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Iron Deficiency With and Without Anemia: Perspectives on Perioperative Management in Pediatric Patients

Claudine Kumba*
https://orcid.org/0000-0002-9748-514
Department of Pediatric Anesthesia and Critical Care, Necker Enfants Malades University Hospital, Paris Descartes University, University of Paris, Paris, France

Abstract

Background: Iron deficiency anemia (IDA) is the most common cause of anemia in children. Iron deficiency (ID) is the most common cause of nutrient deficiency in the pediatric population. ID has various etiologies including decreased iron intake and absorption, increased iron requirement and loss. ID and IDA have been associated with adverse neurodevelopmental outcome in children. Anemia in children has been related with increased mortality. The prevalence of ID and IDA in children in the general population is 6.6% to 15.2% and 0.9% to 4.4% respectively in the USA according to one study. IDA and ID treatment includes iron supplementation and correction of anemia with this therapy can take several weeks. Anticipating treatment of iron deficiency anemia due to blood loss in the perioperative period seems intuitively an important issue to reduce blood transfusion in this setting. Since the latter has been shown to be predictive of adverse postoperative outcome in children. Evidence concerning reduction of blood transfusion requirements perioperatively when IDA and ID were diagnosed, prevented and treated preoperatively is lacking in the pediatric population.

Objective: This narrative review was undertaken to determine the impact of preoperative management of ID and IDA on perioperative blood transfusion in children.

Methods: Narrative review of the litterature.

Conclusion and Results: There are no randomized controlled studies concerning the impact of preoperative management of ID and IDA on perioperative blood transfusion in children. There is evidence that ID and IDA diagnosis, prevention and treatment in the general pediatric population increase hemoglobin levels.

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*E-mail: claudine.kumba@gmail.com

Introduction

The incidence of iron deficiency without anemia (ID) and iron deficiency anemia (IDA) is 7% and 10% respectively in children aged one to three years in the USA [1-6]. The prevalence of ID varies from 6.6% to 75% and that of IDA from 0.9% to 76% with high values found in low income countries [1-6]. Etiologies of ID and IDA varie according to the clinical settings and comprise insufficient dietary iron intake (exclusive breastfeeding, cow milk without supplements, insufficient diet…), malabsorption due to gastrointestinal disease (e.g coelic disease), acute or chronic blood loss (gastrointestinal pathologies, urinary tract disease, blood loss due to surgery), menstruations and genetic disorders like mutations of TMPRSS6 [7-10]. Symptoms and signs of anemia varie depending on the severity, acute and chronic evolution. They can present as fatigue, pallor, low blood pressure, palpitations, tachycardia, cardiac failure, stroke,

neurodevelopmental alteration, growth impairement and pica [7,11,12].

Anemia in the general pediatric population has been related with mortality [13]. The latter has been shown to be reduced with the increase in hemoglobin levels [13]. ID and IDA have been related with neurodevelopment impairement in children less than 24 months [2,3,14-19]. These alterations of brain development can be reversed in some situations with the treatment of ID and IDA and they can be irreversible when ID and IDA occur early in life [19]. These impairements can be prevented with iron supplementations [3,15,16,20-22]. In animal studies, alterations in myelination and dopaminergic pathways with low iron has been evoked as a possible explanation of neurodevelopmental disorders [14,15]. IDA has been reported in one study to affect the neuroendocrine system as demonstrated by low serum cortisol and prolactin levels in patients exposed to IDA in infancy [23]. In the perioperative period it may appear intuitive to diagnose ID and IDA with the aim to prevent blood transfusion in potential hemorrhagic situations in children. This review was undertaken to determine the impact of preoperative ID and IDA mangement on perioperative blood transfusion in children.

Literature Review

No trials were found concerning the management of preoperative ID and IDA on the impact of perioperative blood transfusion, precisely randomized controlled studies comparing iron supplementation to placebo in children. Nevertheless there is a lot of litterature concerning ID and IDA diagnosis, prevention and treatment in the general pediatric population in different parts of the world. Different manuscripts have reported the efficacy of iron supplementation to treat and prevent ID and IDA in risk populations in children like fortification programs in low in come countries where the incidence and prevalence of these issues are the highest [3,4,12,18,20,24-26].

