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BLOOD SUPPLY MANAGEMENT IN AUSTERE CONDITIONS

Medical Science

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ABSTRACT

India has had very tragic experience, on numerous occasions in past with disasters of all kinds. Disasters may be manmade (battlefield, mass causalities by explosion etc) or natural (earthquake, tsunami, floods etc) inflicting massive impact of all kinds on the mankind. Apart from the effect on infrastructure, major irreparable impact is on the lives of those engulfed in the disasters leading to loss of lives and sustaining disabilities due to injury and blood loss. Hemorrhage accounts for the primary cause of death in any austere conditions, and is associated with almost two thirds of the potentially salvageable deaths. All these conditions have a common bottleneck, ie long transit time for definitive care of injury /trauma management in most cases and significant delay in evacuation of those affected. During managing these cases, blood and blood products are literally the life saving element. But unfortunately, there are huge logistical limitations in providing large volumes of transfusion fluids at the place required. Thus, there is a need for specific transfusion policy, enshrining the concept of damage control resuscitation and damage control surgery, to ensure, those injured, receive the best possible transfusion fluid within limited timeframe, to ensure his survival. The use of specific blood & blood products and in specific ratios will improve survival rate and reduce or prevent early and late deleterious transfusion sequelae. In addition, we need to be ready to embrace the latest innovations happening in the world and ensure that the same can be included in our disaster management system, so as to develop a feasible and optimal transfusion policy for stabilization of casualties in any austere condition thus having a positive impact on the whole life and limb saving efforts.

KEYWORDS

Whole Blood, Blood components, Artificial Blood, Freeze dried plasma

INTRODUCTION

Blood and blood products have a critical role to play in saving lives of those impacted by the disasters. Many of these conditions were limited in their impact on lives due to efficient support received from the Transfusion Services. Timely and abundant supply of Blood and blood products also has a special status in war, as many casualties are likely to bleed to death, if timely replacement of blood and blood products are not given.

Most of the blood and blood components are collected, processed, tested and stored at Regional blood banks / Transfusion centers which are to be delivered to the effected areas, before actual transfusion in those requiring it takes place. The issue is compounded by the fact that the life of blood is about 30 days, if preserved in ideal condition. Knowing the wide geographical terrain of India and unpredictable nature and location of these disasters and also the fragile nature of blood and blood components, it becomes imperative to maintain the blood supply chain robust till the far flung areas, where the actual consumption of blood and blood products is expected to take place.

A futuristic Blood supply management system will require close coordination between Transfusion centers and hospitals across the country with developed communication and information system, transportation and logistics support and critical utilities like fuel and power supply to ensure effective transportation and storage of blood and blood products in ideal condition, so as to meet the inescapable demands when required.

Aim.

To highlight the challenges in blood transfusion in austere conditions and to develop a conceptual plan for blood supply management in such conditions.

Haemorrhage, Coagulopathy and Haemorrhage control

In the recent experiences in some of the world's deadliest disasters, haemorrhage has been the most frequent cause of potentially preventable deaths. The older concept of massive transfusion with crystalloids is being challenged at all fronts with evidence pointing towards resuscitation with crystalloid fluids and plasma-poor red cell concentrates rapidly leading to dilutional coagulopathy [1]. Hypothermia and acidosis are also becoming frequent in all the disasters including the battle casualties with increasingly severe injury, which may cause profound coagulopathy by themselves [2]. Further, there is a renewed recognition of a syndrome of Acute Coagulopathy of Trauma [3]. All these findings suggest that there is an emergent need to look at the transfusion practices in the resuscitation of those most likely to progress to massive transfusion in order to actively prevent dilutional coagulopathy and treat the Acute Coagulopathy of Trauma.

The basic pathopysiology of the Coagulopathic bleeding broadly correlates with the concentrations and functional activities of plasma coagulation and anticoagulant proteins and platelets [1]. These concentrations and activities can be affected by a variety of pathophysiological processes occurring in the setting of acute trauma, including blood loss, dilution, acidosis, hypothermia, tissue injury leading to factor consumption and fibrinolysis [4]. The body has small amounts of the structural elements towards formation of blood clots, about 10 g of fibrinogen and 10 ml of platelets (1.25 trillion platelets), circulating in the blood under normal conditions. Shock in an otherwise healthy individual will represent the loss of 30– 40% of the blood volume or even more. The human body normally takes a day to produce that much fibrinogen and several days to replace those many numbers of platelets. Acute replacement of the lost volume, either by physiological vascular refill or with administration of crystalloids or non-plasma colloid solutions results in an equivalent degree of dilution. By the time the platelet count falls below 100×10^9 per litre, the skin bleeding time increases, and when plasma concentration of the individual coagulation factors fall below 25–40% of normal levels, both clinical coagulopathy and increase in the prothrombin time and partial thromboplastin times occur [1].

