Research Article

Conserving Red Cell Use for Good Stewardship and Patient Safety

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Summary

As a resource, the need for allogeneic red cell has never been more in demand than it is today. Escalating elective surgery, an ageing population, periodic shortages arising from a fall in supply, old and emerging threat of transfusion –transmissible infections and spiralling costs due to various safety introductions have all conspired to ensure that allogeneic red cell remains very much a vital but limited asset in healthcare delivery. Conserving blood makes sense. Effective stewardship of our red cell stock is important for economic, supply/demand reasons and to protect the national inventory at times of national blood shortage. There is the need for all stakeholders to think seriously and innovatively about how best to attract and retain new donors as well as sourcing for alternatives to allogeneic red cell transfusion. A successful and sustainable future demands exemplary stewardship from all players in the careful management of both red cell supply and demand issues. We have a significant challenge to reduce unnecessary demand through world class management of this precious product by applying the best available evidenced-based medical practices. To improve outcomes, red cell usage must be optimized and expenditures controlled so that resources may be channelled toward other diagnostic, therapeutic, and technological initiatives. Health professionals involved in the care of anaemic patients has a real and pressing obligation to fulfil their responsibilities, in terms of accountability for the human, financial, clinical and other resources associated with managing blood donations. There is need to reduce the growth in demand for allogeneic red cell transfusion. We must accept the challenge that growth cannot continue at the present rate and take real steps to ensure that any growth reflects real evidence-based clinical need and is not driven by historical practice. Wastage of this precious gift is an unacceptable failure in the stewardship of blood products.

Introduction

As a resource, allogeneic red cell transfusion blood has never been more in demand than it is today. Escalating elective surgery, an ageing population, periodic shortages arising from a fall in supply, old and emerging threat of transfusion –transmissible infections and spiralling costs due to various safety introductions have all conspired to ensure that allogeneic red cells remains very much a vital but limited asset in healthcare delivery. Consequently, allogeneic red cells for transfusion have become much safer but are in increasingly shorter supply and very expensive. Producing blood components costs the UK National Health Service about £500, 000000 (700m euro; $1bn) a year [1], and each unit of red cells costs about £120. In all, 2.5 million units are donated a year [2]. Benchmarking red cell transfusion activity, ensuring that it is clinically indicated and justified will help eliminate inappropriate use of blood products and help conserve our allogeneic blood stock. Erythropoietin (EPO) has drastically and significantly altered red cell transfusion practices. There might be many patients groups who would benefit from the use of erythropoietin analogues and thus help conserve the allogeneic red cell stock for patients in whom EPO is contraindicated. There is increasing advocacy to treat iron deficiency anaemia patients booked for elective surgery with safe, effective and cheap iron (oral or intravenous) supplements prior to surgery to minimize the use of allogeneic red cell transfusion. There is need to formulate policies on ways to seriously and innovatively attract and retain new blood donors. Blood Services and indeed the Department for Health can do well by promoting the appropriate use of red cell transfusion as well as investing in other alternatives therapies to complement the allogeneic red cell transfusion programme in a bid to solving the periodic and envisage future shortages in allogeneic red cells particularly with an aging population in most developed countries and increasing concerns about safety arising from old and emerging transfusion- transmissible infections. The aim of this review is to highlight the need to conserve our valuable allogeneic red cell resource for good stewardship and patient safety.

Challenges of a diminishing blood supply and an aging population

Allogeneic red cell is becoming an increasingly scarce and valuable resource. Shortages occur periodically because of a fall in supply. The challenge facing us today with regards to meeting the red cell transfusion-related needs of most countries is how to draw on the spirit of generosity to inspire even more individuals to donate blood on a regular basis. The UK National Blood Service collect, test, process, store and issue about 2.5 million blood donations yearly. This is vital if we are to address the ever increasing and potentially unsustainable demand on the UK blood supply. We must think seriously and innovatively about how best to attract and retain new blood donors as well as sourcing for alternatives. Current demands over the blood supply in developed and developing nations will compound over time. Development of alternatives to allogeneic red cells has a promising value preposition for transfusion services, because they hold the promise of increasing the availability of red cell products and removing donor contamination risks [3]. The unremitting need and increasing demand for red cell components constantly challenges blood centres to maintain a safe and adequate blood supply from a decreasing pool of eligible donors that is now estimated at only 38% of the US adult population [4,5]. Between 2001 and 2004, the National blood Collection and Utilization Survey

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documented a 0.2% decrease in whole blood and apheresis red blood cell unit collections, during a time when transfusions increased by 2%, implying a diminished reserve and a greater likelihood of episodic shortages [6]. In addition, the incremental restrictions imposed on donor eligibility in recent years, such as geographic deferrals for proven or perceived risk of transfusion-transmitted malaria and bovine spongiform encephalopathy, and the introduction of additional infectious disease tests, including those for Chagas disease and West Nile virus, further diminish the number of eligible blood donors and available screened blood units [7-9]. Although geographic deferrals for proven or perceived risk of transfusion-transmitted bovine spongiform encephalopathy (vCJD) is practiced in the United States of America, it is however not feasible for the UK.

