

SAFETY AND EFFICACY OF IRON SUCRSE IN MILD TO MODERATE ANAEMIA.

ABSTRACT

Background & Objectives : Iron deficiency anaemia (IDA) is the most common nutritional deficiency in pregnancy. Prophylactic oral iron is recommended during pregnancy to meet the increased requirement. Pregnant women with mild to moderate anaemia are to be treated with parenteral iron therapy. This study was undertaken to evaluate the safety and efficacy of intravenous iron sucrose complex (ISC) given to pregnant women with IDA methods : A prospective Randomised control study was conducted (August 2015 to July 2016) in the department of obstetrics & gynaecology, Government Theni Medical College, Theni. One hundred pregnant women with hemoglobin between 7-9 g % with diagnosed iron deficiency attending antenatal clinic were given intravenous iron sucrose in a dose of 200mg twice weekly schedule after calculating the dose requirement.

RESULTS :

The mean hemoglobin raised from 7.51 (+ or -) 0.6 g to 10.9 (+ or -) 0.8 g% after three weeks of therapy. Reticulocyte count increased after 3 weeks of starting therapy (from 1.165 to 4.098). Other parameters including red cell indices were also improved significantly. No major side effects or anaphylactic reactions were noted during study period.

INTERPRETATION & CONCLUSIONS:

Iron therapy was effective in increasing hemoglobin and other hematological parameters in pregnant women with mild to moderate anaemia.

KEY WORDS :

Anaemia – iron deficiency – iron sucrose complex – parenteral iron therapy – Reticulocyte count.

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INTRODUCTION

Anemia is an important problem of the developing country more so in the pregnant period. Of all types of anemia, nutritional anemia is very common and iron deficiency anemia is the most common of these nutritional anemias.

The prevalence of iron deficiency anemia is estimated to be around 18% in developed countries and a staggering 35-75% in developing countries as per WHO report. As against the worldwide incidence, Indian incidence varies between 33-89%. Anemia accounts for about 80% of the global maternal mortality ratio.

Various factors contribute the increased incidence of anemia in India as compared to the world. These factors include:

1. early marriage
2. teenage pregnancy
3. multiple pregnancies
4. inadequate spacing between pregnancies
5. reduced intake of iron and folic acid
6. elevated incidence of worm infestation
7. poor nutrition

Cochrane data review¹ reported anemia as a serious global problem affecting 52% and 23% of pregnant women in developing and developed countries respectively.

WHO defines iron deficiency anemia as hemoglobin <11gm%, in India the ICMR classification of anaemia (IDA) 8-11g% as mild, 5-8gm% as moderate and <5gm% as severe anaemia.

Anemia in pregnancy is a major issue as it results in low birth weight babies, preterm deliveries and preterm deliveries. anemia detected during pregnancy can be a mild condition which can be completely treated if diagnosed early. however anemia becomes life threatening to both mother and fetus if left untreated.

Commonly identified cause of anemia in pregnancy is nutritional anemia ,among which iron deficiency is the leading cause accounting almost 80% of anemic population followed by, folate deficiency and vitamin B12 deficiency anemia. It affects 52% of pregnant women in developing countries and 23% in developed countries. Among these 43% of women from developing countries and 12 % from developed countries are

already anemic pre-conceptionally. WHO has estimated 16800 to 28000 reproductive age women die annually all around the world due to anemia and its related cause.

It is a major contributory factor to maternal morbidity, mortality and perinatal mortality rate. Women between 18-40 yrs have prevalence of iron deficiency anemia of 11 % and non pregnant women of same age with 5%

ANEMIA:

Anemia is a condition of insufficient red blood cells in the human body.

There are various types of anemia world over.

The most common of these types of anemia is iron deficiency anemia which accounts for 15 to 25% of the overall pregnancies complicated by anemia.

Folate deficiency can manifest as macrocytic anemia. This folic acid is an essential micronutrient, the deficiency of which manifests as neural tube defects. Diet rich in folic acid maybe leafy vegetables, bananas, legumes.

Vitamin B12 is another important vitamin that can present with anemia on its deficiency.

There are various causes for anemia, and the occurrence of anemia is most commonly in second trimester because of the associated hemodilution due to disproportionate rise in plasma concentration compared to RBCs.

An anemic mother can be identified by her history of getting tired often, becoming breathless, unable to perform her routine daily work, occasional giddiness.

On examination the mother presents with generalized pallor of the bulbar conjunctiva, hard palate and nails. The diagnosis of anemia is confirmed by estimating her hemoglobin values. Furthermore red cell indices like MCV, MCH and MCHC can be done to identify whether the anemia is microcytic or macrocytic, hypochromic or normochromic.

A smear study can be done to examine the red cells under microscope and confirm the variations in size, colour and shape of the RBCs.

This is then followed up with unusual tests like stool examination for occult blood, parasitic ova and cysts to identify other causes of anemia and correct them with antiparasitic medication. An ultrasound examination of the maternal abdomen can be done to identify rare medical disorders causing anemia like hepatospleomegaly when the anemia is refractory to iron treatment.

The next in line of investigations would be to assess her cardiac status to ensure the heart is capable of taking the volume overload status of pregnancy. Once basic investigations are done, anemia being a clinical diagnosis, iron supplementation is started earlier. The laboratory reports are needed to assess the severity of anemia and thereby decide upon the mode of iron administration to the patient.

IRON DEFICIENCY:

Iron is essential element present in Hb molecule , as its the oxygen carrying pigment in blood. Total iron requirement during pregnancy is 900mg with range of 700-1400mg of which about 500-600 mg is accounted by uterus and its content.150-200mg loss during delievery and same amount through lacactation. There is increased maternal haemoglobin mass which consumes about 500mg .it is returned to stores after delievery. A total iron defecit of about 600-700mg occurs during pregnancy.

Parenteral iron is indicated in women who donnot tolerate oral iron or poor response to oral therapy which 0.8 g% per week .The rate of response to iron therapy is the same whether given orally or parentrally. However parenteral iron eliminate the risk of non compliance and saves critical time in case of non-responders in late gestation.

oral iron should be discontinued before starting parenteral otherwise the Fe receptors sites are competitively inhibited leading to increased iron toxicity leading to Fe circulating iron.

Stages of development of iron deficiency anemia:

1. stage of storage iron depletion

It leads to early functional iron deficiency which shows that iron supply to bone marrow and other tissues is marginally inadequate. still there is no anemia

2. iron deficient erythropoiesis

In this stage peripheral smear shows normocytic cells, laboratory parameters used to detect this phase are serum transferrin saturation, total iron binding capacity, erythrocyte zinc protoporphyrin concentration and soluble transferrin receptor concentration assay.

In iron deficiency anemia, se iron 60 microgm per dl

Total iron binding capacity 400 microgram per dl

Ratio of (iron/TIBC) \times 100 gives transferrin saturation percentage

In anemia of chronic disorders ,se ferritin and TIBC are decreased.

Whereas in fe deficiency anemia, serum ferritina nd transferrin saturation percentage is decreased but TIBC increased

Soluble transferrin receptor concentration is increased in iron deficiency and hematopoiesis. but remains normal in anemia of chronic disorders.

Stage 3.