Hypothermia is a deadly feature of massive haemorrhage, as the injured cannot move to keep warm and are at risk for conductive, radiative and evaporative heat loss. Tissue hypoxia reduces mitochondrial activity, further reducing heat production. Heat loss can be made worse by adverse climatic conditions, exposure for examination and treatment and in the operating room with the exposure of large areas due to evaporative cooling. With a fully open abdomen, evaporative cooling can result in the loss of 1^0C every 40 min [5]. Hypothermia has a direct effect on the enzymatic rates of the coagulation proteins, reducing those rates by half at 30^0C. Hypothermia also decreases the synthesis of fibrinogen [6]. However, the greatest effect of hypothermia is on the activation of platelets through the interaction of von Willebrand's factor with the platelet-activating receptor complex, GPIb–IX. Kermode et al (1999) have shown that below 30^0C, this reaction fails to activate platelets from the majority of individuals [7].

Acidosis also affects clotting, destabilizing the coagulation protein complexes that normally form on the surfaces of activated platelets and profoundly reducing their activity. Thus, half of the normal activity of the Xa–Va complex is lost at a pH of 7.2, 70% being lost at pH 7 and 80% gone at pH 6.8 [8]. Acidosis also increases metabolic degradation of fibrinogen [9]. In pre and post-surgical trauma patients, the most important single factor associated with coagulopathy remains to be acidosis [10] [11].

The end result of all these pathophysiological processes on the clotting mechanism is that blood clots slowly and poorly in injured patients. The resulting weak clots are more likely to be disturbed in the manipulation necessary during evacuation of the injured and patient care, with the clots likely to break down prematurely. To tackle this issue, various approaches have come into play, which include local control of bleeding with tissue sealants such as fibrin glues and fibrin dressings, regional approaches such as abdominal packing in damage control procedures and systemic approaches such as rewarming and administration of procoagulants and antifibrinolytics. These techniques appear to save lives even in those situations where patients have died in the past.

Damage Control Resuscitation

The need for massive transfusion to replenish the massive blood loss sustained by the injured has risen, which has given rise to the concept of *Damage Control Resuscitation,* introduced as a resuscitation strategy, primarily for the most seriously injured patient.

It is a structured intervention that consists of two goals. The first goal is to limit fluid resuscitation, to keep the patient's systolic blood pressure at about 80 mm Hg to minimize renewed bleeding from recently formed blood clots [12]. The second goal is to restore the blood volume using plasma as the primary resuscitation fluid in a ratio close to 1:1 with RBCs to provide haemostatic resuscitation. Other blood products reserved for massive transfusion protocols, such as platelets, cryoprecipitate, and possibly, recombinant activated Factor VII and fibrinogen are being utilized across the world.

Permissive Hypotension

Permissive hypotension, or fluid resuscitation to a blood pressure lower than normal, was recognized as a reasonable approach in the care of casualties in both World Wars I and II [13] [14].

Today, fluid resuscitation practices to normalize the blood pressure rapidly after traumatic hemorrhage are no longer recommended, especially in patients with penetrating injuries [15] [16]. It has been argued that resuscitation to baseline or normal blood pressure can increase bleeding and worsen outcome because of severe hemodilution of remaining coagulation factors and hemoglobin, as well as disruption of newly forming blood clots.

Demand Forecasting : Estimation of quantity and type of blood required to meet the demands.

The prevalence of blood group in the Indian population, as per one of the studies by Javed Ahmed et al [17]is depicted in table below.

Table 1: Prevalence of various Blood group in Indian Population (Javed Ahmed et al)

PHENOTYPE	PREVALENCE in %
A+	22.16
A-	0.79
B+	30.91
B-	1.14
O+	36.47
O-	1.95
AB+	6.35
AB-	0.20
Total	**100**

These data will have to be taken into account while planning for the initial requirement package. In addition, for effective trauma care, use of FWB (fresh whole blood) requires consideration as its use has been proven to be invaluable and indeed life saving in many situations[18].

Large scale storage of blood and components before transpor tation.

Specific controlled space will be required to be earmarked for the purpose of large scale storage. Requisite equipments with adequate provisions for power supply and backups also need to be addressed.

Constraints for an efective Blood Transfusion Policy.

