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Perioperative patient blood management to improve outcomes

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Perioperative patient blood management

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Abstract

Anemia is common in elective surgery and is an independent risk factor for morbidity and mortality. Historical management of anemia has focused on the use of allogeneic blood transfusion but this in itself is not without risk. It too has been independently associated with morbidity and mortality, let alone the costs and relative shortage of this resource. In recognition of this, patient blood management shifts the focus from the product to the patient and views the patient's own blood as a resource that should be conserved and managed appropriately as a standard of care. It consists of three pillars: the optimization of red blood cell mass; reduction of blood loss and bleeding; and optimization of the patient's physiological tolerance towards anemia. Integration of these three pillars in the form of multimodal care bundles and strategies into perioperative pathways should improve care processes and patient outcome.

Preoperative anemia is most commonly caused by functional iron deficiency and should be treated with oral iron, intravenous iron and/or recombinant erythropoietin. An individualized assessment of the thrombotic risk of discontinuing anticoagulant and antiplatelet medication should be balanced against the risk of perioperative bleeding. Neuraxial anesthetic techniques should be considered and minimally invasive surgery undertaken where appropriate. Cell salvage should be used if significant blood loss is anticipated and pharmascological treatments such as tranexamic acid and fibrin sealants have been shown to reduce blood loss. Point of care tests can guide the perioperative management of dynamic coagulopathy. Blood testing sampling should be performed only when indicated and when taken, sample volume and waste should be minimized. Restrictive blood transfusion thresholds and re-assessment after single unit transfusion should be incorporated into clinical practice where appropriate.

Introduction

Anemia is common and is associated with significant morbidity and mortality.[1] In the past, transfusion practice in the perioperative period focused on the use of allogeneic blood to treat and correct anemia which was culturally embedded as default therapy. It has become increasingly clear however that allogeneic blood transfusion (ABT) itself is an independent risk factor for poor clinical outcomes.[2] Moreover, the cost of transfusion continues to escalate and the gap between supply and demand of this scarce resource is ever widening.[3] In response to these drivers, there has been a paradigm shift from a product focus to a patient focus in transfusion medicine.

Patient blood management (PBM), defined by the Society for the Advancement of Blood Management (SABM), is the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin (Hb) concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcomes. It rejects the standard dogma which considers red blood cell (RBC) transfusion to be the primary solution in the correction of anemia and views the patient's own blood as a resource that should be conserved and managed appropriately as a standard of care. PBM can be seen as consisting of three pillars, the optimization of RBC mass, reduction of blood loss and bleeding, and optimization of the patient's physiological tolerance towards anemia.[4] Patient-centred decision-making is crucial when determining an individualized management plan and involves the communication of the risks and benefits of the various potential interventions to decide upon the right course of action.

In 2010, PBM was adopted by the World Health Organization (WHO) and it is supported by NHS Blood and Transplant (NHSBT) and the National Blood Transfusion Committee in the UK. Started at the earliest opportunity prior to surgery and continued into the postoperative period, PBM

addresses the triad of independent risk factors that can affect outcome in surgical patients, namely anemia, blood loss and transfusion. It is in the setting of elective surgery where the most evidence for benefit of PBM has been demonstrated in reducing exposure to ABT and improving patient outcomes.[5]

In this article, we will review the outcomes associated with anemia and ABT and consider how the three pillars of PBM can provide a structure for multidisciplinary and multimodal care bundles and strategies that can be instituted into perioperative pathways with the aim of improving patient outcome.

Anemia: definition, causes and outcomes

Since 1968, the WHO has defined anemia as an insufficient circulating red cell mass with a Hb level <13 g/dL in males and <12 g/dL in menstruating females.[6] More than 30% of the world's population are anemic but the incidence varies with age and comorbidity. In the US National Surgery Quality Improvement Program (NSQIP), the prevalence of anemia in patients undergoing surgery was 30.4%[1] while in Europe, it was found to be 28.7%.[7] Estimates of anemia in surgical patients range widely as the underlying surgical condition can predispose the patient to anemia, from 5% in elderly females with hip fracture to 75.8% in Dukes stage D colon cancer.[8] Postoperative anemia is more common than preoperative anemia and can be present in up to 90% of patients after major surgery.[8]