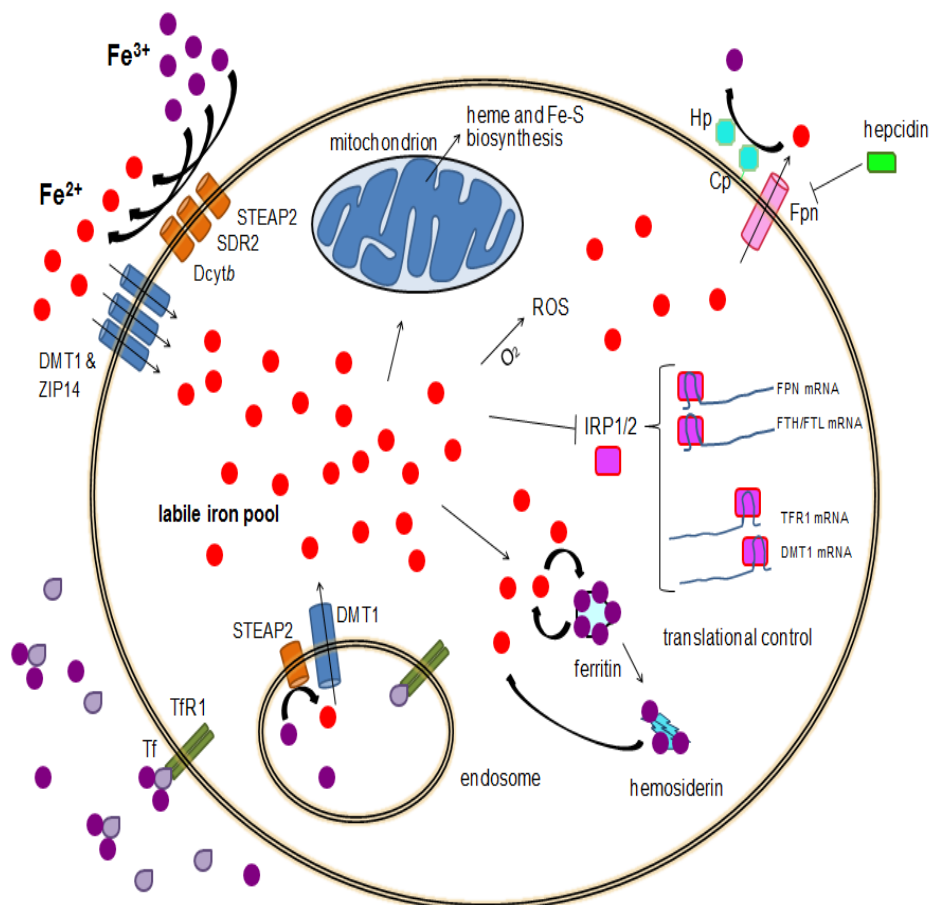
The blood picture shows reduction in Hb ,PCV,MCV and MCHC.

The picture is microcytic hypochromic

New cells are being generated at normal rate.reticulocyte count shows

little deviation from normal.cells are anisocytosis and polychromasia.

Red cell distribution width is a feature to differentiate between iron deficiency anemia and thalassemia.



Cellular iron metabolism

Fe sucrose is second generation IV iron preparation ,safe with few side effects with minimal allergic reactions with no reported fatal death.In this study , a group of 100 anemic mothers were studied and the efficacy and safety of iron sucrose injections is documented.

IRON REQUIREMENT IN PREGNANCY

The iron requirement in various stages of pregnancy are:

Early pregnancy - 2.5 mg/ day

20-32 Weeks - 5.5 mg / day

32 weeks onwards - 6. 8 mg / day

There are various enzymes in the human body in which iron plays a significant role. These enzymes are hemoglobin, myoglobin and some enzymes. Iron serves varied functions in all these enzymes like oxygen carrier, catalyst for oxygenation and hydroxylation, electron carrier through the Fe^{++}/Fe^{+++} cycle.

Various changes occur in pregnancy which result in iron deficiency state in pregnancy. It could be because of

1. Poor iron content in diet
2. Reduced iron stores since early days
3. Supporting the nutritional requirement of baby and placenta

CLINICAL FEATURES OF IRON DEFICIENCY

Iron deficiency anemia manifests with various symptoms. The clinical features are mild initially. The American Society of Hematology says symptoms are so mild initially that many people do not realize they have anemia unless it is identified incidentally on a routine blood test.

The symptoms of moderate to severe iron deficiency anemia include:

Easy fatigability

generalized weakness

generalized pallor of skin and nails

koilonychia

dyspnea

giddiness

PICA

beefy smooth tongue

cold hands and feet

palpitations

brittle nails

headaches

Effects of anemia on mother

Anemia is a major contributor to maternal mortality. case fatality rate 1 – 50% depending on the obstetric care and severity of anemia. cardiac failure is an important cause of maternal mortality in severe anemia. all complications of pregnancy are aggravated by anemia. cardiac patients suffer from greatly increased dyspnea. immune system is suppressed which leads to increased susceptibility to infections ranging from asymptomatic bacteriuria to sepsis.

Antepartum complications associated with and aggravated by anemia are preeclampsia and antepartum hemorrhage.

During intrapartum period, uterine inertia, maternal exhaustion and postpartum hemorrhage are more common.

During puerperium ability to cope up with infection is impaired. postnatal recovery is also retarded leading on to puerperal sepsis, thromboembolism, sub-involution of uterus, delayed wound healing and lactational failure.

EFFECT OF ANEMIA ON FETUS

Effect on fetus depend on severity of anemia. low birth weight incidence increases two fold and perinatal mortality increases three fold when Hb is less than 7 g%.

IUGR and low birth weight leads to poor growth trajectory in infancy, childhood and adolescence.

Gestational period at which fetus is exposed to anemia is important in deciding the perinatal outcome. anemia during first trimester have great adverse affect on fetus.

Physiological hemodilution of pregnancy reaches its nadir at the end of second trimester and early third trimester which improves placental blood flow when the fetal requirements are greatest.

Moderate anemia before 28 weeks has been associated with increased still birth rate.the fetus extracts its iron from maternal storage. so if maternal storage is deficient fetal iron source becomes inadequate. so neonate is at full risks of developing anemia

LABORATORY DETECTION OF ANEMIA

Complete blood cell (CBC) test

A complete blood cell (CBC) test is usually the first test .

CBC test measures the amount of all components in the blood, including:

- Red blood cells (RBCs) and its indices
- White blood cells (WBCs)
- Hemoglobin
- Platelets
- Hematocrit level, which is the percent of blood volume that is made up of RBCs
- the hemoglobin level
- the size of RBCs

The CBC test provides information not only about the deficiency status of Hb but also about the type of anemia through various red cell indices like MCV, MCHC

A normal hematocrit range is 34.9 to 44.5 percent for adult women and 38.8 to 50 percent for adult men. The normal range for hemoglobin is 12.0 to 15.5 grams per deciliter for an adult woman and 13.5 to 17.5 grams per deciliter for an adult man. In iron deficiency anemia, the hematocrit and hemoglobin levels are low. Also, RBCs are usually smaller in size than normal.

Other tests

iron level in blood

RBC size and color

RBCs are pale in color if they're deficient in iron.

ferritin levels

Ferritin is a protein that helps with iron storage. Low levels of ferritin indicate low iron storage.

total iron-binding capacity (TIBC)

Transferrin is a protein that transports iron. A TIBC test is used to determine the amount transferrin that's carrying iron.

Diet

Diets high that include the following foods can help treat or prevent iron deficiency:

red meat

dark green, leafy vegetables

dried fruits

nuts

iron-fortified cereals

Additionally, vitamin C helps your body absorb iron. If you're taking iron tablets, a doctor might suggest taking the tablets along with a source of vitamin C, like a glass of orange juice or citrus fruit.

Iron supplements

Iron tablets can help restore iron levels in your body. Iron tablets should be taken on empty stomach to enable the body to absorb them better. When there is associated nausea and vomiting, these tablets may be taken with meals. These iron tablets need to be taken for long duration to have a significant improvement in iron levels in the body. Iron supplements may cause constipation or stools that are black in color.

Various parenteral iron preparations are available in the market, which can be administered either intravenously or intramuscularly. Initially, iron dextran and iron sorbitol citrate were available in the market for usage. But these formulations required administering a testdose as there was a propensity to cause severe anaphylactic reactions.

Iron sorbitol citric acid and iron dextran were the commonly used parenteral preparations for a long period of time. But they had an anaphylactic reaction adverse effect that was highly unpredictable. And these preparation also had a multitude of local and systemic side effects which limited their widespread use. Despite all these side effects these formulations were capable of providing some improvement in the hemoglobin status of women suffering from anemia.

