Key technologies for improving Patient Blood Management

This white paper provides an overview of the key aspects of patient blood management (PBM) and discusses the role of products and technologies such as viscoelastic hemostatic assays (VHA), cell salvage devices and Point of Care Electronic Blood Management (PoCEBM) systems in enabling and improving PBM.

By João Dias, PhD and Mark Popovsky, M.D.

Patient blood management (PBM) refers to all strategies and approaches to optimizing care of patients that are at risk of anemia and/or might need blood transfusion during hospitalization, with a specific emphasis on reducing allogeneic blood transfusion (ABT) and using a patient's own blood whenever possible.[1,2] Key aspects of PBM include the use of appropriate dose and thresholds for transfusion, intra- and postoperative blood management and the implementation of good practice for blood avoidance, and the use of blood.

The first part of this document discusses the background and rationale of PBM, describes its key aspects and approaches and provides some examples as to the value and importance of its implementation. The subsequent parts detail how VHAs, cell salvage devices and PoCEBM systems can play an important role in enabling and improving key aspects of PBM.

PBM: Background and rationale

An important mechanism of anemia is the loss of red blood cells (RBCs) and a decrease in hemoglobin levels. It can occur due to underlying conditions or from loss of blood, and commonly occurs during surgery, with orthopedic surgery being the leading indication for transfusion.[3-5] The prevalence of preoperative anemia varies across patient populations and is estimated to be between 5–76%.[6] Postoperative anemia is even more common, particularly in orthopedic surgery, where the rate of anemia has been reported to be in the range of 51–87%.[7]

ABT is commonly employed to correct surgical anemia with the goal of improving tissue oxygenation. However, the efficacy of ABT remains poorly demonstrated in clinical studies, and the ability of ABT to improve clinical outcomes and restore tissue oxygenation has been questioned.[8] Extended storage leads to specific deficits in the ability of RBCs to transport and release oxygen to tissues.[9] Furthermore, RBC storage induces a wide range of other deleterious properties, including increased adhesiveness, aggregability and the accumulation of proinflammatory bioactive substances.[10]

Transfusion-related acute lung injury, hemolytic transfusion reactions and transfusion-associated sepsis are the leading causes of transfusion-related deaths.[11] Furthermore, ABT is associated with a range of other infectious, immunologic and nonimmunologic complications, including viral and bacterial infections, allergic and anaphylactic reactions, transfusion-associated graft-versus-host-disease, circulatory overload and metabolic disturbances.[12]

In addition to the clinical risks of ABT, the economic costs are also high. An increase in acquisition costs due to increasing regulatory requirements, disease/infections testing and hospital administration costs make blood and blood products ever-increasingly expensive resources. Both direct and indirect costs of blood products contribute to the total cost of blood transfusion, estimated at USD 1.62–6.03 million per hospital anually for surgical patients alone.[13] In recent years, awareness of the clinical and economic costs associated with autologous transfusions have led to increased interest in PBM.[1,2,14]

PBM: Key aspects and approaches

PBM comprises three main aspects, sometimes referred to as the three pillars of PBM.[15-18] The three pillars, and some examples of each, are shown in Figure 1.

Optimization of Erythropoiesis	Minimization of Blood Loss and Bleeding	Anemia Tolerance Optimization
▪ Identify, evaluate and treat underlying anemia ▪ Time surgery with optimization of erythrocyte mass ▪ Manage nutritional/ correctable anemia ▪ Erythropoietin-stimulating agent therapy where appropriate	▪ Identify and manage bleeding risk ▪ Review medication ▪ Minimize iatrogenic blood loss ▪ Blood-sparing surgical techniques ▪ Anesthetic blood conserving strategies ▪ Cell salvage/reinfusion ▪ Pharmacologic/ hemostatic agents	▪ Compare estimated blood loss with patient-specific tolerable blood loss ▪ Evidence-based transfusion triggers ▪ Maximize oxygen delivery

Figure 1. An overview of the three pillars of patient blood management with some examples

In its broadest sense, PBM encompasses all strategies, from the primary to the tertiary care level that can help reduce the need for ABT. The most critical stage, however, is in the hospital, during all stages of the perioperative period, when the risk of bleeding and anemia is the highest. Here, new products and technologies can be of key importance for guiding evidence-based clinical decision making and improving operational aspects of transfusion within a PBM framework.