Anemia has multiple different causes such as hemoglobinopathy, nutritional deficiencies and renal failure. One of the most prominent causes is iron deficiency[9] and can be either absolute or

functional. In a 70 kg male, total body iron is about 3500 mg, of which most (65%) is found in Hb within the RBC and much of the remainder is stored in the liver, macrophages and bone marrow.[10]

In absolute iron deficiency, there is a reduction in the total body iron which can either be present in isolation, when the level of erythroid iron is still sufficient for erythropoiesis, or in conjunction with anemia. In functional iron deficiency, in contrast, there is iron-restricted erythropoiesis despite normal or even increased total body iron. Inflammation, whether caused by autoimmune mechanisms, infection or malignant cells, can result in functional iron deficiency secondary to its activation of hepcidin and thus functional iron deficiency is the most common cause of anemia of chronic disease.[11] Hepcidin is an amino acid glycoprotein produced in the liver whose normal role is act on ferroportin, a transmembrane iron transporter found in duodenal enterocytes and macrophages. Degradation of ferroportin by activated hepcidin prevents enteral iron absorption and transport of iron from the liver, where it is stored as ferritin, and macrophages to the plasma. Consequent to this, binding of transferrin, the plasma iron transport protein, to iron is reduced and less iron is delivered to the bone marrow affecting effective erythropoiesis.[12]

Of concern, anemia is an independent risk factor for perioperative morbidity and mortality in cardiac[13-16] and non-cardiac surgery[17-19] and is not just a laboratory value but also a disease in itself. Mild anemia leads to impaired functional capacity and performance and a reduced quality of life.[20]

In a retrospective cohort study, which used data from the American College of Surgeons' NSQIP, the effect of mild and moderate-severe anemia was evaluated in 227,425 patients undergoing elective major non-cardiac surgery.[1] Preoperative anemia was associated with a 35% increased odds ratio of composite postoperative morbidity and a 42% increased odds ratio of mortality at 30 days. Of note, this relationship was present for mild anemia as well. Data from NSQIP was used again to

study the effect of anemia in 23,348 patients who underwent elective open and laparoscopic colectomies.[21] Preoperative anemia, even if mild, was found to be a risk factor for a composite outcome consisting of myocardial infarction, stroke, progressive renal insufficiency or death within 30 days of operation and to correlate with a longer hospital length of stay (LOS). Further studies have continued to use NSQIP data to demonstrate the association between anemia and adverse outcomes.[22,23] More recently, a secondary analysis of non-cardiac and non-neurological surgery in 39,309 patients which included elective and non-elective cases showed that moderate and severe anemia resulted in increased postoperative admission to intensive care, hospital LOS and in-hospital mortality.[7]

Blood Transfusion

Compared to comorbidities and severity of illness, anemia is a strong predictor of the likelihood of ABT.[24] ABT has been traditionally used to correct anemia with insufficient consideration of the underlying cause or the associated risks and benefits. If the cause is not addressed, which in most cases is chronic and ongoing in nature, the correction is likely to be transient and the anemia may recur. Considerable variations in transfusion practice have underlined the need for appropriate transfusion use. In orthopedic surgery, for example, the ABT rate varies from 1.5% to 78% for total hip replacement.[25] Indication for ABT should take into consideration patient specific factors, laboratory values, physiological factors and the presence or absence of bleeding. In the emergency setting of acute hemorrhage, ABT could however be the treatment of choice.

In the most recent report from the Serious Hazards of Transfusion (SHOT), 166 patients suffered major morbidity and 26 died, two of which were definitely related, nine probably related and fifteen possibly related to transfusion.[26] Complications from transfusion included acute and hemolytic

transfusion reactions, circulatory overload, dyspnea, transfusion-transmitted infection and transfusion-related acute lung injury (TRALI).

