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Availability of blood components and plasma derived medicines in Iran

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Abstract

Iran is a country with advanced health care system. In 1974 government of Iran established a centralized transfusion system. Since then donations of blood may not be remunerated and therapy with blood and its components is free of charge for all Iranian patients in need of the treatment. Most of donors in Iran are educated middle age men. In 2005 Iranian donated more than 1.6 millions units of blood. Although Iran population has doubled in past three decades blood donation has increased several folds. Donations are meticulously screened through interviewing of donors and lab testing of the donations using serological methods. In contrary to blood and blood components, Iran is heavily depends on importation of plasma derived medicines. Irrational use of blood components and low surveillance on use of plasma derived medicines, which are highly subsidized by the government, is a major challenge in transfusion medicines in Iran.

Keywords: Blood donation; Blood components; Plasma derived medicines; Iran

1. Introduction

Iran, a country with a population over 70 millions, is one of the most populated countries of the Middle East. In past three decades, the government of Iran has invested substantially on primary and secondary cares in Iran and the country now has a substantially advanced health system infrastructure. Iran has a primary healthcare network covering the entire population of the country. Rural health houses throughout the country are staffed by trained personnel and supported by a system of continuing education. In Iran responsibility for health and medical education are merged throughout the health system. In a unique system, Iran Ministry of Health and Medical Education (MOH) is responsible for both health and medical education in the country. Each medical science university in Iran has a vice chancellor responsible for health care [1].

Today blood, blood components and plasma derived medicines are a vital part of the modern medicine and health care systems. Millions of lives each year saved or significantly improved by rational use of these products and it is not currently foreseeable that modern medicine will be able to

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survive without sustained and reliable access to the safe blood and blood/plasma derived products. Although the scarcity of this raw material of human origin brings about legal and ethical consideration, insufficient quantities of these products to treat patients compromise the obvious right of patients to health care.

2. Iranian blood transfusion organization

In Iran blood transfusion is an integral part of the national health system. Blood donation is voluntary and unpaid and blood and its components may not be a source of profit. The costs of collection, fractionating, preserving and distribution of blood and its components is paid by the government. Blood components in Iran are absolutely free of charge and therapy with blood and its components is free of charge for all Iranian patients in need of the treatment.

Although blood transfusion in Iran has a long history, new era of blood transfusion started in 1940s. According to a local newspaper first blood donation in a blood bank was recorded in 1945. Blood transfusion services started in a non centralized and inappropriately supervised manner. However, following the establishment of blood centers both in Iranian Army in early 1950s and Red Lion and Sun Organization (replaced in 1979 with Red Crescent following Islamic revolution in Iran) the country started to experience establishment, growth and coordination of blood transfusion activities in its health sector. Until the early 1970s Iran had no organized blood service and the requirements of hospitals were supplied by commercial ''agents'' who relied mostly upon paid ''professional'' blood donors [2,3].

The basic principles of blood safety are enough safe blood donors, a responsible blood transfusion service which can ensure appropriate and safe processing and testing, and appropriate use of blood. Iran has adopted criteria set by WHO for a national blood organization including well organized nationally coordinated blood transfusion services with quality systems in all areas, the collection of blood only from voluntary non-remunerated blood donors from low risk populations, the quality assured testing of all donated blood, the safe and appropriate use of blood and blood products, and global collaboration for blood safety as principles for Iranian Blood Transfusion Organization (IBTO) [4,5].

In 1974 based on a parliamentary law, IBTO was established in order to centralize all blood transfusion activities from donor recruitment to production of blood components and delivery of blood and blood products under one umbrella. The law banned any other organization, public and private, to perform any activity in blood transfusion section. The establishment of IBTO was a significant progress toward emergence of a developed and scientifically based blood transfusion system in Iran.