Challenges of an aging population

Population ageing is a shift in the distribution of a country's population towards older ages. This is usually reflected in an increase in the population's mean and median ages, a decline in the proportion of the population composed of children, and a rise in the proportion of the population that is elderly. Population ageing is widespread across the world. It is most advanced in the most highly developed countries. It is now recognised as a global issue of increasing importance, and has many implications for health care and other areas of social policy. In 2007 the number of people above state pension age in England exceeded those aged under 16 for the first time ever, and older people above 65 made up the fastest-growing group in the population accounting for 9.8 million of the total population. This figure is projected to increase to 16.1 million by 2032 an equivalent of almost one in four of the total population. At the same time, the number of the 'oldest old' (people aged 85 and over) will more than double, rising from 1.3 million in 2007 to 3.1 million in 2032 [10]. While more people will enjoy longer lives, the ageing of the population and increases in the number of older people will bring new challenges. It is suggested that there will be greater numbers in ill health placing new demands on care services. Over the next 50 years it is envisaged that the populations of many developed countries will decline in size and become predominantly aged. This will impose substantial economic, social and medical costs [11]. The age when we are able to start giving blood is 17, but with fewer babies being born, there are a lot less 17-year-olds around. At the same time, our population is ageing; more persons are reaching old age and requiring operations that need red cell transfusion. In keeping with the general population, the blood donor base in England is aging. In 1990/1991 donors aged 18-19 years accounted for 40% of donors falling to 26% in 2003-2004. Over the same period however donors aged 50 and over rose from 11% to 22%. Although this may of course be due in part to raising the maximum blood donation age over to 70 years, it does also reflect the difficulties which the national blood services have had in maintaining an adequate donor base. Population aging is also a great challenge for the health care systems. As nations age, the prevalence of disability, frailty, and chronic diseases (Alzheimer's disease, cancer, cardiovascular and cerebrovascular diseases) is expected to increase dramatically. Some experts raise concerns that the developed world in particular may become a "global nursing home [12]. Information on the use of red cells, characteristics of transfusion recipients and population based information on transfusion is limited for the United Kingdom. A prospective, observational and population based study of red cell transfusion in hospital blood banks in the North East of England (population 2.9 million) shows that the most common surgical indications for red cell transfusion were total hip replacement (4.6% of all blood transfused) and coronary artery bypass grafting (4.1%). Indications for red cell transfusion, number of units given, and the age

and sex of transfusion recipients were collected. The destination of 9848 units was recorded (97% of expected blood use). In total 9774 units were transfused: 5047 (51.6%) units were given to medical patients, 3982 (40.7%) to surgical patients and 612 (6.3%) to obstetrics and gynaecology patients. Nearly half (49.3%) of all allogeneic red cell was given to female recipients, and the mean age of recipients of individual units was 62.7 years. Haematological disorders accounted for 15.5% of use. Overall use was 4274 units per 100 000 population per year. They concluded that in the North East of England more than half of red cell units are transfused for medical indications, that demand for red cell transfusion increases with age and that with anticipated changes in the age structure of the population the demand for blood will increase by 4.9% by 2008 [13]. Demand for blood transfusion increases with age. A population based study on long-term survival after blood transfusion in the North of England has shown that median age at transfusion was 67 years (mean, 60.9 years) [14].

Similarly, the EASTR Study provides data on National Blood Service (NBS) red blood cell (RBC, n = 9142) recipients independently sampled by monthly quota from 29 representative hospitals over 12 months in 2001-2002. Hospitals were stratified by size according to total yearly RBC issues. Transfusion indications were chosen from diagnostic and procedural codes, and recipients grouped into Epidemiology and Survival of Transfusion Recipients Case-mix Groups (E-CMGs). The main E-CMGs were digestive [19% of RBC recipients; including 5% gastrointestinal (GI) bleeds and 3% colorectal surgery], musculoskeletal (15%; 12% hip and knee replacement), haematology (13%) and obstetrics and gynaecology (10%). Renal failure, fractured neck of femur, cardiac artery by-pass grafting (CABG) and paediatrics, each accounted for 3-4% recipients. Back-weighting gave national estimates of 433 000 RBC recipients/year in England and North Wales, median age 69 years, respectively. Digestive and hepatobiliary indications emerged as the top reason for transfusion in RBC recipients [15].

Similarly a population based study in Finland has shown a marked increase in RBC consumption with increasing age among recipients, beginning at around 50 years of age. The 70 to 80 year olds were found to have an eightfold higher RBC consumption than 20 to 40 year olds. It is envisaged that there may be need in future to consider unprecedented measures such as reversing certain donor deferrals or even exporting blood from country to country [16]. A survey of red cell use in 45 hospitals in central Ontario, Canada has shown that of a total of 101,116 red cell units transfused, more than 74 percent were used in patients discharged with neoplasm, gastrointestinal diseases, circulatory system diseases, and trauma [17]. Similarly a large-scale study of blood recipients and blood use in France has shown that most transfusion recipients (57%) were over 65 years old. The indications most frequently reported for allogeneic red cell transfusion were neoplasms (48%) and those for autologous transfusion were disorders of musculoskeletal (63%) or circulatory (15%) systems [18]. A survey of blood component use, including packed red cells, fresh-frozen plasma, and platelets, in an acute-care University Hospital in the Greater Nurnberg area of Germany has shown that of 28,440 red cell units transfused, 72.4 percent was used in patients with neoplastic diseases, circulatory system diseases, or disorders of the digestive system. Patients less than 65 years old received a significant number of red cell components transfused [19]. A recent epidemiological information obtained from the United States, England, Australia and Denmark on the demographics of blood use has highlighted some major differences between the countries; the incident rate for red cell transfusion varied from 44.7 to 54.1 units, for platelets from 2.0 to 6.0 units and for plasma from 4.8 to 13.8 units transfused per 1000 population per year. Age and sex distribution of

transfused patients was similar in all countries. Most of the red cell and plasma products are transfused to older recipients.