The next to enter the market was intravenous preparation of iron sucrose which significantly improved the hematological indices with negligible side effects or anaphylaxis. This was hence considered a safe alternative for iron supplementation.

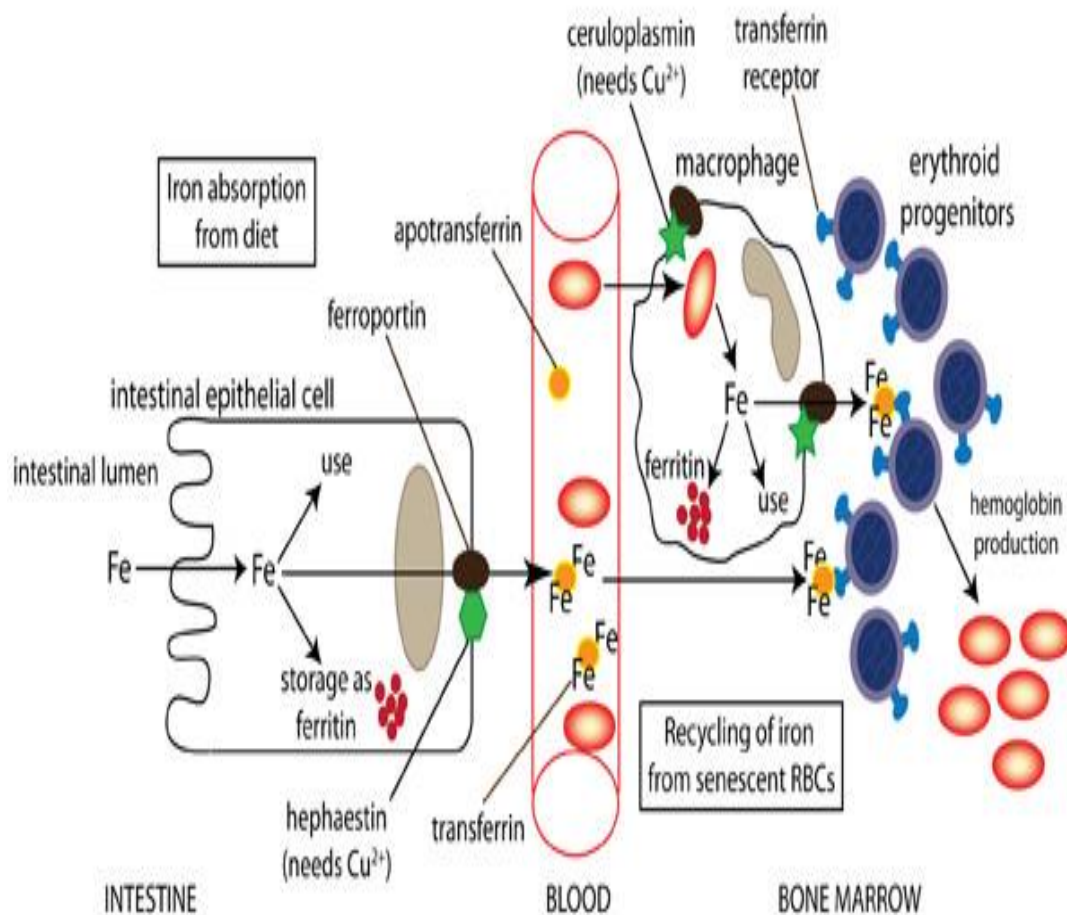
The Cochrane database² suggested that intravenous administration of iron sucrose had a better outcome hematologically with fewer side effects when compared to intramuscular iron injections.

A Cochrane review was conducted in 2007³ by performing a randomized controlled trial to evaluate the effects of treating the iron deficiency anemia during pregnancy. This study concluded that blood transfusion as a method to correct iron deficiency anemia has a significant risk of infection transmission to the receiver like parasitic infections, viral infections such as Hepatitis, HIV, Trypanosomiasis, bovine spongiform encephalitis. The risk of transmitting these infections persisted despite screening of blood. Moreover, in addition to infection risk there was transfusion associated risks like TRALI.

The iron supplementation to correct anemia is important as antenatal anemia can result in postnatal anemia in about 27% of mothers. Postpartum anemia has the associated complication of leading on to

depression, prolonging the duration of hospital stay, and affect the lactation and thereby the infant development.

Hence iron supplementation with intravenous preparations is a safe option to correct iron deficiency anemia and ensure better maternal health and reduce maternal mortality and improve perinatal outcome..



IRON SUCROSE:

Iron sucrose is brown in colour, an aqueous solution, made of polynuclear iron hydroxide with sucrose. This drug is administered intravenously. The molecular weight of this compound is about 34,000 – 60,000 daltons. The formula is



Where n is the degree of iron polymerization and m is the number of sucrose molecules associated with the iron (III)-hydroxide.

One ml of iron sucrose injection contains 20mg elemental iron. This compound is available as vials of 5 ml each, which need to be administered in a single dose. One vial contains 100mg of elemental iron. The sucrose content is about 30% w/v, with pH of 10.5 to 11. There are no added preservatives. The osmolarity is 1250mOsmol/L.

Clinical Pharmacology

Pharmacodynamics & Pharmacokinetics:

After the intravenous administration, this iron sucrose splits into iron and sucrose in the reticuloendothelial system. Iron undergoes first order

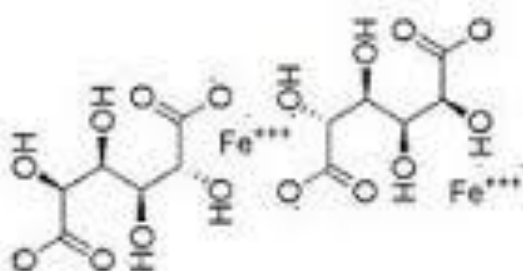
pharmacokinetics, and the half life of the drug is 6 hours. Among the volume of distribution, 10.0L exists in nonsteady state and 7.9L exists as steady state. The clearance of iron from the body depends on stores of iron. Hence clearance of iron following iron sucrose injection is more rapid in iron deficient individuals compared to healthy individuals.

Distribution:

Iron sucrose administration in a healthy adult causes sucrose to enter into blood and a small percentage in the extravascular compartment. Some iron enters into liver, spleen, bone marrow and this store of iron is not available for usage. The iron gets trapped and contributes to non reversible volume of distribution.

Metabolism and Elimination:

After splitting into iron and sucrose, the sucrose component and some iron gets excreted in urine



IRON SUCROSE
COMPLEX
CAS #8047-67-4



Table I. Baseline hematological parameters and effect of iron sucrose therapy

Parameters	Baseline	2 wk	4 wk	8 wk	<i>P</i> value
Mean Hb (g%)	7.63 ± 0.61	7.89 ± 0.60	9.90 ± 0.80	11.20 ± 0.73	0.001
Serum iron (µg/dl)	32.72 ± 5.00	42.94 ± 9.4	59.11 ± 13.7	82.42 ± 12.5	0.001
TIBC (µg/dl)	354.2 ± 37.7	328.8 ± 14.8	320.96 ± 11.3	315.5 ± 11.6	0.001
Serum ferritin (µg/l)	11.2 ± 4.7	17.64 ± 9.3	25.60 ± 10.90	69 ± 23.1	0.001
Reticulocyte count (%)	1.50 ± 0.60	4.6 ± 0.8	4.8 ± 2.1	5.5 ± 1.8	0.001
Mean corpuscular vol. ()	67.24 ± 5.0	76 ± 4.5	79.3 ± 3.2	85 ± 2.3	0.001
Mean corpuscular hemoglobin (MCH) (pg)	22.3 ± 2.6	24 ± 3.2	34 ± 2.2	44 ± 3.2	0.001
Mean corpuscular hemoglobin concentration (MCHC) (g/dl)	26.5 ± 1.9	31 ± 2.3	40 ± 3.2	56 ± 2.4	0.001

IRON METABOLISM

Most of the iron within the body is found in haemoglobin within erythrocytes (about 1800mg of iron). Iron is stored in macrophages (and a lesser extent in hepatocytes), which represents the storage pool of iron (about 1600mg of iron). Small amounts of iron are found in myoglobin and in plasma (bound to transferrin). Iron is conserved within the body.

