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TREATMENT OPTIONS FOR IRON DEFICIENCY ANEMIA IN CHILDREN IN SAUDI ARABIA

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Abstract
Background: Iron deficiency anaemia (IDA) is the most common haematological disorder in children, with a prevalence of 20.1% between the ages of 0 and 4 and 5.9% between the ages of 5 and 14 (39 and 48.1% in developing countries).
Methods: The laboratory reveals microcytic-hypochromic anaemia (low Hb, MCV, MCH, and RDW) with a low reticulocyte count. Low ferritin, sideremia, transferrin saturation, and high unsaturated serum transferrin levels are all observed.
Results: Every day, new frontiers in its diagnosis and therapeutic options emerge; recently, innovative iron formulations for oral and parenteral administration have been launched, with the goal of offering treatment schedules with higher efficacy and lower toxicity.
Conclusion: The current article reports the most recent clinically relevant findings regarding IDA in children and provides practical guidance, particularly in selecting the most appropriate therapy strategies.

Keywords: anemia, iron-deficiency, Children, iron defieciecy in Saudi Arabia, therapy, iron deficiency treatment options,

1. Introduction

Iron-deficiency anaemia (IDA) is a disease caused by a lack of essential iron supplements in the diet. According to the World Health Organisation (WHO), this disease primarily affects women and children around the world. It is the most common nutritional challenge in Asian and African countries [1]. WHO defines anaemia as a condition in which some red blood cells, which are responsible for carrying oxygenated blood, become unable to perform their normal functions in the body. The age groups determine the iron requirements of the human body.

Iron deficiency in children can have long-term consequences; iron supplementation for anaemic children can reverse the anaemia, but it may not fully correct the cognitive impairment [2]. Early detection of iron deficiency, even before the development of anaemia, is thought to be critical in

preventing the disease's systemic complications. This is especially important in developing countries, where other nutritional deficiencies exacerbate the problem.

Iron is required for the development of the foetus, infant, and child. The iron content of the body is determined by its intake and absorption through nutrition. This nutrient's homeostasis is determined by the balance of its uptake and release from the cells where it is stored and recycled [3]. Iron is released into the circulation and carried by the plasma protein transferrin, into the duodenum by enterocytes that absorb dietary iron, and into the stomach by macrophages that recycle senescent erythrocytes and liver reserves. When iron levels in the body are low, intestinal absorption is increased; when levels are high, it is stored in the enterocytes as ferritin and the liver, spleen, and bone marrow as hemosiderin [4]. The release of free iron ions in the plasma, which is required for its homeostasis, is mediated by ferroportin, whose expression is regulated by hepcidin activity [5].

2. Literature review:

2.1 Definition of Anemia:

Anaemia is a condition in which the number of red blood cells (and thus their capacity to carry oxygen) is insufficient to meet the body's physiological needs. [6]

2.2 Definition of iron deficiency anemia:

Anaemia caused by a lack of iron is known as iron-deficiency anaemia.
Iron deficiency anaemia (IDA) is the most common type of micronutrient deficiency in developing countries, caused by a long-term negative iron imbalance. According to the World Health Organisation (WHO), approximately two billion people worldwide suffer from anaemia, with IDA accounting for 50% of all cases. ID typically develops gradually and does not manifest clinically until the anaemia becomes severe.[7]

2.3 Causes of iron deficiency anemia:

Iron deficiency anaemia, which is a major health problem in Saudi Arabia and has multiple aetiologies, is found in varying degrees around the world, depending on age group and geographic location.
Iron deficiency is caused by a long-term negative imbalance between a person's iron intake and physiological demand. Various nonmodifiable and modifiable factors influence an individual's iron balance, either alone or in combination,10 ranging from sociodemographic characteristics (including the individual's age, gender, marital status, level of education, income, and ethnicity) to the amount and quality of food and beverages consumed, their mental and physical health, the medication they take, any abnormalities they have, and their genetic makeup.[8]

