Peri-operative anaemia management in major orthopaedic surgery: the need to find a pathway

Manuel Muñoz[1], Susana Gómez-Ramírez[2], Giancarlo M. Liumbruno[3]

[1]Perioperative Transfusion Medicine, School of Medicine, University of Málaga; [2]Department of Internal Medicine, University Hospital Virgen de la Victoria, Málaga, Spain; [3]Italian National Blood Centre, National Institute of Health, Rome, Italy

Patients undergoing major orthopaedic surgery may be exposed to the effects of anaemia, blood loss and allogeneic blood transfusion (ABT), all of which may adversely influence postoperative outcomes, although there is not agreement on the relative contribution of each of them[1].

Pre-operative anaemia is a frequent condition which is usually regarded as no more than a surrogate marker of the severity of the pathology requiring surgical treatment, and will resolve after it. Obviously, although this can sometimes be true (e.g., anaemia associated with colon cancer), it is not always the case (e.g., anaemia associated with ulcerative colitis in a patient who needs a coronary artery bypass)[1,2].

It is also frequently believed that pre-operative anaemia does not entail an increase in a patient's risk and, therefore, it is not always adequately treated before surgery[2]. In contrast, the association between pre-operative anaemia and worse clinical outcome (longer time spent in hospital, increased rates of postoperative complications and higher mortality) was already described by Lunn and Elwood in 1970[3]. A recent meta-analysis including over 900,000 patients who underwent major surgical procedures (including a large number of orthopaedic operations) confirmed that pre-operative anaemia, even if mild, is an independent risk factor for poorer post-operative outcomes[4].

Pre-operative anaemia, or sub-optimal haemoglobin level (<13 g/dL for both genders), is an independent factor predicting the need for peri-operative ABT. In patients undergoing major orthopaedic surgery, perioperative blood loss and blunted erythropoiesis in the post-operative period may lead to acute severe anaemia[5,6] especially in those whose haemoglobin concentration was low prior to the operation[2]. ABT is usually prescribed to avoid the deleterious effects of anaemia. ABT produces a quick, albeit transient, increase of haemoglobin levels, but its effectiveness in decreasing oxygen tissue debt and/or increasing oxygen consumption in selected patients has rarely been documented[1].

There is great inter-centre variability in the percentages of patients who receive perioperative ABT when undergoing a particular major orthopaedic procedure[7]. In order to reduce this variability different European scientific societies have recommended a more rational, individualised and "restrictive" use of ABT[8-12]. However, even if restrictive criteria are used, ABT is frequently associated with a worse post-operative outcome in surgical and critically ill patients[13-15]. Moreover, in certain settings, such as cardiac surgery, the negative effects of blood loss, ABT and pre-operative anaemia seem to be synergistic[16].

Despite its clinical and economic disadvantages, ABT remains the most frequently used treatment for acute perioperative anaemia. This is likely related to the belief that ABT is innocuous while ABT alternatives are expensive. However, it must be borne in mind that ABT is an expensive therapeutic resource, since the costs of processing, testing, storing and distributing (acquisition costs), as well as those of administering red blood cell units, are high[1]. A systematic review of the literature estimated that the cost of a two-unit transfusion in Western Europe was around € 800[17]. Allogeneic blood is also scarce, as the availability of this product is dependent exclusively on voluntary donors' good will.

Although indispensable, the sole application of restrictive transfusion criteria may not, therefore, be sufficient or adequate, and additional blood-sparing strategies should be implemented. These include optimisation of a patient's pre-operative haemoglobin concentration and reduction of surgical and iatrogenic blood losses. All these measures should be delivered within the context of a multidisciplinary and multimodal "Patient Blood Management" (PBM) programme. However, a patient-centred PBM programme should not be focused only on reducing the probability of ABT, but also on ensuring continuity of care to improve clinical outcomes and, at the same time, reducing treatment costs[18-21].

