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Kyle L. Gress
Karina Charipova
Ivan Urits
Omar Viswanath
Alan D. Kaye

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Supply, Demand, and Quality: A Three-Pronged Approach to Blood Product Management in Developing Countries

Kyle L. Gress, MD,[1] Karina Charipova, MD,[1] Ivan Urits, MD,[2] Omar Viswanath, MD,[3] Alan D. Kaye, MD, PhD[4]

[1]Georgetown University School of Medicine, Washington, DC; [2]Department of Anesthesiology, Beth Israel Deaconess Medical Center, Boston, MA; [3]Valley Anesthesiology and Pain Consultants – Envision Physician Services, Phoenix, AZ; Department of Anesthesiology, University of Arizona College of Medicine-Phoenix, Phoenix, AZ; Department of Anesthesiology, Creighton University School of Medicine, Omaha, NE; [4]Department of Anesthesiology, Louisiana State University Health Shreveport, Shreveport, LA

Abstract While transfusion of blood and blood products is instinctively linked to the provision of emergent care, blood and blood products are also routinely used for the treatment of subacute and chronic conditions. Despite the efforts of the World Health Organization and others, developing countries are faced with a three-part problem when it comes to access to and delivery of transfusions: insufficient supply, excessive demand, and inadequate quality of available supply. Developing countries rely heavily on replacement and remunerated donors rather than voluntary nonremunerated donors due to concerns regarding donation- and transfusion-transmitted infection as well as local and cultural beliefs. While increased awareness of HIV and improved testing techniques have jointly reduced infection-related apprehensions and improved the quality of available blood and blood products, continued efforts are warranted to bolster testing for other bloodborne pathogens. Similarly, although prevalence rates of anemia are high in some areas of the world, success in adequate widespread management of these conditions has been limited. One of the keys to expanding access to high-quality blood and blood products is thus to improve medical management of conditions that would otherwise require transfusion. Through a three-pronged approach to address quantity, quality, and demand, developing countries can enable themselves to build toward self-sufficient blood management services and increased independence from the support of international organizations. (*J Patient Cent Res Rev.* 2021;8:121-126.)

Keywords blood transfusion; developing countries; public health; blood-borne pathogens; anemia; infection

Transfusion of blood and blood products is not only critical in life-threatening emergencies but also facilitates management of subacute and chronic conditions in routine patient care.[1] In developing countries (DCs), such as those in sub-Saharan Africa, the greatest need for transfusions is cited in children with malaria-related anemia and women with obstetric hemorrhage.[1,2] These clinical scenarios are associated with a mortality index of up to 25.5%.[2] Although the World Health Organization (WHO) included fresh-frozen plasma, platelets, red blood cells, and whole blood on its Model List of Essential Medicines in 2019, many DCs lack reliable access to these products.[3]

Adequate blood product management requires a stable supply, a standardized procedure for processing and testing, and appropriate clinical and laboratory skills for use of products.[1] The problem faced by most DCs can be broken down into three basic components: insufficient supply, excess demand, and inadequate quality of available supply. This problem is further complicated by the issue of cost. It has been shown that international organizations such as the Red Cross cannot permanently fund blood transfusion systems and that this responsibility belongs to national authorities.[4] In sub-Saharan Africa many countries have utilized external funding to establish national blood management services, but few have been able to convert to reliable self-sufficient systems.[1]

Herein, we provide a narrative review of published reports on the blood quantity, quality, and demand issues many DCs encounter along with potential strategies for advancing self-sufficient blood management services and independence from international support.

Corresponding author: Kyle L. Gress, MD, Georgetown University School of Medicine, 3900 Reservoir Road NW, Washington, DC 20007 (klg93@georgetown.edu)

Understanding the Problem

Compared to developed countries, DCs lack the voluntary nonremunerated blood donors that are essential to

maintaining adequate supply.[5] Voluntary nonremunerated donors are individuals who give blood products by their own free will without receiving payment in return, be it cash or any other substitute for money.[4] These donors are eligible to receive refreshments or small tokens of low cash value for their donations. Remunerated donors are those who do receive payment for their donations, whereas replacement donors are individuals who elect to donate blood products for direct transfusion to their family and friends, usually on a one-time-only basis.[4] Due to a combination of infection-related apprehension and local and cultural beliefs, DCs rely heavily on remunerated donations.[5,6] As a result, proportions of repeat donors are low, resulting in an unstable supply of blood and a severe lack of plasma derivatives, since very few DCs have the fractionation plants required for their production.[5]