The typical adult human body contains about 3000-4000mg of iron. Only about 1mg of iron is lost from the body per day (through blood loss or sloughed mucosal epithelial cells) and must be replaced through the diet. The majority of iron required by the body is acquired by recycling iron from senescent red cells.

Iron is important in human body because of its occurrence in many hemoproteins such as haemoglobin, myoglobin and cytochromes. Digested in diet as heme or non heme iron.

Most of the iron in the diet is in the ferric (Fe^{3+}) form, whereas it is the ferrous (Fe^{2+}) form that is absorbed. Fe^{3+} will be converted to Fe^{2+} by Fe^{3+} reductase in the brush border of enterocytes

Normally greater proportion of dietary heme iron than non heme iron is absorbed reflecting the greater importance of heme as source of iron. Almost all iron absorption occurs in the duodenum.

Iron absorption is facilitated by reducing substances like ascorbic acid. Sugars especially fructose increase the absorption and may contribute to dietary hemosiderin. Iron absorption is inhibited by alkalies, phosphates, phytates. RDA of iron in menstruating adult female is 1-2mg and in pregnancy is 3-5mg.

Dietary iron is obtained from either inorganic or animal sources. It enters intestinal cells via specific transporters which is then used by the cell (to form enzymes), stored as ferritin or is transferred to plasma. Ferroportins are the specific iron channels which causes the transfer of iron from enterocytes to the transport protein, apotransferrin. This is facilitated by a protein (with ferroxidase activity) called hephaestin. Apotransferrin binds with iron to form transferrin.

Hephaestin contains copper, hence copper deficiency will decrease iron absorption. Heparin is a main iron regulating protein which decreases ferroportin and thus decreases iron absorption. Normal value of transferrin saturation with iron is 35%.

Heme is transported into the enterocyte by separate heme transporter and heme oxidase releases Fe^{2+} from the heme. A part of Fe^{2+} is converted to Fe^{3+} and is bound to ferritin. The rest binds to basolateral Fe^{2+} transporter ferroportin(FP), bound to transferrin and stored in the body as ferritin and hemosiderin.

Transferrin does not cross the placenta but gives up its iron in chorionic villus. Iron is transferred across the placenta against steep concentration gradient, so it is enzyme dependant.

Erythroid progenitors obtain iron for haemoglobin synthesis from plasma transferrin or from recycling of senescent erythrocytes by macrophages in bone marrow, spleen and liver. Iron that is in excess of that required for haemoglobin production is stored in macrophages as ferritin, which is oxidised to hemosiderin.

Iron exists in the circulation as transferrin(bound to apotransferrin).most the iron is obtained by breakdown of senescent RBC(called recycling). red blood cells are phagocytised by macrophages. heme and globins are released by proteolytic digestion of haemoglobin.the iron is released from heme porphyrin ring is released.

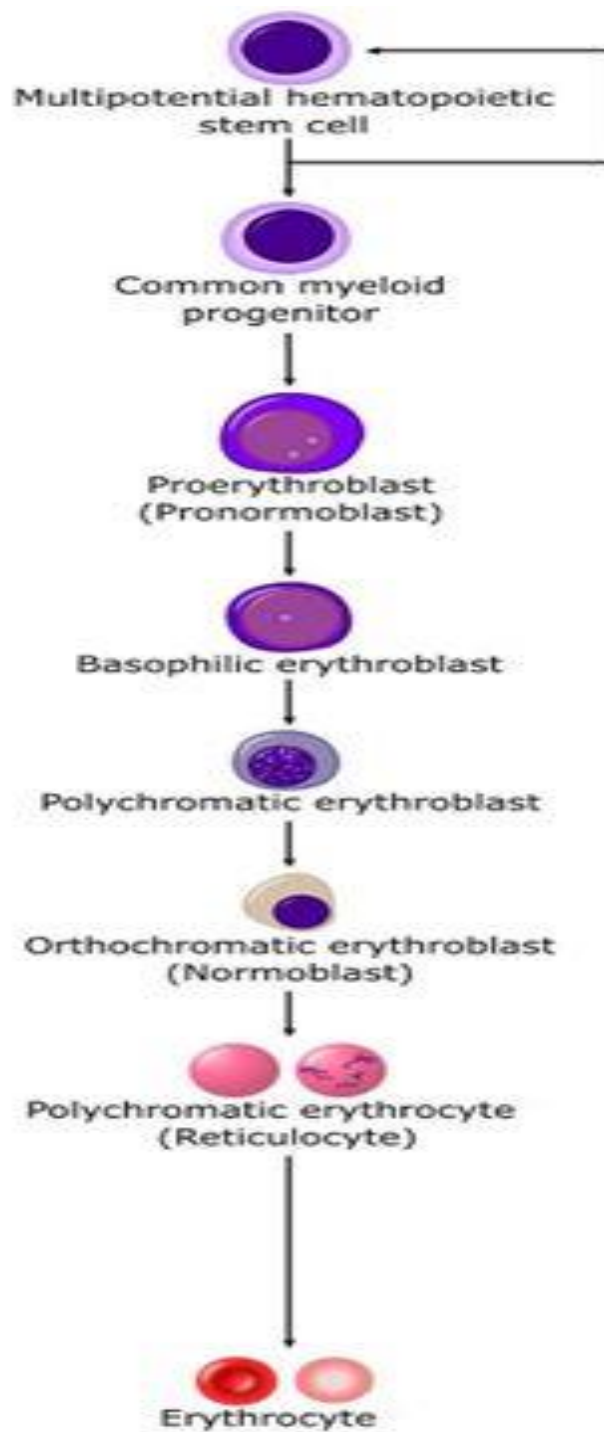
it is converted to bilirubin. In macrophages, ceruloplasmin is a ferroxidase and facilitates transport of macrophage iron to transferrin.

Erythropoiesis

Erythropoiesis is the development of mature red blood cells. Proerythroblast is the first cell of erythroid cells. Then the basophilic erythroblast cell continues to become smaller during development. The cell now will continue to produce haemoglobin and now it is called polychromatophilic erythroblast. Cytoplasm begins more eosinophilic now at this stage the cell is orthochromatic erythroblast. This orthochromatic erythroblast will then extrude its nucleus and enter circulation as a reticulocyte. Reticulocytes lose their polyribosomes and become mature red blood cells.

RBC production starting from stem cells to mature RBC takes about 25 days.

ERYTHROPOISIS



OTHER TYPES OF ANEMIA:

MEGALOBLASTIC ANEMIA:

This anemia is caused due to deficiency of vitamin B12 or folic acid in the general population. But when megaloblastic anemia is identified in pregnancy the cause is most commonly due to deficiency of folic acid.

Mechanism of action:

Folic acid is an important factor required to convert uridine to thymidine. This is a significant step in synthesis of nucleic acids. When there is deficient folic acid in the body, the nucleic acid synthesis is affected and cell get inhibited in division and appear macrocytic and hence the name megaloblastic anemia.

The incidence of this variant of anemia is 0.2 to 5%. But the bone marrow changes could be a lot higher compared to the clinical presentation of megaloblastic anemia.

The megaloblastic red cells undergo rapid destruction and this results in compensatory marrow hyperplasia. Also the demand of RBC is increased in pregnancy and further megaloblastic cells erythropoiesis occurs.

Causes of folic acid deficiency in pregnancy could be inadequate dietary intake, hyperemesis gravidarum, impaired absorption like with sprue. The average daily intake of folic acid is 120 to 300µg .