Similar to anemia, ABT is an independent risk factor for perioperative morbidity and mortality.[27-29] In a prospective study that used NSQIP to collect data from 6301 patients undergoing non-cardiac surgery, ABT was associated with increased postoperative pneumonia, hospital LOS and mortality.[30] Multiple subsequent studies included an increasing number of patients and confirmed the dose dependent relationship between ABT and a composite outcome of myocardial infarction or stroke, pulmonary, renal, septic, thromboembolic and wound complications, and increased hospital LOS.[31-34] Consistent with the results of previous studies, a systematic review of observational studies concluded that ABT does have an adverse effect on mortality but could not exclude the possibility that confounding secondary to unknown and hence unadjusted factors still played a role.[33]

Concerns have also been raised about the influence of ABT on immunomodulation and postoperative infection, metastasis and the recurrence of cancer.[35-43] Immunomodulation of the innate and adaptive immune system occurs after exposure of the recipient to the many cell bound and soluble antigens expressed on viable and decaying cells in the transfusion.[44] In particular, contaminant leukocytes are thought to have a significant role. ABT has been associated with infectious complications after operations for gastrointestinal and pancreatic cancer, hip replacement and spinal fusion.[35-38] Moreover, a systematic review demonstrated that the odds ratio of postoperative bacterial infection was 3.45 subsequent to ABT.[39] It has been widely reported that perioperative blood transfusions increase the risk of colorectal cancer recurrence.[40-42] A Cochrane meta-analysis examined this association in 12,127 patients from 36 trials.[43] It showed that blood transfusion was related to a 42% increase in the odds ratio for cancer recurrence in a dose-related

manner and thus recommended that ABT should be restricted in its use in patients with curable colorectal cancer. Similar trends in recurrence have been found with the use of blood transfusion in surgical patients with various other cancers.[45-48]

Importantly, transfusion is costly and the cost of transfusing a RBC unit, including consumables and labor, is approximately four times higher than to purchase the product.[49,50] In the UK, after including derived costs such as hospital stay, the mean cost for a transfusion of two units in hematology and oncology patients was determined to be £546.12.[51] Evaluation of the cost of blood in a surgical population at two European and two US hospitals found each RBC unit to cost between $522 and $1183.[50] Annual expenditures on blood and transfusion-related activities, limited to surgical patients, ranged from $1.62 to $6.03 million per hospital and were largely related to the transfusion rate.

1st Pillar: optimization of red blood cell mass

In the preoperative period, laboratory investigations should be performed as soon as possible if moderate to high blood loss, defined as more than 500 ml is likely, or there is a ≥10% probability for ABT.[52] They should include a full blood count, serum ferritin, transferrin saturation (TSAT), a marker of inflammation such as C-reactive protein (CRP) and a surrogate of renal function. Guidelines from the Network for Advancement of Transfusion Alternatives (NATA) advocate that the level of Hb should be measured 28 days before elective orthopedic surgery[53] while those from European Society of Anaesthesiology recommend that patients at risk of bleeding be assessed for anemia 4-8 weeks before surgery.[54] In our view, females should be optimized to the same level of Hb as males to 13 g/dL despite the WHO definition of anemia. Both sexes lose comparable amounts of blood in similar surgical procedures but females have a relatively lower circulating volume

which means they lose proportionally more. Females could therefore be at otherwise increased risk of ABT which has been corroborated by the results of previous studies.[55,56]

Treatment of anemia should be directed at the cause. In the case of iron deficiency anemia, either oral or intravenous iron can be used. Oral iron is low cost and a recent meta-analysis demonstrated that it increases the Hb and decreases the proportion of patients who require ABT.[57] Notably however, the bioavailability of ferrous iron is only 10-15% and this may be reduced further by the stimulation of hepcidin in inflammatory conditions. Enteral iron is absorbed at a rate of 2-16 mg per day and if the iron deficit which needs to be replaced is significant, it could take too long for oral iron to effectively replenish stores. Compliance can be a problem as well because of gastrointestinal side effects such as abdominal pain, constipation and diarrhea.[58] Interestingly, high doses of oral iron sulphate in iron deficient but non-anemic females stimulate hepcidin and result in lower iron absorption from the next daily dose. Administration of low dose oral iron on alternate days may increase fractional iron absorption, maximize dosage efficacy, reduce gastrointestinal exposure to unabsorbed iron and improve adherence to treatment.[59] Once oral iron has been commenced, the Hb should be measured again, at least four weeks before surgery.

