when next to the patient and possible labeling multiple tubes.
- iii. Distraction or lack of concentration.

Rejection of sample

There could be a number of reasons a sample may be rejected. There could be missing information or incorrect information supplied to the laboratory. Signature and/or date could be missing. Missing details could be names or date of birth to identify a particular individual patient. The sample itself could be old. There could be simple mistakes like illegible hand writing and crossing out of the information or under filled form. The form may not be signed and the blood sample could be hemolysis or lipemic. The request card may not match the patient details. Finally there could be wrong sample or the blood sample could be sent to the lab in the wrong tube [39]. The lab may reject the samples because of patient safety. They cannot take the risk and make any guess work. Best practice is to follow the BCSH guidelines. These guidelines are of 2009 administration of blood components and 2012 guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. 2007 NPSA Safer practice notice of standardizing wristbands improves patient safety. One has to write the patients last name, first name, date of birth and NHS and hospital number. Human error can result in severe reactions and we must ensure that correct blood reaches the correct patient [40-41].

ACUTE HAZARDS

Fortunately, any serious reactions to transfusions are very rare. But any signs or symptoms arising from transfusion must be taken seriously. Administrative errors are the main reason for a serious reaction caused by transfusion. These reactions included ABO incompatibility and immune reactions to other blood components. Incompatibility with ABO transfusion can cause the breakdown of red cells in the circulation, leading to circulatory and respiratory collapse along with renal failure. The start of blood transfusion should be monitored very closely. Bacterial infection transmitted during blood transfusion can lead to sepsis, causing fever, tachycardia, hypotension, rigors and collapse of the patient's body. Fluid overload by rapid transfusion can result in acute left ventricular failure and signs of pulmonary edema [10-15].

LONG TERM HAZARDS

The risk of transmission of infectious diseases now is very rare due to rigorous donor selection, screening process, and transfusion techniques. Regular transfusions as in the case of chronic anaemia can result in deposits of iron in tissues thus leading to tissue injury. The treatment would be to administer desferrioxamine to the patient. The cross-match represents a special form of the IAT in which the red cells used for testing are from the unit intended for transfusion

(Triulzi). It involves incubation of the patient’s serum with donor RBCs; if no reaction occurs, the donor unit is labelled and reserved exclusively for the identified patient for up to 72 hours. Approximately, 95% of transfusions occur in patients with a negative antibody screen, and such patients can undergo abbreviated cross-match testing in which only ABO compatibility of the unit needs to be established (Triulzi). There are two methods for abbreviated cross-match testing; the “Immediate Spin” Cross-Match (**ISCM**) and the Electronic Cross-Match (**ECM**, Computer CM, Electronic Issue). The ISCM detects major ABO incompatibility between donor and recipient and requires only a five-minute incubation at room temperature with patient serum and donor red cells. ABO compatibility is indicated due to the absence of agglutination. ISCM is beneficial as it makes blood availability quick, it is more cost-effective, and 90% of patients are eligible for ISCM. ECM is an abbreviated crossmatch performed by computer verification of ABO/Rh compatibility of donor and recipient without any serologic testing (Onder). Using a validated computer system the bar code on the unit of blood can be required (scanned?) and the computer compares the ABO of the unit to that of the patient and indicates whether it is compatible. ECM has a faster turn-around; the computer prevents the release of ABO incompatible units; lowers the reagent costs and improves the quality control [10-15].

In 1998, a study conducted by Fordyce, suggested the number of units of cross-matched blood per operation as shown in Table 1.

Table 1: Units of cross-matched blood per operation as suggested by Fordyce, 1998.

Suggested numbers of units of cross-matched blood by operation	
<i>Procedure</i>	<i>Order</i>
Radical Neck Dissection	G&S
Excision of tumour & free flap	G&S
Excision of tumour & neck dissection	2 units
Maxillectomy	2 units
Excision of tumour and pedicled flap	2 units
Excision of tumour, neck dissection & free flap	2 units
Excision of tumour & neck dissection & pedicled flap	2 units

Electronic cross-matching requirements include:

- i. There must be two corresponding results of the patients ABO/Rh status on file, one from historical sample and one from the new current sample.
- ii. In the two samples, there must not be any clinically significant antibodies detected in the patient’s serum upon analysis.
- iii. There must be on-site validation of bar code readers and all relevant computer systems.
- iv. There must be procedures in place to validate the data entered is correct before the blood units are released.
- v. The system should completely prevent the release of ABO-incompatible blood.

There are some disadvantages of electronic cross-matching of blood. Some of these disadvantages include the systems failure to detect weak antibodies and the need for extensive computer validation, competency testing, and employee training. There are other impacts of PAC on transfusion. Patient information should be thoroughly investigated. It is important to know the complete details of medication the patient is taking such as when did they stop their previous medications, and do they have any underlying conditions that the lab needs to know? These conditions include; hemophilia and platelets disorders. The lab also investigates if the coagulation screen shows any other possible problems. If the patient is anemic it should be treated before the operation, if possible [13-15,28,34,40,41].

CONCLUSION

Blood transfusion is an integral part of medical care, but it has certain complications. Full and thorough examination of patients should be carried out before the transfusion. Detailed and precise tests should be undertaken on donor and recipient blood. Care should be taken to eliminate any human errors, and not to cause any unnecessary complications. Transfusion should be closely monitored and carried out by the professionals and in the appropriate setting.

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