PRESERVATION OF BLOOD COMPONENTS BY ADDITIVES TO INCREASE SELF LIFE

Abstract

Blood transfusion (A life-saving procedure) uses whole blood and its element for the treatment. Transfusion of blood fulfil the need and demand of various forms of medical care and thus for blood is frequently amplify. The main motive of blood transfusion is broadly based on a safe and effective blood supply. Whole blood: A mixture of cells, Colloids and crystals, such as red blood cells (PRBC), platelet concentrate, fresh plasma frozen, and frozen, can be divided into several blood components. The utility of a unit of whole blood is maximised by component separation because each blood component has a particular indication. A component must adhere to specific temperature and storage conditions in order to be therapeutically effective. Component treatment has been adopted to ensure adequate blood quality is transfused and to prevent waste. Instead of transfusing complete blood, it entails transfusing a specific component(s). In this chapter we learn about the separation of blood component and blood bags (Single, double, triple, and quadruple bags) use for the storage of different components with suitable preservatives..
The history of storage and the most recent advancements in blood and its component storage techniques are also covered in this chapter. With the addition of preservative solutions, blood and its constituent parts can be preserved in a number of conditions.

Keywords: Introduction, History, Blood Bag System, Component Therapy, Storage and Expiration, , Blood Preservatives

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I. INTRODUCTION

As is common knowledge, blood banks are facilities where transfusion-ready supplies of blood or plasma are stored.

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A blood bank is an area where we donated blood and maintained it for use in blood transfusions in the future. The phrase "blood bank" normally refers to a division of a medical centre, commonly located within a clinical pathology laboratory, where whole blood and its products are stored and pre-transfusion and blood compatibility testing are carried out. However, sometimes collection centre, and some hospitals also perform collection. Blood bank plays an important role in modern medical care.[1] In case of an emergency, they keep blood in advance and can provide it to patients. How then does a blood bank function? Blood is drawn from donors, type-matched (a test transfusion to see how your blood will respond to potential donor blood) and stored or conserved before being given to recipients.

The founder of first blood bank in the country in 1937 at Chicago's Cook County Hospital was Dr. Bernard Fantus. Blood couldn't be kept in storage for more than a few days at the time. Most transfusions, become dangerous process for person-to-person which made it hard to find donors.

Dr. Fantus started testing various blood storage techniques in an effort to find a solution to this issue. He altered the name of the facility from the Blood Preservation Laboratory to "blood bank" because he thought it would be less intimidating to potential donors. The quantity to collect and preservation of blood for a long time revolutionized how medical professionals cared for patients. Blood donation was no longer a dangerous procedure, and patients in need could now get the blood they required to survive. Numerous lives have been saved because of blood banking over the years. Currently, over 13.6 million units of blood are donated annually. Each day, around 36,000 units of blood are required. Blood banks can now keep donations of blood safely and process and test blood to ensure everyone's safety thanks to advancements in medical technology.[2]

II. HISTORY

In 1818, British scientist and obstetrician Dr James Blundell executed the first known transfusion of human blood. Dr Blundell was consulted by a patient suffering from severe bleeding. With no treatment available for this condition back then, Dr Blundell got to thinking. He assumed that if the patient is losing blood, then supplying him with blood would help restore his health. Sounds logical too, right? So, Dr. Blundell injected the patient with 12–14 ounces of blood from numerous donors. Despite these efforts, the patient eventually passed away. Why? Blood groups! Yes, the blood group types were not matched before the transfusion! But there’s no way Blundell knew about this since blood groups weren’t discovered yet. The world, for the first time, got acquainted with the three main blood groups (A, B, and O) after Austrian physician Karl Landsteiner discovered them in 1901. In first blood transfusions, receiver received blood directly from donor before coagulation, later it was used by adding anticoagulant and refrigerating the blood. It was possible to store it for some days, the way of development of blood banks was opening. The first experiment with the use of chemical to prevent the blood coagulation is done in St Mary's Hospital, London,

in the late 19th century by John Braxton Hicks. His attempts, using phosphate of soda, however, were unsuccessful.[3]

On March 27, 1914, the first non direct transfusion was performed by the Belgian doctor Albert Hustin, though this was a diluted solution of blood. The Argentine doctor Luis Agote used a much less diluted blood solution in November in same year. Both choose sodium citrate as an anticoagulant.[1]

1. **Blood Banking Facts:** The American Association of Blood Banks reports that

- 6.8 million volunteers donate blood every year.
- The requirement of blood every day is 36,000 units.
- The donation of blood every year is about 13.6 million units.
- Blood is separated into individual components, included platelets, cryoprecipitate AHF (cryo), a white blood cell, plasma, and red blood cells. One unit of whole blood and its products may used in transfusion for several people. According to their requirement.
- More than 21 million different blood components are transfused every year.