If there has not been an increment in the Hb with oral iron, the patient is intolerant of it or surgery is scheduled in less than six weeks time, intravenous (IV) iron is preferred. Compared to oral iron, IV iron is more effective in raising the level of Hb.[57] In the context of hepcidin up-regulation, IV iron may be more likely to work as it is taken up by macrophages and degraded leading to an increase in intracellular iron.[60] Intracellular iron increases ferroportin expression, partly overcoming hepcidin blockade and allowing iron to be transported by transferrin in the plasma to the bone marrow for erythropoiesis. In multiple studies, IV iron has been associated with a decrease in the need for ABT, a fall in the incidence of acute kidney injury and infections, and a reduction in the hospital LOS.[61-63]

Currently, six different formulations of IV iron are available in Europe and the US (Table 1). Depending on the preparation, the dose can be administered in as little as 15 minutes which is more acceptable to the patient as it incurs fewer hospital visits. A recent meta-analysis demonstrated that IV iron, when compared to oral or intramuscular iron, no iron or placebo, was not associated with an increase in the risk of infection or serious adverse events (SAEs) but did reduce the risk of adverse gastrointestinal events.[64] Serious adverse reactions and death are very rare, occurring in 38 per 10^6 and 0.4 per 10^6 administrations respectively.[65] In a comparison of the cost of IV iron versus ABT, which included consideration of acquisition, administration and transport costs, IV iron was found to be more cost effective.[66]

Use of recombinant erythropoietin (rEPO) to act on progenitors in the bone marrow and stimulate erythropoiesis first became widespread in dialysis patients.[67] A meta-analysis of an overall small sample size evaluated the effect of rEPO in colorectal cancer surgery and demonstrated no significant change in the level of Hb nor the number of units transfused per patient.[68] Subsequent meta-analyses in patients undergoing cardiac or orthopedic surgery have found that rEPO increased the level of Hb[56] and reduced the risk of ABT.[69-72] Guidelines from NATA recommend that, in the setting of orthopedic surgery, rEPO should be used for anemic patients in whom nutritional deficiencies have been corrected or excluded.[53] In one systematic review, subgroup analysis showed that variation in the dose and route of administration of rEPO had no effect on the risk of ABT.[69] Definitive conclusions however about the optimal dose, duration of treatment and route of administration of rEPO cannot be reached because of the significant heterogeneity in the scheduling pattern of rEPO in the individual clinical trials in these meta-analyses. Of note, rEPO has been associated with hypertension and ischemic and thrombotic events, possibly secondary to the

rapidity of rise and potential overshoot in Hb concentration as well as the trophic effect of rEPO on other cells.[73]

2nd Pillar: reduction of blood loss and bleeding

A standardized history to assess the risk of bleeding should be taken. It should ascertain as to whether there is a past history of bleeding after surgery or trauma, menorrhagia in females, drug history related to anticoagulant and antiplatelet medication, and a family history of bleeding diathesis. Increasingly, anticoagulant and antiplatelet medication is being continued into the perioperative period. An individualized assessment of the thrombotic risk of discontinuing these medications should be balanced against the risk of perioperative bleeding.

Surgical blood loss is decreased with neuraxial techniques relative to general anesthesia, probably secondary to a fall in blood pressure and venous tone resulting from sympathetic blockade.[74] Compared to open and invasive surgery, laparoscopic and minimally invasive surgical techniques, such as robotic gastrectomy, are associated with reduced surgery-related blood loss.[75,76] Judicious use of diathermy dissection and meticulous hemostasis is crucial. The patient should be positioned in such a way that venous return is not obstructed which could otherwise increase venous pressure and therefore bleeding at the operative site. Cardiovascular physiology should be manipulated as appropriate to limit bleeding. In hepatic resection, for example, the central venous pressure can be lowered. Maintenance of normothermia and avoidance of acidosis and hypocalcemia is key in the optimization of hemostatic conditions.[77]