The shortage of donors in DCs is compounded by nonindicated transfusion and a large volume of discarded blood.[5] Blood should be transfused only when clinically appropriate. Unfortunately, most clinical transfusion guidelines rely on formal assessments like quality-assured hemoglobin measurements.[1] In places where these services are unavailable, clinicians rely solely on clinical judgment which, when faulty, can result in the transfusion of a unit of blood that costs 40 times more than a single accurate hemoglobin test.[1] Despite the fact that the majority of transfusion-related research has focused heavily on preventing transfusion-transmitted infections rather than addressing blood shortage, the scope for increasing supply by reducing unnecessary transfusion is likely substantial.[1]

Quality of available blood products in DCs has benefited substantially from increased awareness of HIV, but efforts to improve testing for other transfusion-transmissible infectious agents are still warranted.[5] Recent data have shown that transfusion-associated infection rates in sub-Saharan Africa remain astronomically higher than those in high-income countries, with risk of HIV, hepatitis B, and hepatitis C transmission reaching 1, 4.3, and 2.5 infections per 1000 units of blood, respectively.[7] In high-income countries, these rates are approximated to be 1 in 2 million, 1 in 100,000, and 1 in 2.5 million, respectively.[7] Unfortunately, these infection rates likely underestimate true transmission of disease because acquired viruses can be passed on via a wave of secondary infections.[1] As of 2016, antibody to the hepatitis C virus is not part of routine blood screening in many parts of Africa, and only a small proportion of blood banks use enzyme-linked immunosorbent assay (ELISA) kits for hepatitis B surface antigen because testing is not considered cost-effective given the endemic nature of the virus.[1]

The delicate interplay between quantity and quality of supply is exemplified by malaria, a leading cause of anemia requiring transfusion in Africa that also can be transmitted by transfusion.[1] Despite the morbidity and mortality associated with malaria, excluding donors with low-grade parasitemia in endemic areas has the potential to significantly reduce supply of available blood.[1] Of note, it is equally important for DCs to ensure quality of blood products by pairing donors and recipients using appropriate blood groupings and crossmatching techniques.[5] Infection by bacterial components secondary to blood bank contamination and breakdown of the cold chain, often due to frequent power cuts during transport, are factors that are frequently overlooked yet have significant capacity to decrease quality of available supply.[1]

Current Recommendations and Progress

The approaches typically used to secure an adequate supply of high-quality blood in high-income countries are not necessarily appropriate, validated, or practical for implementation in DCs.[8] In DCs, realistic solutions must encourage reliance on local resources, establish networks for research and education, and promote use of guidelines and audits for gradual improvement of clinical practice.[1] In many countries where inadequate supply and lack of funding are significant obstacles, progress can be made by reorganizing existing systems.[4] First, transfusion medicine should be integrated into the national health care system.[1,4] This branch of medicine encompasses all of the aspects of transfusion of blood products, including but not limited to donor recruitment and retention, collection, quality assessment, processing, storage, and administration.[4] Second, a national blood policy must be created to define the organization(s) responsible for providing blood services, means of funding these services, acceptable forms of donation, and regulations for conducting procurement and transfusion.[4]

Unfortunately, while nearly all African states had established a national blood policy as of 2016, more than half were unable to implement their policies.[1] In many cases, inability to carry out a national blood policy stems from a system of organization that relies on the ability of hospitals to run their own blood services without national control or coordination.[4] The International Foundation of Patient Blood Management structures the development of a successful patient blood management (PBM) program around the idea of "giving the right blood products in the right amount to the right patient at the right time."[9] It provides formal recommendations for transparent transfusion guidelines, appropriate education and training for clinical staff, and feedback mechanisms for evaluating appropriateness of

transfusion. Using this framework, countries like Uganda have been able to develop PBM programs featuring national oversight committees and standard operating procedures within individual hospitals. Currently, most sub-Saharan countries, including Uganda, are in the early stages of developing PBM programs.[9]

Bolstering Supply

It has been reported that despite organized humanitarian efforts, up to 80% of the world population currently has access to only 20% of the world's blood products.[10] Unfortunately, the best way to bolster supply is to encourage repeat donation by nonremunerated, voluntary donors who were demonstrated, in a study of 2880 units of blood in Egypt, to have significantly better health profiles than remunerated donors.[11] While it is difficult to stimulate donor motivation, entities like the Federal Ministry of Health in Nigeria have seen success by engaging the media and televising donations by public figures.[1] Nigeria also has implemented strategies like Club 25 to recognize donors under the age of 25 years, while Zimbabwe created the Pledge 25 Club, a program that uses education incentives to attract students to give blood 25 times.[1] In India, issues related to access resulting from a dispersed population were addressed by the institution of a system of "walking blood banks," which consists of a pool of preapproved healthy donors who can be recruited by rural hospitals to provide a reliable and timely supply of blood.[12,13]