Folic acid deficiency can affect the outcome of pregnancy in multiple ways causing abortion of the baby, premature deliveries, anomalous baby and maybe even antepartum hemorrhage. There has been studies demonstrating the association between folic acid deficiency and abruption.

Clinical features:

The time of onset of this variety of anemia is between 5 to 7 months of gestation. Atrophic glossitis, hepatosplenomegaly, purpura can be seen with other manifestations of anemia. Neurological manifestation is rare in pregnancy.

In women on anticonvulsant drugs there occurs an increased demand for folic acid as the anti epileptic drugs interfere with folate metabolism. Prolonged OCP intake prior to pregnancy can interfere with folic acid stores and present with a deficient state.

The neonate of a folate deficient mother is mostly delivered preterm. Periconceptual folic acid supplementation is essential to prevent the incidence of cleft lip, cleft palate, neural tube defects. 400µg of folic acid hence needs to be supplemented in the periconceptual period.

When there is history of earlier child having neural tube defects these women can be administered therapeutic dosage of folic acid at 4mg concentration. The prophylactic dosage of folic acid is advocated in all women as iron deficiency masks the folic acid deficiency and supplementation with just iron interferes with improvement of anemia and makes the anemia refractory to treatment.

Other cause for megaloblastic anemia is B12 deficiency. This B12 deficiency is common in medical disorders like tropical sprue. There is fall in B12 concentration in pregnancy as the B12 stores are diverted to support the nutrition of the fetus. Hence the levels B12 in cord blood tends to be higher than in maternal blood despite folate and B12 being transferred at the same rate through the placenta.

In pregnancy, similar to iron binding capacity, B12 binding capacity is also increased and results in increased deposition of B12 in liver by the

protein transcobalamin. The stores of B12 are in the range of about 3000 μ g in adults.

Treatment:

Treating a megaloblastic anemia is far more essential than correcting iron deficiency as the former is a far more dangerous entity than the latter. When megaloblastic anemia is proven it needs therapeutic dosing of folic acid in the dose of 5mg.

Response of this therapy is evaluated in terms of fall in LDH levels which can occur over 3 to 4 days followed by a rise in reticulocyte count which can occur over 6 to 8 days.

There is no indication for blood transfusion in megaloblastic anemia, the only indication being occurrence of antepartum hemorrhage.

B12 deficiency can be corrected by administering 250 μ g of parenteral cyanocobalamin. This is important because when the megaloblastic anemia is treated with folate without B12 supplementation it can lead on to exacerbation of the neurological symptoms.

APLASTIC ANEMIA:

This is a condition where the bone marrow becomes incapable of producing blood cells and renders the patient anemic. When the diagnosis of aplastic anemia is made, pregnancy should be avoided. If the patient becomes pregnant, it needs to be terminated in early gestation or managed with transfusion of blood and blood products at a later gestation.

HEMOGLOBINOPATHIES:

Hemoglobin is a protein that has heme and globin component. The heme fraction is made up of various polypeptides. When there is defect in these polypeptide chains, it is called as hemoglobinopathy.

The most common hemoglobinopathy is thalassemia. In beta thalassemia, the beta chains are not synthesized and hence the normal HbA is replaced by HbF or HbA₂. In case of alpha thalassemia, the alpha chains are defective and the conditions are called as thalassemia major, thalassemia minor, thalassemia intermedia.

The other hemoglobinopathy is sickle cell anemia where the hypoxic condition manifests as sickling of the red blood cells. This sickling can

obstruct blood vessels and manifest as dactylitis, bone pain and autosplenectomy.

When the anemia is refractory to treatment, suspicion of other rare variants need to be made and diagnosis confirmed by making a bone marrow biopsy for aplastic anemia or smear study to identify sickling after adding a reducing agent.

Management of hemoglobinopathies is mostly by blood transfusion and these conditions do not respond to iron or folic acid supplementation.

These conditions are associated with obstetric complications like pre eclampsia, cardiac failure due to volume overload state of pregnancy. There can occur a high incidence of loss of pregnancy by abortions or intra uterine deaths of fetus, preterm premature deliveries, intrauterine restriction of growth of fetus as a result of the chronic placental insufficiency.

REVIEW OF LITERATURE

Breymann⁴ study showed that iron sucrose releases iron that has a half life of 6 hours with minimal allergic reactions, or overload complications. This resulted in iron sucrose being found to be a safe option for management of iron deficiency anemia.

Geisser et al showed that iron sucrose for parenteral administration and anemia correction is the ideal drug as it is safe and devoid of complications and cost effective.

Moment et al studied by comparing iron sucrose with ferrous sulfate in terms of safety and efficacy. They conducted a prospective, open controlled study by randomly assigning women with anemia to iron sucrose group or ferrous sulfate group. The study sample included 52 and the control group consisted of 59 patients.

In the study group, the administration dose was calculated by the formula $\text{Hb deficit in g/l} * \text{body weight in kg} * 0.3$. This calculated dose was administered by using 2 vials of iron sucrose containing 200mg of elemental iron in 100 ml of normal saline. This solution was administered intravenously slowly over a period of 1 hour. After completing the dose they were also given 10mg/kg of iron to improve the iron stores.

Among the control group, iron supplementation was done by giving 30mg of ferrous sulfate tablets containing 60mg of elemental iron 8th hourly.

Both the groups of patients were stringently observed for adverse effects and improvement of anemia clinically and by laboratory parameters.

The reports of the study showed better outcome in the iron sucrose group with improvement in hemoglobin level of about 128.5 +/- 6.6g/L as opposed to 111.4+/-12.4g/L in the ferrous sulfate group. This improvement in hemoglobin status was achieved in 6.9+/-1.8 weeks in iron sucrose group when compared to 14.9+/-3.1 weeks in the ferrous sulfate group. Both these findings had a p value <0.001 proving a significant superiority of iron sucrose over ferrous sulfate.

The side effect profile was analysed and found to be nil complaints in the iron sucrose group. On the contrary, the control group of ferrous sulfate users had 6% intolerance to the tablet, 30% dyspepsia, 30% poor compliance.

The results of this study showed that iron sucrose is a safer and effective method to correct iron deficiency anemia.

Perwunyk et al studied the effect of iron sucrose therapy in reducing the need for blood transfusion. Iron sucrose has fewer side effects and insignificant allergic reactions, as the release of iron from the iron sucrose complex is slow. This slow release also decreased the storage of iron in liver parenchyma as against increased storage of iron dextran or iron gluconate. The decreased parenchymatous storage lead to increased deposition in bone marrow causing enhanced erythropoiesis. So among patients using iron sucrose the need for blood transfusion was less than 1% of patients per year.

Al ra et al study was a randomized open labeled study that compared iron sucrose with oral iron for correcting iron deficiency. The study sample included 90 women who had hemoglobin levels in the range of 8 to 10.5g/dl. The inclusion criteria for the study required a ferritin level of less than 13mcg/L. The sample was divided into two groups and administered iron sucrose in the study group and oral iron polymaltose in the control group. The iron polymaltose tablet contains 300mg of elemental iron.

The required dosing was calculated by the formula:

Pre-pregnancy weight in kg * Hb deficit from 110g/l * 0.2 + 500mg

The effect of treatment was assessed by repeating the hemoglobin and ferritin values on day 14, day 28, day of delivery, and postpartum day one. The associated adverse effects, weight of the baby, duration of hospital stay, need for blood transfusions were also analysed.

The reports revealed a greater increase in hemoglobin levels in the study group comprising of intravenous iron sucrose administration as compared to control group of oral iron supplementation. On day 14, the hemoglobin improvement comparison between both groups gave a p value of 0.004 while on day 28 the p value was 0.031.

Ferritin values were compared to find the result of the study and it revealed better outcome in those receiving intravenous iron supplementation throughout the pregnancy period.

There was no significant adverse effect in both groups. Likewise there was no variation in terms of weight of baby or duration of hospital stay.

There was need for blood transfusion among oral iron group. This proves the advantage and superiority of intravenous iron sucrose in correcting iron deficiency anemia.