Conventional coagulation tests can in certain circumstances be misleading and have an unacceptably long response time in dynamic situations.[78,79] Viscoelastic tests (VET), in contrast, are

performed at the point of care and can direct the perioperative management of coagulopathy. Both thromboelastography® (TEG®) and thromboelastometry® (ROTEM®) measure changes in clot tensile strength over time and provide information on the kinetics of clot formation and dissolution within 10-20 minutes.[80] Specific patterns of VET measurements can guide the administration of fresh frozen plasma, platelets, cryoprecipitate, factor concentrates and antifibrinolytics. Use of VET has been advocated in cardiac surgery by the National Institute for Health and Care Excellence (NICE) in the UK,[81] where a meta-analysis found it to decrease the need for transfusion in those patients at risk of coagulopathic bleeding.[82] It did not however decrease mortality, reoperation for bleeding, stroke, ventilation time or hospital LOS. In other meta-analyses, where most included studies were undertaken in the setting of cardiac surgery, transfusion requirements were also similarly reduced,[83,84] but in one the use of VET was associated with a reduction in overall mortality.[84]

Pharmacological treatments have demonstrated benefit in reducing perioperative blood loss. Epsilon aminocaproic acid (EACA) and tranexamic acid (TXA) are analogues of the amino acid lysine and reversibly inhibit fibrinolysis by binding the lysine-binding sites on plasminogen, limiting the activation of plasmin which degrades fibrin.[85] A meta-analysis of EACA and TXA in the setting of elective surgery found that the evidence was stronger for TXA than for EACA with a relative risk reduction of 39% and 25% respectively in the need for ABT.[86] Early use of TXA in trauma has been associated with a reduction in mortality due to bleeding and all-cause mortality.[87] Because the hemostatic responses to surgery and trauma are similar, TXA might reduce mortality due to bleeding in surgical patients.[88] TXA can also be used in topical form where a systematic review showed that it reduced blood loss by 29% and the relative risk of receiving a blood transfusion by 45% in cardiothoracic, oral, orthopedic, otorhinolarnygeal, spinal and urological surgery.[89]

Other topical hemostatic agents include fibrin sealants which contain fibrinogen (with or without factor XIII) and thrombin (with calcium) and mimic the final phase of the coagulation cascade.[90] Previously, a meta-analysis demonstrated that fibrin sealant decreased relative exposure to ABT by 54%[91] and a more recent systematic review showed a reduced ABT and blood loss in orthopedic surgery.[92]

Cell salvage is an established technique in cardiac, orthopedic and major vascular surgery[93,94] and should be considered where the anticipated blood loss is greater than 1000 ml.[95] It is performed with the use of a double lumen suction device to collect blood. Blood is stored within a reservoir with added anticoagulant and once enough blood is collected, the RBCs are washed, filtered, suspended in saline to be returned to the patient. Re-transfused RBCs from cell salvage have no clotting factors, platelets or plasma and so additional hemostatic therapies may be required. Use of cell salvage reduces the relative rate of ABT by 38%, saving an average of 0.68 of allogeneic RBCs per patient,[92] and it is cost effective compared with transfusion.[96] Though there have been concerns about the harmful effects of bacteria and malignant cells aspirated from the surgical field, studies have shown that there is no increase in positive culture or postoperative infection despite the aspiration of blood contaminated with microorganisms which the washing process is unable to eliminate completely.[97,98]

Acute normovolemic hemodilution (ANH) is the practice of preoperative withdrawal of whole blood with concurrent infusion of fluids to maintain normovolemia. Potential benefits of ANH include improvement in tissue oxygenation because of decreased blood viscosity, dilution of circulating components reducing the red cell mass lost due to surgical bleeding and the availability of whole blood for re-transfusion at the conclusion of surgery. ANH may be more cost effective than cell salvage[96] and though a recent meta-analysis has suggested that ANH is effective in

reducing ABT, these conclusions were limited by the significant identified heterogeneity and publication bias.[99]