- Higher number of casualties leading to higher need for blood/blood products than planned for.
- Need for resuscitation at various dispersed and even geographically far forward locations.
- Difficulty in transportation due to logistical challenges.
- Need for point of care technological additions/ innovations to enhance care capabilities

Future Products / Transfusion Concepts

Use of Plasma: Platelets: RBCs in 1:1:1ratio.

The evidence of using increased plasma: platelets: RBC ratios in severely injured patients are hard to ignore. Use of plasma, including plasma to RBC ratios that approached 1:1 improved the coagulopathy and reduced 30-day mortality compared to the use of more RBCs or ratios of plasma to RBCs greater than 1:4 [19] [20] [21].

The balanced resuscitation practice is rapidly becoming widespread. This early and increased use of plasma and platelets does place significant stress on the blood banking system. In a logistically challenged system or remote / austere conditions, the supply chain of RBCs, frozen plasma, cryoprecipitate, and freshly drawn platelets will be difficult to maintain and is likely to fail in present conditions. However, such needs cannot be avoided and in near future, mechanisms will have to be put in place to ensure that the transfusion practices are standardized in the correct ratio to ensure maximum casualty survival.

Walking Blood bank and Fresh whole blood transfusion.

One very viable option in many parts of the world like United States and Israel, is the institution of the walking blood bank and fresh whole blood transfusion. Research have validated successful use of warm, fresh, whole blood even in difficult situations like war theater, where, over 6000 units have been transferred over a 4 to 5 year period during operation Desert Storm [17]. Other research have shown improved 30-day survival with warm, fresh, whole blood compared to casualties who received component therapy, as well as acceptable benefit- to-risk ratios under situations where blood components are unavailable or not available in sufficient amounts for transfusion requirements [22] [23] [24].

Freeze dried Plasma and other components.

The field of Transfusion is fast evolving and newer products such as freeze dried plasma, platelets, fibrinogens and RBCs are being continually tried and tested in various parts of world. These products are largely disease free, readily available, easily stored and with a much larger shelf life and will hence provide greater usability.

Various research have validated that freeze-dried plasma was similar to fresh- frozen plasma in its coagulation factor levels and could improve the coagulopathy associated with transfusion [25][26]. In Indian context, with such great geographical diversity and large unpredictable areas where disasters can touch mankind, these newer products will form the basis of future transfusion policies.

Fluid for small volume resuscitation.

Tactical Combat Casualty Care committee of the US army has recommended Hextend, a hetastarch based product in a balanced salt solution, as the fluid of choice for small volume resuscitation, with guidance to limit the total infusion to one liter based on the patients mental status or pulse character. No fluid is recommended if the casualty is not in shock [27]. This recommendation may translate to colloids being selected as the initial fluid of choice while resuscitating casualties in future.

Tranexamic acid (TXA).

Tranexamic acid (TXA), an anti-fibrinolytic agent, has been used to decrease bleeding and the need for blood transfusions. The Joint Theater Trauma System Clinical Practice Guidelines in Operation Iraqi Freedom and Operation Enduring Freedom have recommended use of TXA within 3 hours of injury for cases requiring massive transfusion. A large prospective randomized trial demonstrated a decrease in mortality in trauma patients who received TXA within 3 hours of injury [28].

Artificial Oxygen Carriers [29] [30].

Artificial oxygen carriers have been developed to obviate the shortcomings of packed red cells. It has various benefits as elucidated below:

- These are universally compatible as there is no need for typing or crossmatching, preventing the risk of ABO incompatibility.
- Artificial blood substitutes are universally compatible.

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- Artificial haemoglobin carriers have an extended shelf life of 1-3 years at room temperature, which allows for stock-piling for emergencies, trauma, disasters and warfare.
- Blood substitutes provide a disease-free source of blood.
- Artificial blood substitutes are at full oxygen capacity immediately.

Table 2 : Comparison of Artificial Oxygen carriers and RBC on various parameters [29].

	Hemopure (HBOC -201)	Poly Heme	RBCs
Origin	Bovine	Human	
Haemoglobin(g/dL)	13	10	13
P50 (mm Hg)	38	29	26.8
Half Life	19 Hours	24 Hours	31 days
Shelf Life @ 4oC	>= 3 Years	>= 1.5 Years	42 days
Shelf Life @ 21oC	>= 2 Years	>= 6 Weeks	< 6 hours

Blood supply management.

Demand Forecasting. The demand of blood and blood products for future austere conditions needs to be worked out which will largely depend upon past experience, data and also databanks of the other countries who are better placed in handling such unforeseen conditions. It forms the basic premise for planning and executing our future blood policies.