Benchmarking red cell transfusion activity may help to eliminate inappropriate use. Despite published guidelines, numerous studies have consistently shown that a significant proportion of red blood cell (RBC) transfusions are unnecessary. A prospective, observational, multicentre study in the intensive care units of 18 Australian and New Zealand hospitals to determine the incidence and appropriateness of use of allogeneic packed red blood cell (RBC) transfusion has shown that the most common indications for transfusion were acute bleeding (60.1%) and diminished physiological reserve (28.9%). The rate of inappropriate transfusion was 3.0%. No indication was provided for 31% of the transfusions. Diminished physiological reserve with haemoglobin level > or = 100 g/L was the indication in 50% (22/44) of inappropriate transfusions. A study in Sydney, New South Wales [21] to assess the appropriateness of red blood cell (RBC) transfusions and the effectiveness of an intervention to reduce inappropriate RBC transfusions has shown that about a third of RBC transfusions were assessed as inappropriate and that more RBC transfusions were inappropriate in surgical patients than in those treated by other specialties. Similarly, a retrospective audit over a 1-year period of two Dutch hospitals by So-Osman and colleagues [22] has shown that of the 311 RBC units transfused, 143 units (46%) were possibly inappropriate and that a significant proportion of postpartum RBC transfusions are possibly inappropriate, partly due to over-transfusion. A review of all RBC transfusions given to peripartum inpatients at Sunnybrook and Women's College Health Sciences Centre in Toronto, Ontario, Canada [23] between April 1994 and July 2002 has indicated that a significant proportion of RBC transfusions given to peripartum women were inappropriate. Authors suggest that educational programs that promote adherence to transfusion guidelines might help reduce exposure to RBC transfusion and that aggressive oral and intravenous iron therapy might have prevented transfusion in 11% of the women in the cohort who were possibly iron deficient.

Allogeneic transfusion is a ubiquitous practice. Once an unquestioned adjunct to patient care, it is currently being re-evaluated and alternatives are being considered in response to concerns about dwindling supply and safety. Over the last several years, an increased awareness of diseases transmitted by allogeneic blood coupled with dwindling blood donor stock the world over has resulted in a dramatic increase in the advocacy for the use of alternatives/complementary therapies; use of erythropoietin (EPO), autologous blood transfusion and use of oral and intravenous iron.

Use of erythropoietin

The availability and use of haemopoietic growth factors on a large scale for in vivo and in vitro has opened a new era in transfusion medicine. Erythropoietin (EPO) was the first haemopoietic growth factor identified. Many anaemic patients being managed with erythropoietin alone or with some combined strategy of erythropoietin plus red cell replacement has shown that the red cell transfusion requirement is substantially reduced. EPO has been studied for its potential value in increasing autologous blood donation or reducing the homologous blood requirement in patients undergoing elective surgery. Use of erythropoiesis-stimulating agents (ESAs) has consistently been shown to reduce transfusions and increase the hemoglobin (Hb) level in patients with anaemia that arises during or shortly after myelotoxic chemotherapy [24]. The American Society of Clinical Oncology (ASCO) and the American Society of Hematology (ASH) first published a joint evidence-based clinical practice guideline for the use of erythropoietin

in adults with chemotherapy-induced anaemia in 2002 [25]. Since the 2002 guideline, awareness has grown of risks associated with ESAs, including increased mortality, venous thromboembolism, tumour progression, and stroke [26,27]. Thus, specific guidance on the safe and optimal use of ESAs is warranted. The initial guideline was updated and expanded in 2007 to include recommendations to address the use of darbepoetin alfa and emerging safety concerns [28]. In 2008, the US Food and Drug Administration (FDA) approved revised labels that limit indications for ESA use to patients receiving myelosuppressive chemotherapy for palliative intent, not curative intent, on the basis of clinical trial data suggesting an increased risk of mortality with ESA use [29]. The Update Committee acknowledges the FDA's assessment that the reported benefits of ESAs may be outweighed by risks considered unacceptable in patients who might otherwise expect cure from their chemotherapy. However, the Committee also notes that data are unavailable to compare outcomes of ESA therapy separately in patient subsets defined by the treatment intent of the chemotherapy regimen they are receiving. A recent report [30] to update American Society of Hematology/American Society of Clinical Oncology recommendations for use of erythropoiesis-stimulating agents (ESAs) in patients with cancer. Committee recommends that clinicians discuss the potential harms (thromboembolism, shorter survival) and benefits (decreased transfusions) of ESAs, and compare these with potential harms (serious infections, immune-mediated adverse reactions) and benefits (rapid Hb improvement) of RBC transfusions. The Committee cautions against ESA use under other circumstances. If used, ESAs should be administered at the lowest dose possible and should raise Hb to the lowest concentration possible to avoid transfusions. ESAs should be discontinued after 6 to 8 weeks in non-responders. ESAs should be avoided in patients with cancer not receiving concurrent chemotherapy, except for those with lower risk myelodysplastic syndromes. Caution should be exercised when using ESAs with chemotherapeutic agents in diseases associated with increased risk of thromboembolic complications.

