

## Iron deficiency with or without anemia and perspectives of perioperative management in children

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### Abstract:

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 coeliac 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 impairment 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 impairment 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 impairments 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 constitutes 50% of the etiology of anemia in children [2,7] is postoperative 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 demonstrated 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

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