Management of Pregnancy Anemia - Obstetrician's Dilemma

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Introduction

Pregnancy anemia is one of the most common problem faced by obstetricians, especially in developing countries. Large majority of anemias in pregnancy are nutritional in origin and iron deficiency is the most prevalent deficiency. According to WHO estimates, 500 million women in the world are suffering from iron deficiency. In India most pregnant women are iron deficient. The Fogsi-Who study of maternal mortality in India (Bhatt. 1996) states that anemia was the cause of maternal death in 64.4 percent of cases. Not only this, but anemia can be responsible for adverse obstetric outcome in the form of spontaneous abortion, preterm labour, low birth weight babies and IUGR. In medicine the mortality/morbidity is high for those diseases whose cause or cure is not known or the treatment is very expensive. It is paradoxical but true that the cause of anemia is known and the treatment with iron is one of the cheapest therapy. Still anemia continues to take a heavy toll of maternal lives in most developing countries. WHO has surmised that noncompliance remains a major problem in anemia control programs (1995). The women are usually blamed for noncompliance. Undesirable side effects to iron are mentioned as a common cause. The purpose of the presentation is to provide helpful suggestions to improve compliance to iron therapy.

Facts about Iron

Plasma volume begins to increase after the first trimester to the extent of 25-30%. The normal blood volume varies from 3 to 5 litres. The red blood cells mass also increases but to lesser extent and hence there is a physiological fall in haemoglobin concentration by 30 weeks pregnancy. The total demand for iron throughout pregnancy is about 800 to 900 milligrams. Dietary iron alone cannot provide this much iron and hence there is need for medicinal iron supplementation during pregnancy.

Total iron content of the human body is etimated as 4.5 to 5 grams. Red blood cells carry about 2 to 2.5 grams of iron. Tissue iron is about 200 mg. and 3 mg. of iron is in circulation in plasma. The storage iron in normal women is about 400 to 600 mg. Haemoglobin contains about 0.33 percent iron. Thus 100 ml. of blood would contain 50 mg. of iron (assuming haemoglobin is 15 G. percent). One gram of haemoglobin can combine with 1.34 ml. of oxygen. Thus the oxygen carrying capacity is 15x1.34 = 20 ml. of oxygen per 100 ml. of of blood. There would be fall in oxygen carrying capacity of blood as the haemoglobin values diminish. This would affect tissue perfusion and vital organs like heart, kidney, liver, lungs and brain would show signs of reduced work function. If the heart muscle is in a hypoxic state for long, it may result in cardiac failure. Thus severely anemic women are likely to die of heart failure. During labour and the immediate postpartum period, the blood volume fluctuates widely because of the uterine contractions. This causes sudden increase in blood volume and load on the heart. Therefore, there is a risk of congestive cardiac failure in the first postpartum day. Routine use of oxytocics should be avoided in the third stage of labour for this reason. The iron stores at birth are negligible. The body starts storing iron after birth and by the time the child becomes an adult, the iron stores in woman are about 400-600 mg. Iron is mainly stored in liver, spleen, bone marrow and reticulo-endothelial system. The iron is stored as ferritin. One miligram of ferritin represents 8-10 mg. storage iron. Serum ferritin levels is a good index of iron stores. If serum ferritin levels are below 20 ng/ml. it means there are minimal or no iron stores. The body iron stores try to maintain haemoglobin values to near normal levels.

It is important for the clinician to realize that iron deficiency and iron deficiency anemia are not synonymous. Iron deficiency anemia is a very late manifestation of iron deficiency. It should be realized that iron stores are

almost nil by the time haemoglobin shows a fall.