Conservative indication for blood transfusion

In a bid to protect the national allogeneic red cell inventory and optimally maximize the use of our red cell stock, there is need to develop a conservative approach in deciding whether red cell transfusion is required in the managements of patients. Transfusion of the right unit of blood to the right patient at the right time and in the right condition must be according to appropriate guidelines. A chain of integrated events that begins with a correct decision that the patient needs blood and ends with an assessment of the clinical outcome of the transfusion. Its goal is to achieve optimal use of blood. Optimal use of blood ensures: that transfusion are safe, clinically effective and that there is efficient use of allogeneic red cells. Previous studies of blood use have used different methods to obtain and classify transfusion indications. A pilot study performed over 2 months at two teaching and two district general hospitals to match information from hospital transfusion laboratories with clinical coding data from the hospital's Patients Administration System to determine the indication for transfusion in 2468 recipients revealed major limitations in the conventional use of primary diagnostic International Statistical Classification of Disease and Related Health Problems 10th Revision (ICD-10) or procedure Office of Population, Censuses and Surveys - Classification of Surgical Operations and Procedures - 4th Revision (OPCS-4) codes alone in allocating transfusion indications. A novel algorithm was developed, using both types of code, to select the probable indication for transfusion for each patient. A primary OPCS-4 code was selected for recipients transfused in relation to surgery (43%) and either the primary (36%) or

the secondary (12%) ICD-10 code was chosen for recipients transfused for medical reasons. The remaining patients were unclassified. Selected codes were then collated into Epidemiology and Survival of Transfusion Recipients (EASTR) case mix groups (E-CMGs). The most frequent E-CMGs were haematology (15% of recipients), musculoskeletal (14%), digestive system (12%) and cardiac (10%). The haematology E-CMG includes patients with malignant and non-malignant blood disorders and recipients transfused for anaemia where no cause was listed. Recipients undergoing hip and knee replacement and coronary artery bypass grafting are within the musculoskeletal and cardiac E-CMGs. The digestive E-CMG includes recipients transfused for gastrointestinal (GI) bleeds and those undergoing GI surgery. This methodology provides a more useful means of establishing the probable indication for transfusion and arranging recipients into clinically relevant groups [31]. The Department of Health (DOH) Health Service Circular (HSC 2007/001) [32] on Better blood transfusion-safe and appropriate use of blood stipulates that patients should not normally be transfused if the haemoglobin concentration is above 10 g/dl, that there is a strong indication for transfusion is a haemoglobin concentration below 7 g/dl, that transfusion will become essential when the haemoglobin concentration decreases to 5 g/dl, that a haemoglobin concentration between 8 and 10 g/dl is a safe level, even for those patients with significant cardio respiratory disease. Symptomatic patients should be transfused and that it is appropriate to use a one unit transfusion to exceed the transfusion threshold if necessary. The following measures need to be considered in a bid to reducing blood use in the preoperative, intraoperative, and postoperative stages.

Preoperative situations

Although the practice of autologous transfusion in the UK is low, there is however increasing advocacy for increased use of autologous red cell transfusion. Previous report [33] suggest that the National Blood Service and indeed the Department for Health can do well by promoting the use of autologous blood and other alternatives therapies to complement the UK allogeneic blood transfusion program in a bid to solving the periodic and envisage future shortages in allogeneic blood particularly with an aging UK population and that this will maximize the use of the limited allogeneic blood resource particularly for patients in whom autologous blood transfusion is contraindicated. The blood – sparing benefit of haemodilution is that it produces a decrease in patient's haematocrit and blood viscosity potentially improving tissue perfusion and reducing intraoperative red cell loss and significantly reducing the need for allogeneic transfusion [33]. In orthopaedic and cardiovascular surgery, reduction in allogeneic blood use has been reported after extreme haemodilution [34]. The efficacy of ANH remains uncertain because of the lack of well-designed prospective randomized control trials. Several reports have been undertaken to evaluate the impact of ANH on blood transfusion requirement for various types of surgical operations. Wolowczyk and co-workers [35] investigated 32 patients undergoing ANH during elective Abdominal Aortic Aneurysm repair and concluded that a dedicated surgical team can achieve a significant reduction in the use of allogeneic blood and that ANH patients required less blood transfusion preoperatively (median of 2 units) than non-ANH patients (median 3 units).The efficacy of ANH on allogeneic blood was examined by way of a prospective randomized controlled trial by Sanders and co-workers [36] in Derriford hospital in Plymouth UK. Outcome measured included; number of patients receiving allogeneic blood, complication and duration of stay in hospital. They concluded that pre-operative haemoglobin, blood loss and transfusion protocol are the key factors influencing allogeneic blood transfusion and that ANH did not significantly affect allogeneic transfusion in major

