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EDITORIAL

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Do cardiac children need more red blood cell transfusions than other critically ill children?

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Anaemia is associated with a higher risk of mortality in cardiac adults [1, 2] and children [3]. Only a red blood cell (RBC) transfusion can rapidly increase a low haemoglobin (Hb) concentration. However, there is no such thing as a perfectly safe RBC transfusion: both transfusion-transmitted infections and non-infectious serious hazards of transfusion (NISHOT) can occur [4]. RBC transfusions are associated with a higher mortality rate in cardiac adults [5] and with more morbidity in cardiac children [6–9]. An association between RBC transfusions and worse outcomes does not mean that there is a cause-effect relationship; it means only that such a cause-effect relationship is possible, and it questions the assertion that RBC transfusions are actually more useful than harmful in patients with cardiovascular disease.

In clinical practice, cardiac patients receive more RBC transfusions than other critically ill children [9–11]. The question is what prompts physicians to prescribe an RBC transfusion. According to a self-administered survey, determinants in cardiac children include Hb level, patient's stability, active bleeding, inadequate O_2 delivery (low $ScvO_2$, high lactate level, low SaO_2/FiO_2 ratio) and low blood pressure [10]. However, the Hb level remains the most important determinant of RBC transfusion [10, 11]. Therefore, it makes sense to ask ourselves the following questions: in cardiac children, how much anaemia can we tolerate and when do the benefits of RBC transfusions overcome their harms?

RBC transfusions are given during the perioperative care of paediatric cardiac surgery in the operating room and in the intensive care unit (ICU). While cardiac surgery accounts for only 5 % of anaesthesia episodes, it represents 58 % of perioperative RBC use and 24 % of total hospital RBC use [12]. The lowest Hb level below which an RBC transfusion must be given during a cardiopulmonary bypass (CPB) is not well characterised. Jonas et al. [13] reported that infants randomised at CPB onset to an haematocrit of 20 % (Hb level: about 7 g/dl) had worse 1-year Bayley psychomotor development scores than those allocated to 30 % (10 g/dl); this suggests that the Hb level should be maintained over 7 during a CPB, but it does not tell us what is the best and safest threshold Hb level for transfusion over 7 g/dl.

The uncertainty about the threshold Hb level with the best risk/benefits ratio also arises in the ICU after surgery. Most cardiac children (range: 46–79 %) receive at least one RBC transfusion during their ICU stay after a cardiac surgery [15, 16]. However, recent data suggest that a restrictive transfusion strategy might be as safe, if not safer than a liberal transfusion strategy. A subgroup analysis that focussed on 125 cardiac children enrolled in the Transfusion Requirements in Pediatric ICU (TRIPICU) randomised clinical trial reported that a threshold Hb level of 7 was as safe as 9.5 g/dl in stable non-cyanotic cardiac infants [14].

In this issue, de Gast-Bakker et al. [15] published a randomised clinical trial where they compared the

outcomes of children allocated to receive an RBC transfusion if their Hb level dropped below 8 g/dl (restrictive group) or below 10.8 g/dl (liberal group) in the operating room and in the ICU. All children older than 6 weeks with a planned cardiac surgery were considered for inclusion; cyanotic cases were excluded. Patients were randomised before the surgery, and the research protocol on RBC transfusion was initiated in the operating room and maintained in the ICU up to discharge. One hundred patients were enrolled and retained for analysis. Risk Adjustment for Congenital Heart Surgery (RACHS) scores and the length of surgery, CPB and aortic clamp time were similar in both groups; PRISM III and PIM 2 were low. The Hb value before RBC transfusions and the lowest Hb level in the ICU were not reported, nor was the compliance with the research protocol. The total volume of RBC units given in the operating room and ICU was lower in the restrictive than in the liberal group (186 ± 70 vs. 259 ± 90 ml/patient, $p < 0.001$). Duration of mechanical ventilation, length of ICU stay and incidence of adverse events were similar in both groups, but length of hospital stay was shorter in the restrictive group [median: 8 (IQR: 7–11) vs. 9 (7–14) in the liberal group, $p = 0.047$]. Costs of RBC and plasma were 229 vs. 328 euros per patient. The authors concluded: "For patients with non-cyanotic congenital heart defect undergoing elective cardiac surgery, a restrictive RBC transfusion policy (threshold Hb: 8 g/dl) during the entire perioperative period is safe, leads to a shorter hospital stay and is less expensive".

There is no doubt that an RBC transfusion can be lifesaving in some patients. However, serious hazards of transfusion such as over transfusion, transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI) and transfusion-associated multiple organ dysfunction syndrome must be feared [4, 9, 14]. Data from different haemovigilance systems report that the overall complication rate of transfusion is up to four times higher in children than in adults [4, 16]. On the other hand there is no evidence that the benefit of RBC transfusion is better in children than in adults. Moreover, there is no strong clinical evidence that cardiac children need more RBC transfusions than other critically ill children.

Clinicians must apply the "primum non nocere" principle to cardiac children. It must be recognised that the threshold Hb level below which there are more benefits than harms administrating an RBC transfusion is not well characterised during and after paediatric cardiac surgery. The study by de Gast-Bakker et al. [15] suggests that, in both the operating room and ICU, a threshold of 8 g/dl is safe in infants with non-cyanotic cardiac disease if the RACHS score is ≤ 3 and if their severity of illness is low; however, a large multicentre clinical trial is required before any strong recommendation can be made in this population. Moreover, it must be underlined that these data are not applicable to surgery with RACHS scores >3, to cardiac neonates and to children with cyanotic cardiac disease.

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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