Educational programs and materials created by the Red Cross and WHO have proved helpful in dispelling apprehensions and false beliefs about the process of blood donation, especially in rural areas.[1,5] It is likely that the most effective approaches for recruiting new donors and converting remunerated donors to repeat donors will involve the combined efforts of local and international organizations. While it is promising that global organizations have aimed to educate potential donors and to circulate resources, it is essential that these groups collaborate with local organizations.[1] In many ways, the task of finding donors may be more reasonably assigned to the nonmedical community, such as municipalities, schools, and religious organizations, rather than to medical professionals. At its core, blood product management is a public health issue, not a strictly medical issue. The recruitment of new donors should fall in the realm of public health authorities, partnered with these nonmedical organizations, with the ultimate goal being to change public opinion about donation.

Decreasing Demand

A systems approach to blood product management must reflect a balance of bolstering and conserving supply as well as decreasing demand. A significant proportion of the blood requirement in DCs is dedicated to the treatment of anemia, especially in children. The prevalence of anemia in South Africa is estimated to be 17% in males and 31% in females compared to 3.5% and 7.6%, respectively, in the United States.[14,15] While many cases of anemia in DCs do require treatment, demand can be managed by considering alternative interventions such as use of haematinics for the treatment of nutritional anemia and stimulation of erythropoiesis prior to resorting to transfusion.[5,14] Similarly, treatment with hydroxyurea can be used to decrease transfusion requirements in sickle cell anemia, and high-hematocrit placental blood can be useful for small-volume emergency transfusion in cases of neonatal anemia.[1] Novel strategies have been developed to reduce excessive rates of exchange transfusions in infantile hyperbilirubinemia.[16,17] It is proposed that formally assessing both total serum bilirubin and clinical signs of encephalopathy allows for more accurate prediction of kernicterus risk, helping to reduce transfusion requirements and improve overall health outcomes.[17]

In cases of trauma associated with significant blood loss, investigations like the Clinical Randomisation of Antifibrinolytics Hemorrhage-2 (CRASH-2) study demonstrated that tranexamic acid, an antifibrinolytic, reduces all-cause mortality by 10% when administrated within 3 hours of the initial trauma.[1] Per PBM recommendations, minimizing blood loss through anesthetic and surgical techniques as well as optimizing coagulation status before and during procedures is essential to reducing blood requirements in both emergency and scheduled operations.[14] Educating transfusion prescribers about appropriate protocols and available alternatives, such as saline and colloids, also may help decrease demand.[5] Given that strict enforcement of a transfusion protocol in a Malawian hospital reduced transfusion numbers by 75%, it is possible that implementation of these innovative interventions in conjunction with strict transfusion guidelines may help significantly decrease demand for blood and blood products in DCs without negatively impacting mortality.[1] It is vital to note, however, that in any scenario the enforcement of protocols is as important as their creation, since protocols tend to fade away without adequate means for their enforcement.

Going hand in hand with the use of alternative therapies and approaches as a means to decrease demand is targeted reduction of waste. Some surgical procedures are associated with an inherent risk of blood loss and typically require preemptive crossmatching of blood, but this blood is often wasted (at a cost of approximately $40 per unit).[18] A study out of Pakistan recommended that crossmatching be performed only if audits suggest that there is a greater than 50% likelihood that the unit will

be used.[18] This practice, along with the general practice of auditing usage of blood supply, is likely to promote better stewardship of available products.

Improving Quality

The effective supply of blood products is further hampered by poor quality of those products that are available.[2,5] Lack of adequate resources predisposes some countries to continuously fall short of meeting set standards for screening of transfusion-transmissible infection; in many instances, communities within these countries are acutely aware of this shortcoming, and individuals take this information into account when choosing for or against voluntary donation.[19] As a result, distrust of health systems is one of the key problems that lie at the heart of the issues surrounding blood product management.