Initial Collection and storage. The issue of point of collection of Blood will be the determining factor for the policy of transfusion particularly in geographically far forward areas. This will be determined by the choice of the blood product for transfusion, whether it will be Fresh whole blood or components or a mix of both.

Fresh Whole Blood (FWB). The concept of considering each and every individual as a "walking blood bank" saves the vital transit time of carrying either the casualty or the blood and its components to the desired location. Requisite infrastructure needs to be put in place to implement the concept of Walking Blood Bank. This will require augmenting the whole system by creating multiple small transfusion teams with blood transfusion assistant along with 2 persons with few essential items required to carry onsite transfusion. The standard supply channels will have to provide with materials for the collection and transfusion of FWB, including phlebotomy kits, collection and transfusion tubing, citrated blood bags, and reagents for blood typing. The only limitation/ challenge is the formulation of robust Policies regarding Indications, Collection, Testing, Transfusion, legal and Documentation which needs to be mandatorily in place prior to exercising the concept of FWB Transfusion.

Component Therapy. Newer safe initiatives demand for greater use of plasma, platelets and cryoprecipitates. Shelf life of Platelets is very short, only 05 days, on platelet agitator at 20°C. Hence, if it is to be used in far flung zone, it has to be prepared at the distant medical facility. Platelets can be prepared from whole fresh blood or through cell separator machines (SDPs), as used by US and Israel army. It can be accomplished with adequate numbers of well trained Blood Transfusion Assistants, requisite kits, Blood bags, space for bleeding, basic testing, grouping and cross matching and most importantly platelet agitators.

Platelets FFP

Cell separator Platelet agitators

FFPs and cryoprecipitate can be prepared at base level and transported in remote areas with help of deep freezers/ walk in coolers for transportation and storage.

Freeze dried blood products can be used as these can be easily prepared at the blood banks/ transfusion station/ sub-station and further disseminated as per requirements. It is more feasible keeping in mind that it will increase the shelf life to 4 – 5 years, hence reducing the burden of manpower required at forward areas and relatively less equipment intensive.

Freeze Dried Plasma.

(a) **Initial Push Package.** The initial amount of blood and blood products required will be based on the demand forecast for the initial period as worked up based on the past data. This initial push package will form the basic unit to be provided immediately for meeting the emergent requirements before the actual logistics/ medical supplies system is established and stabilized.

(b) **Transportation**. Timely and adequate transport of blood and blood product is the mainstay of logistics of Transfusion assets. The challenges are to maintain the Cold chain while transporting and timeliness of transport to ensure that the blood products reach the end user as early as possible and in best possible condition. Air transport of Blood and Blood products is a necessity and has to be made available as soon as possible for maximum impact.

(c) **Inventory holding**. Adequate equipments and necessary arrangements for alternate power supply in form of high power generators need to be in place, so as to sustain cold chain requirements in terms of refrigerators and deep freezers. Inventory holding and disposal of waste need to be governed by elucidating fresh set of guidelines and protocols.

(d) **Pull process for re-supply**. Further supply of blood products will depend on the requirements being projected from the far forward locations. In this era of information technology, it is imperative that a proper Medical Logistics Information management system is put in place to ensure smooth, efficacious and effective supply of blood and blood transfusion products for greater effectiveness, and this will form the basis of the pull process for re-supply.

(e) **Final issue and use for damage control resuscitation**. The final issue will be based on the demands being generated from different axis of area affected, the availability of resource in terms of FWB / Components or newer products and feasibility of transport in minimum time period. The protocols for Damage Control Resuscitation will also play an important role in the final issue of blood products. The concept of **LIFO–Last In First Out**, needs to be implemented for cases requiring massive transfusion. This ensures that the freshest set of blood product is made available for patients requiring massive transfusion to decrease chances of deleterious effects of transfusion and avoid the red blood cell 'storage lesions'.

CONCLUSION.

Providing appropriate blood and blood products to save lives, at the time and place required, particularly, in the far flung areas inflicted with disaster, definitely remains a challenge to the best of the countries of the World. Success in the field of blood transfusion is primarily by following the dictum of adequate bleeding, minimum storage time, quick transportation and maximum utilization of blood and blood components. Fresh Whole blood remains the best fluid for resuscitation; hence maximum use of Fresh whole blood in form of capabilities for blood transfusion needs to be addressed and strengthens. The logistical difficulties of FWB can be counter balanced by the benefits of small volume, lightweight, ambient temperature storage; lyophilized products; and recombinant proteins [32]. The present blood policy should also concurrently include the evolutions taking place around the world, in the field of Transfusion Medicine, to take care of the casualties sustained in this geographically diverse country and ensure minimum morbidity and mortality due to Blood loss.

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