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Blood transfusion: What to transfuse?

Abstract

Physiology learns the function of organs like liver and bone marrow. In case of disturbed balances these organs are stimulated to increase their function and strengthen their metabolic processes like protein synthesis and blood cell production and release. These processes are time dependent to compensate loss.

In case of acute blood loss this augmentation bridges a temporarily drop in the presence of red cells and plasma proteins and restores the temporarily shortages.

In such circumstances there are two major principles that play a role: 1. Virchow's trias; and 2. in the logistics of the event, the WHO's definitions of 'need for', 'demand for', and 'use of' blood or blood elements.

A major risk in massive and acute blood loss is the thread of organ failure. Volume (repair of the circulation, perfusion of the vascular system, at a lower blood pressure) and lowering the viscosity of the circulation allows red cells to enter the organ capillary beds and release oxygen restoring a metabolic balance. Massive transfusion with whole blood leads to kind of volume repair but also to increase of the viscosity and transfusion of low concentrations of plasma proteins, in contrast to concentrates.

Blood products are to be manufactured under pharmaceutical conditions realizing that each blood donation represents one unique and sterile batch which needs to be processed keeping the sterility intact. That should also be done when splitting (pediatrics) or combining (platelets, cryoprecipitate).

Today blood products and Plasma-Derived Medicinal Products (PDMPs) produced using fractionation technology are part of the WHO Model List of Essential Medicines and should be accessible and affordable to all in need.

Keywords: Blood transfusion; Need; Demand; Use; Processing; Blood products; Plasma-derived medicinal products; Essential medicines.

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Introduction

Blood transfusion is a relatively young and supportive medical intervention. With the groundbreaking discovery of red cell antigens or AB0 blood group in Vienna end 19th Century an entirely new clinical practice has been initiated in the world. A very interesting and learning epoque of several Centuries of both mystical and scientific experiments in the attempt and expectation to support life through the transfer of animal and human blood into human beings came to an end [1]. However, the new epoque brought the development of a variety of related sciences and practices to life and broadened the scope of the early 20th Century clinical practices – immunohematology, microbiology and virology, anticoagulation and preservation, receptacles, giving sets and polymers, separation and centrifugation, but also organization, structure and infrastructure, education and knowledge economy standardization, quality systems and management, artificial intelligence and digital foot printing, sociology and many more of which a distinctive number resulted in Nobel prizes (close to 25) [2]. The first, as early as 1908, were Ilya Ilyich Mechnikov and Paul Ehrlich.

The science of blood transfusion developed over the 20th Century into a new academic field: Transfusion Medicine, a bridging science and clinical practice supported by the laboratory- and alpha- or soft sciences [1].

Does bloodloss always need blood transfusion?

Physiologically blood loss is compensated by an increased synthesis in the liver of plasma proteins and a strengthening of the bone marrow productivity of cell production [3]. These processes take in general around 24 hours to come to full action. The most important event is the loss of volume leading to a drop in blood pressure, increase in heart rate and constriction of major arteries in the periphery, hence a thread of organ failure and hemorrhagic shock.

To allow the remaining red cells to enter the threatened organs capillary beds one needs a lower viscosity achieved by replacement fluids rather than whole blood to stabilize the blood pressure and initiate organ perfusion. When the viscosity is lowered and perfusion has started, red cells more easily will enter the capillary beds and release their carried oxygen, relieving the thread and bringing back the balance of organ function to normal or close to normal. A single unit of red cells usually is sufficient and effective. Massive transfusion raises the viscosity and hampers adequate tissue perfusion and reoxygenation.

In situations where cardiac or cerebral function are at stake, the approach may be adapted [4]. In general, it is preferable to stabilize the blood pressure and tissue perfusion at a lower level to allow a more effective relieve of the organ failure thread and restore the physiological homeostatic balance.

Whole blood contains all the different elements, proteins and cells. However, concentration of cells and proteins is much lower and therefore less effective than concentrates. Problem in many of the low- and Middle-Income Countries (LMICs) is the availability, and storage and distribution capacity [5].

What blood products are needed?

Depending on the need in the gamma of diseases, all blood elements, cells and proteins, and volume play a supportive therapeutic role. In real life there is a difference between need for, demand for and use of blood and blood components or Plasma Derived Medicinal Products (PDMPs) and volume. WHO developed definitions to evaluate these differences in the blood transfusion practice [6]:

Need: estimation of the amount of blood or its elements needed to meet the transfusion requirements of the patient population according to current up to date policies, clinical guidelines and best practices;

Demand: the amount of blood or its elements that would be transfusion if all prescriptions for transfusion were met. Demand may reflect appropriate or inappropriate indications and practices;

Use: the actual amount of blood or its elements currently transfused; use may be appropriate or inappropriate.