The review of the efficiency of these measures shows that their use translates into a trend towards improved clinical results (lower ABT requirements, fewer post-operative complications and mortality, shorter time spent in hospital and/or improved quality of life). However, the evidence supporting their safety and efficacy derives

Blood Transfus 2017; **15**: *289-91* DOI 10.2450/2017.0296-16

from studies that are very heterogeneous in design and quality. In addition, most studies have evaluated the efficacy or safety of a particular strategy (along with the application of restrictive transfusion criteria in the most recent ones). Although this significantly influences the strength of the recommendations on their use[2], we must bear in mind that, as designing and carrying out a randomised trial on PBM is extremely challenging, we should measure the impact of this multimodal and multidisciplinary approach on outcomes through registries of treated patients rather than randomised controlled trials, since the former more closely resemble those patients we come across in daily clinical practice[22].

Although it is not simple to implement a PBM programme, the benefits for both the patient and the healthcare system, seem indisputable and it is well-known that failure to treat patients with pre-operative anaemia, with the intention of obviating avoidable transfusions, is equivalent to providing sub-optimal healthcare[23]. There are numerous barriers to overcome (planning, leadership, institutional support, funding, legal framework, professional involvement, knowledge)[2]. Implementation of a PBM programme will not occur spontaneously because, simply, it is too easy ask for one or two units of blood from the blood bank[2]. As a consequence, PBM implementation in Europe is variable and inconsistent. While some countries, such as the Netherlands, have been using PBM strategies for years, these measures have been adopted sparsely in other countries[19]. In Spain, many hospitals have implemented some blood-saving strategies for specific interventions, but rarely a genuine PBM programme. Along with the cited barriers, the lack of widely accepted implementation guidelines may be behind the observed variability in the development of PBM programmes[24].

Stimulation of erythropoiesis to optimise pre-operative haemoglobin levels or correct post-operative anaemia constitutes one of the fundamental pillars of a PBM programme[18]. Whenever feasible, pre-operative anaemia should be corrected before an elective major surgical procedure. This may entail re-scheduling surgery, if possible. It is presently unknown whether correction of pre-operative anaemia may completely offset the risk of post-operative complications, but it will at least reduce those associated with ABT and should, therefore, always be attempted. Various clinical guidelines have issued recommendations on the the detection, classification and management of pre-operative anaemia[8,9,20,21,25-29]. However, this is probably the PBM strategy with the most logistical problems for implementation, highlighting the difficulties that arise in the process of moving from guideline recommendations to daily clinical practice[2].

A survey on the use PBM strategies conducted among Anaesthesiology Departments in Spanish hospitals revealed that peri-operative anaemia management (the first pillar of PBM) was less frequently implemented (40%) than the use of cell salvage (67%) and tranexamic acid (75%) (the second pillar of PBM), or restrictive transfusion criteria (the third pillar of PBM)[30]. In this issue of Blood Transfusion, Bisbe and collaborators[31] present a practical tool for the optimisation of peri-operative haemoglobin in surgical patients at risk of requiring red cell transfusions, based on available clinical evidence and their own experience. To this purpose, they developed an algorithm for the diagnosis and treatment of anaemia which will help anaesthesiologists to make patient-tailored decisions, according to the type of surgical procedure (oncological, orthopaedic, obstetric, gynaecological, cardiac, etc.). The economic aspects of the different treatment alternatives are also considered.

We must thank the authors for providing this anaemia management tool. However, they reported that, in the United Kindgom, multidisciplinary collaboration between surgeons, anaesthesiologists, haematologist, physiotherapists and nurses has allowed the implementation of PBM programmes in major orthopaedic surgery which resulted in better outcomes[32]. In Italy, a multidisciplinary PBM programme for major orthopaedic surgery has been recently developed[23] and regulatory guidelines are forthcoming thanks to the endorsement of PBM by the Ministry of Health. At the end of 2015, the Italian Health Minister issued a Decree: according to art. 25 of this Decree (dated November 2, 2015), "for the prevention of avoidable transfusions and with particular reference to the preparation of the patient who will undergo pre-scheduled surgical treatments, specific programmes shall be defined and implemented nationwide (Patient Blood Management) on the basis of guidelines to be issued by the National Blood Centre"[33].

