transplantation
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RECENT ADVANCES IN TRANSFUSION MEDICINE

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ABBREVIATIONS

PCV:	Packed cell volume	FFP:	Fresh frozen plasma
TRALI:	Transfusion related acute lung injury	PRC:	Platelet rich concentrate
TTD:	Transfusion Transmitted Diseases		

KEY WORDS

blood transfusion, blood components, platelet concentrate, fresh frozen plasma, transfusion-transmitted disease.

Blood transfusion is one of the most important milestones of medical science. It is one of the most acceptable therapeutic options where risk-benefit ratio still outweighs the side effects which have been reported to be as high as 20%[1]. A gynecologist did first successful blood transfusion in 1828. Transfusion became safe after discovery of blood group by Landsteiner. First blood bank was established in 1937 in Cook County hospital USA, after invention of anticoagulant. Blood components became routine after the second world war with invention of plastic bag. Blood component therapy evolved as a part of progress of transfusion medicine especially since the limitations of whole blood became more obvious.

LIMITATIONS OF WHOLE BLOOD

(1) Volume over load

(2) Cocktail therapy: Although patient needs one component only, he/she receives all components.

(3) Different components are best preserved at different temperatures e.g. platelets are preserved at 20-22°C, clotting factors are preserved at -18°C, RBCs are preserved at 4^0 C. Since blood is preserved at 4^0 C, platelets and unstable clotting factors are not available.

(4) Each component contributes to side effects thus leading to cumulative side effects to whole blood transfusion.

The only approved indication of whole blood is blood loss of more than two litres. If this guide line is strictly followed only 10 % of total blood demand will be for whole blood.

Blood components are prepared by two methods

(1) **Conventional method** (figure) : Here one unit of blood is tapped from the donor and components are prepared. From a donor only one component of each type is prepared i.e. one packed cell volume (PCV), one platelet concentrate, one unit of fresh frozen plasma (FFP) and one unit of cryoprecipitate. Important features of each component are given in Table 1.

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Component	Volume (ml)	Shelf life	Storage	Contents
Whole blood	350-450	21 d: ACD/CPD 35-42 d: CPDA	2-6° C	RBC, stable clotting (F VIII, V, XI are unstable)
Packed cells	150-200	21 d: ACD/CPD 35-42 d: CPDA	2-6° C	RBC
Platelet rich concentrate (PRC)	30-50	3-5 days on Shaker	20-22° C	Platelets
Fresh Frozen Plasma (FFP)	150-200	1 year	£-18° C	All clotting factors
Cryosupernate	150	21-35 days	2-6° C	Factors not present in Cryoprecipitate
Granulocyte	40-50	24 hours	20-22° C	WBCs
Cryoprecipitate	50	1 year	≤-18° C	Factor VIII, I, XIII, fibronectin, Von-willebrand factor

Table Important Features of Blood Components

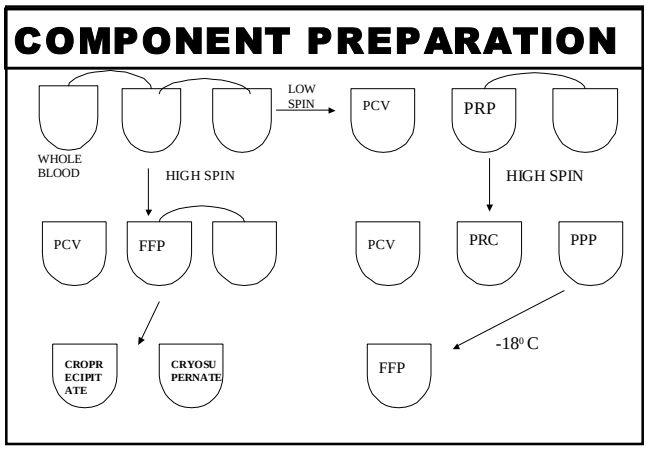

Figure Component Preparation

(2) **Cell separator:** Here blood is tapped and simultaneously the machine separates different components in different bags and returns all other components to the donor. This method is better than the conventional method for several reasons:

