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EDITORIALS

Non-treatment of preoperative anaemia is substandard clinical practice

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It is well known that preoperative anaemia is frequent and associated with increased mortality and morbidity, even if only mild anaemia is present.[1 2] In addition, preoperative anaemia is one of the most significant risk factors in subsequent red blood cell transfusion,[3] which in itself has adverse effects on mortality and morbidity.[4] Therefore, unmanaged preoperative anaemia is a contraindication for elective surgery.[4]

In this edition of the *British Journal of Anaesthesia*, Muñoz and colleagues[5] rightly alerted the medical community, reporting that preoperative anaemia is often left untreated. The paradox of known negative consequences of untreated anaemia and current practice is explained by the presentation of 10 widely held misconceptions. Moreover, we identified two additional reasons why physicians are still hesitating to treat preoperative anaemia systematically. First, the World Health Organization's definition of anaemia with a haemoglobin concentration of <120 g litre^{-1} in women and <130 g litre^{-1} in men is not sufficiently known by the majority of physicians. Furthermore, the notion that very mild forms of anaemia (haemoglobin values between 100–120 and 100–130 g litre^{-1}, respectively) result in adverse clinical outcomes, such as increased mortality and a long list of complications,[1 2] is also not well known. Second, there may be reluctance by some physicians to treat preoperative anaemia actively, because of the fact that they themselves will be held responsible for any adverse events occurring thereafter. In contrast, a perioperative transfusion in a patient who is anaemic before surgery is considered by most an inevitable event, for which medical staff cannot be held responsible. Therefore, some physicians prefer not to be involved in treating preoperative anaemia. We hope that the refuting by Muñoz and colleagues[5] of 10 widely held misconceptions helps pave the way to widespread treatment of preoperative anaemia.

A consortium of four large German University Hospitals (Frankfurt, Münster, Bonn, and Kiel) is engaged in the concept of patient blood management (PBM). The Frankfurt group has shown how to target and implement treatment of preoperative anaemia (ClinicalTrials.gov Identifiers: NCT01820949 and NCT02147795). Their investigation clearly highlights five key success factors (Table 1) for implementing a comprehensive preoperative anaemia treatment programme. The first factor, which is clearly the most important, was establishing a dedicated interdisciplinary PBM steering committee, with preoperative anaemia treatment being the first pillar of PBM.[4] Second, the inclusion and support of senior hospital management is of utmost importance. Only with this support can the necessary reorganization of the preclinical procedures and structures be implemented. Additionally, the understanding of surgical and medical disciplines is crucial to the management and treatment of preoperative anaemia. Last, but not least, focusing our efforts on the knowledge of how operations are regularly performed in anaemic patients, who frequently require allogeneic red blood cell transfusions, is also essential (www.patientbloodmanagement.eu). Such favourable hospital conditions and improvements can be achieved only by continuous education over years and through the coordination of a dedicated interdisciplinary PBM steering committee. Should your hospital not yet have the aforementioned structure, then becoming a leader in PBM and establishing a steering committee is the way forwards.

Table 1 Key success factors for the large-scale implementation of preoperative anaemia treatment

1. Dedicated, interdisciplinary patient blood management steering committee
2. Support from senior hospital management
3. Commitment from surgical and medical disciplines
4. Knowledge of patient blood management background (anaemia, transfusion, alternatives to transfusion)
5. Knowledge of clinical and preclinical management:
   - Surgical procedures associated with frequent preoperative anaemia and considerable blood loss
   - Structure and processes of preclinical evaluation to be reorganized and optimized

Other centres have also succeeded in implementing treatment of preoperative anaemia. Theusinger and colleagues[6] contacted the primary physician of each patient found to be anaemic before surgery. These patients were to undergo major orthopaedic surgery (n=8871), with suggested treatment of anaemia using erythropoietin α, i.v. iron, vitamin B_{12} and folic acid. Despite the fact that not all patients who were anaemic before surgery were treated, the incidence of anaemia on the day of operation decreased from 15 to 10% (P<0.01) and total allogeneic transfusion rate reduced from 20 to 10% (P<0.01). Short-term treatment of preoperative anaemia with erythropoietin and i.v. iron has also been shown to be successful in orthopaedic[7] and cardiac surgery.[8] Likewise, a group of four Spanish hospitals recently published their success in short-term preoperative treatment of anaemia with erythropoietin and i.v. iron in 2547 patients undergoing hip and knee arthroplasty or surgery for hip fracture.[9] They could decrease the allogeneic transfusion rate from 37 to 24% (P<0.01), the postoperative infection rate from 12 to 8% (P<0.01), and the length of hospital stay from 12 to 11 days (P<0.01). In patients undergoing surgery for hip fracture, the 30 day mortality was reduced from 9 to 5% (P<0.01).

