BJMHR
British Journal of Medical and Health Research
Journal home page: www.bjmhr.com

Etiology, Treatment and Prevention of Iron Deficiency Anaemia (IDA) In Women : A Review

Amreen Naqash[1], Rifat Ara[2], G.N.Bader[1]
1.Department of Pharmaceutical Sciences, University of Kashmir, Hazratbal, Srinagar,Kashmir-190006
2. Department of Obstetrics and Gynaecology, SKIMS Medical College and Hospital, Bemina Srinagar, Kashmir

ABSTRACT

Iron deficiency anaemia (IDA) is a significant problem worldwide. It is widespread and a most neglected nutritional deficiency especially in the developing countries. The IDA can be evaluated by low hemoglobin and iron stores value. Women among all age groups, particularly during pregnancy and children should be screened for IDA. In adults, IDA can result in reduced work capacity, immune dysfunction, impaired thermoregulation, Gastrointestinal (GI) disturbances while in children or adolescents it can impact motor and mental development**.** IDA can be treated both by oral and parenteral therapy. In this review etiology, treatment, and prevention of iron deficiency anaemia are discussed.

Keyword: Iron deficiency anaemia (IDA), hemoglobin, iron stores, oral therapy, parenteral therapy.

*Corresponding Author Email: gnbader@kashmiruniversity.ac.in
Received 12 July 2017, Accepted 12 August 2017

Please cite this article as: Naqash A *et al.*, Etiology, Treatment and Prevention of Iron Deficiency Anaemia (IDA) In Women : A Review. British Journal of Medical and Health Research 2017.

INTRODUCTION

The World Health Organization (WHO) defines iron-deficiency anaemia as a condition whereby either individual haemoglobin levels are two standard deviations below the distribution mean, or more than 5% of a given population has haemoglobin levels that are two standard deviations below the distribution mean, in an otherwise normal population of individuals from the same gender and age, living at the same altitude **(WHO/UNICEF/UNU, 2001)** accompanied by the depletion of the iron store or the insufficient intake of iron which is not enough to meet the physiological requirements of a body **(Goddard, *et al.*, 2011).**

Global Prevalence

Half of the world's anaemic burdon is contributed alone by iron deficiency anaemia **(WHO/UNICEF/UNU, 2001)**. In 2013, 1.2 billion people were found to be affected by iron-deficiency anaemia and 183,000 deaths were accounted because of IDA **(Global, 2015)**. In 2004, WHO estimated 273 000 deaths because of IDA: 45% in Southeast Asia, 31% in Africa, 9% in the Eastern Mediterranean, 7% in the America, 4% in the Western Pacific, and 3% in Europe, with 97% occurring in low- and middle-income countries **(Pasricha, *et al.*, 2013)**.

Prevalence In India

Around, 600 million people in South-East Asia are suffering from iron deficiency anaemia, predominantly adolescent girls, women of reproductive age and young children. The condition has an alarming prevalence rate among pregnant women i.e. 88 percent and 74 percent prevalence in non-pregnant women **(WHO/UNICEF/UNU, 2001)**. It ranges from 13.4 percent in Thailand to 88 percent in India **(Kaur, 2014)**

Etiology

Iron deficiency anaemia is particularly common in adolescent girls because of increased demand of iron for haemoglobin, myoglobin and to make up the loss of iron due to menstruation and poor diet **(Kaur, 2014)**. In males, iron need is highest during peak pubertal development **(CDC, 1998; Wharton, 1999)**. In spite of increased iron needs, particularly in adolescent females, the intake of iron is only 10-11 mg/day of the total iron required, resulting in approximately 1 mg of absorbed iron **(Beard, 2001).** Figure 1 and table 1 gives an overlook of Etiology related to IDA.