2. **What are the Components Of Blood?**

Although blood or one of its components can be transported, each one also has a variety of other purposes, such as the following:

- **Red Blood Cells:** The cells, who carry oxygen to the tissues and are commonly help in the treatment of anemia.

- **Platelets:** The cells, who help in forming the blood clot and are help in the treatment of leukemia and various forms of cancer.

- **White Blood Cells:** The cells, who help to fight against infection, and aid in the immune process.

- **Plasma.** The liquid, watery composition of blood in which our platelets, WBC, and RBC are suspended. The components of the blood must be transported through the bloodstream through plasma.

  Many functions are serve by plasma, including the following

  - Helps to maintaining blood pressure
  - Provides proteins for blood clotting
  - Balances the levels of Na and K.

- **Cryoprecipitate AHF.** The portion of plasma help in controlling bleeding and contains clotting factors.

  The separation of Albumin, immune globulins, and clotting factor may also be processed for transfusions.

3. **Disposable Blood Bag System:** A disposable bio-medical equipment called a blood bag system is used to collect, store, transport, and transfuse human blood and blood components. The system is made up of one or more blood bags that are connected to one another by tubes, needles, needle covers, clamps, etc. The blood bags are constructed of plastic that is compatible with blood.

   Blood systems have relied on polyvinyl chloride plastic bags with suitable various anticoagulants inside of them since the 1950s because they offer an amazing storage life of up to 49 days. Now, the next generation PVC blood bags are imminent.[13] PVC blood bags allow a long shelf life for the blood. The blood can last up to 49 days when refrigerated. Despite the fact that most blood is used within a few weeks, a storage period of up to 49 days is essential for a number of reasons. Currently, the plasticizer DEHP is used to make blood bags flexible, stabilising the red blood cells and ensuring a long storage period. However, the substance has come under scrutiny by authorities and regulators. The value chain for PVC medical devices is looking for substitute plasticizers to take its place. DEHT is an acceptable replacement, according to the Swedish Karolinska Institute, while BTHC and DINCH, according to recent study by the national Dutch blood bank Sanquin, can take the place of DEHP. The continued availability of blood bags plasticized with DEHP is essential for patient safety in the meantime.

   The technology has been licensed to four Indian businesses with a combined annual manufacturing capacity of 3 million bags, bringing the nation's overall production capacity to 12 million bags. Currently, it is anticipated that the nation as a whole needs 10 million bags annually. However, the product has gained acceptance on a global scale and there is a substantial market demand for it, providing excellent export possibilities.[14]

   A complete line of blood bags created to improve the quality of blood collection, processing, product separation, and storage. All bags have required international licences and certificates. Products can be customized to fit individual and country- specific requirements, including bag configurations, safety methods, filtration and sampling methods.

4. **Single Blood Bag:** The blood bag which is used for collection of whole blood with anticoagulant CPDA-1 solution is single bag system. The single bag system contain primary bag with anticoagulant CPDA-1 (Citrate-Phosphate-Dextrose-Adenine) which preserve red blood cells up to 35 days at 2-6ºC.

5. **Double Blood Bag:** The blood bag system which is used for separation of two components from whole blood is double bag system. The double bag contain anticoagulant CPDA-1 with one empty satellite bag.

6. **Triple Blood Bag:** The blood bag system which is used for separation of three components from whole blood is triple bag system, the triple system contain one primary bag with anticoagulant CPDA-1 solution with two empty satellite bag. Triple SAG-M blood bag system includes CPD anticoagulant solution in primary bag and SAGM solution in another bag and one empty satellite bag.

7. **Quadruple Blood Bag:** The blood bag system which is used for separation of three components of blood through Buffy coat method is Quadruple bag system. Quadruple blood bag system includes anticoagulant CPD solution in primary bag, SAGM solution in second bag with two empty bags.