IBTO is a public and non-profit organization that relies fully on the government of Iran for its financial budget and therefore delivers all of its produced blood components free of charge both to the public and private hospitals. Although it is an independent organization, Minister of Health chairs IBTO high council. Among other responsibilities IBTO high council is responsible for appointment of IBTO general manager. According to its constitution the main scope and responsibilities of IBTO are as following:

- To define standards for blood collection, storage and delivery of blood and blood components.
- To recruit voluntary donors through educational and non commercial promotional activities.
- To develop blood supply network and blood collection centers throughout the country.
- To conduct necessary tests on donors and donated bloods to ensure blood safety.
- To prepare blood components and deliver blood and blood components to authorized health centers based on their requests.
- To establish educational program for health professionals involve in administration of blood and blood components.
- To establish reference laboratories to diagnose blood borne disease and blood related disorders.

According to the law, IBTO has a monopoly status and currently it is the sole organization receiving donated blood, preparing blood components e.g. red cells, platelets and fresh frozen plasma and distributing them to the hospitals in Iran. However, it has no obliged responsibility for production, importation and distribution of plasma derived medicines.

IBTO has focused on self sufficiently of the country on blood and blood components and therefore has spent enormous efforts on increasing blood collection form volunteer donors. Iran now has one of the most comprehensive blood transfusion systems in the Middle East region. In 2005 Iranian donated more than 1.6 millions units of blood (Fig. 1).

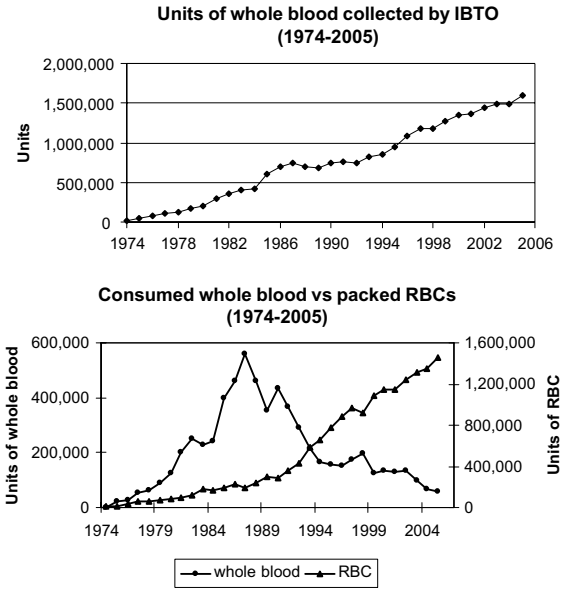

Fig. 1. Collection and consumption of blood and blood components in Iran 1974–2005.

Despite the fact that Iran population has doubled in past three decades Fig. 1 shows a several fold increase in blood donation by the donors. Donated bloods are mainly converted to blood components including RBC, platelets and plasma. Therefore along with this, production of blood components including red blood cells, plasma and platelets has also been increased. Although thalesemic patients consume substantial portion of packed RBCs produced by IBTO, use of whole blood in Iran in past two decades has declined drastically (Fig. 1).

Iran has implemented a comprehensive care program for thalassaemia patients. This even includes a prenatal testing for possible abortion of fetus prior to 16 weeks post gestation. Prenatal diagnosis has resulted in a 70% reduction in the expected annual birth rate of affected infants. Despite this currently there are about 18,000 thalassaemic patients in Iran [6]. This number of patients consumes about 30% of red blood cells produced by IBTO.

Table 1 shows demographic data regarding blood donation in Iran. Participation of women in blood donation in Iran is low and only 9% of donors are female. Most of donors are educated male donors and 20–40 years old. Today developing countries face considerable obstacles to ensuring a safe blood supply and safe blood transfusions. The leading source of blood in the least developed and developing countries is replacement donors (88% and 81% respectively) who tend to be family members or friends [7]. However Iran has successfully removed ''family blood'' from its national transfusion policy. According to published statistics share of family blood in collected blood throughout the country was 3% [8]. This is expected to be less than 1% by end of 2007.

In addition to the traditional safety challenges facing the sector, the emergence of new aggressive infectious disease such as AIDS and hepatitis C caused new concerns to transfusion medicine. Therefore in Iran despite screening the donors through interviewing by trained physicians all donated bloods undergo lab testing for possible presence of important and known blood borne disease including HBV, HCV, HIV and Syphilis. Currently IBTO uses serological (Ab/Ag) methods for screening of donated bloods. IBTO now considering implantation of NAT system in its screening protocol for donated bloods.