These WHO definitions together with (Figure 1) give an idea how to try to measure the need for, demand for and use of blood and its elements. However, globally many factors influence the requirements for to meet the health care needs of a given population for blood and its elements. These include e.g., income levels, economy, current status and rate of development of the health care and blood supply system and accessibilities of health care institutions and their operations to the public.

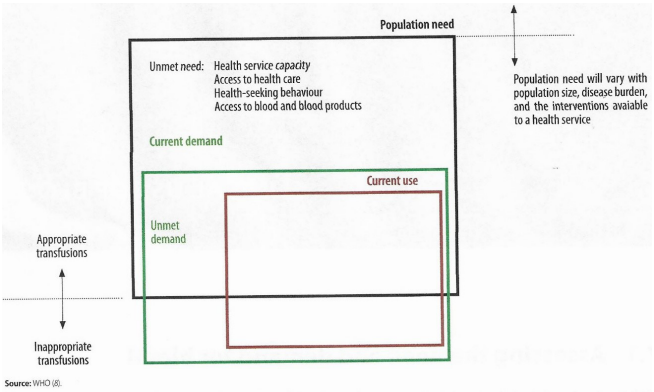

Figure 1: Paradigm of need for, demand for and use of blood or its elements.

The need for, demand for, and use of blood and its elements in a country could be affected by geography, migration of population, epidemiology of diseases for which blood or its elements are needed, e.g., childhood, inherited coagulopathies (e.g., hemophilias and von Willdebrand Disease, thrombocytopenias, etc,), natural disasters and humanitarian emergencies (e.g., Ukraine and Gaza).

Blood manufacturing

Blood is the only liquid tissue in the body, a composite of a fluid matrix plasma containing a.o. the proteins, and the different cell lines of which the white cells are produced in the lymphoid system and the others in the bone marrow. Due to its liquid matrix it can easily be separated by mechanical (centrifugation) or gravity technologies and the elements (proteins) of the matrix (plasma) through fractionation technologies. The processes are in principle pharmaceutical, but differ in some aspects:

Source material: Each unit of donated human blood is a unique sterile batch which needs to be processed keeping the sterility intact, wherein the pharmaceutical production industry source material is acquired in large amounts for the production of several batches of medicinal products.

Intermediate products: In the manufacturing of blood products are a limited number of intermediate products like in platelet concentrate production and the production of cryoprecipitate and leukocyte depletion or washing of red cell concentrates which require containing of the sterility. In the pharmaceutical industry there is a manifold of intermediary or half products.

Finished products: Each finished blood product originates from one single donor unless we need pooling such as with platelet and cryoprecipitate or splitting for pediatric consumption. The entire process is organized and performed with the highest level of disinfection keeping the sterility intact. In the pharmaceutical IV-product industry the finished product has a final batchwise sterilization step to complete.

Quality assurance: In the blood manufacturing, which takes usually place in licensed blood establishments the prime objective is to keep and guaranty the sterility throughout the entire process and testing for sterility is done on a statistical basis of 1% of each type of product manufactured. In the pharmaceutical industry the end point is sterility, performed on each batch including the guarantee of purity or absence of contaminants.

The normal manufacturing of blood [7] leads to the production of red cell concentrates, platelet concentrates, fresh plasma to be snap frozen and cryoprecipitate with also cryoprecipitate poor plasma.

The pharmaceutical fractionation process of plasma, whether fresh or supernatant, leads to the Plasma-Derived Medicinal Products (PDMPs) like albumin, immunoglobulins for IM or IV use, general and specific, clotting factor concentrates such as Factor VIII and IX, fibrinogen and the prothrombin complex II/VII/IX/X besides a small number of orphan proteins for the treatment of rare inherited diseases.

Most of these products manufactured or fractionated are to be found in the WHO List of Essential Medicinal Products (EMP) with the intention that Governments (Ministries of Health) ensure the availability, accessibility and affordability for each patient in the country [8]. On paper that works, but in reality, there is still a lot to develop.

Conclusion

In case of blood loss normal physiological processes are stimulated to increase their function, a time dependent process. Immediate massive whole blood transfusion is not really necessary. In these situations, there are two major principles that play a role: Virchow's triad of hemostasis; and the WHO definition of 'need for', 'demand for', and 'use of' blood or blood elements.

Donated whole blood is a sterile source material. Manufacturing that source material into blood products (red cells, platelets and plasma) should guarantee that sterility and consistency of quality are kept. Plasma proteins are isolated and purified using fractionation technology and final sterilization to obtain Plasma-Derived Medicinal Products (PDMPs) for clinical use.

The WHO Model List of Essential Medicines, first published in 1979, hosts these products and urges Ministries of Health to make these available and affordable for all those in need.

Declarations

Conflict of interest: The author has nothing to declare.

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