Early epoetin for preventing red blood cell transfusion in premature infants

NICE has developed the Cochrane Quality and Productivity topics to help the NHS identify practices that could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care. Each topic has been derived from a Cochrane systematic review that has concluded that the evidence shows that the practice is harmful or ineffective and should not be used, or that there is insufficient evidence to support widespread use of the practice.

NICE summary of Cochrane review conclusions

Use of epoetin (also known as EPO) may reduce the use of blood transfusions but not sufficiently to reduce donor exposure. Use of epoetin appears to lead to an increase in the incidence of retinopathy of prematurity (ROP). As such the Cochrane review determined that the use of epoetin is not recommended.

The 'Implications for practice' section of the Cochrane review stated:

'Early administration of epoetin reduces the use of one or more red blood cell (RBC) transfusions, the volume of RBCs transfused, and the number of donors and transfusions the infant is exposed to following study entry. Donor exposure is probably not avoidable, as most studies included infants who had received red cell transfusions prior to trial entry. Although statistically significant, the reductions are of limited clinical importance. There was a significant increase in the rate of ROP (stage≥3) with early epoetin use. Animal data and observational studies in humans support a possible association between treatment with epoetin and the development of ROP. Epoetin does not significantly reduce or increase any of many other important adverse outcomes including mortality. In view of the limited clinical benefits and the increase in ROP (stage≥3) the administration of early epoetin is not recommended.'

Details of Cochrane review

Cochrane review title

Early erythropoietin for preventing red blood cell transfusion in preterm and/or low birth weight infants (Review).

Citation

Ohlsson A, Aher SM. Early erythropoietin for preventing red blood cell transfusion in preterm and/or low birth weight infants. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD004863. DOI: 10.1002/14651858.CD004863.pub3.

When the review content was assessed as up to date

24 March 2012.

Quality and Productivity category

Medicines use and procurement, Right care.

Relevant codes	OPCS	ICD10	HRG
	X321	PO23	N/A

Programme budget:

Maternity and reproductive health.

Evidence

Relevance to the NHS

Physiologic anaemia of infancy (Strauss 1986) is a process whereby after birth, the haemoglobin concentration of new-born infants normally falls to minimal levels of 11 g/dL. In extremely low birth weight (ELBW) infants, the decline in haematocrit to levels below 7.0 to 10.0 g/dL is known as anaemia of prematurity which is associated with pallor, poor weight gain, decreased activity, tachycardia and feeding problems. Infants with anaemia of prematurity require RBC transfusions.

Infants born prematurely have low levels of epoetin, a constituent of blood that encourages RBC production. Administering epoetin could boost epoetin production to prevent or treat anaemia. The principal aim of epoetin therapy is to decrease the number of transfusions. Most transfusions are given during the first 3-4 weeks of life. Transfusions can lead to potentially serious complications so it is beneficial to reduce the incidence where possible.

According to Cohen and Manno (1998) the diagnostic accuracy of different clinical signs and laboratory findings has not been studied. A rational guide for transfusion therapy for anaemic neonates is not available. However, 'top-up' transfusions to treat low haemoglobin or low haematocrit levels are frequently used. As many as 80% of very low birth weight (VLBW) infants and 95% of ELBW infants receive blood transfusions during hospitalisations (Widness,1996).

Vamvakas and Strauss (2001) reported that there is great variation in the results of epoetin studies and until this variation is better understood it is not yet possible to recommend epoetin as standard treatment for anaemia of prematurity. Some 27 studies that included 2300 infants born prematurely have been enrolled.

Early epoetin treatment reduces the number of RBC transfusions but the overall benefit of epoetin may not be clinically important. This is because many patients had already been exposed to RBC transfusions before entering the clinical trials. Results showed that treatment with early epoetin did not have any significant effects on common complications of premature birth or mortality but treatment with epoetin did increase the possibility for ROP, a serious complication that can cause blindness in premature infants. Juul (2002) and Dame et al (2001) found that the administration of epoetin may have a neuro protective effect in preterm infants, particularly infants with perinatal asphyxia. However no systematic reviews have been conducted to confirm effectiveness of this aspect of epoetin use in neonates.

Epoetin is not recommended for routine use in preterm infants. The update in 2012 did not identify any additional studies for inclusion.

Relevant NICE guidance and products

No relevant NICE guidance was available at the time of publication (April 2014).

Other accredited guidance

No relevant accredited guidance was available at the time of publication (April 2014).

Potential productivity savings

Estimate of current NHS use

- Approximately 38,000 preterm deliveries were recorded in England in 2013[1]. Based on the 2012/13 Hospital Episode Statistics about 730 blood transfusions for new-born infants were carried out.[2].
- There is no data available relating to the number of preterm infants who received early administration of epoetin.

Level of productivity savings anticipated

- No productivity savings expected.

Type of saving

- The cost of epoetin beta is £10.53 per week and £63 for 6 weeks of treatment. This is based on an average dosage of 400 units/kg, 3 times a week[3].
- Actual cash savings range from £10.53 to £63 per new-born infant requiring a blood transfusion (who does not receive early administration of epoetin). However, because early epoetin significantly reduces the number of red blood cell transfusions per new-born infant and the number of donor exposures these savings may even out with additional cost of increased transfusions once epoetin is stopped.

Any costs needed to achieve the savings

- No additional resources required.

Other information

- Potential savings are likely to benefit NHS provider trust budgets.

[1] The Health and Social Care Information Centre. Table 7.a: Delivery complications recorded by age of mother, 2012-13.
[2] The Health and Social Care Information Centre. Hospital Episode Statistics for England. Inpatient statistics, 2012-13. Main procedures and interventions: 4 character code and description.
[3] BNF for Children January 2014

Potential impact on quality of NHS care

Impact on clinical quality

Not anticipated to have any impact on quality of care delivered to patients. Early use of epoetin only slightly reduces the number of RBC transfusions that may be required but the reductions are of limited clinical importance.

Impact on patient safety

Not administering early epoetin is anticipated to have a significant improvement in patient safety. Studies indicate that there is a significant increase in the risk of ROP associated with administering early epoetin [RR; 1.65, (95% CI 1.12 to 2.43); typical RD; 0.05 (95% CI 0.01 to 0.08); number needed to harm (NNTH); 20, (95% CI 13 to 100); eight studies, 984 infants]. Due to the limited benefits and the increased risk of ROP, early administration of epoetin is not recommended.

Impact on patient and carer experience

Not anticpated to have an impact on patient and carer experience.

Likely ease of implementation

Time taken to implement

It is assumed that stopping the administration of epoetin can be achieved quickly (within 3 months).

Healthcare sectors affected

Affects one department or team.

Stakeholder support

Likely to achieve good buy-in from key influencers.

References

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