2.4 Pathophysiology

Iron is a trace element that is primarily controlled by dietary intake, intestinal absorption, and iron recycling.12 There are two types of dietary iron: haem iron and non-haem iron. Haem iron is easily absorbed and is derived from haemoglobin (Hb) and myoglobin, which can be found in animal meat, poultry, and fish. Non-haem iron is found primarily in plant foods but is less easily absorbed. Plant compounds such as phytate, oxalate, polyphenols, and tannin, as well as some drugs such as proton pump inhibitors, reduce non-heme iron uptake.[9]

3. Methodology:

3.1 Diagnosis:

The absence of stainable bone marrow iron is the gold standard test for absolute ID. Unless they also have absolute ID, patients with functional ID have detectable stainable bone marrow iron. Although bone marrow aspiration is invasive and rarely used routinely to diagnose ID, it is still useful in complex cases. Blood biomarkers are commonly used to diagnose ID.[10]

Anaemia, microcytic, hypochromic red blood cells with increased red blood cell distribution width (anisocytosis), and elongated (pencil shaped) cells can all be detected by a film blood count.
Ferritin in serum (or plasma) is the gold standard for ID diagnosis.

Soluble transferrin receptor (sTfR) is a useful index of tissue iron needs, and the sTfR:log(ferritin) ratio has predictive value for bone marrow iron stores, particularly in inflammatory patients. sTfR is also an erythropoiesis biomarker. Because different sTfR tests have not been formally standardised, it has limited clinical availability and different thresholds between assays. [11]

Several modern automated haematology analyzers can measure reticulocyte haemoglobin content, hypochromic red blood cell percentage, and other indices. The proportion of hypochromic red blood cells reflects iron-restricted erythropoiesis over the previous 2-3 months.

4. Results:

4.1 Treatment options of Iron deficiency anemia:

If anaemia is present, the goal of treatment is to replenish iron stores and normalise haemoglobin concentrations. Anaemia, symptoms, critical periods that risk poor outcomes, and when progression is likely to be due to uncorrected underlying factors, such as ongoing growth in children, poor iron intake, or blood losses, are all indications for therapy in ID. Most patients with non-anaemic ID who are seen clinically will have symptoms and should be treated, whereas patients who are completely asymptomatic should probably still be treated to prevent further iron store decline.[12]

4.2 Oral iron supplementation

There are numerous oral iron products available in various doses and formulations. Ferrous salts (for example, ferrous sulphate) and other agents, such as iron polymaltose, are used in oral iron formulations. The dose is determined by the elemental iron content (for example, 325 mg ferrous sulphate contains 105 mg elemental iron). The use of ferrous salts for iron therapy is restricted due to gastrointestinal side effects. A systematic review of placebo-controlled trials found that ferrous salts increased gastro intestinal symptoms (OR 232 [95% CI 175-308]), especially constipation (12%), nausea (11%), and diarrhoea (8%). Gastrointestinal symptoms limit adherence and cause therapy discontinuation. Slow-release iron formulations aim to reduce side effects; however, clinical studies show that this type of formulation is ineffective. [13]

Historically, doses of elemental iron as high as 100-200 mg per day were recommended in two to three divided doses. Stable isotope studies, on the other hand, have redefined optimal oral regimens.

When the sustained absorption of elemental iron from twice daily, daily, and alternate daily dosing was measured, alternate daily dosing absorbed 33% more iron over 14 doses than daily dosing; dividing doses worsened fractional absorption. In women with mild IDA, frac- tional iron absorption was higher when iron was given on alternate days rather than consecutive days, and it was higher from 100 mg doses rather than 200 mg doses.