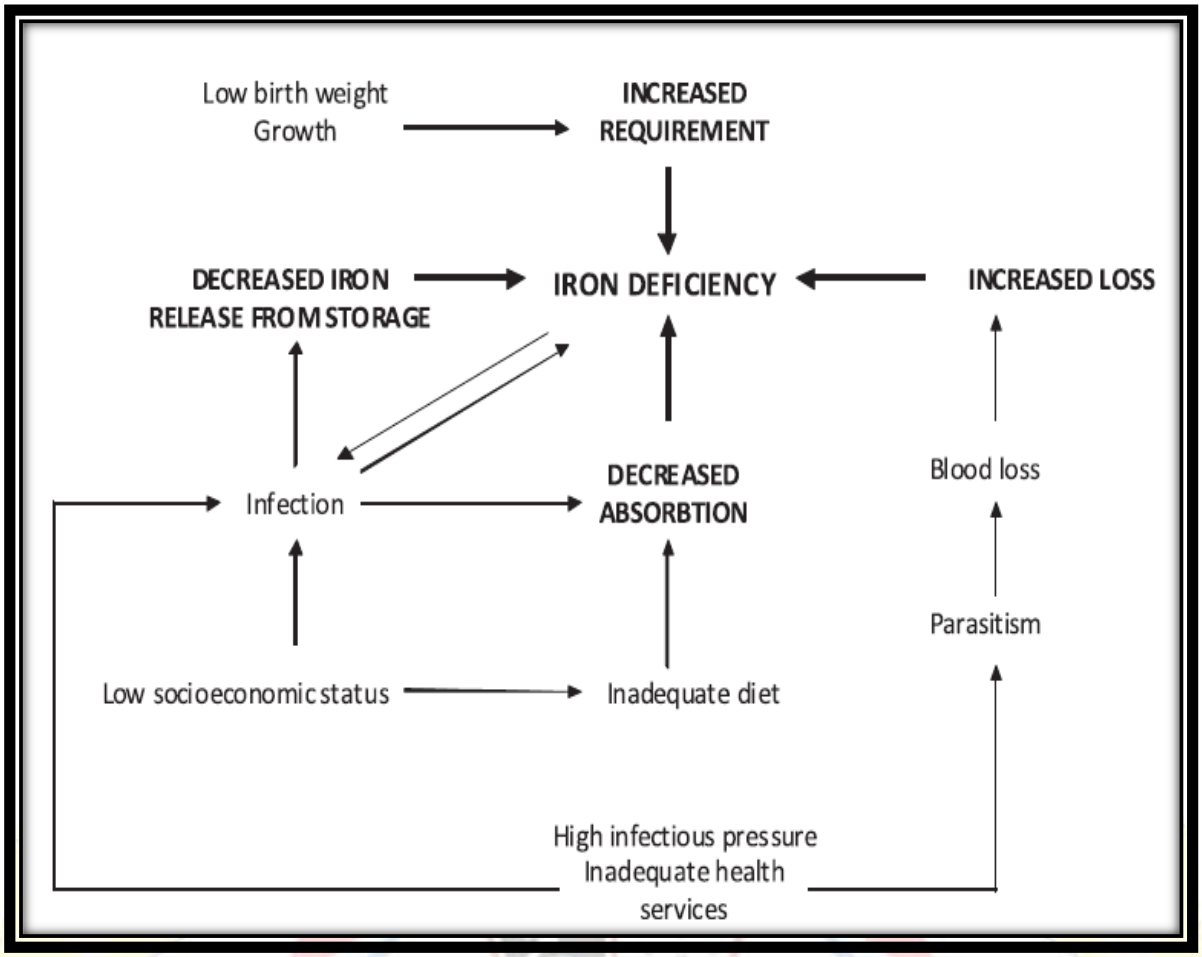

Figure 1: Etiology of Iron deficiency anaemia (Jonker and van Hensbroek, 2014).

Table 1: Etiologies of Iron Deficiency Anaemia

Etiology	Prevalence (%)
Abnormal uterine bleeding	20 to 30
Long- term use of NSAIDs	10 to 15
Colonic Carcinoma	5 to 10
Angiodysplasia	5
Blood donation	5
Gastric carcinoma	5
Peptic ulcer disease	5
Celiac disease	4 to 6
Gastrectomy	<5
Helicobacter pylori infection	<5
Esophagitis	2 to 4
Esophageal carcinoma	1 to 2
Gastric antral vascular ectasia	1 to 2
Small bowel tumors	1 to 2
Hematuria	1
Ampullary carcinoma	<1
Bacterial overgrowth	<1
Cameron ulcer (i.e., ulcer in large hiatal hernia)	<1
Epitaxis	<1
Intestinal resection.	<1

Source: Short and Domagalski, 2013.

Diagnosis

The Center for Disease Control and Prevention (CDC) recommends screening of adolescent females for anaemia at least once every five years unless risk factors for anaemia are present, resulting in the need for annual anaemia screening **(CDC, 1998)**. To diagnose iron deficiency anaemia certain laboratory confirmed parameters are required. Diagnostic algorithm (Figure 2) is adapted to determine if a patient has IDA or not. This algorithm is adapted with the primary modification that serum iron (SI), total iron-binding capacity (TIBC), and transferrin saturation (TS) are recommended as follow-up tests in patients with an intermediate serum ferritin (SF) level as a strategy to reduce the need for bone marrow biopsy **(Johnson-Wimbley and Graham, 2011)**.

It is important to find cause for IDA, as it has both physiologic and pathophysiologic causes, or serious disease may be overlooked.