A retrospective study of 195 children in a single center showed that intravenous iron supplementation in children diagnosed with ID and or IDA increased hemoglobin levels [12]. A systematic review and meta-analysis in more than 12000 children aged 28 days to 12 years showed that mortality was high in anemic children and every increase of 1g/dL of hemoglobin level with blood transfusion reduced it by 24% [13]. This trial where anemia had several etiologies did not determine the impact of iron supplementation on mortality due to anemia. This meta-analysis also found that intravenous iron supplementation was more efficient in increasing hemoglobin levels than oral iron which was more efficient than placebo. A systematic review and meta-analysis of more than one thousand school aged children showed that iron deficiency and anemia were reduced with iron supplementation compared to placebo. This meta-analysis also found that global cognitive performance was increased in the iron group compared to placebo [20]. Another meta- analysis in more than 4000 school aged children found that ID and IDA were decreased with fortified beverages with iron supplements [24]. Iron supplements also were shown to reduce ID and IDA in low birth infants [25]. In a Cochrane systematic review of 33 trials in more than thirteen thousand children less than 12 years daily supplementation with iron was more effective to reduce ID and IDA than intermittent supplementation which was more effective than placebo [26].

Discussion

Transfusion which has been evidenced to be related to adverse outcome in terms of organ dysfunction, infections, length of hospital stay (LOS), length of mechanical ventilation (LMV) in critical ill children [27] can be a life saving therapy in anemic children [13]. Anemia is also a risk factor of mortality. The issue raised here is if there are preventable causes of anemia like iron deficiency which constitues 50% of the etiology of anemia in children [2,7] is postperative IDA prevention possible ? There are reports on the efficacy of iron supplementation to prevent and treat ID and IDA in children in the general population [3,4,12,18,20,24,25,26]. There are no randomized controlled trials showing that in children iron supplementation reduces mortality related to anemia, nonetheless iron supplements have been demontstrated to increase hemoglobin levels [13].

In adults, a meta- analysis in colorectal and gynecological surgery showed that iron supplements decreased blood transfusion compared to placebo [28]. Hemoglobin levels were also higher in patients with intravenous iron supplementation than oral iron administration

[28,29]. Another issue here is whether ID and IDA diagnosis, prevention and treatment in the preoperative period can contribute to reduce red blood cell transfusion and thus reduce adverse outcome related to transfusion in hemorrhagic surgeries. This is yet to be evidenced in children scheduled for potential hemorrhagic surgery. Since increase in hemoglobin levels after iron supplementation is not immediate and demands several weeks to be effective patients scheduled for potential hemorrhagic elective surgery should benefit from an elective anesthesia consultation several weeks before surgery to be screened for ID and IDA. These latter should equally benefit from iron supplementation if diagnosed. Laboratory test that contribute to ID and IDA diagnosis are hemoglobin levels, mean corpuscular volume (MCV), red blood cell distribution width (RDW), serum ferritin levels which can be high in case of infection or inflammation should be dosed with C-reactive protein concomittantly, serum transferrin, soluble transferrin receptor, iron saturation on transferrin, serum iron, erythrocyte zinc protoporphyrin, reticulocyte hemoglobin concentration, red blood cells count (RBC), serum hepcidin levels (not systematically in routine diagnosis) [7,8,30].

Other causes of microcytic anemia should also be excluded like beta thalassemia, hemoglobinopathies where iron supplementation is not recommended and sideroblastic anemia [1,30]. Once ID and IDA are diagnosed oral or parenteral supplementation should be instaured. Oral iron supplements have proven efficacy in inceasing hemoglobin levels within several weeks. Some patients cannot tolerate oral iron and patients who have genetic disorders which cause iron refractory iron deficiency anemia (IRIDA) like mutations of TMPRSS6 may benefit from intravenous iron [31]. The latter is a recessive autosomal disorder characterized by refractory IDA to oral iron, low or normal ferritin levels which increase after oral iron supplementation and partial responsiveness to parenteral iron [9,10]. IRIDA is a rare disorder and 41 muations of TMPRSS6 have been identified [32]. The latter encodes for hepatic type II transmembrane serine protease which regulates the expression of hepcidin which is the serum iron regulator. In children one type of IV iron has shown its efficacy which is iron sucrose (venofer) with minimal side effects [31]. There are no randomized controlled trials concerning the impact of preoperative iron supplementation in iron deficient and iron anemic children on perioperative blood transfusion.