gastrointestinal surgery. McGill and colleagues [37] in Southampton general hospital in the UK examined the safety of ANH in patients with known coronary artery disease and concluded that ANH is safe and can significantly reduce the use of allogeneic blood in patients with known coronary artery disease and that there is no attendant ischaemic burden after haemodilution. Verma and colleagues [38] at the Royal Manchester hospital in the UK studied 70 consecutively recruited patients with adolescent idiopathic scoliosis who underwent corrective surgery. They concluded that the use of blood conservation measures, lowering of the haemoglobin trigger for transfusion and education of the entire team involved in the care of patients can prevent the need for allogeneic blood transfusion. Predeposit autologous donation (PAD) involves repeated phlebotomy 4-5 weeks before surgery, during which time 4-5 units of in-date blood can be collected with ease [32]. Criteria used for selecting autologous donors are less stringent than those of allogeneic donors. The current standards of the American Association of Blood Banks [39] states that a patient may donate autologous whole blood if his or her haemoglobin level is 11g/dL or greater. This clinical benefit is claimed to be a consequence of the haemodilution induced by PAD and ANH [40]. Although modest haemodilution may be beneficial, it is not acceptable to all [41]. PAD is associated with increased risk of donation associated vasovagal reaction and angina, or trauma due to venepuncture and are thus contraindicated in patients with severe aortic stenosis, unstable angina and severe left main coronary artery disease [42]. To reduce these risks, the British Committee for Standards in Haematology (BCSH) advocates that a patient may donate autologous whole blood if they are free from cardiovascular and respiratory diseases and active infection, have a confirmed and reliable surgical date, have a good venous access and be free from anaemia [43]. Pregnancy with impaired placenta blood flow, intrauterine growth retardation, pregnancy-related hypertension, pre eclampsia, renal disease and insulin-dependent diabetes mellitus are all contraindications [44]. In deciding to collect autologous blood from a patient, the benefit of decreased exposure to allogeneic blood must be weighed against the risk of making the donation and of delaying surgery for the time needed for adequate regeneration of red blood cells (RBCs). To try to boost the haemoglobin concentrations between donations, preoperative autologous donation may be combined with iron supplementation, erythropoietin, or dietary advice. Typical cases for which preoperative autologous donation is indicated in major orthopaedic surgical procedures (knee replacement, total hip replacement and scoliosis correction), major urologic and gynaecologic oncology cases for which transfusion is anticipated. Elective total hip arthroplasty (TAH) or total knee arthroplasty (TKA) is frequently associated with allogeneic red cell (RBC) transfusion [45]. Pre-operative autologous blood donation in children presenting for elective surgery decreases the life-time complications associated with allogeneic blood and should be considered a component of paediatric blood conservation programmes [46].

Pre-operative assessment of patient billed for surgery is critical in assessing the blood transfusion –related need of a patient. It is important that every patient should have a defined transfusion and blood conservation strategy. Preoperative assessment should be early enough to identify patients who need more complicated interventions, such as erythropoietin and preoperative autologous donation. Simple measures include those that aim to increase the patient's haemoglobin concentration. This is most applicable to patients who undergo planned elective surgery and can be achieved by dietary advice, eating foods rich in iron, for example, red or organ meat. Specific iron supplements can also be given orally or intramuscularly. Oral supplementation is the commonest way for a patient to receive iron. It is easy for the patient to

take; it avoids painful, possibly skin marking injections; and it doesn't require the help of a clinician. Oral administration is not without complications. Gastrointestinal side effects-for example, nausea, epigastric pain, constipation, or diarrhoea-tend to decrease compliance. Intravenous iron is not generally recommended. Its advantage, however, is that it bypasses the gastrointestinal tract, but it can cause allergic reactions, which can be reduced by using lower molecular weight iron dextran [47]. The preoperative administration of intravenous iron sucrose increases haemoglobin by about one gram a week and reduces blood transfusions in patients undergoing hip surgery [48]. Oral and Intravenous Iron is often given concomitantly with erythropoietin, but may also be given independently to treat iron deficiency anaemia (either when the patient has overt iron deficiency anaemia, or when the patient is in negative iron balance and blood loss). Concomitant periopertaive use of intravenous iron and erythropoietin preserves iron stores and may fasten the recovery from post-operative anaemia [49,50]. There is increasing advocacy to treat iron deficiency anaemia patients booked for elective surgery with safe, effective and cheap iron (oral or intravenous) supplements prior to surgery to minimize the use of allogeneic red cell transfusion.

