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Low Dose Oral Iron Supplementation in Non Anemic Pregnant Women

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ABSTRACT:

Iron deficiency continues to be the leading cause of single nutrient deficiency in the world. In India 62-88% pregnant women suffer from anemia, out of which 80% is due to iron deficiency. Iron deficiency anaemia is completely preventable with iron supplementation. This study was conducted to know whether low dose weekly oral iron regimen is an effective alternative to daily regimen in preventing iron deficiency in pregnancy.

Keywords: Iron deficiency anaemia, iron supplementation, oral iron, weekly regimen, daily regimen.

INTRDUCTION:

Iron deficiency continues to be the leading cause of single-nutrient deficiency in the world, affecting the lives of > 2 billion persons although considerable efforts are done to decrease its prevalence for the past 3 decades. Nutritional iron deficiency is seen highest in populations which are at peak rates of growth mainly infants, young children, and pregnant women[1]. In India 62-88% pregnant women suffer from anemia. Approximately 80% of all anemia cases in pregnancy occur due to iron deficiency[2].

The iron requirement during pregnancy is drastically more than that in the non-pregnant state despite the temporary break from iron losses which occur during menstruation in non pregnant state[1]. Pregnant women require supplementary iron and folic acid to meet their own nutritional needs as well as those of the developing fetus[3]. Although daily iron and folic acid are provided free or cheaply in most countries, the major problem is none or poor compliance. This might be due to personal behaviour, cultural issues, and environmental factors, lack of awareness, socio-demographic status, economic factors, inadequate service delivery or side-effects. Unpleasant side-effects of iron such as constipation, diarrhoea, gastric cramping, nausea, vomiting, metallic taste and black coloured stool also decrease the compliance in patients[4].

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The use of daily intake of iron and folic acid throughout pregnancy has been the standard approach to prevent and treat iron deficiency anemia. Despite its proven efficacy, the use of daily iron supplementation has achieved limited success in program settings, may be due to less compliance as well as concerns for the safety of iron overload among women with an adequate iron intake, and erratic availability of the supplements at community level. Studies have shown that intermittent regimens may be more accepted by women, with amplified devotion to supplementation programs[5]. So low dose weekly iron supplementation could be an effective alternative to high dose conventional daily supplementation in pregnancy in non anemic pregnant women in preventing anemia and iron deficiency during pregnancy.

International Federation of Obstetric and Gynecological Society (FIGO) defines anemia as hemoglobin less than 10g/dl. Centre of Disease Control recommends a cut-off point of 10.5 g/dl hemoglobin during the second trimester and <11 g/dl in first and third trimester[6].

Anemia is a global problem. It is a direct cause of 5-25% of maternal death and indirect cause in 20%-40% of maternal deaths. The overall prevalence of anemia during pregnancy is estimated by the World Health Organization (WHO) to be 47.4%. According to recent WHO figures, India is included in the list of countries with high occurrence of anemia in pregnant women (>40%). The relative risk of maternal mortality due to moderate anemia was 1.35 and for severe anemia is 3.51[7].

The risk of maternal mortality increases 8-10 fold when hemoglobin falls <5 g/dl. Iron deficiency anemia is one of the leading nutritional disorders and presents as a widespread public health problem in the world and especially in developing countries including India[2].

Total requirements of iron in pregnancy differ with the body weight of the mother and the size and maturity of the foetus. In an average, demands for iron in pregnancy come to a total of around 900 mg (700-1400 mg)[8]. Uterus and its contents-500 to 600; Blood loss at delivery -150 to 200 mg ; Red cells mass expansion -500 mg; average saving due to amenorrhea -225 mg; iron deficit -600 to 700mg. Requirements are 4mg/day approximately (2.5 mg/day in early pregnancy, 5.5 mg/day in 20-32 week/ 6-8 mg/day from 32 weeks onwards). As absorption is around 10%, for 4-6 mg absorption of iron 40-60 mg of iron should be available in the diet[8].

Pathophysiology of Anemia:

Haematopoiesis is the production of circulating erythrocytes and others blood components from stem cells. Over 200 billion cells are produced daily in a normal person this way and in larger numbers in people with anemia or iron deficiencies. Haematopoietic system mainly in bone marrow in adults and requirements are iron, vitamin B12, folic acid and growth factors.

Inadequate supply of any of this leads to anemia[9].

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Iron metabolism:

Body has an extended system for the supply of Iron for haematopoiesis which requires specialised transport and storage proteins according to body's demand[9].

Majority of Iron used for haematopoiesis is recovered from the catalysis of old erythrocytes and only a small iron is lost each day. So dietary requirements are small for iron easily replenished by different foods but in special population where iron is required more (e.g. growing children, pregnant woman, lactating mother) or increased losses e.g. menstruating woman iron requirements exceeds normal dietary supply thereby causing iron deficiency anemia[9].