Diagnosis of Anemia

There are lot of investigations available to diagnose anemia. They are expensive and time consuming and not necessary in every pregnant woman. Clinically woman would complain of lassitude, fatigue, lack of interest, etc. She may have pallor which can be seen in fair skinned woman but difficult to notice in dark skinned woman. Peripheral smear of blood can help in finding out the type of anemia. If there is iron deficiency, the smear looks pale hypochromic and microcytosis. In megaloblastic anemia, there would be macrocytosis, hypersegmentation of neutrophils and fully haemoglobinised red blood corpuscles. In hemolytic anemia, there would be target cells, reticulocytosis and sickle cells (in sickle cell disease). If there is a family history of hemolytic anemia or there is a strong suspicion on clinical grounds or on examination or peripheral smear, haemoglobin electrophroresis and all other tests for hemolytic anemia should be done. If hemoglobin is less than 5 gm. percent, therapy should be initiated only when the type of anemia is diagnosed. It is dangerous to give parenteral iron if it is hemolytic or megalobastic anemia. Serum iron, total iron binding capacity of the serum (TIBC), serum ferritin, serum folate and B12, bone marrow are some of the investigations needed to confirm the type of anemia. Normal values of some hematological parameters are given in Table. 1. Various blood indices in anemias are shown in Table 2. Inspite of its limitations, hemoglobin estimation remains a good screening test to diagnose anemia.

Table 1:
Normal Values of Some Haematological Parameters

Investigation	Normal Values
Serum iron	100 microgram/dl.
Total iron bindings capacity of serum	300-350 microgram/dl.
Serum ferritin	40-340 ng/ml in male 14-150 ng/ml in female
Serum Folic acid	5-15 ng/ml.
Red blood cell folate	> 1.9 ng/ml.
Serum B 12	140-820 pg/ml.

Table 2
Blood Indices in Nutritional Anaemias

Blood Indices	Normal	Iron Deficiency	Folate& B12 Deficiency
MCV (cubic mirons)	75-100	<75	110/140
MCH (micro - microns)	24-33	<25	33-40
MCHC (Percent)	30-36	< 30	32-38

Treatment of Iron Deficiency

The oral iron is the best, cheap, safe and effective method of treating iron deficiency anemia. The clinician is worried about noncompliance. The compliance rate improves if the woman is properly counselled and properly explained about the benefits. Titration method of iron therapy also improves compliance. In titration method the dose is gradually built upstarting from low dose. Initially only 30 mg. elemental iron may be given and then the regular dose gradually established. Iron after food reduces side effects but the phytates in serial diet may reduce absorption. Tannins present in tea and coffee and other poly phenols, found in nuts and pulses, also inhibit iron absorption. Though ideally, iron should be given without food, one has to compromise and advise iron to be taken after meals if there is intolerance.

Prophylactic Iron Therapy

There is general agreement among clinicians about iron supplementation during pregnancy if the haemoglobin is less than 11 G. percent. There is no firm guideline whether routine iron should be given prophylactically to all pregnant women in India and other developing countries. Hallberg (1988) reviewed iron supplementation need in pregnancy and concluded that in both industrialized and developing countries, all pregnant women should be given iron supplementation. Iyenger (1970) concluded from his studies that daily supplements of 30 mg. elemental iron be given to all women during the last 100 days of their pregnancy. Mohamed and Hytten (1989) conclude that healthy well nourished pregnant women in developed countries should be screened for anemia, but only treated if anemia is found. They further state, "To treat all pregnant women as if they were iron deficient is thera-

peutically misguided and possibly harmful". We feel that in India there is a need for prophylactic iron supplementation to all pregnant women in second half of pregnancy. However, we strongly suggest that prophylactic supplementation should NOT be started in the first half of pregnancy because of the normal phase of nausea and vomiting in the first trimester. Moreover, the fetal demand for iron is very minimal in the first half of pregnancy.

