Is best transfusion practice alone best clinical practice?

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The review by Shander *et al.* in this issue of the journal highlights the progress made in transfusion medicine since the 1980s, including the tremendous decrease in the risk of transfusion-transmitted infections (TTIs) and the development of remarkably similar (and uniformly restrictive) transfusion guidelines by five major professional societies and the American Association of Blood Banks[1]. These guidelines aim at reducing the number of a patient's allogeneic donor exposures as much as possible, by administering transfusion only when proven (rather than postulated) benefit can be expected from the transfusion. Proven benefit, exemplified by a red-blood-cell (RBC) transfusion to a stable and non-bleeding patient triggered by a haemoglobin of 7 g/dL, is based on findings from randomised controlled trials (RCTs) using clinical endpoints[2]. In contrast, transfusing stable and non-bleeding patients at a haemoglobin of 8 g/dL and higher is largely based on postulated benefits based on what can be theoretically deduced from pathophysiology[3,4].

Adherence to these restrictive transfusion guidelines constitutes best transfusion practice, which may decrease mortality according to the findings of a recent meta-analysis of 19 RCTs enrolling over 6,000 subjects[2]. The optimisation of transfusion practice that these restrictive transfusion triggers allow, however, does not remove the risks of RBC transfusion[5,6]. The latter include the currently-leading causes of death from transfusion (transfusion-related acute lung injury, haemolytic transfusion reactions, and transfusion-associated circulatory overload), other infectious and immunologic transfusion complications, as well as the cardinal threat to transfusion safety today, namely the next "HIV-like" pathogen to emerge in the future[5,6]. For these reasons, best transfusion practice alone may not necessarily represent best clinical practice.

One reason why it is necessary to optimise clinical practice beyond the improvement afforded by the adoption of restrictive transfusion guidelines is that preoperative anaemia is a major risk factor for RBC transfusion[7] and, in addition, even mild preoperative anaemia increases perioperative mortality and morbidity by at least 30%[8]. Detection and treatment of preoperative anaemia is thus a necessary component of best clinical practice. The success of this approach has been demonstrated by RCTs conducted in orthopaedic[9] and cardiac surgery[10]. Preoperative treatment of anaemia reduced transfusion needs[9,10], decreased acute renal failure[10] and correlated with reduced length of hospital stay[10].

Another reason why best transfusion practice alone does not represent best clinical practice is that excessive blood loss and the need for early reoperation are independently associated with increased mortality, acute kidney injury[11], stroke and myocardial infarction[12]. Blood loss can be reduced by blood-sparing surgical and anaesthetic blood-conservation techniques which minimise perioperative bleeding, while they optimise intraoperative cardiac output, ventilation and oxygenation. In addition, perioperative blood recovery reduces the need for RBC transfusion and the length of hospital stay[13], making meticulous surgical and anaesthetic technique, as well as perioperative blood recovery where indicated, necessary components of best clinical practice. Indeed, the combination of preoperative treatment of anaemia, meticulous surgical and anaesthetic technique, perioperative blood recovery, and restrictive haemoglobin transfusion triggers has been shown to reduce RBC transfusion needs and the length of hospital stay, as well as to decrease mortality and costs[13-16].

It is all these strategies together that represent best clinical practice, according to the concept of Patient Blood Management (PBM)[17] adopted by the World Health Organization in 2010[18]. PBM identifies a patient at risk of transfusion and formulates a multidisciplinary and multimodal, yet individualised, plan for reducing or eliminating the need for allogeneic transfusion[19]. PBM encompasses the adoption of restrictive transfusion guidelines, but it includes a lot more than the mere adoption of restrictive transfusion guidelines[13-21]. In addition to transfusing only when proven benefit is expected, PBM encompasses treating anaemia and coagulopathy before admission to the hospital, minimising iatrogenic blood losses throughout the hospitalisation, using blood-sparing surgical and anaesthetic blood-conservation techniques, and employing perioperative blood recovery

and acute normovolaemic haemodilution where indicated. In this way, PBM integrates many hospital departments and services in a common effort to reduce allogeneic-donor exposures as much as possible, and to thereby prevent the infectious and immunologic complications of transfusion.

When the standard for transfusion medicine is set as reducing the transfusion risk for each patient to the level of the "as-low-as-reasonably-achievable" (ALARA) risk[20-22], clinical practice has to be further improved by meeting a patient's allogeneic-transfusion needs through fewer donor exposures than the number mandated by the number of components that the patient receives. Hitherto, PBM has been mainly used to avoid RBC transfusion in surgical patients, but multicomponent apheresis can expand the domain of PBM to platelet and plasma transfusion and to medical patients[20,21,23,24]. Multicomponent apheresis is now limited to collecting any combination of RBCs, platelets, and/or plasma from the same donor during the same donation (with at least 2 components collected from each donation: 2 RBC units, 2-3 plasma units, 2-3 platelet units or 1 RBC unit together with plasma and/or platelets)[24]. In the future, all components collected from the same multicomponent apheresis donation should be reserved for transfusion to the same recipient[20,21,23]. Because multitransfused patients -such as patients with acute blood loss- need multiple units of RBCs and plasma (and sometimes of platelets as well), multicomponent apheresis can reduce their number of donor exposures by at least 2-fold, thereby also reducing the risk of infectious and immunologic complications of transfusion by at least 2-fold[20,21].

Together, PBM and multicomponent apheresis represent a new paradigm -the patient-centric paradigm- of transfusion medicine that will hopefully replace the current (component-centric) paradigm in the 21st century[20,21,25]. Whereas now each blood component is a drug to be dispensed, in the future we will hopefully be meeting each patient's transfusion needs through an individualised combination of (PBM and multicomponent-apheresis) approaches. Whereas our current focus is on the quality of the component, in the future we should concentrate on the quality of the medical service (or individualised combination of PBM and multicomponent-apheresis approaches) that we provide each patient. And whereas now our overriding concern is to avoid blood shortages, in the future should aim to reduce the transfusion risk for all patients to the level of the ALARA risk[20-22].

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