The process of iron absorption is dependent on the body iron stores and the activity of haematopoietic system. Low stores of iron and increased haematopoiesis causes more of intestinal iron absorption where as normal iron stores and decreased haematopoiesis result in decreased iron absorption. The iron stored in erythrocytes as haemoglobin and in muscles in myoglobin. A very small amount of iron is attached to transport protein called transferrin though majority of iron stored in liver and bone marrow attached to ferritin[10].

Iron is absorbed through intestinal brush border of enterocytes in proximal small intestine. Once internalized iron may be transported to plasma or may be stored inside intestinal cells. There is flow of iron from intestine continuously to tranferrin and from there to ferritin then to erythrocytes. Finally from erythrocytes to monocytes – macrophage system back to tranferrin and ferritin[10].

Stages of iron deficiency[9]

Iron deficiency anaemia has a clear evidence of iron deficiency. It occurs in 3 different stages. The first stage is negative iron balance where the requirement for iron exceeds the body's capacity to absorb iron from diet. Causes for this may be numerous physiological mechanisms like blood loss in menstruation, pregnancy, growth spurt in adolescents. Most commonly the growing needs of the foetus or adolescent exceeds the individual ability to absorb the total iron necessary for haemoglobin synthesis. Blood loss if more than 10-20 ml per day then it exceeds the amount of iron absorbed from a normal diet. This stage is recovered by mobilisation of iron from RES sites. In this stage iron majors like serum ferritin or the appearance of stainable iron on bone marrow aspiration depletes. So long as iron stores are not exhausted and can be mobilised the serum iron, TIBC and red cells protoporphyrin remains within the normal range. Red cell morphology and indices are normal[9].

As the iron supplies also deplete further, the serum iron starts to fall as well. Slowly the TIBC increases. There comes a stage when marrow iron reserve is also absent when serum ferritin level goes below 15µg/L. So far the serum iron is normal; haemoglobin synthesis is unaffected despite the decreasing iron stores. When the transferrin saturation falls below 15 to 20% haemoglobin synthesis becomes impaired. This stage is called iron deficient

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erythropoiesis. A careful observation of peripheral blood smear reveals the first appearance of microcytic cells, as well as hypo chromic reticulocytes in circulation. Gradually, haemoglobin and hematocrit starts falling, causing iron deficiency anaemia. The transferrin saturation is around 10-15%[9].

With moderate anaemia the bone marrow is hypo proliferative. In severe anaemia

(Haemoglobin 7- 8 g/dl), hypochromia and microcytosis becomes prominent, blood cells become poikilocytic and dismorphic and bone marrow becomes ineffective. With severe iron deficiency, hyperplasia of erythrocytes develops rather than hypoplasia[9].

HEMATOLOGICAL CHANGES IN PREGNANCY:

BLOOD VOLUME:

Blood volume in pregnancy increases significantly. In non anaemic pregnant women blood volume at or near term is 40-50% above the non pregnant state. This expansion of blood volume differs in different women. Some have mild increase and in some volume doubles. In fact by 12 weeks the plasma volume expands by 15% of pre pregnant state. 2nd trimester volume expansion is maximum but in 3rd trimester this expansion is comparatively slower and platue in last several weeks[11]. Blood volume expansion occurs due to increase in both plasma and erythrocytes. Though plasma is more as compared to erythrocytes in maternal circulation, the increase in erythrocytes is around 450ml which is significant[12]. Moderate erythroid hyperplasia is present in bone marrow, and the reticulocyte count is elevated slightly during pregnancy. This corresponds to the increase in erythropoietin levels, which peaks in early 3rd trimester[13, 14].

HEMOGLOBIN CONCENTRATION AND HEMATOCRIT:

Even though there is augmented erythropoiesis, haemoglobin concentration as well as hematocrit slightly decreases during pregnancy. Hence whole blood viscosity also decrease[15]. Haemoglobin concentration in an average is 12.5 g/dl near term and in around 6% pregnant women it is below 11g/dl[16].

IRON METABOLISM DURING PREGNANCY:

IRON STORES:

The overall iron content of normal adult female is between 2.0- 2.3 which is half the amount of normal male. But iron stores of normal young are only about 300mg[9].