Intraoperative conservation of Blood and Blood products

Perioperative cell salvage entails the collection and re-infusion of blood lost during or after surgery. Perioperative cell salvage (PCS) is typically accomplished with a semi continuous flow device that utilizes special suction tubing that allows the mixing of recovered blood with an anticoagulant solution and the content is filtered to remove clots and debris. It is indicated in a variety of surgical procedures associated with a significant blood loss thus minimising the use of allogeneic blood [51]. Contraindications to the use of PCS include infection from bacterial contamination of the operative field and presence of malignant cells. However, a recent study [52] suggests that the risk of dissemination of malignant disease is minimal. Perioperative cell salvage produces a significant reduction in allogeneic blood transfusion use in revision surgery of the hip [44] and cardiac surgery [53]. Transfusion of predeposit or salvaged blood has continued to grow since the 1980's. Issues such as indication for use, cost effectiveness as well as safety of autologous blood salvaged for use particularly during cancer surgery have emerged a huge challenge. Blood salvage allow for the collection and processing of surgical blood loss with the eventual reinfusion of washed cells back to the patient. However the use of salvaged blood in patients undergoing surgeries for malignancy has been a matter of debate. Controversies exist as to the risk of haematogenous tumour dissemination [54]. Gamma irradiation of salvaged erythrocyte concentrate leads to inactivation of malignant cells and allow for the retransfusion in oncologic surgery [55,56]. Catling and co- workers [57] in Singleton hospital in Swansea in the UK salvaged and filtered using the Pall RS leuco depletion filter, the intraoperative blood loss in 50 consecutively recruited gynae-oncology patients undergoing surgeries for endometrial, cervical and ovarian cancer. Result showed that no remaining viable nucleated malignant cells were detected in any of the filtered sample. Similarly Liang and colleagues [58] investigated the use of leucocyte depletion filter among 32 patients with hepatocarcinoma (HCC) undergoing orthotropic liver transplantation (OLT) and concluded that the use of leucocyte depletion filter after the use of the cell saver remarkably reduces the risk of tumour cell re-introduction during OLT in HCC recipients with unruptured tumours. These findings suggest that the use of leucodepletion filters and irradiation after intraoperative blood salvage may make auto transfusion safe in tumour surgery.

Simple measures can reduce intraoperative blood loss, such as optimal positioning of the patient-for example; raising the head in ear, nose, and throat procedures; the use of tourniquets in certain sites; and effective haemostasis-for example, applying compression at the surgical incision, ligation of cut vessels, and thermal coagulation. Hypotension (reducing systolic blood pressure to less than 90 mm Hg) can also lessen bleeding, but elderly patients are at risk of ischaemic events. Intraoperative cell salvage can be used during surgery [59]. Shed blood is collected, filtered, anticoagulated, and stored in a sterile container. The red cells are centrifuged out, washed, concentrated, and suspended in saline. The process can return up to 70% of the shed cells. To be cost effective, a minimum volume of 1litre of shed blood is required to justify washing and reinfusion. The advantages of the principle of intraoperative salvage are that; it reduces the chances of allogeneic blood use, suitable for procedures with anticipated risk of massive blood loss (revision joint replacement and vascular surgeries), it is acceptable to religious groups like the Jehovah's witnesses who frown against and would not accept a blood transfusion and it eliminates clerical errors. It may however not be suitable in patients with infection or malignant cells undergoing bowel surgeries because of the risk of bacterial contamination and formation of emboli. Pharmacological methods entail the use of drugs, such as antifibrinolytics. For example, tranexamic acid reduces blood loss in surgery associated with excessive bleeding or hyperfibrinolysis.It is also useful in patients who have mild haemostatic defects, or in patients who refuse blood transfusion. These drugs target specific steps of the coagulation cascade and the fibrinolytic pathway. Side effects include anaphylactic reactions and increased incidence of thrombosis. Prothrombin complex concentrate is a virally inactivated blood product containing clotting factors II, VII, IX and X, and is available as an alternative to fresh frozen plasma for the rapid warfarin reversal when the patient has major haemorrhage [60]. Recombinant activated factor VIIa: is a synthetic version of the activated coagulation factor VII [61-63]. It is not licensed for use in massive haemorrhage but is often used 'off-label' for this indication when a patient has suffered extreme blood loss and conventional blood products are not effecting haemostasis. Vitamin K may be used to prevent excessive bleeding caused by a functional deficiency of factors II, VII, IX and X, either due to treatment with warfarin or vitamin K deficiency caused by malnutrition or malabsorption [64].

Avoidance of wastage of blood components

Allogeneic red cell is becoming an increasingly scarce and valuable resource. Shortages occur periodically because of a fall in supply. There is the need to avoid unnecessary wastage. A successful and sustainable future demands exemplary stewardship from all players in the careful management of both red cell supply and demand issues. Wastage of this precious gift is an unacceptable failure in the stewardship of our products. It is not something to be discarded casually because it was left out of a fridge for too long. Information from the national blood stocks management project reported wastage of 2.25% in 40 NHS hospitals [65]. In the United States Wallace et al. [66] reported that 9.7% of available allogeneic red cell units were wasted in 1994. Red blood cell (RBC) product wastage in hospitals is reported to range from 0.1% to 6.7% [67]. Blood wastage study in a hospital in Maryland in the United States averaged 4.4% of 63,000 issued RBC products. Data indicated that approximately 87% of wasted RBC units were either individual unit that were out of blood bank for more than 30 minutes and that the implementation of Lean Sigma methodology was an effective tool for reducing RBC wastage in the large academic hospital. Overall RBC product wastage decreased from 4.4% to a sustained rate of less than 2%. Factors identified as contributors to RBC wastage most amenable

to improvement were lack of awareness and training of staff ordering and handling RBC products, management of temperature-validated containers, inconsistent interpretation of RBC temperature indicators, and need for accountability when ordering blood products [68].