8. **Top to Bottom Blood Bag:** Top to bottom blood bag also used for separation three components of blood through buffy coat method however it provides process to extract red blood cells from the bottom and plasma from the top side.

III. COMPONENT THERAPY

Instead of entire blood transfusions, component therapy uses specific component transfusions.

. Component therapy are carried out in two ways:

- Separation of blood components through centrifugation method after collection of whole blood or
- Aphaeresis .

The only medical procedure that uses the aphaeresis method is component therapy. Component therapy is a process of removal of blood from the donor, separation of the product needed for transfusion, and after that transfusion of the other components back into the donor.[4]By guaranteeing that one unit of whole blood is utilized in numerous patients, The danger of blood exposure and negative transfusion-related consequences is reduced by component therapy. In cases of severe blood loss, whole blood is transfused. Transfusion of Erythrocytes is done in cases of anaemia; Transfusion of Platelets is done in cases of thrombocytopenia and clotting issues. In cases of liver illness and coagulation factor deficiency, plasma and its accompanying factors are transfused.[5]

IV. WHOLE BLOOD TO COMPONENTS

A specific equipment known as a cooled centrifuge was developed in 1960 to separate blood components from a single unit of whole blood. In contrast to platelet concentrates (PLTCs), PRBC concentrates, and fresh frozen plasma (FFP), only PRBC and fresh frozen plasma (FFP) are manufactured utilising a single-step heavy spin centrifuge. The two primary methods for preparing PLTC are the platelet-rich plasma (PRP) method and the BC method.[6] These two separation techniques are based on Algorithms 1 and 2. The main elements of the basic PRP technique are the PRBC, PLTC or random donor platelet (RDP), FFP, cryoprecipitate, cryo poor plasma (CPP), and Plasma fractionation products.[7]

V. EXPIRATION AND STORAGE

Presently, Whole blood is collected in polyolefin or PVC tubes that have undergone various plasticizing processes, such as triethyl hexyl trimellitate and butyryl-tri-hexyl citrate.[10] In addition to maintaining pH levels above 6, In comparison to first-generation Di-ethyl hexyl phthalate plasticized PVC containers, these bags provide roughly twice the oxygen permeability. In order to maintain the biological activity of the constituents, lower

their metabolic activities, and stop bacteria from growing on the blood components, adequate component storage is required. Red blood cells should be stored between +2°C and +6°C, platelets and leucocytes between +20°C and +24°C, and plasma products should be stored below -18°C, according to standard guidelines. All components must be kept in one of three compartments: untested, tested and safe for release, and tested but unsafe or quarantined for disposal.[11] If available, additional equipment is also needed to keep cross-matched units safe. If kept at recommended temperatures, the components can be transported and stored for a maximum of 24 hours. The PRBC must be kept between +2 and +10 degrees. All parts are routinely shipped and stored at temperatures between +20°C and +24°C.[8] All frozen components should be shipped in a way that keeps them frozen. Either personally inspecting each component for signs of deterioration or using indicators fixed to units are two ways to track and record temperature changes. All blood components should be kept in the cold chain up until the point of transfusion.[9]

1. **The Following are the Storage and Transportation Tools:** Refrigerators (+4–2°C) in which Whole blood and PRBC is stored, as well as thawed FFP and other plasma products stored, Agitators for platelet incubators in which all platelet component is preserved, operating at a temperature of (+222°C) and 70 cycles/minute, Deep freezers (80°C) are used to freeze blood components or FFP. Mechanical blast freezers can quickly freeze materials, and they can store frozen PRBC or platelets at temperatures as low as 65 C. Freezers (40 °C): In which all plasma products is stored at a temperature of −30°C or even lower degrees, Transport containers: Transport containers are used to move blood or blood components quickly between two storage locations. Even blood mobiles are equipped with backup power and built-in cold chain storage systems. The choice to transfuse should not be made solely on the basis of test data, but rather should be preceded by a detailed assessment of each patient's clinical condition. The main objective of transfusion medicine in a health care facility is to ensure that "the right blood is given to the right patient at the right time and at the right place."[12]