PBM: Value and importance of implementation

The World Health Organization has urged its member states to implement PBM strategies, yet the extent to which they are implemented varies significantly between countries.[1] In Europe, for instance, transfusion guidelines are considered to be moderately implemented. Although hemoglobin levels are regularly used as a transfusion trigger, hypotension and tachycardia remain the most widely used, and these physiological triggers may have low discriminative power for tissue hypoperfusion.[19] Furthermore, full implementation of a PBM strategy involves more than adopting transfusion guidelines, as PBM aims for the implementation of a wide range of strategies in the pre-, intra- and postoperative setting, aimed at minimizing patient blood loss and, consequently, the need to use allogeneic blood (see Figure 1). Countries including Australia, the United Kingdom and the Netherlands have already made significant progress in implementing PBM; the United States, Switzerland, Austria, Germany and Spain are also now beginning to implement PBM.[1]

The United Kingdom PBM guidelines are primarily aimed at implementing PBM at a hospital level.[20] The guidelines comprise a wide set of recommendations aimed at reducing blood use during the pre-, intra- and postoperative period, including: the use of appropriate dose and thresholds for transfusion; preoperative management of Haemostasis; intra- and postoperative blood management, such as the use of cell salvage where appropriate; and, importantly, implementation of good practice for blood avoidance and use of blood. The Australian guidelines contain similar recommendations but takes a more holistic approach and also provide recommendations regarding diagnosis and testing at the primary and secondary care level prior to hospitalization, in order to further optimize the handling of anemia and reducing ABT during upcoming surgery.[21] Other PBM guidelines include the Seville document[17] in Spain and the Italian PBM guidelines.[18]

In addition to reducing patient exposure to potentially detrimental ABT, implementation of PBM can also lead to significant cost savings. Nine years after the introduction of PBM in Dutch hospitals there was a 12% nationwide decrease in ABT, resulting in a EUR 100 million net cost saving annually.[1] In Scotland and England, a 22% reduction in RBC transfusion between 2001 and 2012 has led to savings of around GBP 100 million annually.[22] In New South Wales, Australia, implementation of PBM has reduced blood usage by 27.4% over a five year period, which has led to a 7.8% reduction in hospital expenditure on acute care inpatients and represents an annual cost saving of AUD 8.5 million.[23] Similar reductions in RBC use and associated costs have also been reported other hospitals that have implemented PBM strategies, including the Johns Hopkins hospital.[24,25]

Summary

- PBM refers to a set of approaches aimed at reducing the need for ABT, which is often ineffective and is associated with increased risk of complications, morbidity and mortality.
- Implementation of PBM can reduce RBC requirements by more than 20%. In the United Kingdom and the Netherlands, countries which have made significant progress in implementing PBM, this has led to estimated annual cost savings of around GBP 100 million and EUR 100 million, respectively.
- PBM strategies include:
  - Use of appropriate dose and thresholds for transfusion
  - Preoperative management of Haemostasis
  - Intra- and postoperative blood management and the use of cell salvage, where appropriate
  - Implementation of good practice for blood avoidance and use of blood

Managing bleeding risk and using appropriate blood component and dose

Coagulation testing for managing bleeding and guiding transfusion

The use of near-patient testing enables rapid and accurate assessment and diagnosis of coagulopathy providing clinicians with the information they need to correctly manage hemorrhage and reduce blood loss, thereby reducing unnecessary ABT.