- Less WBC contamination: Newer versions of cell separators give 3 log reduction of WBCs, thus eliminating chance of allo-antibody production, transfusion related acute lung injury (TRALI), CMV infection and reduces chance of transfusion graft versus host disease (GVHD) [2, 3, 4].
- One unit of single donor platelet is equal to 8-10 units of random donor platelets, thus reducing donor exposure and alloantibody formation.
- Cell separator can remove 3 units of RBCs or Plasma from a donor thus reducing donor exposure and alloantibody formation. This is very useful with rare blood groups, as donor pool may be very restricted.
- Plasma exchange, stem cell separation, leucopheresis are possible with cell separator only.
- Donor for plasma and platelets can re-donate after 3 days since there is no RBC loss; thereby reducing the chances of donor sensitization.

PACKED CELLS

They should be transfused when there is significant deficit of red cells leading to anemia and blood loss up to 2 liters. Decision to transfuse depends upon the cause and patient's general condition, e.g. a patient with cardiac problem should be transfused if Hb falls below 10 gm %. However a patient with pure iron deficiency whose Hb is 7 gm % may not need transfusion. A patient with autoimmune hemolytic anemia should not be transfused unless he has evidence of hypoxia; transfusion itself is hazardous here. In severe anemia, 2-3 ml packed cells /kg BW should be given in a day. In other conditions, 10 ml/kg BW can be given. An infusion of RBCs, 3 ml/kg BW will increase Hb by 1 gm %. PCV flows as fast as whole blood with 17-18 gauge needle and hence can be used during surgery also [5].

FFP

FFP is indicated in following conditions: clotting factor deficiencies (e.g. hemophilia), oral anti-coagulant reversal, massive blood transfusion, anti-thrombin deficiency, protein C/ S deficiency, open heart surgery and disseminated intra vascular coagulopathy. Use of FFP in thrombotic thrombocytopenic purpura, liver disease and anti-thrombotic agent (streptokinase, urokinase) overdose is controversial.

CRYOPRECIPITATE

It is used in hemophilia A, afibrinogenemia or hypofibrinogenemia, factor XIII deficiency and von-Willebrand disease. One unit contains 80-100 I.U. of factor VIII and 200-250 mg of fibrinogen. Cryoprecipitate can be given irrespective of blood group and does not need cross matching.

PLATELET RICH CONCENTRATE (PRC)

It is used whenever patient has thrombocytopenia /platelet function disorder. Platelet transfusion is reserved for life threatening bleeding or surgery when thrombocytopenia is due to immune mechanism (i.e. ITP, drug induced) or when patient has acquired platelet function disorder (i.e. in uraemia or liver disease). PRC can be given irrespective of blood group and does not need cross matching. Anti-D immunoglobulin, 20 ug per one bag of PRC should be given when Rh-negative person is given Rh-positive PRC to avoid Rh immunization. Platelet count should be 1,00,000 /cmm for any surgical procedure and >60,000/ cmm to arrest a bleeding episode. One random donor platelet contains 8 x 10^{10} platelets while one single donor platelet contains 3x10^{11} platelets[6]. One random donor platelet increases platelet count by 10000/cmm in a person with body surface area of 1 sq.meter.

GRANULOCYTE TRANSFUSION

It is used in neutropenic severe febrile illness and neonatal sepsis. Its use is decreased with easy availability of colony stimulating factors.

IS TRANSFUSION SAFE ?

Each transfusion has 20% chance of transfusion reaction. Majority of the reactions are mild and self-limiting.