Although hemovigilance systems are identified as a powerful tool to influence transfusion safety, currently there is not any recording and reporting system for adverse events due to transfusion in Iran. Therefore most of the time such events cannot be traced. The implemented ''look back'' system in IBTO is mainly concern with reports about safety of the blood and blood components. Every report indicating possible breach of safety of the donated bloods and/or patients receiving blood and blood components will be seriously traced through the product identity to the donors for appropriate actions. However, IBTO is in process of implementing centralized automated software based on bar code system. The system is based on ICCBBA international standard and ISBT 128 coding system. This will pave the way for the implementation a through national homovigilance system.

Table 1
Demographic facts for blood donation in Iran (2005)

Marital status of donors	Married 72%	Single 28%
Nature of donation	Voluntary 97%	Replacement 3%
Sex distribution	Male 91%	Female 9%
Age distribution	>51 yr (8%); 41–50 yr (18.5%); 31–40 yr (29%); 21–30 yr (36%); <20 yr (8.5%)	
Educational distribution	University (23%); High School Diploma (39%); Elementary (35%); Illiterate (3%)	

3. Plasma derived products

Significant roots of transfusion medicine and the use of plasma proteins lie in the military need for battlefield treatment. Therefore, traditionally many governments and not for profit organization became involved in the development of blood collection, plasma proteins and delivery of these products. Although albumin, immunoglobulins and clotting factors are among the most familiar products that are developed from human plasma, there are many other products that are of importance and often go unnoticed.

Blood and plasma are unique national resources and availability of safe blood and plasma products is essential to modern healthcare in countries with national health policy. Provision of concentrates of coagulation factors is an essential component of the provision of comprehensive care for hemophilia patients.

For most countries self sufficiency in safe and reliable plasma derived products remains an unachievable goal. Some countries believe that sufficiency rather than self sufficiency is the appropriate objective and accordingly source their plasma products from other countries. Other countries collect enough plasma domestically to be self sufficient in plasma derived products and may also export plasma to other countries. Although there has been a well accepted and rational choice, there is no officially formulated policy of self sufficiency for plasma derived medicines in Iran.

Since 1977 IBTO started production of plasma derived medicines in its own fractionation facility. However, the production of clotting factors was stopped in 1997 due to lack of a valid and efficient viral inactivation/removal step in production procedure. Since then Iran has mainly relied on importation of plasma derived medicines. Although self sufficiency in plasma derived medicines has always been part of Iran national health policy, no firm action plan has ever been announced and/or implemented. Establishing a new fractionation facility has been part of Iran national health policy. However, due to technical difficulties encountered efforts to establish such facility have not been fruitful yet. Iran now relies on offshore toll fractionation and importation of commercially available products, while pursuing a plan for future domestic production of the plasma derived medicines.

It is also clear that recovered plasma from donated blood in IBTO is not sufficient to cover needs of Iran market to such products. According to the law, blood can only be collected by IBTO from voluntary and non remunerated donors. Consequently there are no commercial blood collection centers in Iran. However, this is not the case for plasma collection and commercial plasma collection centers are allowed in the country. In 2005 first commercial plasmapheresis center established by private sector started its activity in Iran.

In order to furnish Iran pharmaceutical market with medicines derived from plasma recovered from blood donations, IBTO has started a toll fractionation activity since 2004. So far the plasma fractionation has been based on tendering and yearly contract. In 2004–2005 about 100 ton of plasma produced by IBTO has been send to two commercial companies in Germany and France for fractionation. Medicines produced from this, has played a substantial role in improving access of patients to plasma derived medicines. However, MOH still needs to import these medicines in order to respond to increasing demand of market in Iran. Paul-Erlich Institute (PEI) as a reputable EU health authority and responsible regulatory authority in Germany along with regional health authorities inspected blood collection centers in Iran for several time and following verification of quality system of these centers issued a time limited certification for exportation of recovered plasma produced in these centers to Germany for fractionation. These inspections have also played a positive role in improving quality system in IBTO blood collecting centers.