The understanding of coagulopathy and optimal transfusion algorithms is continuously evolving. A number of parameters are known to be useful in managing bleeding and guiding transfusion: for instance, hemoglobin levels are generally used as a trigger for RBC transfusion; prothrombin time/activated partial thromboplastin time/international normalized ratio are used for fresh frozen plasma (FFP) transfusion; platelet count for platelet transfusion; and fibrinogen levels for cryoprecipitate transfusion.[26] The use of near-patient coagulation tests for transfusion management of massive hemorrhage has been well-established and is recommended in guidelines.[27,28]

The Haemonetics thromboelastography (TEG) system

Viscoelastic hemostatic assays (VHAs) are performed to assess coagulation in a sample of whole blood. The Haemonetics thromboelastography (TEG) system is a real-time analyzer of whole blood measuring the viscoelastic properties of the hemostasis process and allows for individualized goal-directed therapy. It provides rapid, comprehensive and accurate identification of an individual's hemostasis condition, in a laboratory or in the context of near-patient testing, which allows clinicians to drive personalized, clinically and economically sound treatment and monitoring decisions.

A variety of assays can be run on the TEG device, providing insights into different aspects of coagulation. Although von Willebrand factor is not detected, the effects of most whole blood components (e.g. coagulation factors, platelets, fibrinolytic factors and inflammatory cells) are included in TEG analysis. Also, the full process of coagulation and subsequent clot lysis is followed. TEG results therefore provide a good reflection of the cell-based model of hemostasis

Application and benefits within a PBM framework

In addition to the potential beneficial effects of optimizing transfusion on patient outcomes, there are also significant economic benefits. The reduction in blood components achieved by preoperative platelet mapping prior to surgery led to a 45% cost saving on blood components.[30] Based on modelling data assuming 500 patients per year, the use of TEG in cardiac surgery could lead to an annual net cost saving of EUR 302,250 while reducing transfusion-related adverse events by 26.[43] A United Kingdom NICE study confirms that the use of VHAs such as TEG was cost saving and more effective than standard coagulation tests, with the cost-efficacy of TEG being superior.[44]

Summary

- Viscoelastic hemostatic assays (VHAs), such as thromboelastography (TEG) enable rapid and accurate assessment and diagnosis of coagulopathy in a sample of whole blood
- TEG assays form an integral part of PBM by providing clinicians with key information about a patient's hemostasis condition, thereby reducing the amount of unnecessary ABT
- TEG can assess several parameters simultaneously and provide results faster than standard laboratory tests, reducing the time needed to make accurate transfusion decisions and potentially leading to improved outcomes
- In addition to the potential clinical benefits, implementation of TEG can produce a net annual cost saving of approximately USD 300,000 per average size hospital.

Intra- and postoperative blood management

Reducing the need for ABT with intra- and postoperative cell salvage and reinfusion

Anemia due to blood loss is common during surgical procedures,[3-5] and cell salvage management aimed at reducing the need for ABT is therefore a vital aspect of PBM. In addition to reducing ABT through accurate assessment and diagnosis of coagulopathy, the need for ABT can be further reduced by intraoperative and postoperative recovery and reinfusion of a patient's own blood using cell salvage devices.

There is a wide range of data from randomized controlled trials and systematic reviews that support cell salvage as an effective and cost effective method for reducing the need for ABT in a variety of surgical settings.[45-50] The use of cell salvage in trauma is also being investigated.[51] Current guidelines recommend the use of cell salvage in a number of operative scenarios, including cardiac surgery, major orthopedic surgery, surgery and blood loss in obstetric settings and in oncological surgery.[28,52,53]

Several devices employing different technologies are available for reinfusing a patient's own blood. In the direct transfusion method, the salvaged blood is returned to the circulation without hemoconcentration or washing. With ultrafiltration, water, electrolytes and small molecules are first removed by passing the blood through a semipermeable membrane. The cell saver method is based on the separation, washing and selective reinfusion of RBCs.[54] Due to issues with quality and safety of blood, PBM guidelines have specifically suggested using washed blood for reinfusion in surgical settings.[18]

The Haemonetics Cell Saver and Autotransfusion Systems

- **The Cell Saver® 5+/Cell Saver® Elite®** autologous blood recovery system is designed for use in procedures where medium- to high-volume blood loss occurs, and has the ability to deliver moderate hematocrit and to help remove traces of undesirable components such as free hemoglobin.