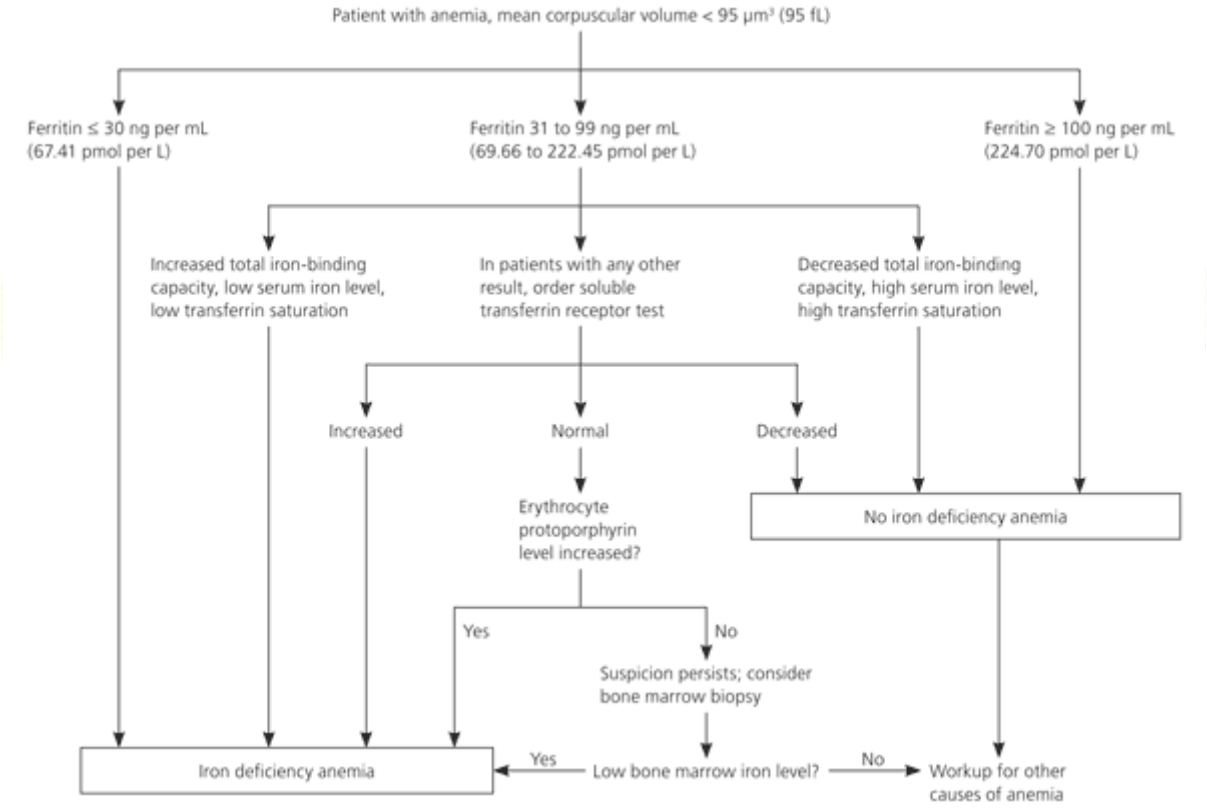

Figure 2: Algorithm for diagnosis of IDA (Short and Domagalski, 2013).

Iron Deficiency Anaemia in Premenopausal Women

In developed countries, the excessive menstruation is a common cause of iron deficiency anaemia in premenopausal women. In younger patients, aged 20-40, coeliac disease often presents with IDA. Gastrointestinal lesions account for 6 to 30 percent of iron deficiency anaemia cases **(Carter, *et al.*, 2008; Green and Rockey, 2004, Park, *et al.*, 2006)**. Also, attention should be paid to unexplained weight loss, diarrhoea, and abdominal pain **(Todd and Caroe, 2007)**.

In some premenopausal women, drugs like anticoagulants, aspirin, and non-steroidal anti-inflammatory drugs may cause or worsen blood loss.

In 9-14% of all women, excessive or irregular menstrual bleeding can lead to varying degrees of iron deficiency anaemia **(Fraser, *et al.*, 2009)**.

Iron Deficiency Anaemia in Pregnant Women

Approximately 75% of all anaemias diagnosed during pregnancy are due to iron deficiency. Iron deficiency anaemia leads to characteristic hypochromic, microcytic erythrocytes on the peripheral blood smear **(Sifakis and Pharmakides, 2000)**. The American Academy of Family Physicians, U.S. Preventive Services Task Force, and Centres for Disease Control and Prevention recommends routine screening of asymptomatic pregnant women for IDA **(U.S, 2006; WHO/CDC, 2005)**.