IRON REQUIREMENTS:

Total requirements of iron during pregnancy differ with the body weight of the mother and the size and maturity of the foetus. In an average, demands for iron in pregnancy come to a total of about 900 mg (700-1400 mg)[8]. Uterus and its contents-500 to 600; Blood loss at

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delivery -150 to 200 mg ; Red cells mass expansion -500mg; Average saving due to amenorrhea -225 mg; Iron deficit -600 to 700mg. Requirements are 4mg/day approximately (2.5 mg/day in early pregnancy, 5.5 mg/day in 20-32 week/ 6-8 mg/day from 32 weeks onwards). As absorption is around 10%, for as little as of 4-6 mg absorption, 40-60 mg of iron should be available in the diet[8].

BLOOD LOSS:

In normal vaginal delivery as well as in caesarean delivery and in subsequent days after delivery only half of the erythrocytes added to maternal circulation are lost in the form of placental implantation site bleeding, episiotomy, surgical site and lochia. In an average, an amount of maternal erythrocytes corresponding to about 500ml to 600ml of pre-delivery blood is lost during and after vaginal delivery of a single fetus[17,18]. The average blood loss with caesarean is 1000ml same as twin vaginal delivery [17].

THE PROBLEM AND PREVALENCE OF ANEMIA:

Anaemia is the most prevalent nutritional deficiency affecting pregnant females. Iron deficiency is the primary reason for anaemia followed by folic acid deficiency. The prevalence varies worldwide in different socio economic conditions, life style and health seeking behaviour. Anaemia affects 52% of developing nation's pregnant women as compared to 23% of developed nations[19].

Prevalence is higher in India as compared to other developing countries. Prevalence is highest in South Asian countries. According to WHO among Southern Asian countries India has highest prevalence. India contributes to 80% of the burden of maternal deaths due to anaemia. Anaemia is a major concern for perinatal morbidity and mortality as well[19].

According to NFHS survey 2005-2006 incidence of anaemia in pregnant women in India is 54.6% in urban areas and 59% in rural areas[19].

The functional outcome of iron deficiency in women of child bearing age group is well documented in literature.

MANAGEMENT OF IRON DEFICIENCY ANAEMIA:

Along with volume replacement, treatment options include the administration of oral iron, parenteral iron and hetrotologus (donor) blood. Another option to be considered is the administration of recombinant erythropoietin (rhEPO)[20].

The severity and reason for iron deficiency anemia will decide the suitable approach to management. For instance, indicative patients with severe iron deficiency anemia and cardiovascular volatility may require red cell transfusions. Patients who have compensated for their anemia can be treated more predictably with iron replacement[9].

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For the majority of cases of iron deficiency, oral iron therapy will suffice. For patients with unusual blood loss or mal-absorption, specific diagnostic tests and appropriate therapy take priority. Once the finding of iron deficiency anemia and its cause is made, and a therapeutic approach is planned, there are three major approaches-donor blood transfusion, oral iron therapy and parenteral iron therapy[9].

DONOR BLOOD TRANSFUSIONS

Transfusion therapy is reserved for those individuals who have symptoms of anemia, cardiovascular instability, and continued and excessive blood loss, from whatever source, and those who require immediate intervention. Not only do transfusions rectify the anemia acutely, but the transfused red cells offer a source of iron for reutilization, assuming they are not lost through unrelenting bleeding. Transfusion therapy will alleviate the patient while other alternatives are reviewed[9].

Situations that can lead to a donor blood transfusion [20]

- Postpartum anemia with signs of shock.
- Severe acute blood loss following spontaneous delivery or caesarean section

ORAL IRON THERAPY

In the patients with established iron deficiency anemia who are asymptomatic, therapy with oral iron is usually sufficient[9].

Typically, for iron replacement therapy, up to 300mg of elemental iron per day is given, usually as three or four iron tablets (each containing 50 to 65 mg elemental iron) given over a day. The goal of therapy in individuals with iron deficiency anemia is not only to repair the anemia, but also to provide stores of at least 0.5 to 1 g of iron. Sustained treatment for duration of 6 to 12 months after correction of the anemia will be necessary to achieve this[9].

Of the complications of oral iron, gastrointestinal stress is the most prominent and is seen in 15 to 20% of patients. For these patients, abdominal pain, nausea, vomiting or constipation often leads to noncompliance. The gastrointestinal complications are a major barrier to the effective treatment of a many patients[9]**.**

Daily and weekly administration iron supplement in non-anemic pregnant women has similar hematological response. Regarding the side effects of iron supplementation, weekly supplementation seems preferable to daily intake. There is also improved compliance to the therapy and reduced cost of supplementation.

Also intermittent supplementation showed to reduce the number of women with increased hemoglobin concentrations during mid and late trimester compared with daily regimens thereby reducing the unacceptable high hemoglobin concentrations which are harmful as they may be associated with an increased risk of having a premature birth and low birth weight

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baby. Thus weekly supplementation of non-anemic pregnant women with 120mg of elemental iron is a helpful alternative to daily regimen for prophylaxis.

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