- **The OrthoPAT®** orthopedic perioperative autotransfusion system is a fully automated device that collects, washes, and returns a patient's blood during and after orthopedic surgery helping to give the best chance at avoiding unnecessary allogeneic transfusions and related risks of infection. The system consistently delivers fresh RBCs with high hematocrit, reducing the need for ABT. The processing of autologous blood, separation of plasma and washout of cell debris, and undesirable contaminants, as well as collection into the retransfusion bag, is performed automatically.

Applications and benefits within a PBM framework

By recovering and re-infusing a patient's own blood, the need for potentially unnecessary ABT and its associated risks is reduced. Cell salvage is a safe,efficient and cost effective method for reducing the need for exposing a patient to ABT.[47,50]

Summary

- Cell salvage and reinfusion of a patient's own blood can reduce the need for ABT

- Several methods for cell salvage and reinfusion exist, but guidelines specifically suggest the use of washed blood for reinfusion in surgical settings

- The Haemonetics Cell Saver® and OrthoPAT® are autotransfusion systems capable of returning a patient's RBCs after washing and removal of debris and contaminants

- Cell salvage is a safe, efficient and cost-effective method for reducing the need for exposing a patient to ABT

Implementation of good practice for blood avoidance and use of blood

Point of Care Electronic Blood Management (PoCEBM) systems offer a way to implement and improve end-to-end control of hospital blood transfusions. By improving storage and tracking of blood components, such systems may improve efficiency and have a beneficial impact on several aspects of transfusion where errors are likely to be made.[20,55-62] As such, PoCEBM play an important role in the implementation of good practice for blood avoidance and the use of blood within a PBM framework that can be used in addition to other strategies in order to further improve operational aspects of transfusion and reduce blood wastage.

Hemovigilance systems as a tool for improving the blood transfusion chain

Errors of transfusion are common and can be divided into different types of errors:

- **Avoidable, delayed or under-transfusion (ADU):** Occurs when the intended transfusion is carried out, and the blood/blood component itself is suitable for transfusion and compatible with the patient, but where the decision leading to the transfusion is flawed. It also occurs where a transfusion of blood/blood component was clinically indicated but was not undertaken or was significantly delayed. Finally, it occurs during avoidable use of emergency O RhD negative blood where group-specific or crossmatched blood was readily available for the patient.

- **Handling and storage errors:** All reported episodes in which a patient was transfused with a blood component or plasma product intended for the patient, but in which, during the transfusion process, the handling and storage may have rendered the component less safe or not suitable for transfusion.

- **Incorrect blood component transfused:** Comprises two types of errors, wrong component transfused (WCT) and specific requirements not met (SRNM). WCT occurs when a patient was transfused with a blood component of an incorrect blood group; a blood component which was intended for another patient and was incompatible with the recipient; a blood component which was intended for another recipient but happened to be compatible with the recipient; or a blood component which was different than that prescribed (e.g. platelets instead of RBCs). SRNM occurs where a patient was transfused with a blood component that did not meet their specific transfusion requirements, for example irradiated components; human leucocyte antigen (HLA)-matched platelets when indicated; antigen-negative RBC units for a patient with known antibodies; RBCs of extended phenotype for a patient with a specific clinical condition (e.g. hemoglobinopathy); or a component with a neonatal specification where indicated. Notably, the above does not include cases where a clinical decision was taken to knowingly transfuse components not meeting the specification in view of clinical urgency.