In Iran plasma derived products are regarded as pharmaceuticals and no specific legislation on production and importation of plasma derivatives exists. Therefore plasma derivatives in Iran are treated as any other medicinal products by the national authorities. Plasma derived medicines, both locally produced and imported, should obtain a marketing authorization from national regulatory authority in MOH. Plasma derived clotting factors are still dominating the market in Iran and so far there is not any recombinant clotting factors on the market.

In order to reduce price of medicines for patients some medicines including plasma derived medicines in Iran are heavily subsidized by the government. It means that government of Iran pays ''direct subsidies'' to the importers of these medicines [9]. Therefore availability of these medicines in Iran market depends mainly on financial situation of MOH. As it is illustrated in Fig. 2, due to fluctuations of

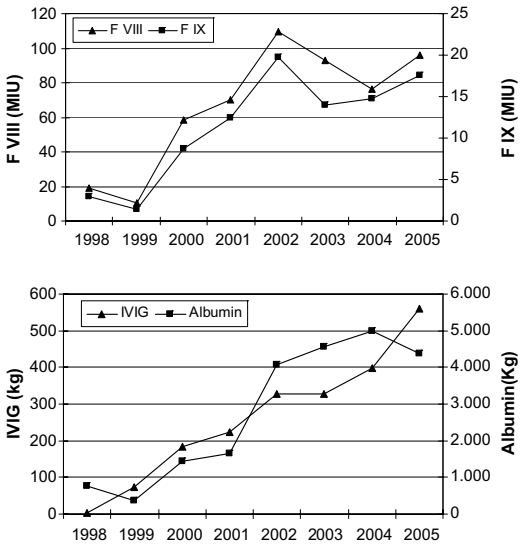

Fig. 2. Consumption of plasma derived medicines in Iran 1998–2005.

MOH budget importation of the plasma derived medicines does not follow any predictable trend. Therefore the story of the availability of plasma derived medicines in Iran is characterized by periodic shortages and steadily increasing demand. As standard of medical care continues to rise in Iran, the country is experiencing an increased demand for plasma products. However, the high cost of these products means that there are limitations to access to these products. Despite a steadily increase in consumption of albumin and immunoglobulins in past decade importation of clotting factors experienced substantial fluctuation (Fig. 2).

Currently there are about 5000 hemophilia patients in Iran [10]. Although treatment of these patients supported by the national health system and they receive clotting factors in highly subsidized prices, there is not a comprehensive policy of optimal use of plasma derived medicines including clotting factors and presently no reliable national registry for hemophilic patients has been established. Therefore, treatment and medicine supply strategies cannot be assessed. MOH relies on individual physicians who treat the patients for rational use of expensive imported clotting factors.

In 2005 per capita consumption of factor VIII in Iran was 1.4 IU which is in range of countries with GNP per capita more than 10,000 USD [10]. However the fact that Iran GNP per capita is reported to be 2767 USD indicates that the country spends more on these products than expected [11]. However, due to presence of very cheap plasma derived medicines on the market and lack of national protocols for prescription and use of these medicines, irrational use of plasma derived medicines and smuggling the products into the neighboring countries are major concerns regarding use of these medicines in Iran.

4. Conclusion

In conclusion IBTO as a not for profit organization is the sole responsible organization for collecting, processing and distribution of blood and blood components in Iran. Although Iran currently is self sufficient in blood and blood components and all patients in need of such products receive these products free of charge, Iran market is heavily depends on importation of plasma derived medicines. Due to absence of a national protocol for use of blood and blood components and availability of these products free of charge for both public and private sectors, irrational use of these products is the major challenge of transfusion medicine in Iran. Unanimous subsidy of the government of Iran for plasma derived medicines which made them very cheap in the market and low surveillance on use of these medicines in Iran has caused irrational allocation of limited resources available in Iran health sector without proportional improvement of patients' quality of life.

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