



REVIEW ON IRON-DEFICIENCY ANEMIA

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ABSTRACT

Many studies have shown an association between iron-deficiency anemia (IDA) and less than optimal behavior in infants and children, demonstrated by lower scores on tests of development, learning, and school achievement. A problem with interpretation is that IDA is associated with other adverse conditions that may independently affect behavior. New studies have shown that iron therapy in children with IDA results in improvements in certain behavioral tests. This research on children and experimental animals suggests that IDA is causally associated with less than optimal behavior. Therefore, it is important that IDA be prevented and treated in all children. Because the specific mechanism and functional significance of these behavioral changes are not completely understood, further studies are essential to clarify effects of IDA itself, to assess the reversibility of these effects, and to determine the importance of lesser degrees of iron deficiency in children.

KEYWORDS: Iron, iron deficiency, behavior

INTRODUCTION

is anemia caused by a lack of iron.^[2] Anemia is defined as a decrease in the number of red blood cells or the amount of hemoglobin in the blood.^[2] When onset is slow, symptoms are often vague such as feeling tired, weak, short of breath, or having decreased ability to exercise.^[1] Anemia that comes on quickly often has more severe symptoms, including: confusion, feeling like one is going to pass out or increased thirst.^[1] Anemia is typically significant before a person becomes noticeably pale.^[1] Children with iron deficiency anemia may have problems with growth and development.^[2] There may be additional symptoms depending on the underlying cause.^[1] Iron-deficiency anemia is caused by blood loss, insufficient dietary intake, or poor absorption of iron from food.^[2] Sources of blood loss can include heavy periods, childbirth, uterine fibroids, stomach ulcers, colon cancer, and urinary tract bleeding.^[7] Poor absorption of iron from food may occur as a result of an intestinal disorder such as inflammatory bowel disease or celiac disease, or surgery such as a gastric bypass.^[7] In the developing world, parasitic worms, malaria, and HIV/AIDS increase the risk of iron deficiency anemia.^[9] Diagnosis is confirmed by blood tests.^[3]

Iron deficiency anemia can be prevented by eating a diet containing sufficient amounts of iron or by iron

supplementation.^[8] Foods high in iron include meat, nuts, spinach, and foods made with iron-fortified flour.^[9] Treatment may include dietary changes and dealing with underlying causes, for example medical treatment for parasites or surgery for ulcers.^[2] Iron supplements and vitamin C may be recommended.^[4] Severe cases may be treated with blood transfusions or iron injections.^[3] Iron-deficiency anemia affected about 1.48 billion people in 2015.^[5] A lack of dietary iron is estimated to cause approximately half of all anemia cases globally.^[10] Women and young children are most commonly affected.^[2] In 2015 anemia due to iron deficiency resulted in about 54,000 deaths – down from 213,000 deaths in 1990.^{[6][11]}

Signs and symptoms

Iron deficiency anemia may be present without a person experiencing symptoms.^[12] If symptomatic, patients may present with the sign of pallor (reduced oxyhemoglobin in skin or mucous membranes), and the symptoms of fatigue, lightheadedness, decreased exercise tolerance, headache, and weakness.^[12] None of these symptoms (or any of the others below) are sensitive or specific. The symptom most suggestive of iron deficiency anemia in children is pallor of mucous membranes (primarily the conjunctiva). Even so, a large study showed that pallor of the mucous membranes is only 28% sensitive and 87%

specific (with high predictive value) in distinguishing children with anemia (defined as hemoglobin < 11.0 g/dl) and 49% sensitive and 79% specific in distinguishing severe anemia (hemoglobin < 7.0 g/dl).^[13] Thus, this sign is reasonably predictive when present, but not helpful when absent, as only one-third to one-half of children who are anemic (depending on severity) will show pallor.

Iron deficiency anemia tends to develop slowly; therefore the body has time to adapt, and the disease often goes unrecognized for some time.^[14] In severe cases, shortness of breath can occur.^[15] Pica may also develop; of which consumption of ice, known as pagophagia, has been suggested to be the most specific for iron deficiency anemia.^[14] Other possible symptoms and signs of iron-deficiency anemia include.^{[2][14][15][16]}

CAUSES

A diagnosis of iron-deficiency anemia requires further investigation into its cause.^[23] It can be caused by increased iron demand, increased iron loss, or decreased iron intake.^[23] Increased iron demand often occurs during periods of growth, such as in children and pregnant women.^[24] For example, during stages of rapid growth, babies and adolescents may outpace their dietary intake of iron which can result in deficiency in the absence of disease or a grossly abnormal diet.^[24] Iron loss is typically from blood loss.^[24] One example of blood loss is by chronic gastrointestinal blood loss, which could be linked to a possible cancer.^[24] In women of childbearing age, heavy menstrual periods can be a source of blood loss causing iron-deficiency anemia.^[24] People who do not consume much iron in their diet, such as vegans or vegetarians, are also at increased risk of developing iron deficiency anemia.^[22]