Similarly a study to determine the normative rates of blood unit cross matched to transfused (C:T) ratios, red blood cell (RBC) unit wastage, and RBC unit expiration throughout the United States has shown that hospital blood bank personnel can achieve C:T ratios below 2.0, RBC unit expiration rates below 1.0%, and RBC unit wastage rates below 0.5%. Lower C: T ratios and/or RBC unit expiration rates were associated with blood bank personnel setting C: T thresholds of 2.0 or less, monitoring requests for blood components by transfusion indication criteria, monitoring categories of health care workers responsible for blood wastage, not accepting short-dated units from blood distribution centres, and if short-dated units were accepted, being allowed to return those units to the blood distribution centre. These practices were not associated with lower blood wastage rates [69]. RBC inventory/disposition data for a 21-month period from 156 hospitals in Canada were analyzed using logistic regression techniques to identify factors that affected RBC outdating (month of the year, distance from the blood supplier, monthly transfusion activity, hospital type, and provincial region). The results were used to categorize hospitals into groupings that accounted for the factors affecting wastage. Data has shown that three factors can significantly affect RBC outdating; distance from the blood supplier, mean monthly transfusion activity, and month of the year and that a method can be developed for establishing evidence-based benchmarking targets for RBC outdating that allows for hospitals to be grouped with similar peers taking into account logistic factors that impact on product outdating [70,71]. Many remote hospitals in Canada keep small on-site stocks of red blood cell (RBC) units for emergency use and to support patient care programs. The blood supplier does not accept returned units into inventory. Discard rates can, therefore, be high. Previous report has suggested the need to transport near-outdate RBC units to a high-usage hospital site, which would reduce overall discard rates, thereby increasing overall stock levels available in the blood system and that such redistribution systems can be an effective way to reduce RBC unit discard rates. Even simple transportation systems have many factors affecting the RBC unit temperature. Novel temperature stabilizing materials may make future transportation of RBC units more reliable [72]. A previous report in the Prince of Wales Hospital Shatin, Hong Kong analyzed the pattern and rate of donor blood outdating between 1986 to 1990. Report indicated that outdating rate varied among different blood groups (group 0 less than A = B less than AB) and that there was a sharp drop in blood outdating since the implementation of the Type and Screen cross match protocol. The outdating rate was reduced from 11.5% to 1.3% for whole blood and from 4.9% to 0.4% for red cells. In absolute numbers, wastage of blood due to outdating was cut from 2,570 units in 1986-87 (a 2 yr period before Type and Screen) to only 227 units in 1988-89 (a 2 yr period after Type and Screen) [73]. Blood product production planning can bring about a significant reduction in outdating and substantial economic savings for a regional blood supplier. A previous study used daily information exchange and product production planning to establish an optimum platelet concentrate production goal for each weekday. This procedure has resulted in the ability to meet 100 percent of the hospital demand while reducing platelet concentrate outdating from greater than 20% to 2.95 percent over a 6-month period [74]. Limited information exists on home transfusion practices. There are increasing concern about effective cold chain monitoring of blood products intended for home transfusion. Home care nurses face many challenges in transporting and storing medications and blood products in the vehicles and in patients' homes. Unlike climate-controlled institutions, products subject to the cold of winter and the heat of summer can easily be damaged, which can be harmful to the patient. Additionally, several regulations and protocols demand that products be cared for in a certain manner, stored in the proper container, and labelled appropriately to reduce the incidence of blood product wastage [75]. Despite considerable advances in the safety of blood components, transfusion associated bacterial infection (TABI) remains an unresolved problem. Bacterial contamination of blood product also plays a significant role in blood product wastage [76-78].

Restrictive use of red cells transfusion in ICU and paediatric ICU patients

The past two decades have witnessed an extensive re-evaluation of transfusion therapy in the intensive care unit (ICU). Red blood cell (RBC) transfusions should usually be given only to restore or maintain oxygen delivery to vital organs and tissues. Medical history has clearly documented the importance of blood transfusion in saving lives threatened by acute haemorrhage or severe anaemia. The availability of component therapy has facilitated many surgical and medical advances, allowing the support of patients who hitherto may not have survived invasive therapies. Consequently, the use of blood products has increased steadily over the past half century. However, recent years have seen much greater emphasis on the consequences and costs of transfusion, leading to widespread attempts to restrict blood product use. Balancing the risks and benefits of transfusion has becoming increasingly complex; while restricting transfusion reduces unwanted effects and cost, the thresholds at which the risks of poor oxygen carriage outweigh these have not been clearly appreciated. Accumulating evidence suggests a lack of efficacy with red blood cell (RBC) in the majority of critically ill patients. Evidence has also increasingly exposed previously under-recognized transfusion risks. This has resulted in a growing number of recommendations for more restrictive RBC transfusion strategies. An important exception to a more conservative transfusion practice occurs in patients with major trauma and life-threatening bleeding. Delaying RBCs therapies in this population can result in higher mortality [79]. Prospective, multiple centre, observational cohort study of intensive care unit (ICU) patients in the United States has shown that anaemia is common in the critically ill that the number of RBC units transfused is an independent predictor of worse clinical outcome [80]. International clinical practice has recently changed, with a decrease in the "trigger" haemoglobin concentration used for red blood cell transfusions in critically ill patients. This change has been driven by increasing awareness of the infectious and non-infectious complications of allogeneic red blood cell transfusion, the perennial blood supply shortages, and most importantly by the Transfusion Requirements in Critical Care (TRICC), which suggested that a restrictive transfusion strategy (a transfusion trigger of 70 g/L and a post-transfusion goal of 70-90 g/L) may be equivalent to a liberal transfusion strategy (a transfusion trigger of 100 g/L and a post transfusion goal of 100-120 g/L) in non-shocked ICU patients [81]. However, patients with ischemic heart disease may benefit from red blood cell transfusion at a haemoglobin trigger level higher than advocated by such a restrictive transfusion strategy. In determining the appropriate trigger for transfusion of allogeneic blood, the physician should ideally weigh the risk-benefit profile for each individual patient, for each unit of blood administered [82]. The Transfusion Requirements in Critical Care (TRICC) trial clearly established the safety of a restrictive transfusion strategy, suggesting that physicians