Haemoglobin levels less than 11 g/dL (110 g/L) in the first or third trimester, or less than 10.5 g/dL (105 g/L) in the second trimester are the values defined for anaemia in pregnancy **(Baker and Greer, 2010)**.

The factors responsible for high incidence of anaemia during pregnancy in India are early marriage, teenage pregnancy, multiple pregnancies, phytate rich Indian diet, low iron and folic acid intake less birth spacing, and high incidence of worm infections **(Singh and Toteja, 2003)**.

Iron Deficiency Anaemia in Postmenopausal Women

In postmenopausal women the signs and symptoms for iron deficiency should be screened and complete evaluation must be done **(Barmejo and García-López, 2009)**. In case of asymptomatic postmenopausal women malabsorption of iron, gastrointestinal blood loss, or *Helicobacter pylori* colonisation are the most common factors of iron deficiency anemia.

FACTORS AFFECTING IRON AVAILABILITY IN BODY

Iron status in a body depends on long-term iron balance and is favoured by ingestion of adequate amounts of iron in the diet. The balance is adversely affected by the loss of Iron through intestinal mucosal turnover and excretion, skin desquamation, menstruation and lactation **(Hunt, 2005)**.

Iron availability can be regarded mainly as a characteristic of the diet, but for human comparative studies to evaluate the factors affecting iron absorption require normalization of the iron status of the subjects. Person with low iron status can substantially increase their iron absorption from diets with moderate to high availability **(Brune, *et al.*, 1992)**. Both, dietary as well as non-dietary factors are responsible for enhancing or inhibiting the iron availability in the body. Table 2 highlights the factors that affect the iron availability in a body **(Sharma and Shankar, 2010)**.

Non dietary factors (Medicine) that affect the absorption of iron include: antacids, proton pump inhibitors **(IDI, 2016)**, cholesterol lowering medication (cholestyramine and colestipol.), concurrent use of NSAIDs **(Wolfenden, 2011)** or calcium supplements **(Grinder-Pedersen, *et al.*, 2004; Rosado, *et al.*, 2005)**. Diseased conditions that limit iron absorption include insufficient stomach acid, lack of intrinsic factor (hormone needed to absorb vitamin B12), coeliac disease, inflammatory conditions such as Crohn's disease, and in autoimmune diseases and hormone imbalances **(IDI, 2016)**.

Table 2: Factors influencing dietary iron absorption

Heme Iron Absorption	
Iron status of subject	
Amount of dietary heme iron, especially as meat	
Content of calcium in meal (e.g., milk, cheese)	
Food preparation (time, temperature)	
Non-Heme Iron Absorption	
Iron status of subjects	
Amount of potentially available non-heme iron (adjustment for fortification iron and contamination iron)	
Balance between enhancing and inhibiting factors	
Enhancing factors	**Inhibiting factors**
Ascorbic acid (e.g., certain fruit juices, fruits, potatoes, and certain vegetables)	Phytates and other inositol phosphates {e.g., bran products, bread made from high extraction flour, breakfast cereals,
Meat, chicken, fish and other seafood	oats, rice (especially unpolished rice), pasta products, cocoa, nuts, soya beans,
Fermented vegetables (e.g., sauerkraut),	and peas}
Fermented soy sauces, etc.	Iron-binding phenolic compounds (e.g., tea, coffee, cocoa, certain spices, certain vegetables, and most red wines)
	Calcium (e.g., milk, cheese) Soy proteins.

PREVENTION

Counselling, prophylaxis of non-pregnant women, treatment to hook worms and other gastrointestinal infections, Iron supplementation to pregnant women, proper dietary habits, improvement of iron availability, food fortification, maintenance of hygiene and better education about balanced diet **(Sharma and Shankar, 2010)**. In addition, improvements in access to health care, infant feeding, food security, and socio-economic status are important factors. Recently, WHO has revised global guidelines for anaemia control **(Pasricha, *et al.*, 2013)**.

IMPLEMENTATION OF ANAEMIA CONTROL PROGRAMMES

Population level anaemia control should involve relevant government and non-government health and non-health organisations. Proper monitoring should be involved to assure safety and efficacy of the community **(Parischa, *et al.*, 2013)**.

TREATMENT OF IRON DEFICIENCY ANAEMIA

Different types of therapies are used to address the iron deficiency anaemia. The aim of the treatment is to restore the iron stores and return back the normal haemoglobin levels. The iron treatment improves quality of life, physical condition as well as alleviates fatigue and cognitive deficits **(Falkingham, *et al.*, 2010)**. Also, the patients with underlying disease that causes IDA should be referred for a proper consultation and evaluation to the specialist (gynaecologist, gastroenterologist, or the one concerned to respective disease) for proper definitive treatment **(Short and Domagalski, 2013)**.