In the postoperative period, efforts to avoid coagulopathy and reduce bleeding should be continued. Cell salvage can be used after the operation[95] but surgical drains can increase the rate of ABT in orthopedic surgery[100] though its use is declining with the establishment of enhanced recovery programmes. Repeated blood sampling can result in iatrogenic blood loss, contribute to postoperative anemia and should be minimized. In cardiac surgery, cumulative median phlebotomy volume for the hospital stay was 454 ml and increased with LOS.[101] Patients with similar risk factors for mortality in the intensive care environment were subjected to more blood tests if they had an indwelling arterial catheter.[102] Because of this, non-invasive monitoring should be considered where appropriate. Blood tests should be performed only when indicated and when taken, the smallest collection tube size that is practical for the required analysis should be used. In a study, replacement of adult blood tubes with pediatric ones reduced blood loss associated with diagnostic testing by 47%.[103] Transition to the use of pediatric blood tubes is not however simple as the patient identification labels are often larger than the tube, process costs are higher and the analysis can be delayed. Discard volume should be as low as possible and blood waste minimized by the use of closed in-line flush blood sampling devices for arterial and central venous devices.[104]

3rd Pillar: optimization of the patient's physiological tolerance towards anemia

Oxygen uptake, transport, delivery and utilization are complex biological processes and any deficiency in any link in this chain, such as anemia, can be compensated for by other links.[105] Adaptive responses include increased minute ventilation and cardiac output, improved ventilation-perfusion in the lungs, preferential oxygen delivery to vital organs and higher tissue oxygen

extraction. A patient's physiological tolerance of anemia can be harnessed in several ways.[106] Oxygenation can be optimized by increasing the inspired fraction of oxygen and hemodynamics can be manipulated with the use of vasopressors to maintain organ perfusion. Consumption of oxygen can be decreased by ensuring adequate analgesia and minimizing infection.

Evidence suggests that transfusion with RBCs fails to improve tissue oxygenation within the first 24 hours and might in fact decrease it.[107,108] In the seminal Transfusion Requirements in Critical Care (TRICC) trial, a restrictive strategy with a transfusion threshold of less than 7 g/dL was as effective as a liberal strategy with a transfusion threshold of less than 10 g/dL in 838 critically ill patients.[109] Further studies have supported these findings and a restrictive threshold of less than 8 g/dL was compared to a liberal transfusion threshold of less than 10 g/dL in patients with a history of or risk factors for cardiovascular disease who were undergoing hip fracture surgery.[110,111] A restrictive transfusion strategy did not reduce functional capacity or increase 60 day and long-term mortality. Multiple meta-analyses have shown that the use of a restrictive transfusion threshold across a broad range of specialities does not impact adversely on morbidity and mortality compared to a liberal transfusion threshold.[112-114]

In recognition that restrictive transfusion thresholds are non-inferior to liberal ones, NICE advocates that RBC transfusion should be considered at a Hb threshold of 7 g/dL in patients who do not have acute coronary syndrome or major hemorrhage, aiming for a target concentration of 7-9 g/dL after transfusion.[115] After each single unit of RBC transfusion, a clinical re-assessment should be made and the level of Hb checked to evaluate the appropriateness of further transfusion. Such practice could improve RBC utilization and decrease patient exposure to ABT.[116]

Patients with cardiovascular disease could represent a specific high risk group at the limits of their physiological reserve for which liberal transfusion thresholds should be recommended. In a feasibility study of transfusion thresholds in 110 patients with acute coronary syndrome or stable angina undergoing cardiac catheterization, a liberal transfusion strategy of 10 g/dl was associated with a decreased risk of death compared to a restrictive transfusion strategy of 8 g/dl.[117] Evidence from randomized controlled trials in cardiac surgery refutes findings from observational studies that liberal thresholds for RBC transfusion are related to a substantially increased risk of morbidity and mortality.[118] In the Transfusion Indication Threshold Reduction (TITRe2) trial, 2007 patients with a postoperative Hb level of less than 9 g/dl after cardiac surgery were randomized to either a restrictive transfusion strategy of less than 7.5 g/dl or a liberal transfusion strategy of less than 9 g/dl.[119] No difference in a composite outcome of serious infection or ischemic events was found but it did show that restrictive transfusion resulted in more deaths. NICE, as it stands, recommends that RBC transfusion should be considered at a Hb threshold of 8 g/dl in patients with acute coronary syndrome, aiming for a concentration target of 8-10 g/dl after transfusion.[115]