could easily minimize exposure to allogeneic RBCs by lowering their transfusion threshold [83]. It is now clear that most critically ill patients can tolerate haemoglobin levels as low as 7 g/dl and therefore a more conservative approach to RBC transfusion is warranted. Strategies to minimize loss of blood and increase the production of RBCs are also important in the management of all critically ill patients [84].

Children have different physiology and pathology than adults and many aspects of transfusion practice are poorly researched in the young [85]. In a previous non-inferiority trial, we enrolled 637 stable, critically ill children who had haemoglobin concentrations below 9.5 g per decilitre within 7 days after admission to an intensive care unit. Result indicated that in stable, critically ill children a haemoglobin threshold of 7 g per decilitre for red-cell transfusion can decrease transfusion requirements without increasing adverse outcomes [86]. Similarly a review to discuss the implications of transfusion strategies in stable critically ill children indicated that using a restrictive transfusion protocol with a transfusion threshold of 7 g/dL in stable critically ill children is as safe as using a liberal protocol and can decrease the number of patients exposed to RBC transfusions [87].

Conclusion

As a resource, red cell has never been more in demand than it is today. Escalating elective surgery, an ageing population, new and emerging threat of transfusion –transmissible infections and spiralling costs due to various safety introductions have all conspired to ensure that allogeneic red cells remains very much a vital but limited asset to the health service. The need to use blood more appropriately is paramount. Hospitals and clinicians must introduce methods and techniques to decrease its use. Mechanical and pharmacological techniques are available for this purpose; however, each has its own separate risk. It is important to establish contingencies for shortages, appropriate guidelines, and correct indications for using these techniques in order to protect resources and minimise the risk of harm to patients and maximise the use of the limited allogeneic red cell resource. Blood transfusion is not a zero-risk procedure and must only be prescribed for patients when no alternative therapy is possible. We must ensure all use is appropriate, and work collaboratively to reduce the overall volume of transfusions that are required. Internationally this is being pursued through an approach known as patient blood management. There is an urgent need for the clinical community, academic community and governments to better understand the overall risk-benefit equation for patients receiving a blood transfusion. All patients should be managed in a more evidence-based and holistic manner to reduce the likelihood of transfusion. For instance, treatment of iron deficiency anaemia with iron therapy rather than transfusion could reduce the need for a significant proportion of red cell transfusions. The availability of effective use of haemopoietic growth factors (EPO) on a large scale has opened a new era in transfusion medicine. Many anaemic patients being managed with erythropoietin alone or with some combined strategy of erythropoietin plus red cell replacement has shown that the red cell transfusion requirement is substantially reduced. We challenge everyone – from the manufacturer to the hospital porter, the blood bank scientist, the ward nurse and the prescribing doctors - to understand and consider the longer term sustainability of this precious resource. In particular, we need to urgently address the ordering and prescription of too many units and discontinue outdated prescribing practices. We must help people understand the limitations of supply. Each and every donation is a precious commodity that should be treated as such. It should not be given as therapy without clear evidence of its benefits and it should not be given as therapy without clear understanding of its risks. Preventing or minimising the requirement for transfusion is also an important pre-emptive approach when managing a patient who is likely to experience blood loss/be at risk of anaemia due to surgery or pregnancy/child-birth. Where practically and clinically possible, patients should be offered a range of strategies to avoid the development of anaemia, minimise blood loss and treatment with non-blood pharmacological approaches. We must avoid unnecessary wastage. A successful and sustainable future demands exemplary stewardship from all players in the careful management of both red cells supply and demand issues. Wastage of this precious gift is an unacceptable failure in the stewardship of our products. Autologous blood transfusion has been effectively used as alternatives to allogeneic blood transfusion for many years. The recent growth in popularity of this procedure and other alternatives, related directly to heightened awareness of the risks of allogeneic blood exposure, is a justification to the medical community to address issues of safety and utility of autologous blood collection in groups of patients particularly those billed for elective surgeries. Effective stewardship of our allogeneic red cells is important for economic, supply/demand reasons and to protect the national inventory at times of national blood shortage.

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