IRON ADMINISTRATION

Presently, iron supplements have become an integral part of the management of patients receiving epoetin therapy, and clinicians have found it necessary to learn how and when to use it to the best advantage **(Crosby, 1984)**. Two routes of iron administration are there:

1. Oral Administration
2. Parenteral Administration

- Intravenous Administration (IV)
- Intramuscular Administration (IM)

The treatment has to be carried systematically and watched for laboratory parameters. Also, the signs and symptoms need to be checked for correction.

ORAL IRON

Oral Iron replacement therapy is the first line drug treatment for patients suffering from iron deficiency anaemia **(Crosby, 1984)**. The iron absorption in the intestine is limited. Of the oral 100 mg, only 20-25% is absorbed.

In adults, 120 mg of elemental iron per day for three months is required and in children, 3 mg per kg per day up to 60 mg per day is required to treat IDA **(WHO/UNICEF/UNU, 2001)**. Increase in the haemoglobin level by 1g/dL per month shows the effectiveness of the treatment and confirms the diagnosis **(Baker, *et al.*, 2010)**. However, oral therapy should be restricted to patients with mild anaemia i.e. when haemoglobin level is between 11 – 11.9 g/dL in non-pregnant women.

Patients suffering from IDA have 10 to 13% of iron absorption rates, while in healthy females it is 5.6% **(Werner, *et al.*, 1976)**. Studies have revealed that the iron that remains in the intestinal lumen may cause mucosal injury **(De Silva, *et al.*, 2005; Abraham, *et al.*, 1993)**. Moreover, almost 50% patients have dose related gastrointestinal side effects which result in non-adherence of the drug therapy **(Tolkien, *et al.*, 2015)**.

Many therapeutic formulations of oral iron are available over the counter and are composed of ferrous salts e.g. Ferrous sulfate, Ferrous glycine sulphate, Ferrous gluconate, Ferrous

fumarate, Ferrous calcium citrate, Ferrous ammoniate, Ferric ammonium citrate, and Ferrous ascorbate. Other newer oral preparations available include Iron polysaccharide complex (iron polymaltose), Carbonyl iron, Sodium feredetate, Combination of iron salts with Vit C, succinate, and fructose, and Haemoglobin preparations **(Sharma and Shankar, 2010)**.

Advantages of Oral Iron

- Easy availability,
- Cheap,
- Convenient and effective when intestinal absorption is not impaired.

Disadvantages of Oral Iron

These formulations have many disadvantages as well. Their absorption is interfered by many dietary as well as non-dietary products. Since, daily absorption is limited, thus, it takes time for repletion of iron stores. Patient noncompliance is often a concern for continuing medicine.

PARENTERAL IRON

Parenteral iron therapy is a choice for patients who are intolerant or experience gastrointestinal side effects or are unresponsive to oral iron therapy **(Schröder, *et al.*, 2005)**. Parenteral Iron therapy is indicated in rapid correction of severe anaemia **(Silverstein and Rodgers, 2004)**, in patients undergoing elective surgery **(Theusinger, *et al.*, 2007)**, in women with near term or in postpartum with severe anaemia, or in patients with haemoglobin level less than 6 g per dL (60 g per L) with poor perfusion signs, who would otherwise receive transfusion (e.g., patients having religious objections) **(Hamstra, *et al.*, 1980)**.

Parenteral iron therapy helps in increasing the serum ferritin levels immediately after administration which diminish the recurrence of iron deficiency anaemia in the long term as compared to oral iron therapy **(Khalafallah, *et al.*, 2012; Evstatiev, *et al.*, 2013)**.The main disadvantage associated with parenteral iron therapy is the necessity for administration by a health care professional, with the associated costs and proper measures to avoid any anaphylactic reaction or any drug related adverse effect.

Parenteral iron is administrated by two techniques:

1. Intramuscular Iron Administration
2. Intravenous Iron Administration

Intramuscular Iron Administration

Intramuscular (IM) iron preparation is usually injected deep into the muscle of the buttock by Z- technique. A smaller test dose is required to check for any hypersensitivity reaction. Disadvantages of intramuscular route are pain, sterile abscess formation, nausea, vomiting, headache, fever, lymphadenopathy, allergic reactions and rarely anaphylaxis. Iron dextran and Iron sorbitol are given IM **(Sharma and Shankar, 2010)**.

Intravenous Iron Administration

Intravenous (IV) preparations have been put in use to reduce the requirement for red blood cell transfusion in various acute clinical settings **(Hofmann, *et al.*, 2012; Shander, *et al.*, 2010)**. IV transfusion requires proper facilities for resuscitation if the patient experiences any hypersensitivity reaction which can be fatal **(Lowes, 2013)**. Patients are closely monitored for signs and symptoms of hypersensitivity reactions during and for at least 30 minutes following each injection of an intravenous iron medicine **(Rampton, *et al.*, 2014)**.