There was better correction of anemia in intravenous group receiving iron sucrose as they had better iron stores improvement at a faster rate and better efficacy without causing significant adverse effects.

Al moment et al conducted another randomized prospective controlled study. The study sample in this was 111 women at various stages of pregnancy and hemoglobin level less than 9g/dl and proven iron deficiency anemia on smear study. This sample was randomly divided into two groups and 55 women were given intravenous iron sucrose and 55 women were given intramuscular iron dextran.

Iron sucrose was given as 100mg of elemental iron in 100ml of normal saline intravenously. Iron dextran was administered as 100mg intramuscular dose on alternate days upto a maximum of completing the calculated iron requirement.

The reports of this study showed that better improvement of hemoglobin, with a shorter time duration was achieved with intravenous therapy compared to control group. The side effect profile was non existent in iron sucrose group. But 6% developed intolerance, 30% developed nausea, 32% turned non compliant in the control group.

Wali et al conducted a prospective controlled study where they compared iron sucrose with intramuscular iron sorbitol. This study was done on 60 pregnant women. The inclusion criteria for the study was 12 to 34 weeks of gestation and proven iron deficiency anemia.

These patients were then randomly divided to three groups.

15 women were given iron sucrose intravenously at a dose of pre-pregnancy weight in kg * Hb deficit from 110g/L * 0.24 +500mg.

20 women were given iron sucrose intravenously at a dose of pre-pregnancy weight in kg * Hb deficit from 110g/L * 0.24 +200mg

25 women were managed with intramuscular iron sorbitol.

The effects of treatment was analysed by hemoglobin estimation after 3 weeks of treatment. The hemoglobin increase was by about 2.8g/dl in the first group, 1.9g/dl in the second group and 1.4g/dl I the third group. The total increase in hemoglobin was 3.8g/dl in the first group and 2.4g/dl in the second group over a period of 6.6.weeks.

The end point was kept at achieving 11g/dl of hemoglobin levels. This end point was achieved in 80% patients in the first group, 70% patients in the second group, and only 28% in the third group.

The results of this study prove that the intravenous mode of administration is far effective method of anemia correction that is safe and convenient as compared to intramuscular mode of iron administration.

Hogine et al study involved comparison of iron sucrose with iron dextran in causing adverse effects. One set involved a sample of 206 patients, of which allergic reaction to iron dextran occurred in 4 women.

Among these allergic reaction, 1 patient manifested with severe dyspnea and the remaining 3 patients presented with generalized reactions.

Another study was conducted at Zurich hospital involving 400 patients who required treatment with intravenous iron sucrose administration. Among this group, generalized skin reactions occurred in 7 women, flushing occurred in 4 women, exanthema occurred in 3 women.

A retrospective was conducted among 8100 patient years. They were managed with 100mg elemental iron each using up about 160,000 ampoules of iron sucrose. Flushing occurred in 10 women, reversible hypotension occurred in 7 women, urticaria in 1, diarrhea in 1 woman.

Dede et al studied the correction of anemia occurring in postpartum period with iron sucrose. This study comprised of 75 women in their puerperal period who had hemoglobin levels of 9g/dl. This sample size was divided into two groups where one group was administered iron sucrose intravenously and another group was given oral tablets containing 60mg of elemental iron on a 8th hourly basis. The effects were analysed by hemoglobin, ferritin, iron and hematocrit, TIBC estimation at day 7 and day 28. The reports revealed significant improvement of serum ferritin levels within shorter time duration and fewer adverse profile among women managed with intravenous iron therapy rather than with oral iron therapy.

Wali A, Mushtaq A performed a prospective study on 60 women who were 12 to 24 weeks pregnant. One group of 30 women received 500mg of iron sucrose and another group of 30 women received iron dextran. The baseline hemoglobin was obtained and repeat hemoglobin estimation was done 3 weeks alter which showed a increase of 2.8g/dl in first group and 1.4g/dl in the second group. Adverse effects were analysed and it showed 1 complaint of abdominal pain, 2 complaints of shivering, 3 complaints of phlebitis in intravenous group. The

intramuscular group presented with injection site pain in almost all patients.

Breyman et al conducted a prospective randomized trial for correcting iron sucrose anemia with iron sucrose with use or without use of recombinant human erythropoietin. The inclusion criteria in this study was more than 20 weeks of pregnancy with hemoglobin levels of less than 9g/dl. 20 patients belonging to first group were given 200mg iron sucrose intravenously and 300IU/kg recombinant human erythropoietin. 20 patients belonging to second group were given biweekly injections of 200mg iron sucrose for upto 4 weeks. Hematocrit values and reticulocyte counts were assessed in both groups and the reports revealed better outcome with erythropoietin therapy. There were no reports of adverse effects, no blood transfusion requirement. This study suggested usage of iron sucrose for correcting iron deficiency anemia initially in pregnancy and addition of erythropoietin in severe anemia that was not responding to intravenous iron sucrose.

Scoff et al studied and reported that usage of intravenous iron therapy reduced the need for blood transfusion.

Sal Mommen et al studied iron sucrose therapy with ferrous sulphate and discovered that there was better improvement of hemoglobin levels in the range of 128.5+/-6.6 in intravenous group as compared to 111.4+/-2.4g/dl in the ferrous sulphate group. There was no side effect reported with iron sucrose and 6% incidence of side effects with control group.

Gravier et al conducted a study to identify ability of iron sucrose in reducing the need for postpartum blood transfusion and concluded that when pregnant mothers were treated with iron sucrose antenatally the need for postpartum blood transfusion was reduced and iron sucrose also has a better outcome in correcting postpartum anemia.

Scott B, Silvestein study reported that the incidence of anaphylaxis was 0.002% following intravenous iron administration and 0.6-0.7% following intramuscular iron administration.

American College of Nursing Journal published a study citing the safety of iron sucrose usage in patients with cardiac disease along with anemia complication.

ACOG Journal published a study reporting iron sucrose corrected anemia effectively without any adverse effects.

BJOG reported that the increase in hemoglobin levels was high with intravenous iron sucrose therapy and there also occurs replenishment of the iron stores.

European Journal issued a study citing the safety and efficacy of iron sucrose in correcting iron deficiency anemia.

All these studies prove that irrespective of the ethnicity and racial differences intravenous iron sucrose is capable of correcting iron deficiency anemia clinically and also improve the hematologic indices in a safe efficacious way.

In a study of Kriplani A et al on Intravenous iron sucrose therapy for moderate to severe anaemia stated that parenteral iron therapy was effective in increasing haemoglobin, serum ferritin and other haematological parameters in pregnant women with moderate anaemia

Another study conducted on 50 pregnant anaemic women by Khurshid Shabbir Raja, Nusrat Batool Janjua and Nasir Khokhar stated that, Iron

sucrose complex when given to pregnant women with IDA significantly improved the haematological parameters

In a study conducted by Abdul Kareem Al-Momen et al on 52 patients and 59 controls concluded that Iron sucrose therapy resulted in a significantly higher Hb level in a shorter period with no major side effects. Hence they stated that Iron sucrose therapy as safe and effective in the treatment of iron deficiency anaemia during pregnancy.

Bhandal et al performed a study by randomized controlled trial method involving a total of 400 women in their postpartum period, with laboratory reports showing hemoglobin values less than 9g/dl, ferritin values being less than 15 μ g/L, in their postpartum period of 24 to 48 hours post delivery.

The sample was divided into two groups and administered intravenous iron sucrose in one group and oral ferrous sulphate in the control group. Both the groups showed a good improvement in their hemoglobin levels following therapy on day 5 and day 14 estimation.

Westad et al performed another study by involving women from five different obstetric centres. This was a randomized controlled study done

on 129 women in their postpartum period. These women had a hemoglobin value in the range of 6.5 to 8.5g/dl and were in their immediate postpartum period of 48 hours post delivery.