PoCEBM and other systems can play a key role in hemovigilance and improving the blood transfusion chain by:

- **Reducing the number of allogeneic blood units transfused.** By facilitating the implementation of the transfusion committee guidelines as, for example, one unit policy and behavior change from just-in-case to just-in-time.

- **Facilitating improved blood availability.** Blood availability can be facilitated by optimizing the transport, availability and other operational aspects of transfusion. Potential areas for optimization include: blood inventory management; time to get the right blood; just-in-time instead of just-in-case point of care blood storage and allowing for re-routing of blood units in the blood bank that would otherwise be on hold.

- **Reducing human error.** The majority of transfusion-related adverse events are due to preventable clerical errors[47] such as errors of storage and handling and transfusion of incorrect blood components. PoCEBM systems have the potential to significantly reduce the amount of human errors in the blood transfusion chain.

Due to the potential benefits associated with PoCEBM, the use of these systems has been recommended in several guidelines. The United Kingdom NICE transfusion guidelines recommend that hospitals consider using a system that electronically identifies patients in order to improve the safety and efficiency of the blood transfusion process and to reduce wastage.[63] The Joint Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee also recommends the use of electronic transfusion management systems using barcodes on ID bands and blood components; handheld scanners linked to the laboratory information systems are also recommended.[64] In Italy, proper patient identification using wristbands is now regulated by law, and it is possible other countries will adapt a similar approach in the future.[65]

The Haemonetics BloodTrack System

BloodTrack is a modular blood management and bedside transfusion solution that combines software with hardware components to act as an extension of your blood bank transfusion management system. Through integrated modules, BloodTrack solutions provide the control, visibility, and traceability needed to safely and properly store, dispense, and transfuse blood products at the point-of-care and verify that the right blood is transfused to the right patient at the bedside. BloodTrack can improve hemovigilance within a PBM framework through several features, as shown in Figure 2.

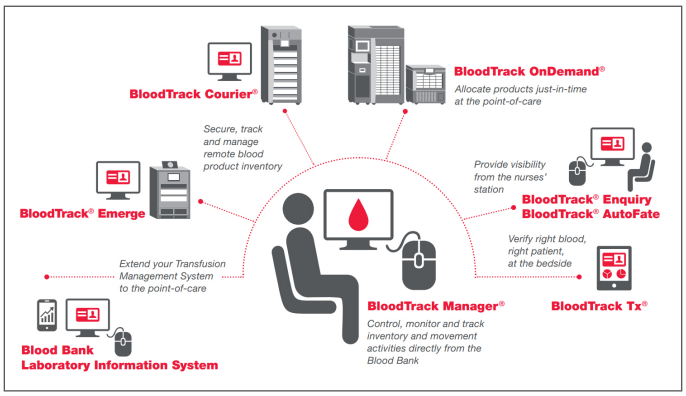

Figure 2. BloodTrack comprises a range of modules that can improve various aspects of the transfusion workflow, such as blood inventory management; just-in-time blood product allocation; clinical transfusion workflow; bedside transfusion verification and transfusion management

Applications and benefits within a PBM framework

There is a significant body of evidence demonstrating that implementation of PoCEBM systems in hospitals can reduce the amount of blood components used and lead to a substantial reduction in transfusion-related costs. In one hospital, the median time needed to deliver urgently needed RBC units was 24 minutes prior to implementation of PoCEBM. After the implementation of an PoCEBM system, which included the use of a nearby blood refrigerator, the median time taken to deliver RBCs was reduced to 59 seconds.[66] In addition to the reduction in delivery time, a number of other important benefits were observed: the number of unused requests were reduced from 42% to 20%; the total number of RBCs issued was reduced by 52%; the number of issued units that were actually transfused was increased from 40% to 62%; and a significant reduction was observed in the workload of both blood bank and clinical staff. In another hospital, the introduction of PoCEBM reduced the amount of unused blood orders from 70% to 25%.[67] The implementation of PoCEBM was also shown to reduce the percentage of preoperative blood orders by 38% and the ratio of crossmatch-to-transfusion by 27%.[68]