There are various IV iron preparations available in the market. They are either dextran containing or non-dextran containing iron preparations **(Silverstein, 2008)**. The dextran preparations have comparatively more adverse effects than non-dextran iron preparations. Ferric gluconate and iron sucrose. IV iron preparations that do not contain dextran have a better safety profile better safety profile. On 25th July 2013, the FDA approved ferric carboxymaltose a new single-dose preparation **(Macdougall, 2012; Gozzard, 2011)**.

Another preparation, ferric pyrophosphate is a new iron formulation in phase III development **(Krikorian, *et al.*, 2013)**.

To administer the intravenous iron the total iron deficit is calculated and dose is adjusted accordingly. There are two formulas for calculating the iron dose

- Modified Ganzoni's Formula
- Haldane's Formula

Ganzoni formula

The Ganzoni formula is ideally the best way to select dose as product labels state specific dosing regimens **(Koch, *et al.*, 2015; Ganzoni, 1970)**.

Total body iron deficit is calculated using the Ganzoni formula as below **(Kulnigg, *et al.*, 2008)**:

$$\boldsymbol{Total\ iron\ dose} = \{(\boldsymbol{Body\ weight})\ [\boldsymbol{kg}] \times (\boldsymbol{Target\ Hb} - \boldsymbol{Actual\ Hb})\ [\boldsymbol{g/L}]\} \times \mathbf{0.24} + \boldsymbol{Iron\ stores}\ [\boldsymbol{mg}]$$

Where,

0.24 is a correction factor that takes into account the patient's blood volume, estimated at 7% of body weight and haemoglobin iron content; which is 0.34% **(Bayoumeu, 2002)**.

Iron Store = 500 mg if body weight >35 kg

= 15 mg if body weight<35 kg

Haldane Formula (Ikan, 2015).

$$\boldsymbol{Total\ iron\ dose} = \mathbf{0.3}\ \boldsymbol{x\ weight}\ (\boldsymbol{lbs})\ \boldsymbol{x}\ (\mathbf{100} - \boldsymbol{Hb}\ \%) + \mathbf{50}\%$$

Where,

0.3 is the multiplication factor

50% is the iron stores.

Advantages of IV Iron Therapy

IV iron preparations allow high doses of iron to be administered rapidly in a single treatment. Thus, resulting in fast repletion of iron stores. Intestinal impairment doesn't affect the absorption of the iron **(Auerbach, *et al.*, 2007)**. IV preparations have shown improvement in symptoms, physical performance, and the quality of life in patients suffering from chronic heart failure **(Anker, *et al.*, 2009)**.

Disadvantages of IV Iron Therapy

The main drawback of IV iron therapy is that it requires administration by a health care professional, with associated increased cost: an important factor in the developing world. There is a potential for iron overload and transient increase in oxidative stress. IV iron preparations have been associated with severe adverse drug reactions.

Follow up/ Management

Once the normal haemoglobin and iron profile values are attained, a regular follow up should be considered at an interval of one month for first three months, followed by 3 monthly for 1 year. If during this period, symptoms of IDA reoccur or the haemoglobin value or red cell indices fall below normal then oral iron should be given and again the laboratory parameters should be evaluated. If Hb and red cell indices aren't maintained this way then a further investigation is necessary.

Counseling of Patients

Counseling of the patients having IDA is very important both before starting the iron therapy and after the therapy for adherence to the treatment.

REFERENCES

1. WHO/UNICEF/UNU. Iron deficiency anaemia assessment, prevention, and control: a guide
2. For programme managers. Geneva, World Health Organization, 2001. Available at: http://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf Accessed on: 2017 Mar 5.
3. Goddard AF, James MW, Mclntyre AS, Scott BB. on behalf of the British Society of Gastroenterology. Guidelines for the management of iron deficiency anaemia. Gut. 2011;60:1309-16.
4. Global Burden of Disease Study 2013, Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic

diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386(9995):743-800.