There is enough evidence concerning the efficacy of this therapy to increase hemoglobin levels in ID and IDA in the general pediatric population. Randomized controlled studies to determine the impact of preoperative iron supplements in ID and IDA on perioperative blood transfusion in children are to be developed.

Conclusion

Although there are no studies concerning the impact of preoperative ID and IDA management that is to say diagnosis, prevention and treatment on perioperative outcome (namely reduction of red blood cell transfusion, reduction of transfusion related adverse outcome mentioned above) in the pediatric population, there is a lot of evidence in the general pediatric population concernig the importance of iron supplementation programs in high risk children around the world. These programs have proven reduction in adverse outcome related to chronic ID and IDA in terms of low hemoglobin levels, cognitive and neurodevelopmental impairement. Iron supplementation in the preoperative period in potential hemorrhagic settings when ID and IDA are diagnosed can be an economic mean to prevent and treat anemia related to iron deficiency. Randomized controlled trials are to be developped to clarify the impact of preoperative iron supplementation on perioperative blood transfusion in potential hemorrhagic surgeries in children with ID and IDA.

References

1. Irwin J, Kirchener J. Anemia in children. Am Fam Physician. 2001;64:1379-86.
2. Moshe G, Amitai Y, Korchia G, Korchia L, Tenenbaum A, Rosenblum J, et al. Anemia and iron deficiency in children: Association with red meat and poultry consumption. JPGN. 2013;57: 722–727.
3. Backer R, Greer R. The Committee on Nutrition. Clinical Report—Diagnosis and Prevention of Iron Deficiency and Iron-Deficiency Anemia in Infants and Young Children (0 –3 Years of Age). Pediatrics. 2010; 126(5): 1040-1050.
4. Paes Leme Coutinho GG, Goloni-Bertollo EM, Pavarino Bertelli EC. Iron deficiency anemia in children: A challenge for public health and for society. Sao Paulo Med J. 2005;123(2):88-92.