The reduction in the number of issued blood components is associated with significant cost savings. At the hospital mentioned above,[68] the annual cost savings on blood components was USD 298,966. In a costing statement issued by NICE, it was concluded that implementation of PoCEBM was associated with significant cost savings both in terms of reductions in the amount of blood used and increased productivity.[69] Expenditure on blood was reduced by 10% because access to blood was quicker and less components were wasted. After taking into consideration the system management and service costs, this led to a net saving of GBP 4.561 per 100,000 population, in addition to a productivity saving of GBP 500,000.[69] Based on modelling data assuming 500 patients transfused with three RBC units each, the introduction of Haemonetics BloodTrack in a hospital produces an annual net cost saving of USD 317,660.[70]

Summary

- Common errors that occur during transfusion include avoidable, delayed or under-transfusion; handling and storage errors and transfusion of incorrect blood components
- Point of Care Electronic Blood Management (PoCEBM) systems can play a key role in improving the transfusion chain by:
  - Reducing the amount of allogeneic blood units transfused
  - Facilitating improved blood availability
  - Reducing human error
- In addition to clinical benefits associated with a reduction in the number of potentially detrimental transfusion errors, implementation of PoCEBM systems can lead to annual net cost savings of approximately USD 300,000 per average size hospital

Summary

Allogeneic blood transfusion (ABT) is associated with increased risk of infectious diseases and other complications as well as increased morbidity and mortality.

- **Patient blood management (PBM)** refers to all strategies and approaches to optimizing care of patients that are at risk of anemia and/or might need blood transfusion during hospitalization, with a specific emphasis on reducing ABT and using a patient's own blood whenever possible. Key aspects of PBM include optimization of erythropoiesis; minimization of blood loss and bleeding; and anemia tolerance optimization.

Several key technologies exist that enable and improve the implementation of PBM:

- **Thromboelastography (TEG) assays** and other viscoelastic hemostatic assays (VHAs) allow for rapid and accurate assessment and diagnosis of coagulopathy at the point of care and provides clinicians with the information they need to correctly manage hemorrhage and reduce blood loss, thereby reducing unnecessary ABT.
- **Cell Saver/OrthoPAT** and other cell salvage devices allow for intraoperative and postoperative salvage and re-infusion of a patient's own blood, further reducing the need for ABT.
- **BloodTrack** and similar Point of Care Electronic Blood Management (PoCEBM) systems improve the operational aspects of transfusion by reducing transfusion errors, improving blood availability when needed and reducing blood wastage.

These technologies represent valuable tools for reducing the need for ABT within a PBM framework. In addition to reducing patient's exposure ABT and its associated risks, the reduction in ABT and blood components leads to significant net cost savings.

About the Authors

Dr. Mark Popovsky was Clinical Associate Professor of Pathology at Harvard Medical School and Beth Israel Deaconess Medical Center for more than 20 years. He has served on 7 editorial boards, authored more than 375 peer-reviewed publications, published 2 reference books on transfusion medicine, and served on many national and international committees. He served as Chief Medical Officer of Haemonetics for 15 years and is currently serving as a medical consultant to the company.

Dr. João Dias is an honors graduate of the University of Helsinki faculty of Medicine in Biomedicine. He has authored several publications in Oncology, Immunology and Hemostasis and served as a reviewer in several journals. Prior to his tenure at Haemonetics Dr. Dias has worked in the R&D development of new products in cancer gene therapy and served as life sciences consultant in multiple global life-science companies. He currently serves as medical science expert for the Haemonetics EMEA region for the complete portfolio of products including in vitro coagulation diagnostics, and specialized blood management devices utilized in Hospitals and Blood centers.

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