Parasitic Disease

The leading cause of iron-deficiency anemia worldwide is a parasitic disease known as a helminthiasis caused by infestation with parasitic worms (helminths); specifically, hookworms. The hookworms most commonly responsible for causing iron-deficiency anemia include *Ancylostoma duodenale*, *Ancylostoma ceylanicum*, and *Necator americanus*.^{[22][26]} The World Health Organization estimates that approximately two billion people are infected with soil-transmitted helminths worldwide.^[26] Parasitic worms cause both inflammation and chronic blood loss by binding to a human's small-intestinal mucosa, and through their means of feeding and degradation, they can ultimately cause iron-deficiency anemia.^{[22][26]}

Blood loss

Red blood cells contain iron, so blood loss also leads to a loss of iron. There are several causes of blood loss including menstrual bleeding, gastrointestinal bleeding, stomach ulcers, and bleeding disorders.^[27] The bleeding may occur quickly or slowly. Slow, chronic blood loss within the body — such as from a peptic ulcer,

angiodyplasia, inflammatory bowel disease, a colon polyp or gastrointestinal cancer (e.g., colon cancer)— can cause iron-deficiency anemia.

Menstrual bleeding

Menstrual bleeding is a common cause of iron deficiency anemia in women of child bearing age.^[27] Women with menorrhagia (heavy menstrual periods) are at risk of iron-deficiency anemia because they are at higher-than-normal risk of losing a larger amount blood during menstruation than is replaced in their diet. Most women lose about 40 mL of blood per cycle. Iron is lost with the blood. Some birth control methods, such as pills and IUDs, may decrease the amount of blood, therefore iron lost during a menstrual cycle.^[27]

Gastrointestinal bleeding

The most common cause of iron deficiency anemia in men and post-menopausal women is gastrointestinal bleeding.^[27] There are many sources of gastrointestinal tract bleeding including the stomach, esophagus, small intestine, and the large intestine (colon). Gastrointestinal bleeding can result from regular use of some groups of medication, such as non-steroidal anti-inflammatory drugs (e.g. aspirin), as well as antiplatelets such as clopidogrel and anticoagulants such as warfarin; however, these are required in some patients, especially those with states causing a tendency to form blood clots. Colon cancer is another potential cause gastrointestinal bleeding, thus iron deficiency anemia. Typically colon cancer occurs in older individuals.^[28] In addition, some bleeding disorders can cause gastrointestinal bleeding.^[27] Two examples of bleeding disorders are von Willebrand disease and polycythemia vera.^[27]

Diagnosis

Diagnosis of iron deficiency anemia requires laboratory-confirmed evidence of anemia, as well as evidence of low iron stores.⁴ Anemia is defined as a hemoglobin level two standard deviations below normal for age and sex (Table 1).⁵ A complete blood count can be helpful to determine the mean corpuscular volume or red blood cell size. Although iron deficiency is the most common cause of microcytic anemia, up to 40 percent of patients with iron deficiency anemia will have normocytic erythrocytes.² As such, iron deficiency should still be considered in all cases of anemia unless the mean corpuscular volume is greater than 95 μm^3 (95 fL), because this cut-off has a sensitivity of 97.6 percent.⁶ Other causes of microcytosis include chronic inflammatory states, lead poisoning, thalassemia, and sideroblastic anemia.^{1.}

Table 1: Age-Related Variations in Hemoglobin Level and MCV.

| <i>Hemoglobin level (g per dL [g per L]) MCV (μm^3 [fL])</i> | | | | |
|--|-------------|-----------------------------|-------------|-----------------------------------|
| Age | Mean | Diagnostic of anemia | Mean | Diagnostic of microcytosis |
| 3 to 6 months | 11.5 (115) | 9.5 (95) | 91 (91) | 74 (74) |
| 6 months to 2 years | 12.0 (120) | 10.5 (105) | 78 (78) | 70 (70) |
| 2 to 6 years | 12.5 (125) | 11.5 (115) | 81 (81) | 75 (75) |
| 6 to 12 years | 13.5 (135) | 11.5 (115) | 86 (86) | 77 (77) |
| 12 to 18 years (female) | 14.0 (140) | 12.0 (120) | 90 (90) | 78 (78) |
| 12 to 18 years (male) | 14.5 (145) | 13.0 (130) | 88 (88) | 78 (78) |
| 20 to 59 years (white men) | NA | 13.7 (137) | 90 (90) | 80 (80) |
| 60 years and older (white men) | NA | 13.2 (132) | 90 | 80 |
| 20 years and older (white women) | NA | 12.2 (122) | 90 | 80 |
| 20 to 59 years (black men) | NA | 12.9 (129) | 90 | 80 |
| 60 years and older (black men) | NA | 12.7 (127) | 90 | 80 |
| 20 years and older (black women) | NA | 11.5 (115) | 90 | 80 |