In contrast, the proposal by Bisbe *et al.* is basically an anaesthesiologist-centred approach to peri-operative anaemia management[31]. Although this is operatively acceptable, the contributions from others specialists and general practitioners would have provided their approach to PBM with the important added value of multidisciplinarity[21,27,34].

In conclusion, we believe that a clear-cut, multidisciplinary peri-operative anaemia diagnostic-therapeutic care pathway can still not be taken for granted even though several useful international, multidisciplinary recommendations aimed at preventing avoidable transfusions and ensuring better outcomes for patients are available.

Disclosure of conflicts of interest

MM has received honoraria for consultancy or lectures and/or travel support from Wellspect HealthCare (Sweden), Roche (Spain), CLS Behring (Spain), Vifor Pharma (Spain and Switzerland), PharmaCosmos (Denmark) and Zambon (Spain) but not for this work. GML is the Editor-in-Chief of Blood Transfusion and this manuscript has undergone additional external review as a result. SG-R has nothing to declare.

References

1) Muñoz M, Gómez-Ramírez S, Campos A, et al. Pre-operative anaemia: prevalence, consequences and approaches to management. Blood Transfus 2015; **13**: 370-9.
2) Muñoz M, Gomez-Ramirez S, Kozek-Langeneker S, et al. 'Fit to fly': overcoming barriers to preoperative haemoglobin optimization in surgical patients. Br J Anaesth 2015; **115**: 15-24.
3) Lunn JN, Elwood OC. Anaemia and surgery. Br Med J 1970; **3**: 71-3.
4) Fowler AJ, Ahmad T, Phull MK, et al. Meta-analysis of the association between preoperative anaemia and mortality after surgery. Br J Surg 2015; **102**: 1314-24.
5) Liumbruno GM, Grazzini G. Double bull's eye for post-operative intravenous iron in patient blood management: better outcome and cost-effective. Blood Transfus 2014; **12**: 7-9.
6) Liumbruno GM, Bennardello F, Lattanzio A, et al; Italian Society of Transfusion Medicine and Immunohaematology Working Party. Recommendations for the transfusion management of patients in the peri-operative period. III. The post-operative period. Blood Transfus 2011; **9**: 320-35.
7) Gombotz H, Rehak PH, Shander A, Hofmann A. Blood use in elective surgery: the Austrian benchmark study. Transfusion 2007; **47**: 1468-80.
8) Leal-Noval SR, Muñoz M, Asuero M, et al. Spanish Consensus Statement on alternatives to allogeneic blood transfusion: the 2013 update of the "Seville Document". Blood Transfus 2013; **11**: 585-610.
9) Kozek-Langenecker SA, Afshari A, Albaladejo P, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesth 2013; **30**: 270-382.
10) Liumbruno G, Bennardello F, Lattanzio A, et al. Recommendations for the transfusion of red blood cells. Blood Transfus 2009; **7**: 49-64.
11) Klein AA, Arnold P, Bingham RM, et al. AAGBI guidelines: the use of blood components and their alternatives 2016. Anaesthesia 2016; **71**: 829-42.
12) National Institute for Clinical Excellence guidance. Blood Transfusion. Available at: https://www.nice.org.uk/guidance/ng24/resources/blood-transfusion-1837331897029. Accessed on 01/10/2016.
13) Ferraris VA, Davenport DL, Saha SP, et al. Surgical outcomes and transfusion of minimal amounts of blood in the operating room. Arch Surg 2012; **147**: 49-55.
14) Acheson AG, Brookes MJ, Spahn DR. Effects of allogeneic red blood cell transfusions on clinical outcomes in patients undergoing colorectal cancer surgery - Systematic review and meta-analysis. Ann Surg 2012; **256**: 235-44.
15) Leal-Noval SR, Muñoz-Gómez M, Jiménez-Sánchez M, et al. Red blood cell transfusion in non-bleeding critically ill patients with moderate anemia: is there a benefit? Intensive Care Med 2013; **39**: 445-53.