Challenges and practicalities in the implementation of PBM

In view of its demonstrable benefits, there is an increasing awareness of the need to integrate the pillars of PBM within routine surgical care. In the US, PBM has been successfully introduced in some centers[120] while in Western Australia, it has become the standard of care.[121] PBM initiatives in Europe however has been variable and inconsistent, reflecting the difficulties that can be met with its implementation.[122] Multiple barriers, including lack of knowledge, interdisciplinary commitment, resources and concerns, limit translation of PBM guidelines into clinical practice.[123-126]

National health care quality change initiatives set the agenda for change, but the patient centered approach to PBM needs to be delivered in a way that is also hospital centered so it is practical, feasible and socially acceptable with each institution.

In each institution, clinical champions and strong leadership are needed to establish PBM and overcome clinical inertia. Hospital Transfusion Committees (HTC) could offer a multidisciplinary leadership role, providing effective hospital governance that would cater for all transfusion related issues within the institution. The HTC oversee the implementation of national policies on blood transfusion and guidelines on the clinical use of blood. One discipline cannot manage the shift in the paradigm alone and hence consensus among disciplines on the bundles of diagnostic and therapeutic interventions is required.[127] Cooperation and engagement of the main stakeholders, such as health authorities, hospital administrators, blood services, patients and practitioners, can harmonize their different backgrounds and philosophies and pave the foundation for the effective institution of PBM. Communication and understanding the motivational frameworks and principles of various specialities such as anesthesiology, hematology and surgery is critical to success. In order to evaluate the cost effectiveness of the introduction of PBM, registries for systematic data collection should be considered. Moreover, incentives for the adoption of newer measures and disincentives against older practices are needed. Otherwise, the assumed initial costs of setting up a PBM program could discourage individual hospitals, even though PBM is expected to decrease longer term health care costs.

Characterization of the current practice of PBM at each hospital is needed and benchmarking of performance should be instituted to identify areas of need. Information should then be shared with stakeholders to enable the planning of appropriate interventions which should be put in place under the precondition of applied change management principles after the identification of drivers for

change. Constructive criticism and suggestions from the multidisciplinary field are crucial to adjust and improve the program and should be welcomed.

Barriers to effective PBM implementation need be recognised and acted upon. Before practice guidelines can affect patient outcome, doctors of all specialities must have a shared understanding of the evidence and principles driving the paradigm shift towards the practice of PBM. Doctors, familiar with the ease and established use of ABT, may not appreciate the risks associated with transfusion and the benefits related to PBM. Education and training should be considered to increase awareness of the clinical implications of anemia and the need for alternatives to transfusion. Once any deficiencies in underlying knowledge have been addressed, their attitude and finally behavior should change.[128] All recommendations and standard operating procedures must be easily accessible and aimed at supporting clinical judgement as the cornerstone of patient care. An increased appropriateness of RBC utilization, for example, can be encouraged by the introduction of electronic real-time clinical decision support systems.[129]

Individualized multimodal PBM care bundles, defined by the Institute for Healthcare Improvement as a straightforward set of evidence based interventions that when implemented together will result in significantly better, more penetrating and sustainable outcomes than when implemented individually,[130] could provide a clinical and pragmatic template for hospitals to follow.[131] Outside PBM, such care bundles have improved compliance with guidelines and resulted in a beneficial impact on care processes and outcomes.[132-134]

Practice needs to be continuously audited and progress monitored to achieve sustainability. Focus should be shifted to the reporting of data on transfusion rates and patient outcomes. Iterative feedback should serve to reinforce the attitudes and motivations of the main stakeholders.

Institutions must collaborate and learn from centers of excellence in PBM in order to accelerate their own success in the implementation of PBM.

Conclusions

It is clear that the establishment of PBM offers the prospect of reduced risk and improved patient outcomes in perioperative pathways. All three pillars of PBM are equally important and can structure the decisions and interventions relating to anemia and blood transfusion. A more considered approach to blood transfusion, acknowledging its risks, preventatives and alternatives should be adopted. Collaborative and continuous efforts to translate PBM guidelines into clinical practice, if done in an engaged, multidisciplinary, organized and structured way, could make PBM the norm.

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