

Iron therapy: a piece in the puzzle of allogeneic blood saving strategies with a relevant role in patients' blood management

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Recently, the combination of increasing costs for the provisions of blood products¹, increasing recognition of the risks associated with transfusion and growing awareness of the possible future shortage of blood supply has raised the interest of the scientific community in the concept of "blood management"².

Blood management should not be confused with the concept of bloodless medicine, which is a programmatic approach to dealing with a small subset of patients who refuse blood transfusions³.

Patients' blood management is "the timely application of evidence-based medical and surgical concepts designed to maintain haemoglobin concentration, optimise haemostasis and minimise blood loss in an effort to improve patient outcome"⁴. The principle at the basis of this concept is the improvement of patients' outcome through the integration of all available techniques to ensure safety, availability, and appropriate allocation of blood products⁵.

This new strategy covers the whole peri-operative period and is characterised by a patient-specific multidisciplinary and multifaceted team approach which entails a partnership between transfusion medicine specialists and the many different health care specialists who interact with the blood bank^{1,6}.

It does, therefore, represent "a model of multidisciplinary care where the changes in culture are system directed on the basis of evidence-based medicine", as stated by Kumar and colleagues⁵. It also includes the appropriate provision of blood components in compliance with transfusion guidelines and suggests alternatives when they are appropriate¹.

Sharing and multidisciplinary work are really the best ingredients to ensure success and safety in multimodal approaches to blood management which comprises an array of different strategies that exploit appropriate combinations of drugs, technological

devices and surgical and medical techniques in the pre-, intra- and post-operative periods⁷.

The creation of "multidisciplinary blood management team (including surgeons, perfusionists, nurses, anesthesiologists, intensive care unit care providers, housestaff, bloodbankers, cardiologist and so forth)" is fundamental for any blood management programme and has also been recently recommended by the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists as a "reasonable means of limiting blood transfusion and decreasing perioperative bleeding while still maintaining safe outcome (level of evidence B)"⁸. All blood saving protocols adopted should also be shared with patients.

Implementation of blood management strategies not only reduces transfusion requirements but also improves post-operative outcomes, at least in patients undergoing orthopaedic and cardiac surgery^{9,10}.

The first strategy to contain the use of blood is an early diagnosis of anaemia in patients who are to undergo elective surgery. In fact, the leading risk factor for allogeneic blood transfusion is the presence of anaemia before surgery. Furthermore, pre-operative anaemia, even if only mild, is independently associated with an increased risk of 30-day morbidity and mortality in patients undergoing major non-cardiac surgery¹¹, as recently shown by a large retrospective cohort study by Musallam and colleagues. This study obtained data from 227,425 patients and strongly suggests that implementation of detection and treatment of anaemia as part of a universal patients' blood management strategy should become standard of care in patients undergoing elective surgical procedures, particularly in those in whom substantial blood loss is expected⁶.

Pre-operative anaemia is easy to detect and, in many situations, cheap to treat. Previously undiagnosed anaemia before elective surgical interventions is common¹². The overall prevalence

of pre-operative anaemia (defined, according to World Health Organization's sex-based criteria¹³, as a haematocrit of less than 36% in women and less than 39% in men) in the general population increases with age and it has been estimated that in the elderly (over 65-year olds) it is 11% and 10.2% for men and women¹⁴, respectively.

An algorithm for the detection, evaluation and management of pre-operative anaemia in elective orthopaedic surgery was recently proposed by the Network for Advancement in Transfusion Alternatives (NATA) which issued practice guidelines on the topic¹⁵. This algorithm is based on a few simple tests useful to detect the various forms of anaemia and treat them with the relevant pharmacological therapies (iron, vitamin B₁₂ and/or folic acid, and erythropoiesis-stimulating agents). Early diagnosis of pre-operative anaemia should be undertaken at least 28 days before the scheduled surgery in order to enable adequate treatment and reduce exposure to allogeneic blood transfusions.

In this issue of Blood transfusion, Manuel Muñoz and colleagues of the Anaemia Working Group España (AWGE, <http://www.awge.org>), a multidisciplinary group for the study and clinical management of anaemia in the surgical patient, published an interesting and updated review on the role of iron therapy in reducing allogeneic blood transfusion in orthopaedic surgery¹⁶. The authors pragmatically suggest the possible clinical and laboratory approaches to the diagnosis of iron deficiency and propose a simplified and very easy-to-adopt algorithm for the diagnosis of iron deficiency anaemia.

Although it is widely recognised that the objective of successful treatment of iron deficiency anaemia is the adequate and quick supply of iron to increase haemoglobin levels to normal values within 4-6 weeks and to replenish iron stores, the route for iron administration is still a matter of debate.

Because of the limitations of oral iron therapy in patients scheduled for surgery, Muñoz and co-workers correctly suggest that intravenous iron be preferred, even though many patients will respond to oral iron. They clearly show that peri-operative intravenous iron reduces allogeneic blood transfusion requirements in orthopaedic and

trauma surgery, and may hasten recovery from post-operative anaemia, while preserving iron stores. These effects seem to be augmented by the addition of a single dose of erythropoietin. In addition, with the exception of high molecular weight iron dextran, the safety profile of intravenous iron preparations is optimal and quite homogeneous, and higher than that of allogeneic red cell transfusion.

In conclusion, although misinterpretation of adverse events caused underuse of this important treatment modality, intravenous iron has earned an undeniable, relevant role in blood saving protocols due to the large amount of available clinical and experimental data. Indeed, the value of intravenous iron in blood management is continuously and progressively increasing as it has changed "from anathema to standard of care"¹⁷.

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