5. Pasricha SR, Drakesmith H, Black J, Hipgrave D, Biggs BA. Control of iron deficiency anemia in low- and middle-income countries. Blood. 2013:121(14).
6. Kaur K. Anaemia 'a silent killer' among women in India: Present scenario. European Journal of Zoological Research. 2014;3(1):32-36.
7. CDC. Recommendations to prevent and control iron deficiency in the United States. Centers for Disease Control and Prevention. MMWR Recomm Rep. 1998;47(RR-3):1-29.
8. Wharton BA. Iron deficiency in children: detection and prevention. Br J Haematol 1999;106(2):270-80.
9. Beard JL. Iron biology in immune function, muscle metabolism and neuronal functioning. J Nutr. 2001;131(2S-2):568S-79S.
10. Jonker FAM, van Hensbroek MB. Anaemia, iron deficiency and susceptibility to infections. J. Infect. 2014;69(1):S23-S27.
11. Short MW, Domagalski JE. Iron Deficiency Anemia: Evaluation and Management. Am Fam Physician. 2013;87(2).
12. Johnson-Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. Therap Adv Gastroenterol. 2011;4(3):177-84.
13. Carter D, Maor Y, Bar-Meir S, Avidan B. Prevalence and predictive signs for gastrointestinal lesions in premenopausal women with iron deficiency anemia. Dig Dis Sci. 2008;53(12):3138-44.
14. Green BT, Rockey DC. Gastrointestinal endoscopic evaluation of pre-menopausal women with iron deficiency anemia. J Clin Gastroenterol. 2004;38(2):104-09.
15. Park DI, Ryu SH, Oh SJ, Yoo TW, Kim HJ, Cho YK, et al. Significance of endoscopy in asymptomatic premenopausal women with iron deficiency anemia. Dig Dis Sci. 2006;51(12):2372-76.
16. Todd T, Caroe T. Newly diagnosed iron deficiency anaemia in a premenopausal woman. Br Med J. 2007;334(7587):259.
17. Fraser IS, Langham S, Uhl-Hochgraeber K. Health-related quality of life and economic burden of abnormal uterine bleeding. Expert Rev Obstet Gynecol. 2009;4(2):179-89.
18. Sifakis S, Pharmakides G. Anemia in Pregnancy, Ann N Y Acad Sci. 2000; 900(1):125-36.

19. U.S. Preventive Services Task Force. Screening for iron deficiency anemia, including iron supplementations for children and pregnant women: recommendation statement. Am Fam Physician. 2006;74(3):461-64.
20. WHO/CDC. Assessing the iron status of populations: report of a joint World Health Organization/ Centers for Disease Control and Prevention technical consultation on the assessment of iron status at the population level. Geneva: World Health Organisation, 2004 April 6-8.
21. Baker RD, Greer FR. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). Pediatrics. 2010;126(5):1040-50.
22. Singh P, Toteja GS. Micronutrient profile of Indian children and women: summary of available data for iron and vitamin A. Indian Pediatr. 2003;40(5):477-79.
23. Bermejo F, García-López S. A guide to diagnosis of iron deficiency and iron deficiency anemia in digestive diseases. World J Gastroenterol. 2009;15(37):4638-43.
24. Hunt JR. Dietary and physiological factors that affect the absorption and bioavailability of iron. Int J Vitam Nutr Res. 2005;75(6):375-84.
25. Brune M, Rossander-Hulthén L, Hallberg L, Gleerup A, Sandberg AS. Iron absorption from bread in humans: inhibiting effects of cereal fiber, phytate and inositol phosphates with different numbers of phosphate groups. J Nutr. 1992;122:442-49.
26. Sharma JB, Shankar M. Anemia in Pregnancy. J Int Med Sci Acad. 2010;23(4).
27. Wolfenden E. Medication that inhibits the iron absorption [Internet]. California: Livestrong; 2011 Jul 03. Available at: http://www.livestrong.com/article /484289-medications-that-inhibit-iron-absorption/. Accessed at: 2017 Mar 5.
28. Grinder-Pedersen L, Bukhave K, Jensen M, Højgaard L, Hansen M. Calcium from milk or calcium-fortified foods does not inhibit nonheme-iron absorption from a whole diet consumed over a 4-d period. Am J Clin Nutr. 2004;80(2):404-09.
29. Rosado JL, Díaz M, González K, Griffin I, Abrams SA, Preciado R. The addition of milk or yogurt to a plant-based diet increases zinc bioavailability but does not affect iron bioavailability in women. J Nutr. 2005;135(3):465-68.
30. Falkingham M, Abdelhamid A, Curtis P, Fairweather-Tait S, Dye L, Hooper L. The effects of oral iron supplementation on cognition in older children and adults: a systematic review and meta-analysis. Nutr J. 2010;9(1):4.
31. Crosby WH. The rationale for treating iron deficiency anemia. Arch Intern Med 1984;144:471-72.