Choice of Iron Preparation

There are hundreds of iron containing preparations each claiming advantage over other preparations. We would like to simplify the choice. There are oral iron preparations in the form of tablets or liquids. The liquid preparations are more expensive than tablets. Therefore the first choice should be iron in tablet form. However, some women cannot tolerate tablet or swallow the tablet. In such cases, liquid preparations should be offered. Ferrous salts of iron are better absorbed than ferric form. Iron from colloidal ferric hydroxide and iron carbohydrate complex is also poorly absorbed. Ferrous sulphate, ferrous fumarate, ferrous succinate, etc. are better absorbed. The sustained release iron preparations are also available in the market. They claim significant reduction in side effects as compared to conventional iron preparations. It must be realized that iron is mainly absorbed in the duodenum and upper jejunum. In sustained release preparations, if iron is released lower down in gut, it will reduce the absorption. Thus the reduction in side effects is due to reduced absorption of iron and not due to any special feature in sustained release preparations. Moreover, such preparations are more expensive and hence not cost effective. Iron preparations containing haemoglobin iron are also available. They are not recommended because one gram of haemoglobin contains 3.4 mg. of iron. Most such preparations have about 10 G. of haemoglobin and so iron content of most of these preparations is 15-20 mg. which is not sufficient for prophylactic or therapeutic use. Addition of vitamin C is known to enhance iron absorption. In most nutritional anemias, there is also deficiency of folic acid. Hence 350 micro gram of folic acid is advisable along with iron. Intolerance is an important problem in oral iron therapy. The symptoms most commonly encountered are, nausea, vomiting, abdominal discomfort, constipation or diarrhoea, pruritus and accentuation and inflammation of hemorrhoids.

Sometimes, noncompliance is related to colour of the tablets, size and shape of the tablet. It is our experience that changing the brand of iron preparation does improve compliance. It is known that some women tolerate iron preparation of a particular pharmaceutical company and develop reaction or intolerance to iron preparation of another pharmaceutical company. Clinicians must respect patients perceptions and feelings and provide proper counselling, build the dose slowly and gradually increase the dose, change the brands of iron preparation and provide sympathy and reassurance. Compliance to iron improves if the advantages of iron to her and her unborn child are properly explained. Many women and even some clinicians feel that need for iron therapy is over as soon as she delivers. This is a wrong concept. There is need to develop iron stores in all anemic women. Iron stores start building up after the haemoglobin values come to normal. Therefore it is advisable to take oral iron for 3-4 months after the haemoglobin values become normal.

Parenteral Preparations

Though oral iron is cheap, safe and cost-effective, there are occasions when it is not possible to give oral iron. This may be due to genuine gastro-intestinal problems, real intolerance or patient cannot be relied to take oral iron. Many clinicians face such problems. There is certainly a place for parenteral iron in such conditions. Advantage with parenteral iron is that there is virtually, complete absorption of iron in due course. This is not affected by gastro-intestinal disease, dietary factors or intolerance. Reduction in absorption of oral iron which accompanies improvement in anemia is not a problem with parenteral iron. Hence parenteral iron may be a more rapid method of replenishing iron stores. There are two popular iron preparations available for intramuscular use. These are iron dextran complex (Imferon) and iron sorbitol citric acid complex (Jectofer). Iron sorbitol has a much lower molecular weight than iron dextran and is absorbed much more rapidly and completely How-

ever, unlike iron dextran, about 30 percent of iron sorbitol is excreted in urine and hence should be avoided in pyelonephritis and other renal conditions. Iron dextran is mainly absorbed by the lymphatics, iron sorbitol is largely directly into the blood stream. Therefore lymphadenopathy occasionally occur with iron dextran but not with iron sorbitol. Intramuscular iron may be given daily or alternate days depending on the need. The injection site should be changed every time and should be injected deeply into muscle (preferably gluteal or lateral thigh) by Z technique to prevent staining of the skin. The needle should be 1½ inch long. Prema (1982) has reported favourably by giving 10 injections of iron-dextran complex containing 100 mg. elemental iron per injection. Bhatt (1996) has also reported on two injections (250 mg. each) of iron-dextran complex intramuscularly. The problems with intra-muscular iron are pain at injection site, risk of abscess at injection site and lymphadenopathy. Moreover, the patient has to be hospitalized or has to come for injection.

