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Review Article

An Overview on Artificial Blood

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ABSTRACT

The 21st century is a challenge for people. Population growth, aging population, generation of new infectious agents, and natural disasters are some of the factors that threaten the status quo of blood transfusions. Artificial blood is designed solely to carry oxygen and carbon dioxide into the body. Depending on the type of blood replacer, it can be produced with a variety of techniques using chemical separation, synthetic production, or recombinant biochemical techniques. The technologies focused on the two major alternatives to blood are perfluorocarbons and hemoglobin-based oxygen carriers (HBOCs). With the availability of blood products, the United States alone is expected to generate more than $ 7.6 billion annually.

HISTORY

The concept of artificial blood sounds simple, but it's not. In 1616, William Harvey first described blood circulation, and scientists began to wonder if blood could be taken and replaced with other liquids such as wine and milk. 6 Milk was one of the first ingredients in 1854, and patients used milk to treat cholera in Asia. The patient died of bleeding due to a serious injury and needed a blood exchange. [1] Since World War II, research on blood proposals has been taken seriously in order to overcome large-scale situations such as private sector events. The composition of blood and the function of each substitution are clear except for the mobility of oxygen. [3] They wanted to change a person's blood for a variety of beneficial effects, including healing of illness and personality. In 1667, the first successful human blood transfusion took place.

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Unfortunately, the patient who received a subsequent blood transfusion died and was discontinued. The ancient Incas were the first recorded cause of blood transfusions. [1] Amberson et al. They conducted experiments on cats and replaced animal blood with cell-free hemoglobin with Ringer's lactate solution, demonstrating that the solution can sustain life [6]. However, the effect was short-lived and the treatment caused serious kidney damage.[9] Amberson et al. They abandoned their study and concluded that hemoglobin solution needed further development due to concomitant nephrotoxicity and vascular hypertension. In the 1950s, the US Navy treated 47 anemia and fever seafarers with one or more injections of free hemoglobin solution.[10]

INTRODUCTION:

To be alive is impossible without blood, the complex liquid containing millions of chemical products and different cells. Blood is a special kind of connective tissue consisting of white cells, red blood cells, platelets and plasma.[1] In the membrane of these cells, proteins that recognize the body as their own. For this reason, the person can only use blood that is compatible with its type. This is the main component of red blood cells, containing about 33% of the cell mass. Artificial blood was highlighted in 1980 after the incidence of HIV due to the risk of blood transfusion transfusion, which imposes the highest cost due to the necessary detection tests.[4] in Japan, the "field of developing artificial blood" in 1997 as a Frontier Advanced Frontier Medical Research Project, so intensive research activities in the three sub-fields, it is artificial red blood cells, artificial platelets and artificial antibodies are performing.[12] Artificial blood is a product that is set as a substitute for red blood cells.[1] Blood replacements: It is also called therapeutic oxygen or oxygen carriers, based on hemoglobin (HBOC): They offer the promise of new and important medical treatments that redeemes.[2] The term "substitute for blood" does not describe the current can accurately describe Didatare products because they usually alone have two functions that transport and increase oxygen and increase blood volume.[9] Today, there is a significant shortage of blood supplies in developing countries, which is inhabited by 80% of the world's population, but has less 32% of the Total blood supplies of worlds collected. Low safety standards. Therefore, artificial blood will be of great value to developing countries. [4] The main purpose of providing an alternative to blood transfusion, conveying the blood product or in the blood of one person to another person. Artificial blood can be safely archived and hospitals and then patients are rapidly administered in emergencies. In addition, patients whose religious beliefs prevent them from accepting blood from donors will benefit from blood substitutes, such as PFC (perfluorochemical) that are not derived from blood products.[2]

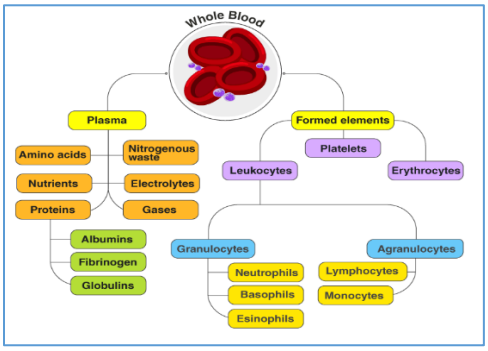

Fig No. 1: Blood components

How to make artificial blood:

Artificial blood can be produced in a variety of ways using synthetic production, chemical separation, or recombinant biochemical techniques. Synthetic hemoglobin products are made from hemoglobin collected from strains of E. coli. Hemoglobin is grown and fermented in seed tanks. [7] This artificial blood is used to reflect the function of biological blood as much as possible so that it is accepted by the body as if it were natural. [13] Premium hemoglobin-producing blood substitutes are based on molecular modifications of hemoglobin, which either chemically cross-link the molecules or modify them using recombinant DNA technology. So-called bifunctional drugs can cross-link hemoglobin molecules to form polyhemoglobin. [6] Special techniques have been developed during surgery to minimize the need for blood transfusions. These techniques included the use of erythropoietin, drug therapy, surgical techniques, and the minimum acceptable levels of hemoglobin and blood substitutes. [3] Unlike red blood cells, blood substitutes can be sterilized by filtration, pasteurization, and chemical cleaning. These steps eliminate the microorganisms that cause diseases such as AIDS and hepatitis.

Surrogate does not have cell membranes containing blood group antigens, so no typing or crossover is required before use.[6]

Composition of artificial blood:

Perfluro-octyl bromide – 28%

FO-9982 – 12%

Yolk lecithin – 2.4%

DSPE -50 H - 0.12%

Distilled water - 48%.[1]

On the other hand, these first generation blood substitutes remain in the body's circulation for only 20-30 hours (normal red blood cells last a few days). We use this term because of the long circulation time. It also does not contain the enzymes needed to protect the body from oxidants such as oxygen radicals[6]. The most promising blood products developed as blood substitutes are oxygen transporters based on perfluorocarbons and hemoglobin. PFC is a long chain compound similar to Teflon and has the ability to carry oxygen [14]. Even in the second generation alternative, the hemoglobin molecule is not protected by the red blood cell membrane. Therefore, researchers are working on a more complex third-generation blood substitute that encapsulates the hemoglobin contained in artificial red blood cells and the necessary enzymes [6].

Perfluorochemicals (PFCs):

Perfluorinated chemicals (PFCs) are colorless, non-abrasive, and are clearly water-resistant at low temperatures for fragrance and cannot be washed off with water and alcohol.

In addition to particle size, PFCs containing carbon 9-11 should be used as a substitute for abnormal blood to be completely removed from the body after parental control [2].

Fig No 2: Perfluorochemicals

PFC has vertical or cyclic hydrocarbon fibers containing the general chemical structure of CnF2n+2, and the vertical type is oxygen better than the cyclic type. [4] The PFC can cause flu in some patients when 'They move these compounds. [2] The advantage of perfluorocarbons is that they allow increased solubility of oxygen in plasma, PFC does not react with oxygen. PFC allows oxygen to be transported more rapidly into the body and reduces the effects of factors such as pH and blood temperature.[5] perfluorinated chemicals are an inert substance that can break down oxygen 50 times more than blood plasma , a fluid that surrounds red blood cells. Perfluorinated chemicals are inexpensive to produce and are completely free of organic matter. Therefore, there is no risk of contamination from infectious bacteria. [6] Through a chemical process called polymerization, more than two cells combine to form a large HBOC molecule. HBOC is smaller than natural red blood cells. Although naturally

occurring red blood cells remain in the bloodstream for up to 100 days, HBOC only circulates in human blood for one day. their ability to support long life. [7] The first (and only) FDA-approved PFC, called Fluosol-DA-20, was manufactured in Japan. [7] PFC stays in the bloodstream for about 48 hours. Because of their ability to break down oxygen, pfcs are the first group of artificial blood products researched by scientists. [2] It contains two pfcs, perfluorodecalin (PFD) and perfluorotripropylamine (FTPA). PFD is the main component in the oxygen carrier, whereas FTPA provides critical stability. Each of the two had a half-life with PFD only 3 to 6 hours due to its rapid elimination. FTPA, on the other hand, remains in the tissue. [7] The desirable characteristics of the second generation PFC include high oxygen depletion, rapid detoxification and minimal tissue depletion, no significant side effects, malaria increased purity, large production and availability.[7]

Hemoglobin-Based Oxygen Carriers (HBOC):

