

# PostScript

## LETTERS

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### Blood transfusion in preterm neonates

The paper by Wardle *et al*<sup>1</sup> puts forward the interesting concept of the use of peripheral fractional oxygen extraction to guide blood transfusion in preterm infants. The clinical dilemma of deciding when to and when not to transfuse preterm neonates is always a major topic of debate among professionals involved in caring for preterm neonates. Ideas vary greatly about whether the cut off of haemoglobin concentration or packed cell volume should be used for transfusions in preterm babies.

There are not many randomised studies in the literature that examine this, and the few we know about either have methodological limitations or are not published in their full form.<sup>2-6</sup> Therefore, as Wardle *et al*<sup>1</sup> state, there is no doubt that we need more studies to produce evidence based guidelines for blood transfusion in preterm neonates. These studies should not only look at the number of transfusions, acute mortality, and morbidity but also developmental outcomes at 2-3 years of age. Can a more serious consideration of physiological basis assist us in deciding about when to transfuse? These may have benefits in terms of oxygen delivery to the tissues.<sup>7</sup>

The risks and benefits of transfusion include those associated with maintaining a high or low haemoglobin concentration and some additional risks and benefits of the transfusion itself. A high haemoglobin level,

maintained by frequent transfusion, enhances arterial oxygen content and oxygen transport to the tissues. However, this usually far exceeds need, and so oxygen delivery (equal to oxygen uptake or consumption) is not limited by haemoglobin content. However, in chronic ischaemic or hypoxic hypoxia, in which oxygen delivery may be limited by oxygen transport, a high haemoglobin content may be required to maintain oxygen delivery to the tissues. Expected consequences of chronic anaemic hypoxia are poor growth or impaired neurodevelopmental outcome. On the other hand, if allowing haemoglobin concentration to decrease has no critical or limiting effects on oxygen delivery, growth and development will continue unimpaired without the potentially adverse effects of blood transfusion, such as transfusion borne infection or iron overload. Complicating these physiological considerations even further is the decrease in oxygen affinity of haemoglobin with postnatal age, which increases the ability of the blood to deliver oxygen, and the effect of transfusion of adult haemoglobin, which enhances this effect.

The paper by Wardle *et al*<sup>1</sup> raised several questions in my mind.

(1) In the abstract it is stated that the primary outcome measures were number of transfusions received, rate of weight gain, and postmenstrual age at discharge. In contradiction to this, in the main methodological details of the article, the authors state the single primary outcome measure as "number of transfusions received after randomisation", and all others were secondary outcome measures.

(2) The first criterion stated in group 1 (conventional group) for transfusion, "transfused at Hb of 140 g/l if inspired oxygen concentration > 0.35 or mean airway pressure > 6 cm H<sub>2</sub>O" appears liberal.

(3) It is stated that one of the transfusion criteria set for group 2 (NIRS group) is "transfused at FOE > 0.47". In the "blinding" paragraph, it is stated that "forearm FOE measurements were made on all infants in both groups. These results were only available to researchers and not to the clinical team". This statement implies that clinicians were not aware or notified of the FOE values even in the "NIRS group".

(4) The frequency of Hb measurement is described as "daily in first week of monitoring, then about 4 times a week until the infant was 30 weeks postconceptional age, and then about twice a week". Going through the

paper, it is evident that these infants were enrolled in the study when they were not ventilated or ventilated with Fio<sub>2</sub> < 40%, and the postnatal median age at randomisation was 5 days. Taking these two facts into account, I think that Hb monitoring during the study was too frequent, contributing to excess iatrogenic blood loss.

(5) In the footnote of table 1, it is mentioned that the results are given as "median (range)". For example, the birth weight in the NIRS group is 1200 g (range 1004-1373). The reader will initially interpret this as meaning that the lowest birth weight was 1004 g. However, further down the table it is mentioned that nine infants were ≤ 1000 g. It is left to the poor reader, after serious thought, to conclude that this "range" in reality means "interquartile range".

(6) In the discussion, the authors state that many infants in the NIRS group were transfused because of low Hb or clinical symptoms, even though FOE was not > 0.47. They state that these clinical symptoms could have been due to clinical reasons other than anaemia—for example, infection. It would have been useful, as this is a prospective study, if they had given us some data on infection rate differences in the two groups.

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