Transfusion Clinique et Biologique 26 (2019) 195–196

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Mise au point

Transfusion in neonates and older children: Principles and updates

Transfusion chez les nouveau-nés et enfants : principes et mises à jour

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ARTICLE INFO

Article history:
Available online 14 July 2019

Keywords:
Transfusion
Children
Neonates

Mots clés :
Transfusion
Enfants
Nouveau-nés

Transfusions for neonates and older children follow similar principles as in adults. In many areas the age-appropriate evidence base is lacking, with consensus guidance extrapolated from adult studies and practice, but there have been several key paediatric randomised controlled trials (RCTs). 'Patient Blood Management' is the evidence-based approach to optimising the care of patients who might need transfusion thereby reducing transfusion requirements. Although the focus in many countries to date has been largely on adults, the principles of PBM are likely to be equally appropriate for neonates and children [1,2]. Specific examples include the use of delayed cord clamping [3–5] and of small sample tubes and laboratory analysers to reduce the requirement for neonatal top-up transfusions. As for adults, there is evidence that pre-operative anaemia in neonates [6] and older children [7], is associated with worse post-operative outcomes, suggesting that measures to diagnose and correct pre-operative iron deficiency, commonly occurring in the paediatric age group [8], may also be beneficial.

Clinical decisions to transfuse are based on risk-benefit analysis. Pre-term low birthweight neonates, most of whom will receive at least one red cell transfusion, are a particularly vulnerable group of recipients with a potentially long life span. For this reason blood transfusion services frequently provide additional safety features for neonatal components [9,10]. Haemovigilance schemes vary in their focus on paediatric reporting internationally, and few attempt to use modified definitions for neonates and children [11]. From the UK 'Serious Hazards of Transfusion (SHOT) scheme, approximately 8% of reports are in children < 18 years of age [12]. Comparison of SHOT data with a population based epidemiological study of transfused patients suggested that a disproportionate number of adverse events occur in paediatrics compared to adults [13]. In recent years, the disproportionate representation is particularly high in a subset of error categories: where the wrong component is transfused, specific requirements not met, or the transfusion is categorised as 'avoidable, delayed or under transfusion'. These reflect the complex nature of paediatric transfusion. Errors are a high percentage of neonatal/infant reports (89% in 2017; [12]), with only a small number of neonatal reactions reported, possibly due to under-recognition or to fewer reactions as the result of immunological immaturity.

The literature also reflects the increased vulnerability of neonates and infants to the metabolic effects of large volume transfusions to neonates and infants [14,15]. To reduce the risk of transfusion associated hyperkalaemia, it is recommended that 'fresh' (in the UK < 5 days) red cells for neonatal and infant large volume transfusions should be used, and that for cardiac surgery potassium concentrations should be checked in the bypass fluid before connecting to the patient to ensure that they are within the normal range [10]. This risk has also been highlighted by the identification of a genetic variant causing Familial pseudohyperkalaemia, (FP) occurring in approximately 1:400 individuals, where red cells leak potassium more rapidly on red cell storage in the cold [16]. In red cells from FP individuals, supernatant potassium in the first few days of storage reaches similar levels to those seen at the end of storage in controls. The UK blood services have recently taken the decision not to use red cells from identified FP donors for the neonatal/infant blood supply, to avoid using them for large volume transfusion for this age group.

A number of specific guidelines are available for neonatal and paediatric transfusion (for example, [17,10]), which review the literature and provide recommendations and good practice points. Key for all are the interpretation of the results of the RCTs on preterm neonatal red cell 'restrictive' vs. 'liberal' haemoglobin

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https://doi.org/10.1016/j.tracli.2019.07.003

(Hb) thresholds [18,19], with Hb levels stratified by postnatal age and level of respiratory support. The RCTs are the subject of systematic reviews [20,21], with overall no evidence that 'restrictive' transfusion practices for this age group have a significant impact on mortality or major morbidity. The recent guidelines on Hb thresholds for preterm neonates are compared by Lopriore [22]. Nonetheless, data on long term outcomes following restrictive and liberal neonatal transfusions is limited and inconsistent. Therefore the results of two large trials with outcomes including 2 year neurodevelopmental impairment are awaited with interest: the ETTNO trial (Effects of Transfusion Thresholds on Neurocognitive Outcome of extremely low birth weight infants, NCT01393496) and the TOP trial (Transfusion of Prematures, NCT01702805).

Platelets are commonly prescribed to thrombocytopenic preterm neonates on hospital neonatal units, usually prophylactic in the absence of bleeding [23]. Guidelines have been consensus based [10], with wide variation in practice. Recently, the PlaNeT2/MATISSE trial a multicentre RCT of 660 preterm babies comparing prophylactic platelet transfusions at two different platelet count thresholds (25×10^9/L vs. 50×10^9/L; [24]) has been published. The results of the study showed, somewhat unexpectedly, a significantly higher rate of major bleed or death in the group of preterm neonates receiving most platelet transfusions (the 50×10^9/L threshold group), suggesting that the platelets were associated with clinical harm. The reasons for this finding are not known but possibilities could include an immunomodulatory process, or an impact of donor ABO mismatch or platelet storage age [25]. A haemodynamic effect of the platelet transfusions cannot be excluded, and it is of note that the platelet dose of 15 mL/kg used for the study reflects common practice [10] but is approximately 3–5 times the equivalent weight-based volume transfused for adults receiving a single standard platelet pack.

Relatively higher red cell volumes are also often prescribed for neonates, despite increasingly restrictive transfusions outside of the newborn period. The UK 'NICE' guidelines (2015) [26] recommended that single unit red cell transfusions should be considered for adults without active bleeding (or equivalent volumes calculated based on body weight for children). This takes into account risks such as Transfusion Associated Circulatory Overload (TACO). For children, the British Society for Haematology (BSH) guidelines [10] suggested that transfusion volumes for non-bleeding infants and children should generally be calculated to take the post-transfusion Hb no more than 20 g/L above the transfusion threshold (approximately 8 mL/kg if starting Hb is at the threshold) usually a maximum of one unit, as a pragmatic balance between restrictive dose and reducing donor exposure. However, this guidance is not evidence-based. For neonatal small volume 'top-up' transfusions, traditionally volumes of 10–20 mL/kg have been used. In the UK National Comparative Audit of Blood Transfusion (2010) [27], the overall median volume prescribed for the baby's first transfusion was 18.7 mL/kg, with 24% above 20 mL/kg (with similar findings for subsequent transfusions). As volumes greater than 20 mL/kg may increase the risk of volume overload, and in the context of data supporting restrictive Hb thresholds across all age groups, the UK guidelines made a consensus recommendation for 15 mL/kg in non-bleeding neonates [10]. The precise incidence and appropriate definitions of TACO in infants and children are not known. However, there are cases reported to SHOT which, together with the outcome of the PlaNeT study, emphasise the need to re-evaluate the non-evidence based yet common practice for neonatal transfusion volumes, and the need for caution in providing precise recommendations where there is a lack of evidence.

Disclosure of interest

The author declares that she has no competing interest.

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