Iron supplementation for postoperative anaemia following major paediatric orthopaedic surgery

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ABSTRACT

INTRODUCTION There is increasing evidence that the anaemia of surgery is not iron deficient and is, therefore, unresponsive to iron supplementation. Oral iron is best avoided postoperatively, particularly in children, due to its dose-dependent side effects. We undertook a national survey of major paediatric orthopaedic surgical units in the UK to investigate the current management of postoperative anaemia with particular reference to iron supplementation.

MATERIALS AND METHODS Middle-grade doctors and charge nurses at 23 major paediatric orthopaedic units in the UK were contacted by telephone and a structured questionnaire was used to determine the management of postoperative anaemia in major hip, pelvic and spinal surgery.

RESULTS Only one (4.3%) of the units surveyed had a formally established protocol for the management of postoperative anaemia. Only 10 out of 23 units (43.5%) did not routinely prescribe iron postoperatively. Of the remaining units, 11 commenced iron based on the postoperative haemoglobin level while only 2 used iron supplementation after investigation of serum haematinics for iron deficiency. One unit used erythropoietin in the treatment of postoperative anaemia.

CONCLUSIONS Iron supplementation continues to be used in major paediatric orthopaedic surgery in the treatment of postoperative anaemia in the absence of iron deficiency. Given the current available evidence, we call for an end to the practice of routine iron supplementation for postoperative anaemia following major paediatric orthopaedic surgery in the UK.

KEYWORDS

Postoperative anaemia – Iron supplementation – Survey

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Postoperative anaemia secondary to haemorrhage is a common complication following major surgery. Transfusion is best avoided particularly in children, due to the risks of infection, immunosuppression, and allo-immunisation, and is reserved for patients with severe anaemia.¹ Strategies that have been developed to reduce the severity of anaemia and minimise exposure to allogeneic blood transfusion include the use of erythropoietin, intra-operative cell salvage and autologous blood donation.² Moderate anaemia following surgery is commonly treated empirically with iron.

There has been an improved understanding of the pathophysiology and the role of iron in postoperative anaemia in the past decade. There is now strong evidence that the anaemia of surgery is not iron deficient and does not respond to iron supplementation.^{3,4} Oral iron is generally safe but there are dose-dependent side-effects, particularly in children.⁵ As it has been shown to be ineffective, its use cannot be recommended. Nevertheless, iron supplementation

continues to be used in postoperative anaemia in various departments, including our own. This prompted us to undertake a national telephone survey of major paediatric orthopaedic surgical units in the UK to investigate the management of postoperative anaemia.

Materials and Methods

We conducted a telephone survey of the use of iron supplementation, blood transfusion, erythropoietin therapy and blood conservation techniques in the management of paediatric orthopaedic postoperative anaemia in the UK. Units which do not carry out major open hip, pelvis or spine surgery in children were excluded from this study. We interviewed middle-grade doctors (senior house officers and specialist registrars) and charge nurses at 23 major paediatric orthopaedic surgical centres. Using a structured questionnaire, we examined how postoperative anaemia is

managed in children undergoing major hip, pelvic and spinal surgery (Appendix 1). We determined whether iron supplementation was used and the indications for iron supplementation, blood transfusion, erythropoietin and blood conservation techniques.

Results

Of the 23 units surveyed, only one (4.3%) had a formal protocol for the management of postoperative anaemia. Ten out of 23 units (43.5%) did not routinely prescribe iron for postoperative anaemia due to the associated side effects and the lack of current evidence. Importantly, the other 13 units (56.5%) did routinely prescribe iron. Of these, 53.8% (7/13) units commenced iron for a haemoglobin (Hb) < 10.0 g/dl, 15.4% (2/13) at Hb < 9.0 g/dl, and 15.4% (2/13) at Hb < 8.0 g/dl without investigation of serum haematinics (Fig. 1). Also, 15.4% (2/13) units commenced iron only if indicated following investigation of serum haematinics.

All the units interviewed transfused children with symptomatic postoperative anaemia. Only one (4.3%) of the units surveyed used erythropoietin in their management of postoperative anaemia at Hb < 8.0 g/dl. None of the units surveyed used vitamin B₁₂, folate supplementation or blood conservation techniques, such as autologous transfusion, in major hip, pelvic or spinal surgery in children.

Discussion

Chronic blood loss results in iron deficiency, which can be effectively treated with iron supplementation. This principle has been extended to the management of acute surgical blood loss. However, there is evidence that iron supplementation is not effective for the treatment of postoperative anaemia in emergent hemi-arthroplasty⁵ or in elective total joint replacement.⁴ Furthermore, significant adverse effects was reported in over 20% of patients.⁴

In the presence of adequate iron stores, acute blood loss does not usually result in iron deficiency, even in children.⁶ Observations in blood donors show that erythropoiesis is only modestly stimulated after phlebotomy and does not improve with oral iron supplementation.^{7,8} Furthermore, the degree to which erythropoiesis is stimulated is not dependent on the level of storage iron present.⁹ This suggests that iron is not a limiting factor for haemoglobin recovery after acute blood loss in iron-replete individuals.