16) Ranucci M, Di Dedda U, Castelvecchio S, et al; Surgical and Clinical Outcome Research (SCORE) Group. Impact of preoperative anemia on outcome in adult cardiac surgery: a propensity-matched analysis. Ann Thorac Surg 2012; **94**: 1134-41.
17) Abraham I, Sun D. The cost of blood transfusion in Western Europe as estimated from six studies. Transfusion 2012; **52**: 1983-8.
18) Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology 2010; **113**: 482-95.
19) Shander A, Van Aken H, Colomina MJ, et al. Patient blood management in Europe. Br J Anaesth 2012; **109**: 55-68.
20) National Blood Authority. Patient Blood Management Guidelines: Module 2 – Peri-operative. Available at: https://www.blood.gov.au/pbm-module-2. Accessed on 01/10/2016.
21) Vaglio S, Prisco D, Biancofiore G, et al. Recommendations for the implementation of a Patient Blood Management programme. Application to elective major orthopaedic surgery in adults. Blood Transfus 2016; **14**: 23-65.
22) Liumbruno GM, Vaglio S, Grazzini G, et al. Patient blood management: a fresh look at a fresh approach to blood transfusion. Minerva Anestesiol 2015; **81**: 1127-37.
23) Guerra R, Velati C, Liumbruno GM, Grazzini G. Patient blood management in Italy. Blood Transfus 2016; **14**: 1-2.
24) Meybohm P, Richards T, Isbister J, et al. Patient blood management bundles to facilitate implementation. Transfus Med Rev 2017; **31**: 62-71.
25) Beris P, Muñoz M, García-Erce JA, et al. Perioperative anaemia management: consensus statement on the role of intravenous iron. Br J Anaesth 2008; **100**: 599-604.
26) Goodnough LT, Maniatis A, Earnshaw P, et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient - NATA guidelines. Br J Anaesth 2011; **106**: 13-22.
27) Kotzé A, Harris A, Baker C, et al. British Committee for Standards in Haematology guidelines on the identification and management of pre-operative anaemia. Br J Haematol 2015; **171**: 322-31.
28) Muñoz M, Gómez-Ramírez S, Kozek-Langeneker S. Pre-operative haematological assessment in patients scheduled for major surgery. Anaesthesia 2016; **71** (Suppl 1): 19-28.
29) Liumbruno GM, Bennardello F, Lattanzio A, et al; Italian Society of Transfusion Medicine and Immunohaematology Working Party. Recommendations for the transfusion management of patients in the peri-operative period. I. The pre-operative period. Blood Transfus 2011; **9**: 19-40.
30) Colomina MJ, Basora Macaya M, Bisbe Vives E. [Implementation of blood sparing programs in Spain: results of a survey of departments of anesthesiology and resuscitation]. Rev Esp Anestesiol Reanim 2015; **62** (Suppl 1): 3-18. [In Spanish.]
31) Bisbe E, Basora C, Colomina MJ. Perioperative anaemia treatment in major orthopaedic surgery: Spanish practical approach. Blood Transfus 2017; **15**: 296-306.
32) Kotze A, Carter LA, Scally AJ. Effect of a patient blood management programme on preoperative anaemia, transfusion rate, and outcome after primary hip or knee arthroplasty: a quality improvement cycle. Br J Anaesth 2012; **108**: 943-52.
33) Decreto del Ministro della Salute del 2 novembre 2015. Disposizioni relative ai requisiti di qualità e sicurezza del sangue e degli emocomponenti. Gazzetta Ufficiale della Repubblica Italiana N. 300 of 28 December 2015 (S.O.N. 69).
34) Theusinger OM, Kind SL, Seifert B, et al. Patient blood management in orthopaedic surgery: a four-year follow-up of transfusion requirements and blood loss from 2008 to 2011 at the Balgrist University Hospital in Zurich, Switzerland. Blood Transfus 2014; **12**: 195-203.

Correspondence: Manuel Muñoz
Medicina Transfusional Perioperatoria
Facultad de Medicina
Campus de Teatinos, s/n
29071 Málaga, Spain
e-mail: mmunoz@uma.es