Through sound scientific evidence, they disproved 10 misconceptions of perioperative anaemia treatment. Moreover, this medical need can be met with successful treatment options. Therefore, we conclude that there is no reason why treatment of preoperative anaemia anaemia should not be widely practised. Untreated preoperative anaemia is indeed a contraindication for elective surgery, and failure to treat preoperative anaemia is substandard clinical practice.

Declaration of interest

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Early cryoprecipitate for trauma patients is feasible, but will it improve outcome?

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In this issue of *BJA*, Curry and colleagues[1] demonstrate the feasibility of administering cryoprecipitate as a fibrinogen source within 90 min of admission of trauma patients. This study is important because cryoprecipitate contains fibrinogen and fibronectin, which are critical to clotting; data are variable on the need for cryoprecipitate in trauma patients, and no randomized controlled trials looking at the administration of fibrinogen concentrate or cryoprecipitate in trauma patients have been performed. However, the completion of the randomized clinical trial on the early use of cryoprecipitate is needed before implementation of this practice. Trauma patients receive plasma, which also contains fibrinogen and fibronectin, but at lower amounts and not in therapeutic doses. In some countries, prothrombin complex concentrates are used, which contain some but not all of the clotting factors. Also, fibrinogen concentrates are being used in trauma patients and require less volume for administration.

Fibrinogen (factor I) is a 340 kDa protein comprised of two sets of disulfide-bridged Aα, Bβ and γ chains. Thrombin cleavage of fibrinopeptide A from the Aα chains creates fibrin, which polymerizes and forms the proteinaceous structural basis for blood clots.[2] As such, maintaining adequate fibrinogen concentrations in bleeding patients seems to be a rational objective. However, our understanding of what constitutes an adequate concentration in a bleeding patient, how to determine fibrinogen concentrations rapidly and meaningfully, and what products to use for replacement is relatively poor. [3 4] A 2013 review in the Cochrane Collaboration examining the use of fibrinogen concentrates in bleeding patients found only six randomized controlled trials (248 subjects), of which two had mortality data.[5] While they concluded that there was a suggestion of benefit on reduction of red blood cell (RBC) transfusions, the authors were unable to draw any conclusions on mortality. Interestingly, the studies reviewed showed no effect on other outcomes, including thrombotic adverse events. A systematic review of fibrinogen concentrate in trauma revealed 12 articles, including a single prospective study.[6] Again, conclusions by the authors were limited, but suggested a reduction in the use of RBC transfusions in this setting. Taken together, these studies suggest that administration of fibrinogen may result in earlier haemorrhage control.

Given that 40% of trauma-related mortality is attributable to uncontrolled bleeding, a deeper understanding and optimization of fibrinogen supplementation is of great interest. There has been a substantial focus on the early administration of plasma and platelets (plasma:platelet:RBC transfusion ratio); a ratio of 1:1:1 compared with 1:1:2 did not demonstrate improved survival, but showed that more plasma and platelets help to achieve earlier haemostasis (although there was no decrease in the use of RBC transfusions within the two groups).[7] However, cryoprecipitate has not been as well studied. Indeed, fibrinogen deficiency (as defined by concentrations below 100 mg dl^{-1}) develops early in trauma.[8] The lower amount of fibrinogen administration via blood products, including whole blood, plasma, and cryoprecipitate, and defined as fibrinogen:RBC ratio has been associated with higher mortality in military trauma,[9] a lower cryoprepitate:RBC ratio has been associated with higher mortality in civilian trauma,[10] and data from an observational cohort study relates low fibrinogen at admission to higher trauma mortality at 24 h and 28 days.[11] These studies indicate that increasing fibrinogen concentrations in trauma patients may be beneficial. However, there are no randomized trials looking specifically at fibrinogen or cryoprecipitate in trauma patients. It is from this perspective that the study by Curry and colleagues,[1] published in this issue of the *BJA*, takes on importance.

In their study, Curry and colleagues[1] performed a feasibility study to determine whether it is possible to administer cryoprecipitate as a fibrinogen source within 90 min of admission of trauma patients. This is operationally complex because cryoprecipitate must be thawed and then delivered and cannot be stored for more than 6 h. Secondary objectives included laboratory