- **Major group incompatibility** is almost always an administrative error rather than a technical error[7].
- **Transfusion transmitted diseases (TTD)**

  Various infections can be transmitted by blood transfusion. Commonly encountered infections are HIV, hepatitis B, hepatitis C, bacterial, malaria and CMV. HIV can be transmitted in spite of proper screening as HIV antibodies take an average time of 3 months to develop after infection (known as window period). HBsAg may be negative during acute HBV infection /early convalescence and can be missed. Anti HBc IgM will be positive during this period and it is done routinely in some countries like U.S.A. Like HIV, HCV also can be missed during window period.

As blood transfusion always carries risk of TTD, the following strategies need to be adopted:

1. To exclude donors of high-risk behavior (like drug addict, multiple sex partners, homosexuals). This can be found out by personal interview of the donor or by using self-exclusion form.
2. To screen donor twice at the interval of three months before tapping blood to avoid window period (quarantine).
3. Artificial blood: This eliminates immunization problem and TTD completely. It can be stored in a pharmacy like IV fluid and hence becomes extremely handy during accidents. Many compounds are tried but none is available for routine clinical use.
4. Virucidal method: If this method can be applied to blood components, like in clotting factor concentrate, risk of TTD can be almost eliminated. So far no method is found to be useful for widespread clinical use.
5. Autologous blood transfusion**:** Here patient's own blood is transfused back and hence there is no risk of TTD. There are three ways of giving autologous blood transfusion.

A. Pre-operative Autologous blood transfusion[8].

One unit of blood can be collected every third day for total 5-6 units. Hb should be more than 10 gm % each time. There is no age restriction for donation. Last donation should be 72 hours before surgery. If for any reason surgery is delayed, oldest unit is re transfused and fresh unit is drawn (leapfrog technique). Elemental iron, 5-mg/kg BW/ day, must be given from the beginning to prevent iron deficiency.

B. Acute Isovolaemic haemodilution[9].

Blood is collected just before surgery and can be re transfused after surgery. Due to haemodilution, blood lost during surgery contains less red cells. Blood tapped is replaced by crystalloid (3.0 ml for every 1.0 ml blood) or (colloid 1 ml for 1 ml of blood). Hb should not fall bellow 9 gm % and total blood tapped should not be more than 40 % of patient's estimated blood volume. The volume of blood to be collected is estimated by following formula :

Volume of blood to be removed = Estimated blood volume X (initial PCV – desired PCV) / Mean of (Initial + desired PCV)

Estimated blood volume = body weight (kg) x 70 (adult)/ 80 (pediatric)

Blood should be re-infused within six hours or else should be stored at 4°C.

C. Intra-operative blood salvage[10].

Blood should be re-infused with in six hours. This procedure is used when anticipated blood loss is more than 20 % of blood volume. Four methods are commonly used:

1. Gauze filtration: Blood is collected in sterile container with anticoagulant and filtered using 4-6 layers of gauze pieces.

2. Suction collection devices: reusable or disposable.

3. Semicontinuous-flow centrifugation cell-washing system.

D. Post-operative blood salvage

It is required when blood loss is more than 200 ml or >5 % of total blood volume. Blood must be collected in sterile bottle containing anticoagulant.

WBC removal[11].

Removal of WBCs from the blood components is now a routine practice as it has many advantages:

It reduced incidence of CMV infection, GVHD, HLA antibody production, non-hemolytic febrile reaction, TRALI, etc.

WBC removal in the blood bank can be done using various systems: WBC filter, saline washes, cell separator and various collection systems like Optipress. Saline wash is very cheap method but since it makes system open, it carries risk of infection. Filters are very easy to use but are very costly. Saline wash and various collection systems like Optipress reduce WBC by one log and so are effective in preventing non-hemolytic febrile reaction only while WBC filters and some cell separators reduce WBC by 3 log and hence prevent other side effects also.

WBCs can be removed using WBC filters just before transfusion to the patients. WBC filters achieving 3 log reduction are effective in reducing all side effects except transfusion GVHD while filter producing 1 log reduction (macro-aggregate filter) is useful to eliminate non-hemolytic febrile reaction.

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