32. Baker RD, Greer FR. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). Pediatrics. 2010;126(5):1040-50.
33. Werner E, Kaltwasser JP, Ihm P. Intestinal absorption from therapeutic iron doses (author's transl) [in German]. Arzneimittelforschung. 1976;26(11):2093-2100.
34. De-Silva AD, Tsironi E, Feakins RM, Rampton DS. Efficacy and tolerability of oral iron therapy in inflammatory bowel disease: a prospective, comparative trial. Aliment Pharmacol Ther. 2005;22(11-12):1097-105.
35. Abraham SC, Yardley JH, Wu TT. Erosive injury to the upper gastrointestinal tract in patients receiving iron medication: an underrecognized entity. Am J Surg Pathol. 1999;23(10):1241-47.
36. Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ. Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. PLoS One. 2015;10(2):e0117383.
37. Schröder O, Mickisch O, Seidler U, De Weerth A, Dignass AU, Herfarth H, et al. Intravenous iron sucrose versus oral iron supplementation for the treatment of iron deficiency anemia in patients with inflammatory bowel disease—a randomized, controlled, open-label, multicenter study. Am J Gastroenterol. 2005;100(11):2503-09.
38. Silverstein SB, Rodgers GM. Parenteral iron therapy options. Am J Hematol. 2004:76(1):74-78.
39. Theusinger OM, Leyvraz PF, Schanz U, Seifert B, Spahn DR. Treatment of iron deficiency anemia in orthopedic surgery with intravenous iron: efficacy and limits. Anesthesiology. 2007;107(6):923-27.
40. Hamstra RD, Block MH, Schocket AL. Intravenous iron dextran in clinical medicine. JAMA. 1980;243:1726-31.
41. Khalafallah AA, Dennis AE, Ogden K, et al. Three-year follow-up of a randomised clinical trial of intravenous versus oral iron for anaemia in pregnancy. BMJ Open. 2012;2(5).
42. Evstatiev R, Alexeeva O, Bokemeyer B, Chopey I, Felder M, Gudehus M. et al. Ferric carboxymaltose prevents recurrence of anemia in patients with inflammatory bowel disease. Clin Gastroenterol Hepatol. 2013;11(3):269-77.
43. Hofmann A, Farmer S, Towler SC. Strategies to preempt and reduce the use of blood products: an Australian perspective. Curr Opin Anaesthesiol. 2012;25:66-73.

44. Shander A, Spence RK, Auerbach M. Can intravenous iron therapy meet the unmet needs created by the new restrictions on erythropoietic stimulating agents? Transfusion. 2010;50(3):719-32.
45. Lowes R. New Precautions Recommended for IV Iron Supplements [Internet]. Medscape. 2013 Jun 28. Available at: http://www.medscape.com/viewarticle/ 807081. Accessed on: 2017 Mar 7.
46. Rampton D, Folkersen J, Fishbane S, Hedenus M, Howaldt S, Locatelli F, et al. Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. Haematologica. 2014;99(11):1671-76.
47. Silverstein SB, Gilreath JA, Rodgers GM. Intravenous iron therapy: a summary of treatment options and review of guidelines. J Pharm Pract. 2008;21:431-43.
48. Macdougall IC. New anemia therapies: translating novel strategies from bench to bedside. Am J Kidney Dis. 2012;59:444-51.
49. Gozzard D. When is high-dose intravenous iron repletion needed? Assessing new treatment options. Drug Des Devel Ther. 2011;5:51-60.
50. Krikorian S, Shafai G, Shamim K. Managing Iron Deficiency Anemia of CKD With IV Iron. US Pharm. 2013;38(8):22-26.
51. Koch TA, Myers J, Goodnough LT. Intravenous Iron Therapy in Patients with Iron Deficiency Anemia: Dosing Considerations. Anemia 2015;2015:763576.
52. Ganzoni AM. Intravenous iron-dextran: therapeutic and experimental possibilities. Schweiz. Med. Wochenschr. 1970.
53. Kulnigg S, Stoinov S, Simanenkov V, Dudar LV, Karnafel W, Garcia LC, et al. A novel intravenous iron formulation for treatment of anemia in inflammatory bowel disease: the ferric carboxymaltose (FERINJECT) randomized controlled trial. Am J Gastroenterol. 2008;103(5):1182-92.
54. Bayoumeu F, Subiran-Buisset C, Baka NE, Legagneur H, Monnier P, Laxenaire MDMC. Iron therapy in iron deficiency anemia in pregnancy: Intravenous route versus oral route. Am J Obstet Gynecol. 2002;186(3):518-22.
55. Ikan. Medicowesome [Internet]. Mumbai: Ikan; 2015. Available at: http://medicowesome.tumblr.com/post/104594246241/total-dose-infusion-formula-haldane-and-ganzoni Accessed on: 2017 Mar 9.
56. Auerbach M, Ballard H, Glaspy J. Clinical update: intravenous iron for anaemia. Lancet. 2007;369(9572):1502-04.

57. Anker SD, Colet JC, Filippatos G, Willenheimer R, Dickstein K, Drexler H, et al. Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency. N Engl J Med. 2009;361:2436-48.