One group of women received intravenous iron sucrose while another group of women received oral ferrous sulphate. The follow up was done at 4, 8 and 12 weeks by withdrawing blood and estimating their hemoglobin values. This study report was issued as improvement of hemoglobin by 2g/dl in the treatment group following intravenous administration.

Meghan Crowley et al performed a widespread study in the form of six trials involving a mammoth 1140 women. These studies yielded results as shortened duration of time to achieve improvement in hemoglobin levels when iron was supplemented intravenously.

Both iron sucrose and ferric carboxymaltose were thus proven to be successful in managing anemia and improving the hemoglobin status of the patient. They also showed that both these being intravenous preparations had an edge over the oral preparations by eliminating the gastrointestinal side effects.

GUIDELINES FOR PREVENTION OF MATERNAL ANAEMIA

Anemia is an important risk factor that affects the maternal morbidity and mortality and also influences the health of newborn and hence health promotion strategies were developed to prevent maternal anemia.

Maternal anemia is associated with poor intra-uterine growth and conceiving of low-birth-weight babies and the incidence of abortion is 12 to 28%, perinatal death is 30%, and neonatal death is 7 to 10%. There occurs a fivefold increase in preterm delivery and 15 to 20% incidence of maternal mortality in anemia complicating pregnancy.

As anemia can significantly impair the health of the mother and cause maternal mortality and perinatal morbidity, the National Rural Health Mission issued guidelines to prevent anemia in pregnancy.

Classification of Anaemia (ICMR-1989)

Hb level	Classification
<4g/dl	Very severe
4-6.9 g/dl	Severe
7-9.9 g/dl	Moderate
10-10.9 g/dl	Mild

a. Compulsory Haemoglobin estimation

Haemoglobin estimation is done by Cyanmeth-haemoglobin method at 14-16 weeks, 20-24 weeks, 26-30 weeks and 30-34 weeks of pregnancy

mandatorily for all pregnant mothers. Repeat estimation of hemoglobin should be done with 4 week interval between estimations.

b. Deworming at 14-16th week of gestation

Deworming is done with one tablet of albendazole in all women at 14 to 16 weeks of pregnancy.

I. At 14-16 weeks

First Hb estimation is done at 14-16th week for all the antenatal mothers.

At Hb levels more than 11g, prophylactic dose of iron folic acid tablet with 100mg iron and 0.5mg of folic acid supplementation is sufficient. These tablets are administered daily for 100 days. When the Hb levels are between 7 to 11g, therapeutic dose of iron folic acid tablets administered by giving the tablets twice daily. When the Hb levels are less than 7g, patient needs blood transfusion and further evaluation for cause of anemia.

II. At 20-24 weeks

Second estimation of hemoglobin is done between 20 and 24 weeks

At Hb levels more than 11g, prophylactic dose of iron folic acid tablets are sufficient. When the Hb levels lie between 9-11g, the same tablets are

administered at therapeutic dose of twice daily. When the Hb levels are between 7 to 9g, iron sucrose is administered intravenously at a dose of 100mg of elemental iron containing iron sucrose is mixed in 100ml of normal saline and administered slowly over 20 to 30 minutes on alternate days upto 4 doses. Oral iron supplementation should be discontinued when using intravenous supplementation. When the Hb levels fall below 7g, blood transfusion is required.

III. At 26-30 weeks

Next hemoglobin value is done at 26 to 30 weeks of gestation. But when there has been history of iron sucrose administration, the estimation should be done one month after last dose.

When Hb levels are more than 11g, patient can continue with prophylactic dose of iron folic acid tablets. When the Hb levels come to 9 to 11g, there need to be a changeover to therapeutic dose of iron folic acid tablets. When the Hb levels become 7 to 9g, if there is history of iron sucrose administration, two top up doses of iron sucrose is sufficient. If there is no history of iron sucrose usage, start the patient on 4 doses of iron sucrose administration intravenously over a period of 2 weeks. At Hb levels less than 7g, patient needs to be managed with blood transfusion.

IV. At 30-34 weeks

Irrespective of previous anemia management all pregnant women need Hb estimation at 30-34 weeks.

At Hb levels more than 11g, continue prophylactic iron supplementation.

At Hb levels of 9 to 11g, manage with therapeutic iron dosage. If Hb levels do not improve more than 9g at 30-34 weeks of gestation there is a need to correct anemia with blood transfusion.

b) History

a. History of blood transfusions repeatedly point to hemoglobinopathies and bleeding disorders.

b. Rule out any history of drug allergy or bronchial asthma.

Avoid injection iron sucrose if there is positive history.

c) Tests to be done

Hb estimation by Cyanmeth-hemoglobin method ^[L]_[SEP]

Peripheral smear for cell morphology

MCV/RBC ratio

Serum iron binding capacity ^[L]_[SEP]

Urine should be checked for albumin, sugar and deposits and urine culture to be done if there is presence of 4-6 cells

d) Safety aspects

Iron sucrose infusion has to be administered as 20-30 drops per minute in the first 5 minutes, and then increased to 80-90 drops per minute and completed in 30 minutes to avoid free radical release. Administering the iron sucrose injection should be done cautiously to avoid extravastation of drug. Standard Emergency tray should be made available at the bedside for handling any reactions. Pulse and BP to be recorded before, during and after the administration of Inj. Iron Sucrose infusion

e)Dietcounselling

All the mothers should be encouraged to take iron rich foods and avoid coffee and tea.

f)Vitamin supplementation Water soluble vitamins like folic acid, B12 need not be withheld during iron sucrose infusion.

AIMS AND OBJECTIVES

1. To evaluate the response and effect of intravenous iron sucrose complex given to pregnant women with IDA.
2. To study the acceptance of drug among anemic mothers
3. To study the side effects of the drug

MATERIALS AND METHODS

STUDY SETTING: Govt. Theni Medical College and Hospital,
Department of Obstetrics and Gynaecology

STUDY DESIGN :prospective randomized control study

SAMPLE SIZE: determined by statistical analysis

100 pregnant women with haemoglobin between 7-9% with diagnosed iron deficiency attending antenatal clinic, were given intravenous iron sucrose complex in a dose of 200mg twice weekly schedule after calculating dose requirement

DURATION OF STUDY: one year study From July 2015 to June 2016

INCLUSION CRITERIA

Age 18-40yrs

Pregnancy between 18 to 24weeks

Hb 7-9 gm%

EXCLUSION CRITERIA

Underlying disease such as heart disease, hypertension

H/o allergy to iron metabolism

Hb <7g%

Thalassemia

Bleeding diathesis

METHODOLOGY:

Red cell indices, peripheral blood smear and detailed serum iron studies were also conducted.

100 women were recruited for intra venous iron sucrose therapy. Ethical clearance for the study protocol was taken from the Ethics Committee of the institute. Informed written consent was taken from all the patients before starting the therapy.

Baseline investigations including liver and kidney function tests, urine (routine microscopy and culture sensitivity), stool examination (for ova and cyst) were done. Folic acid tablets were given to all women during therapy.

The formula used for calculation of iron sucrose dose was as follows:

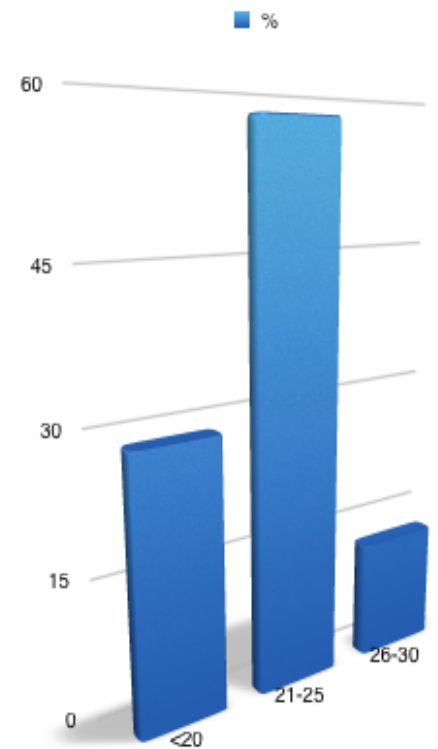
$$\text{Required iron dose (mg)} = \frac{2.4 \times (\text{target Hb} - \text{actual Hb}) \text{ pregnancy}}{\text{Weight(kg)}} + 1000 \text{ mg for replenishment of stores}$$

The required iron dose varied depending upon index Hb level and pre-pregnancy weight. Average dose requirement was 1777 ± 168.5 mg (1400-2160 mg). Mean duration to complete total therapy was 4.5 ± 1.0 (3.5-5.5 wk).