Intravenous Iron

Iron dextran can be given intramuscularly as well as by intravenous route. Advantage of intravenous route is that there is less risk of pain or infection at the injection site and patient does not have to come frequently for injections if total dose technique is used. The total dose is calculated by the formula 0.3W(100-Hb%). W stands for patients weight in pounds and Hb. stands for haemoglobin concentration. The total dose calculated can be given neat or diluted in 500 ml. of normal saline. The reaction rate is directly related to the dose, we found 20 ml. as optimal dose at one sitting though higher dose may also be given. It is obligatory that intravenous iron is given in a hospital setting where facilities exist to combat serious reactions.

The test dose should be given earlier. The local reactions may be venous spasm and infusion of iron in the tissues causing pain. General reactions may be muscular and body pain, headache, vertigo, tachycardia, dyspnoea. Rarely there may be syncope, shock or convulsions. Bhatt (1977) has reported on a large series with intravenous use of iron dextran.

Management of Severe Anemia in Pregnancy

Clinicians are often faced with pregnant women with severe anemia in early or frank heart failure. Some of them are in imminent labour. These are very dangerous cases and ideally should be jointly dealt with the physician. The main object is to prevent death due to anoxemia and cardiac failure. The blood volume is already high and further increase in blood volume may precipitate further crisis. Partial exchange transfusion of blood keeping slight negative balance is recommened. If this is not feasible, packed cells can be transfused slowly giving diuretics. Oxygen should be administered. Digitalis may be gien on physicians recommendation. Patient should be given light sedation to prevent excitement. She should not be allowed to bear down in second stage of labour and outlet forceps or vacuum is advisable. There is risk of puerperal infection and hence prophylactic antibiotics should be given. There is risk of cardiac failure in the immediate postpartum period due to sudden rush of blood from uterus to the heart. Routine use of oxytocics should be avoided unless she has postpartum bleeding.

Haemolytic Anemias in Pregnancy

Severe haemolytic anemias are rarely seen in pregnancy. Obstetricians till recently were not much aware about these conditions. Now with much improved facilities for diagnosis, thalassemia minor or thal trait is well recognized. These women in pregnancy present with 6-8 grams haemoglobin and show little or no improvement with iron therapy. Specific investigations at this stage would confirm the diagnosis. There are three normal haemoglobins, designated by the letters A, A2 and F.A. is that which occurs as the normal haemoglobin of adults. Haemoglobin A2 is present in normal adult blood as not more than 3% of the total haemoglobin. Haemoglobin F is that which occurs as about 50-100% of the newborn infants haemoglobin, disappearing in the first year of life. It is normally present in low concentration, in the blood

of the pregnant women. In thalassemia, there is a genetic defect in haemoglobin A synthesis. Thalassemia occurs in two clinical forms, a major homozygous form in which the abnormal gene is inherited from both parents and the clinical features are severe. The thalassemia minor, the abnormal gene is inherited from one parent only and the clinical features are mild. The deficiency in haemoglobin A synthesis is compensated by increased synthesis of haemoglobin A2 and persistence of haemoglobin F. The abnormal haemoglobins are designated as C,D and S. Sickle cell disease and sickle cell trait may be occasionally associated with pregnancy. Like thalassemia trait, sickle cell trait runs a mild course. It is advisable for obstetricians to consult a physician / haematologist in such cases and go by his advice. Parenteral iron in such conditions is contraindicated. In anemic pregnant women with thal trait, low dose oral iron (30 mg.) may be necessary along with folic acid. Blood transfusion may be needed sometimes.

Supportive Therapy

Worm infections are common in India and it may be the cause of anemia. Therefore deworming is advisable. Malaria takes a heavy toll and hence patient should be advised to use mosquito repellents, mosquo nets and/or prophylactic chloroquine in areas which are endemic for malaria. Balanced diet with high protein should be advised.

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