VI. BLOOD PRESERVATIVES

1. **For Whole Blood and Erythrocytes:** Rous and Turner reported successful blood preservation in 1916. Blood was stored in the solution and then transferred to rabbits via transfusion. The solution contained citrate and dextrose. Oswald Robertson employed the same remedy during World War I.[15] During the Spanish Civil War and World War II, Loutit and Mollison developed the acid-citrate-dextrose (ACD) solution. For storing whole blood, the CPD solution (citrate, phosphate, and dextrose) was used. However, Simon's inclusion of adenine led to the formation of CPDA or CPDA-1 solutions (adenine, citrate, phosphate, and dextrose). There was a parallel growth of fresh and enhanced storage containers as were many different "additive remedies," each with its own variations on the prior solutions that were accessible.16] Bags allowed to facilitate the separated storage of blood components in place of the antiquated practise of storing blood in bottles, which increased demand for and the supply of solutions for each distinct component. After being collected in a CPD solution, the blood's constituent parts were separated., and each part was subsequently put in a separate vessel.[17] The first erythrocyte storage solution, known as BAGPAM, was developed by Beutler and contained adenine, glucose, mannitol, $NaHCO_3$ sodium bicarbonate (sodium bicarbonate), Na2CO3(sodum carbonate), and Na_3PO_4 (sodium phosphate). [18-19] During storage, the

decrease in ATP in this solution is because of the SAG solution, which is made up of NaCl (saline), $C_5H_5N_5$ (adenine), and $C_6H_{12}O_6$ (glucose). Mannitol was added to the same mixture later to develop SAGM, which is the most widely used commercial RBC storage technique today.[20-23] Mannitol has been demonstrated to significantly lower hemolysis by scavenging free radicals and defending the erythrocyte membrane. Only for 21 days Blood is stored in CPD, however whole blood is stored for 35 days in CPDA-1. On the other hand, SAGM allows the erythrocyte preservation for 42 days.[24-25]

2. **For Platelets:** The existence and role of platelets in haemostasis were first described in the 1870s. However, it wasn't until 1910 when transfused platelets were shown to reduce the risk of bleeding in thrombocytopenic patients.[26] Platelet transfusions weren't routinely available until the 1970s. When Scott Murphy and Frank Gardner discovered that platelets could be kept at 22°C for up to 3 days while still performing their haemostasis function, this became possible. Platelets can now be transfused even after being stored for 5-7 days because to innovations like the use of creative platelet addition solutions (PAS) and better storage containers. Studies are currently being carried out to improve the likelihood of continuous platelet preservation. The majority of the plasma in platelet suspensions is currently replaced with PAS during storage [27]. So there is less likelihood that germs and viruses may contaminate the leftover plasma. It also enhances storage conditions and lessens the negative consequences of plasma transfusion. In PAS, there are various concentrations of glucose, citrate, PO_4 (phosphate), K (potassium), Mg (magnesium), and acetate. Acetate, a substrate which acts as aerobic respiration, keeps the pH in check. The effectiveness and shelf life of preserved platelets are being studied. According to Gulliksson, if ageing of the platelets is avoided, platelets can be preserved for 18 to 20 days at 20 to 24°C with an improved additive medium. Natural life span of platelets is 8 to 12 days. At 22–24 °C with agitation, the shelf life of platelets collected for therapeutic or prophylactic transfusion is now only 5-7 days. The effects of platelet storage lesion (PSL) and the risk of bacterial growth are both reduced by this restriction. PSL is associated with impaired in vivo recovery and reduced post-transfusion hemostasis activity [28]. PSL refers to any detrimental changes that occur from the time blood is collected from the donor until platelet concentrate (PC) is administered to the recipient.[29]

3. **For Plasma:** Because plasma depicts the alterations taking place in blood, it is an excellent biomarker of oxidative stress. Human plasma has a potent antioxidant defence mechanism to counteract changes brought on by storage. Protein sulfhydryl groups have also been shown to have antioxidant properties, and the oxidation of these groups is a sign of protein oxidation [30]. Neutrophils and mononuclear phagocytes that are active, lysed, or dying release the proteases (serine, cysteine, aspartic, and matrix metalloproteases) that are present in plasma. Plasma must be chilled as soon as it is separated to prevent proteases from degrading proteins. Plasma also has the natural ability to inhibit these proteolytic enzymes via protease inhibitors, such as tissue inhibitor of metalloprotease, 2-macroglobulin, and -protease inhibitor. Another approach is to use protease inhibitors in the storage solution. Citrate and ethylene-diamine-tetra-acetic acid (EDTA), two Ca2+ chelators, help to inhibit Ca2+-dependent proteases in addition to preventing coagulation [31].

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