low transferrin saturation, and a high total iron-binding capacity.^[18] Soluble transferrin receptor and erythrocyte protoporphyrin testing, or bone marrow biopsy can be considered if the diagnosis remains unclear.^[18] The soluble transferrin receptor level is an indirect measure of erythropoiesis and is increased in patients with iron deficiency anemia.^[19] Another benefit of this test is that the soluble transferrin receptor level is unaffected by inflammatory states and can help identify concomitant iron deficiency anemia in patients with anemia of chronic disease.^[20] Erythrocyte protoporphyrin is a heme precursor and accumulates in the absence of adequate iron stores.^[21] If other tests are indeterminate and suspicion for iron deficiency anemia.

Treatment

Treatment should take into account the cause and severity of the condition.^[29] If the iron-deficiency anemia is a result of blood loss or another underlying cause, treatment is geared toward addressing the underlying cause.^[29] Most cases of iron deficiency anemia are treated with oral iron supplements.^[30] In severe acute cases, treatment measures are taken for immediate management in the interim, such as blood transfusions or intravenous iron.^[29]

For less severe cases, treatment of iron-deficiency anemia includes dietary changes to incorporate iron-rich foods into regular oral intake and oral iron supplementation.^[29] Foods rich in ascorbic acid (vitamin C) can also be beneficial, since ascorbic acid enhances iron absorption.^[29] Oral iron supplements are available in multiple forms. Some are in the form of pills and some are drops for children.^[29] Most forms of oral iron replacement therapy are absorbed well by the small intestine; however, there are certain preparations of iron supplements that are designed for longer release in the small intestine than other preparations.^[30] Oral iron supplements are best taken up by the body on an empty stomach because food can decrease the amount of iron absorbed from the small intestine.^[30] The dosing of oral iron replacement therapy is as much as 200 mg per day.

This is generally spread out as 3-4 pills taken throughout the day.^[30] The various forms of treatment are not without possible adverse side effects. Iron supplementation by mouth commonly causes negative gastrointestinal effects, including constipation.^[31] Constipation is reported by 15-20% of patients taking oral iron therapy.^[30] Preparations of iron therapy that take longer to be absorbed by the small intestine (extended release iron therapy) are less likely to cause constipation.^[30] It can take six months to one year to get blood levels of iron up to a normal range and provide the body with iron stores.^[30]

As iron-deficiency anemia becomes more severe, if the anemia does not respond to oral treatments, or if the treated person does not tolerate oral iron supplementation, then other measures may become necessary.^{[29][31]} Two options are intravenous iron injections and blood transfusion.^[30] Intravenous can be for people who do not tolerate oral iron, who are unlikely to respond to oral iron, or who require iron on a long term basis.^[30] For example, people receiving dialysis treatment who are also getting erythropoietin or another erythropoiesis-stimulating agent are given parenteral iron, which helps the body respond to the erythropoietin agents to produce red blood cells.^{[31][32]}

Intravenous iron can induce an allergic response that can be as serious as anaphylaxis, although different formulations have decreased the likelihood of this adverse effect.^[31] In certain cases intravenous iron is both safer and more effective than the oral route.^[33] For patients with severe anemia such as from blood loss, or who have severe symptoms such as cardiovascular instability, a blood transfusion may be considered.^[30]

CONCLUSION

Abstract. In our bloodstream, there are plenty of red blood cells (RBC), which function as an important oxygen carrier in our bodies. Each RBC consists of millions of haemoglobin (Hb), which is made up from globin and iron. If any deficiency/malfunction of any globin, it will

lead to anaemia as indicated in low Hb level while iron deficiency anaemia (IDA) is anaemic due to the lacking of iron as indicated in low Hb and ferritin levels. IDA affects almost two billion people globally while anaemia without iron deficiency, such as thalassaemia, affects almost 4.5% in Malaysian population. These anaemic conditions have similar clinical symptoms like fatigue, dizziness, in which disturb their cognitive development and productivity in workplace. In areas without proper medical access, many anaemic individuals were misdiagnosed and treated with iron tablets because they were thought to have iron deficiency anaemia due to low Hb content. But, excess iron is toxic to the body. Misdiagnosis can be avoided by iron status assessment. We hereby review the currently available iron status parameters in laboratory and field study with the conclusion of demonstrating the importance of a need for iron reader, in the effort to reduce the prevalence of IDA globally.

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