Effect of recombinant erythropoietin on "late" transfusions in the neonatal intensive care unit: a meta-analysis

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Authors' objectives
To assess whether the administration of recombinant erythropoietin (rEpo) to very low birth weight (VLBW) infants after the first week of life resulted in fewer 'late' transfusions.

Searching
MEDLINE was searched from January 1990 to December 2000; the search terms were reported. In addition, the authors reviewed personal files and checked the references of all subsequently retrieved articles. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised, placebo-controlled double-blind trials were eligible for inclusion in the review.

Specific interventions included in the review
Studies that assessed treatment with rEpo or placebo after the first week of life were included in the review. The standardised cumulative dose of rEpo ranged from 100 to 1,400 U/kg per week across the included studies. One of the studies used intravenous administration whilst the other seven used subcutaneous administration. All of the studies used enteral iron at doses ranging from 2 to 6 mg/kg per day.

Participants included in the review
The participants included were newborn infants with VLBWs of 1,500 g or less. The mean age of the infants at study entry was 25.1 days (range: 8 to 91).

Outcomes assessed in the review
The outcomes assessed were the proportion of patients who received erythrocyte transfusions and the number of transfusions per patient that were given after the third week (day 22) and before hospital discharge.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed quality.

Data extraction
The authors stated that the included studies were reviewed independently. However, they did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on study demographics, participant age, number of participants, rEpo dose and the number of transfusions. The effect sizes for each of the individual studies were presented as odds ratios, with corresponding 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis. The authors did not state whether a random-effects or fixed-effect model was used. Publication bias was not assessed.
How were differences between studies investigated?
Differences between the studies were explored using regression models, with rEpo dose, birth weight and whether or not transfusion guidelines were in place at the time of the study, being entered as covariates. A dose-response curve that modelled the probability of receiving a transfusion as a function of weekly rEpo dose was generated.

Results of the review
Eight RCTs with a total of 357 participants (183 rEpo and 174 placebo recipients) were included in the review.

The odds ratio of receiving a transfusion for any dose of rEpo compared with placebo was 0.33 (95% CI: 0.21, 0.51). The probability of receiving any erythrocyte transfusion (whether one or multiple) was a function of the rEpo dose received. Birth weight and having guidelines in place were not significantly correlated with the probability of receiving a transfusion. The number-needed-to-treat was also found to be a function of the dose received. For every 10 patients treated with placebo, 6.5 would be expected to receive a 'late' transfusion. For every 10 treated with an rEpo dose of 500 U/kg per week, 3.8 would receive a transfusion; for every 10 treated at 1,000 U/kg per week, 1.7 would receive a transfusion; and for every 10 treated at 1,500 U/kg per week, 0.6 would receive a transfusion. The average number of transfusions per patient was also significantly correlated with rEpo dose, whilst birth weight and having transfusion guidelines in place were not.

Authors' conclusions
The administration of rEpo to VLBW infants reduced 'late' erythrocyte transfusions in a dose-dependent manner.

CRD commentary
The review question was well defined in terms of the intervention, participants, outcome measures and study designs. Only one database was searched and the references of included studies were checked. Efforts were made to reduce language bias, but no efforts were made to search for unpublished studies. Little information on the review process was given, so it is not known whether any efforts were made to reduce bias and errors. In addition, the quality of the included studies was not assessed. Therefore, it is not known whether bias in the included primary studies could have influenced the results of the review, and the authors did not explore this.

The statistical analysis appeared appropriate but, again, there was little information on how the studies were combined. The authors adequately explored differences between the studies in terms of dose, concomitant medication and whether or not guidelines were in place. Overall, because of the level of reporting of the review methods, it was unclear whether any attempts were made to minimise bias and errors, and how these might have impacted on the results. Further research in this area is therefore warranted to support the authors' conclusions.

Implications of the review for practice and research
Practice: The authors stated that if reducing erythrocyte transfusions in the neonatal intensive care unit was a goal, then implementing transfusions criteria guidelines, minimising phlebotomy losses, and administering rEpo to patients who were likely to require 'late' transfusions, could facilitate this goal.

Research: The authors did not state any implications for further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.