There are two main strategies for improving quality of available blood and blood products: predonation testing and postdonation pathogen reduction. Recommendations for blood product monitoring include testing for direct antiglobulin and screening all donations for HIV, hepatitis B virus, hepatitis C virus, syphilis, and regional pathogens like arboviruses, *Trypanosoma cruzi*, and human T-lymphotropic virus.[1,5,20] Unfortunately, the specificity, sensitivity, ease of use, and costs associated with anti-HIV, anti-hepatitis C, and hepatitis B surface antigen testing vary.[1] For instance, widespread use of nucleic acid testing is limited in most DCs by cost.[1,11] Fortunately, more cost-effective substitutes for nucleic acid testing, such as the use of two anti-HIV ELISA tests performed in parallel, are being investigated.[1] Similarly, data out of Egypt suggest that core antigen testing is more effective than RNA testing for determining the presence of hepatitis C without sacrificing specificity.[20] Rapid immunochemical tests, such as those developed for the HIV antibody, are under development for other infectious agents.[1] Successful development of these tests has the potential to cut costs by decreasing the need for highly skilled staff and advanced processing equipment.[1]

Alternatively, researchers are considering the option of prophylactically treating recipients of red blood cells in endemic regions with antimalarial agents instead of excluding donors with low-grade parasitemia.[1] Pathogen reduction refers to a series of interventions that involve using heat or alcohol fractionation to eliminate viral components from plasma products. Pathogen reduction is promising but cannot be used for whole blood or packed red blood cells and is associated with logistic concerns, including cost and requirements for complex equipment and skilled personnel.[19]

It is important to note that as long as the prevalence of these viruses remains high, residual risk of transmission will not decrease even in the setting of adequate testing given the existence of the window period.[1] While it is essential to channel efforts into developing adequate screening protocols, it is equally if not more vital to address the availability of antiretroviral therapy. Thus, poor quality of available blood products can serve as a motivating factor for both tighter usage guidelines and compliance enforcement. This approach provides a simultaneous solution to two important issues by helping to reduce transmission of infection and by improving quantity and quality of available supply for true emergency use.

Looking Forward

Uganda and other sub-Saharan countries that have taken steps toward developing PBM programs serve as examples of the implementation of novel, practical strategies for blood delivery in lower-resource settings (Table 1). Of

Table 1. Strategies for a Three-Pronged Approach to Blood Product Management

Bolstering supply
• Engage the media, televise donations by public figures
• Target youth audiences using education initiatives
• Create “walking blood banks” to serve as a supply of blood for rural hospitals
Decreasing demand
• Consider alternative interventions (ie, hydroxyurea, stimulation of erythropoiesis, tranexamic acid)
• Improve education for use of fluids for resuscitation (ie, saline, colloids)
• Enforce strict transfusion protocol
• Reduce waste by limiting preemptive crossmatching
Improving quality
• Screen all donations for HIV, hepatitis B, hepatitis C, syphilis, and regional pathogens
• Consider alternative cost-effective techniques for predonation testing
• Implement prophylactic treatment of recipients for endemic diseases
• Increase availability of antiviral therapy to decrease transmission risk

note, these approaches are often quite different than those strategies utilized in higher-resource areas where the majority of health care leaders are trained. The challenges faced by health systems across the income spectrum vary significantly, and it has become evident that DCs must forge blood programs that complement not only their health care infrastructure but also the culture of their communities.[21] When the literature and public media highlight the shortcomings of blood product management programs in low- and middle-income countries by comparing them directly to wealthier nations, they often overlook the nuances that require these delivery programs to be innately different.[22] While beyond the scope of this review, a more beneficial approach may be to shed light on novel strategies used by lower-resource health systems such that others may use these examples as a starting point to addressing shortcomings of their own programs.

Summary

Problems associated with transfusion of blood and blood products in developing countries stem from insufficient supply, excessive demand, and inadequate quality of available supply. While initiatives of international organizations have bolstered blood transfusion systems in DCs across the world, progressive improvement of these systems is greatly needed. DCs should focus on increasing repeat volunteer donor rates through enriched education materials, advancing testing techniques to audit the quality of available blood, and improving medical management of subacute and chronic conditions that would otherwise require transfusion. International organizations can aid DCs in the pursuit of these goals by addressing barriers like access to resources and cost. These efforts, however, should be supportive rather than enabling, since the long-term success of any independent blood transfusion system is determined by the ability of national authorities to maintain it over time.

Patient-Friendly Recap

- Developing countries can face considerable obstacles to making high-quality blood, platelets, plasma, and other blood products available to patients in need of transfusion.
- The authors reviewed three approaches to bettering blood management in these countries — bolstering supply, decreasing demand, and improving quality.
- Strategies described in this review may enable developing countries to build more efficient and self-sufficient blood management systems that are less dependent on support from international health organizations.

Author Contributions

Concept: Viswanath, Kaye. Literature search: Gress, Charipova. Manuscript drafting: Gress, Charipova, Urits. Critical revision: Viswanath, Kaye.

Conflicts of Interest

None.

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