4.3 Intravenous iron

Parenteral iron administration is an alternative to oral iron supplementation. The primary benefit of intravenous iron is that it avoids GI tract absorption, avoiding further mucosal aggravation and inflammation and producing fewer side effects. Clinicians also do not have to worry about patient medication adherence.[14]
The equation is used to calculate typical transfusion volumes.[15]

$$\text{Transfusion volume} = \frac{\text{weight(kg)} \times \text{desired increment in Hb}\left(\frac{\text{g}}{\text{L}}\right) \times \text{transfusion factor}}{10}$$

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4.4 Red blood cells transfusion:

Red blood cells, or erythrocytes, account for approximately 45% of whole blood and 99% of its cellular components, with white blood cells and platelets accounting for the remainder. Circulating blood volumes vary with age, but as a guide, term infants under 3 months should have 90ml/kg, older infants and children should have 80ml/kg, and adolescents should have 70ml/kg. For the sake of simplicity, a figure of 80ml/kg could be applied to all ages. Red blood cells are made up of the oxygen-carrying proteins haemoglobin, which is composed of four protein subunits and a central haem moiety (an iron-containing molecule). Haemoglobin serves as an oxygen store, supplying the tissues with dissolved oxygen.

Normal haemoglobin (Hb) levels vary with age, gender, race, and ethnicity. Infants develop a physiological anaemia from birth to three months of age, with high Hb levels of >140 g/L in healthy term infants at birth, dropping to a nadir of around 110 g/L at six to nine weeks of age. The average Hb level in older children is around 130 g/L. The World Health Organisation defines anaemia in children as Hb values less than 115 g/L, and severe anaemia as Hb values less than 80 g/L.[16]

Transfusion of red blood cells thus increases overall circulating blood volume and, to some extent, systemic oxygenation. However, this does not always imply improved oxygen delivery, especially to peripheral vascular beds. Furthermore, factors associated with tissue activity influence haemoglobin's affinity for oxygen. Increased body temperature, acidosis, hypercarbia, and increased DPG (2,3diphosphoglycerate - a by-product of glycolysis) cause oxygen to dissociate from haemoglobin at a higher pO2 than normal, as described by the oxygen-haemoglobin dissociation curve. This means that oxygen can be delivered more easily in active tissues.

Pre-transfusion testing and transfusion safety

Blood transfusion is a complex, high-risk, multi-step procedure that relies on collaborative teamwork and strict adherence to well-defined procedures to reduce errors and negative outcomes.[17]

5. Discussion:

A small randomised controlled trial (RCT) comparing treatment of IDA with alternate day dosing at 120 mg with 60 mg twice daily dosing was conducted. Patients who received twice daily dosing had faster increases in haemoglobin concentration, but patients who received alternate day dosing had similar increments after receiving the same total amount of iron and had fewer gastrointestinal adverse events.[18]

In some patients, intravenous iron is the preferred route of administration, and it is becoming more .popular due to its rapid correction of Hb, fewer side effects, and improved safety profile

Children with rare inherited anaemias, such as unstable haemoglobins and Diamond Blackfan anaemia, require regular transfusions as well.

Transfusion volumes for non-bleeding infants and children, excluding those on chronic transfusion programmes, should be calculated in such a way that the post-transfusion Hb is no more than 20 g/L above the transfusion threshold. In non-bleeding children over 50kg (as in adults), NICE recommends a single unit of red cells transfusion. There is no current evidence-based ideal Hb for children under 50kg; however, a target Hb of 120 g/L is reasonable, but should not exceed 140 g/L. For infants and children, the volume transfused should be kept to a minimum, taking into account the possibility of needing additional transfusions, and should not exceed 20ml/kg for top-up transfusions.

6. Conclusions:

Iron deficiency anaemia is the most common type of anaemia in children.

Heme iron has a higher bioavailability because it is derived from the breakdown of haemoglobin and myoglobin in meat and fish. The amount of iron that the body is able to absorb and use for bodily functions is referred to as its bioavailability; the bioavailability of a nutrient is determined by several factors, including its bioaccessibility, For example, the amount that can be released from the matrix during food digestion and pass into the soluble fraction, becoming available for absorption by the body via the gastrointestinal mucosal epithelial cells. The first step in making a nutrient bioavailable is to remove it from the food matrix and convert it into a chemical form capable of binding to and entering between intestinal cells. The processes of chewing and enzymatic digestion of food make nutrients bioavailable. The small intestine is the primary site of nutrient absorption. [19]

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