5. Engle-Stone R, Nankap M, Ndjebayi AO, Erhardt JG, Brown KH. Plasma ferritin and soluble transferrin receptor concentrations and body iron stores identify similar risk factors for iron deficiency but result in different estimates of the National Prevalence of Iron Deficiency and Iron-Deficiency Anemia among Women and Children in Cameroon. J. Nutr. 2013; 143: 369–377.
6. Murray-Kolb LE. Iron supplementation in early life and child health. The Lancet Global Health. 2013; 1: e56-e57.
7. Miller JL. Iron Deficiency Anemia: A common and curable disease. Cold Spring Harb Perspect Med. 2013;3:a011866
8. Zhu A, Kaneshiro M, Kaunitz JD. Evaluation and treatment of iron deficiency anemia: A gastroenterological perspective. Dig Dis Sci. 2010;55:548–559
9. Khuong-Quang D, Schwartzentruber J, Westerman M, Lepage P, Finberg KE, Majewski J, et al. Iron refractory iron deficiency anemia: Presentation with hyperferritinemia and response to oraliron therapy. Pediatrics. 2013;131:e620–e625.
10. Finberg KE, Heeney MM, Campagna DR. Mutations in TMPRSS6 cause iron-refractory iron deficiency anemia (IRIDA). Nat Genet. 2008; 40(5): 569–571.
11. Janus J, Moerschel SK. Evaluation of anemia in children. Am Fam Physician. 2010;81(12):1462-1471.
12. Powers J, Daniel C, McCavit T, Buchanan G. Deficiencies in the management of iron deficiency anemia during childhood. Pediatr Blood Cancer 2016;63(4):743–745.
13. Scott SP, Chen-Edinboro LP, Caulfield LE, Murray-Kolb LE. The impact of anemia on child mortality: An updated review. Nutrients. 2014; 6: 5915-5932.
14. Black MM. Integrated strategies needed to prevent iron deficiency and to promote early child development. J Trace Elem Med Biol. 2012; 26(0): 120–123.
15. Lozoff B. Iron deficiency and child development. Food and Nutrition Bulletin. 2007; 28(4): S560-S571.
16. Carter RC, Jacobson JL, Burden MJ, Armony-Sivan R, Dodge NC, Angelilli ML, et al. Iron deficiency anemia and cognitive function in infancy. Pediatrics 2010; 126(2): e427–e434.
17. Joo EY, Kim KY, Kim DH, Lee JE, Kim SK. Iron deficiency anemia in infants and toddlers. Blood Res. 2016;51:268-73
18. Stoltzfus RJ. Iron interventions for women and children in low-income countries. J. Nutr. 2011; 141: 756S–762S.
19. Kazal LA. Prevention of iron deficiency in infants and toddlers. Am Fam Physician 2002;66:1217-24,1227.
20. Low M, Farrell A, Biggs B, Pasricha Q. Effects of daily iron supplementation in primary school aged children: systematic review and meta-analysisof randomized controlled trials. CMAJ. 2013;185(17):E791-E802.
21. Detzel P, Wieser S. Food fortification for addressing iron deficiency in Filipino children: Benefits and cost-effectiveness. Ann Nutr Metab. 2015;66 (2):35–42.
22. Eicher-Miller HA, Mason AC, Weaver CM, MaCabe GP, Boushey CJ. Food insecurity is associated with iron deficiency anemia in US adolescents. Am J Clin Nutr. 2009;90:1358–1371.
23. Felt BT, Peirano P, Algarín C, Chamorro R, Sir T, Kaciroti N, et al. Long-term neuroendocrine effects of iron-deficiency anemia in infancy. Pediatr Res. 2012 ; 71(6):707–712.
24. Aaron G, Dror D, Yang Z. Multiple micronutrient fortified non-dairy beverage interventions reduce the risk of Anemia and iron deficiency in school-aged children in low-middle income countries: A systematic review and meta-analysis. Nutrients 2015;7:3847–3868.
25. Long H, Yi J, Hu P, Li Z, Qiu W, Wang F, Zhu S. Benefits of iron supplementation for low birth weight infants: A systematic review. BMC Pediatrics. 2012;12:99.
26. De-Regil LM, Jefferds MED, Sylvetsky AC, Dowswell T. Intermittent iron supplementation for improving nutrition and development in children under 12 years of age (Review). Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD009085.
27. Kumba C, Cresci F, Picard C, Thiry C, Albinni S, Orliaguet G. Transfusion and morbi- mortality factors: An observational descriptive retrospective pediatric cohort study. J Anesth Crit Care Open Access. 2017;8(4):00315.
28. Ng O, Keeler BD, Mishra A, Simpson A. Iron therapy for pre-operative anaemia.Cochrane Database of Systematic Reviews 2015, Issue 12. Art. No.: CD011588.
29. Gurusamy KS, Nagendran M, Broadhurst JF, Simpson A, Neal K, Brookes MJ, et al. Iron therapy in anaemic adults without chronic kidney disease (Review). Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD010640.
30. Short MW, Domagalski JE. Iron deficiency anemia: Evaluation and management. Am Fam Physician. 2013; 87(2):98-104.
31. Pinsk V, Levy J, Moser A, Yerushalmi B, Kapelushnik P. Efficacy and safety of intravenous iron sucrose therapy in a group of children with iron deficiency anemia. IMAJ 2008;10:335–338.
32. Poggiali E, Andreozzi F, Nava I. The role of TMPRSS6 polymorphisms in iron deficiency anemia partially responsive to oral iron treatment. Am J Hematol. 2015; 90:306–309.