In addition to simple blood loss, the anaemia following surgery is complicated by a state of anaemia of chronic disease (ACD) induced by the acute phase inflammatory response.¹⁰ This form of anaemia is characterised by low serum iron in the presence of adequate iron stores. In other words, iron is sequestered at the storage sites and not made available for erythropoiesis. It is known that iron supplementation does not benefit patients with ACD.¹¹ The iron given is rapidly transported to the reticulo-endothelial storage sites and not incorporated into haemoglobin.¹² Furthermore, the removal of iron by chelation therapy in ACD is associated with a rise in haemoglobin.¹⁵ The resemblance of postoperative anaemia to ACD and not to iron-deficiency anaemia explains the lack of effect of iron on this group of patients.

There is strong evidence that erythropoietin therapy promotes haemoglobin recovery and reduces the need for transfusion in both children and adults with postoperative anaemia.¹⁴ It is, therefore, of great interest that only one of the 23 units surveyed uses erythropoietin. A similarly low uptake of erythropoietin use in surgery was noted in the US.¹⁵

The wide-spread variability in anaemia management seen in this study is an example of how dissemination and application of clinical evidence to everyday clinical practice still remains inadequate. Based on the current evidence, we recommend an end to the practice of iron supplementation for postoperative anaemia in major paediatric orthopaedic surgery in patients who are not iron deficient. Consideration should be given to extending this principle to other paediatric and adult surgical procedures. Alternatives with proven efficacy such as erythropoietin and blood conservation techniques, including acute normovolaemic haemodilution and autologous transfusion, should be considered instead.

References

1. Mercuriali F, Inghilleri G. Transfusion risks and limitations. *Minerva Anesthesiol* 1999; **65**: 286–92.
2. Goodnough LT, Shander A, Spence R. Bloodless medicine: clinical care without allogeneic blood transfusion. *Transfusion* 2003; **43**: 668–76.
3. Zauber NP, Zauber AG, Gordon FJ, Tillis AC, Leeds HC, Berman E *et al*. Iron supplementation after femoral head replacement for patients with normal iron stores. *JAMA* 1992; **267**: 525–7.
4. Sutton PM, Cresswell T, Livesey JP, Speed K, Bagga T. Treatment of anaemia after joint replacement. A double-blind, randomised, controlled trial of ferrous sulphate versus placebo. *J Bone Joint Surg Br* 2004; **86**: 31–3.

5. Rohling RG, Zimmerman AP, Breymann C. Intravenous versus oral iron supplementation for preoperative stimulation of hemoglobin synthesis using recombinant human erythropoietin. *J Hematother Stem Cell Res* 2000; **9**: 497–500.
6. Han P, Stacy D. Response of the erythron and erythropoietin to autologous blood donations in paediatric subjects. Is erythropoietin supplement necessary? *Vox Sang* 1997; **73**: 24–7.
7. Goodnough LT, Mercuriali F. Compensatory erythropoiesis during routine autologous blood donation. *Transfusion* 1998; **38**: 613–5.
8. Weisbach V, Skoda P, Rippel R, Lauer G, Glaser A, Zingsem J *et al*. Oral or intravenous iron as an adjuvant to autologous blood donation in elective surgery: a randomized, controlled study. *Transfusion* 1999; **39**: 465–72.
9. Price TH, Goodnough LT, Vogler WR, Sacher RA, Hellman RM, Johnston MF *et al*. The effect of recombinant human erythropoietin on the efficacy of autologous blood donation in patients with low hematocrits: a multicenter, randomized, double-blind, controlled trial. *Transfusion* 1996; **36**: 29–36.
10. van Iperen CE, Kraaijenhagen RJ, Biesma DH, Beguin Y, Marx JJ, van de Wiel A. Iron metabolism and erythropoiesis after surgery. *Br J Surg* 1998; **85**: 41–5.
11. Roy CN, Weinstein DA, Andrews NC. The molecular biology of the anemia of chronic disease: a hypothesis. *Pediatr Res* 2003; **53**: 507–12.
12. Jensen NM, Brandsborg M, Boesen AM, Yde H, Dahlerup JF. Low-dose oral iron absorption test in anaemic patients with and without iron deficiency determined by bone marrow iron content. *Eur J Haematol* 1999; **63**: 103–11.
13. Salvarani C, Baricchi R, Lasagni D, Boiardi L, Piccinini R, Brunati C *et al*. Effects of desferrioxamine therapy on chronic disease anemia associated with rheumatoid arthritis. *Rheumatol Int* 1996; **16**: 45–8.
14. Tamir L, Fradin Z, Fridlander M, Ashkenazi U, Zeidman A, Cohen AM *et al*. Recombinant human erythropoietin reduces allogeneic blood transfusion requirements in patients undergoing major orthopedic surgery. *Haematologia* 2000; **30**: 193–201.
15. Goodnough LT, Monk TG, Andriole GL. Erythropoietin therapy. *N Engl J Med* 1997; **336**: 933–8.

APPENDIX 1

Structured telephone interview questionnaire as used in the survey

HOSPITAL:

Do you carry out major open hip, pelvis, or spine surgery in children?

If yes, proceed on to questionnaire

Are you familiar with the unit's transfusion practices?

Contact registrar/SHO/charge nurse whoever is more familiar with the unit practices

Is there a protocol for haemoglobin check and transfusion?

If YES, what is the protocol?

If NO

Do you routinely check haemoglobin?

If so, do you have a cut-off threshold for treatment?

Haemoglobin	Action

Management

Do you routinely consider use of the following in postoperative anaemia?

Iron

Vitamin B₁₂

Folate

Erythropoietin

Cell salvage or autologous transfusion

What would you do for a child with a postoperative

Hb < 9

Hb < 9 and symptomatic anaemia