Hemoglobin is obviously a need for blood substitutes that exhibits many of the most desirable traits. [3] HBOC is made from strong hemoglobin and looks a little like real blood. Red blood cells are often used to represent red blood cells from damaged human blood, cow's blood, hemoglobin-producing bacteria, or human placentas. and at the same time seems to be successful. [2] Oxygen containing hemoglobin can be divided into two broad categories; solution of pure hemoglobin and modified hemoglobin. Modified hemoglobin can also be divided into polymerized hemoglobin, hemoglobin binding to intramolecular cross-linked, hemoglobin recombinant, and hemoglobin vesicles. [7] Oxygen-dependent hemoglobin (HBOCs) carry the same molecular protein molecule oxygen as found in the blood. Oxygen binds chemically to the hemoglobin molecule, where it dissolves only in perfluorocarbon emulsion. HBOC is different from red blood cells because hemoglobin is not present in the skin. [7] Overall, these findings suggest that HBOC caused only a small amount of blood loss during and after surgery, there is no improvement in mortality and increased adverse effects. [10] Some products have come close, no HBOC is recommended for hospital use in the United States or Europe. This study focuses on the history and clinical trials of three HBOCs that passed the Phase II or Phase III clinical trials: HemAssist, PolyHeme, and Hemopure. [10] The process is called α-Hb by at the hands of the US military and the dclhb or hemassist of Baxter. The source of hemoglobin is the red blood cells that humans collect, cleanse, lysed and filter. The product was then deoxygenated, combined with bis (3,5-dibromosalicyl) fumarate and re-oxygenated. One unit of Baxter dclhb was made from 25 g of hemoglobin and 250 ml to give a total of 10 g / dl.

Dclhb solution forms P50 of 32 mmhg, colloidal osmotic pressure (COP) of 42 mmhg, as well as methemoglobin content <5%. [15] It also exhibits long life when stored in the freezer. Examples of HBOC blood transfusions are Hemopure, PolyHeme, MP4OX (Hemospan), Hemotech, Hemoglobin Engineered.4, None of the HBOCs are approved for clinical use in the United States. As shown in Table 4, all Hb disconnected for storage is discontinued. In a multicenter, randomized, single, small dose infusion of hemoglobin diaspirin-crosslinked hemoglobin (DCLHb) for 3 days did not affect adverse outcomes in patients with severe stroke. rue 1960. [6]

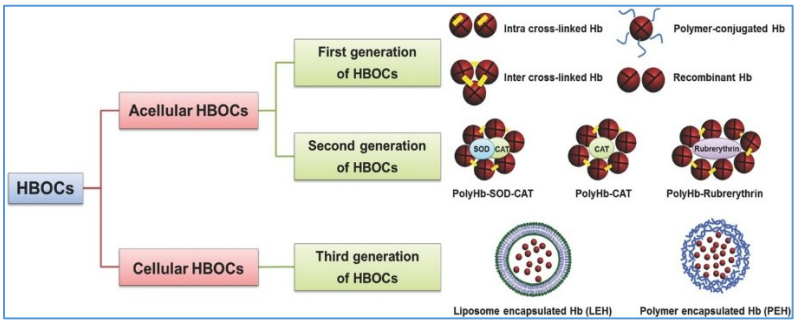

Fig No. 3: Hemoglobin-Based Oxygen Carriers

Advantages:

Improper blood flow has many benefits than human blood. Since blood substitutes belong to the same group of O blood, patients can be given regardless of their blood type. compatibility, can be injected through pasteurization. [5] The advantage of PFCs over living blood is that it can be stored for more than a year at room temperature. [11]

Disadvantages:

It causes effects on the kidneys, neurotoxicity, platelet aggregation, antigenicity, increase in pancreatic and liver enzymes. They also cause the effects of intestinal obstruction, vasoactivity / hypertension, nephrotoxicity, coagulopathy, and anemia. [11] People who receive a blood transfusion are three times more likely to have a heart attack than those who receive blood transfusions. reduces the half-life distribution, disrupts certain physiological organs, especially the intestinal tract and red blood cells, hemoglobin. PFCs should be prepared as emulsions because they cannot remain in the liquid phase. [11] Side effects of HBOC may include high blood pressure, abdominal discomfort, and temporary redness of the eyes or 2 mouths. platelet count in the blood will decrease and it will cause flu-like symptoms.[11]

CONCLUSION:

Based on the documents obtained, oxygen therapy is still in experimental phase. There is no FDA approved product for clinical use in the United States, except Fluosal-DA. There is ample evidence of adverse effects of oxygen therapy. Further research is needed to develop products that are safe for human consumption. The current goal of active red blood cells is to supplement blood transfusion therapy to save lives during emergencies. With advances in biotechnology, there will be more alternatives to blood, which could completely replace normal blood. However, new technology must develop an effective and more robust method than blood transfusions. Currently, the use of blood due to low half-life on toxins and potential costs, access to equipment by the FDA is difficult. It is stated that prompt treatment with blood-borne trauma conditions will be of great benefit. These blood substitutes do not contain any antigens that determine a single blood type 11, so they can be used in all forms without immunological reactions.

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