RESULTS:

Age Distribution (Table 2)

Age (yrs)	Cases	%
<20	29	29
21-25	58	58
26-30	13	13
Total	100	100%



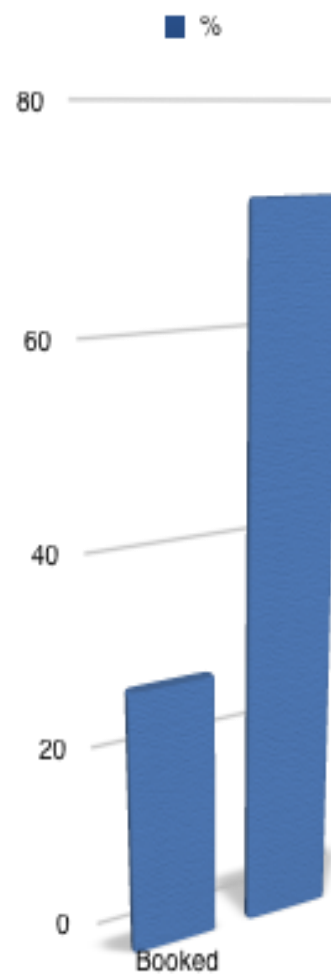
INFERENCE

Among 100 patient studied 29% were less than 18 yrs,58% belong to age group of 21-25 yrs,13% belong to 26 to 30 yrs.

TABLE 3

Booking Status

Booking status	Cases	%
Booked	28	28
Unbooked	72	72
Total	100	100%



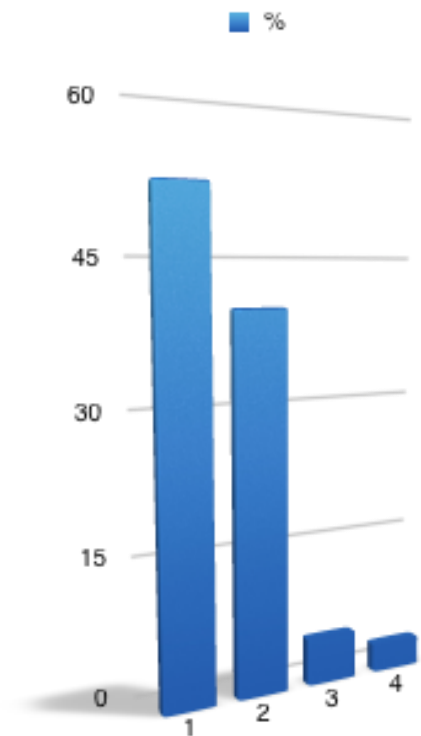
INFERENCE:

Among 100 patients 28% were booked case and 72% were unbooked case. with iron sucrose therapy given more to unbooked cases than booked cases.

Table 4

Obstetric Code

Obstetric Code	Cases	%
1	52	52
2	40	40
3	5	5
4	3	3
Total	100	100



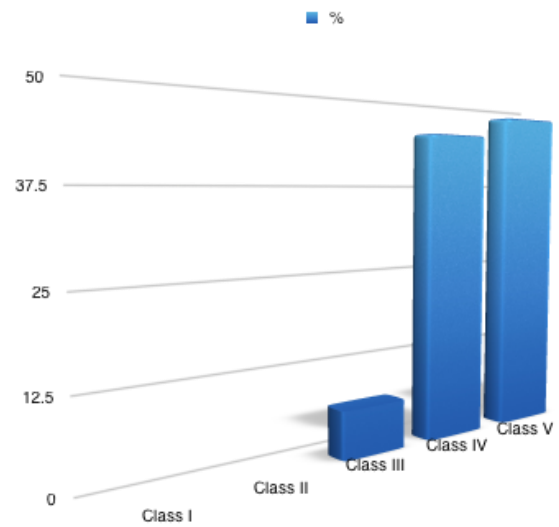
INFERENCE:

Among 100 patients 52% are primigravida, 40% gravida 2, 5% gravida 3, 3% gravida 4. With mean parity

Table 5

Socio Economic Status

SE status	Cases	%
Class I	0	0
Class II	0	0
Class III	7	7
Class IV	45	45
Class V	48	48
Total	100	100



INFERENCE:

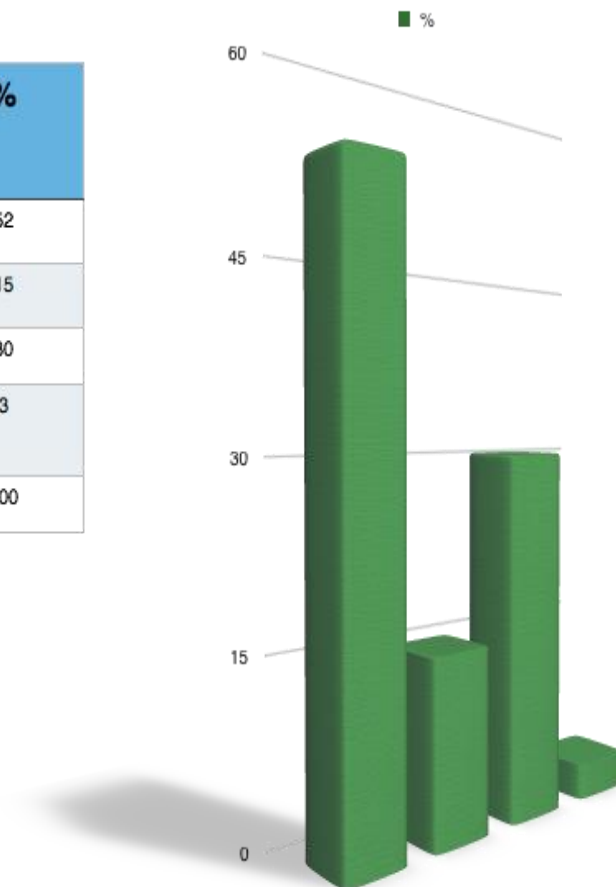
7% belong to class 3, with 45% belong to class 4, 48% belong to class v.

with mean socioeconomic status

Table 6

clinical features

Symptoms	Cases	%
Easy Fatiguability & Pallor	52	52
Breathlessness & Pallor	15	15
Pallor	30	30
Easy Fatiguability & Pallor & Breathlessness	3	3
Total	100	100

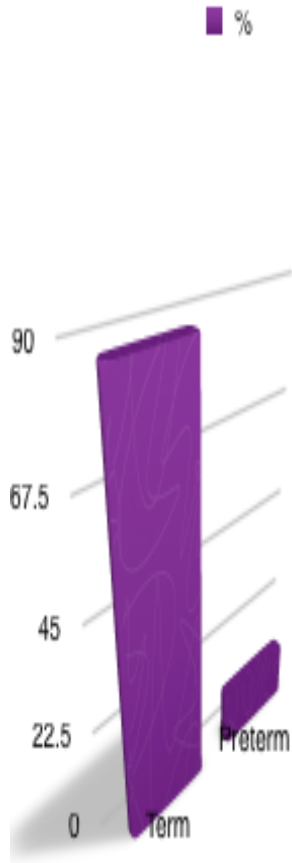


INFERENCE:

Symptom of easyfatiguability and pallor 52% which was in higher number than pallor alone or easy fatiguability,pallor and breathlessness.

Table 7

Gestational Age



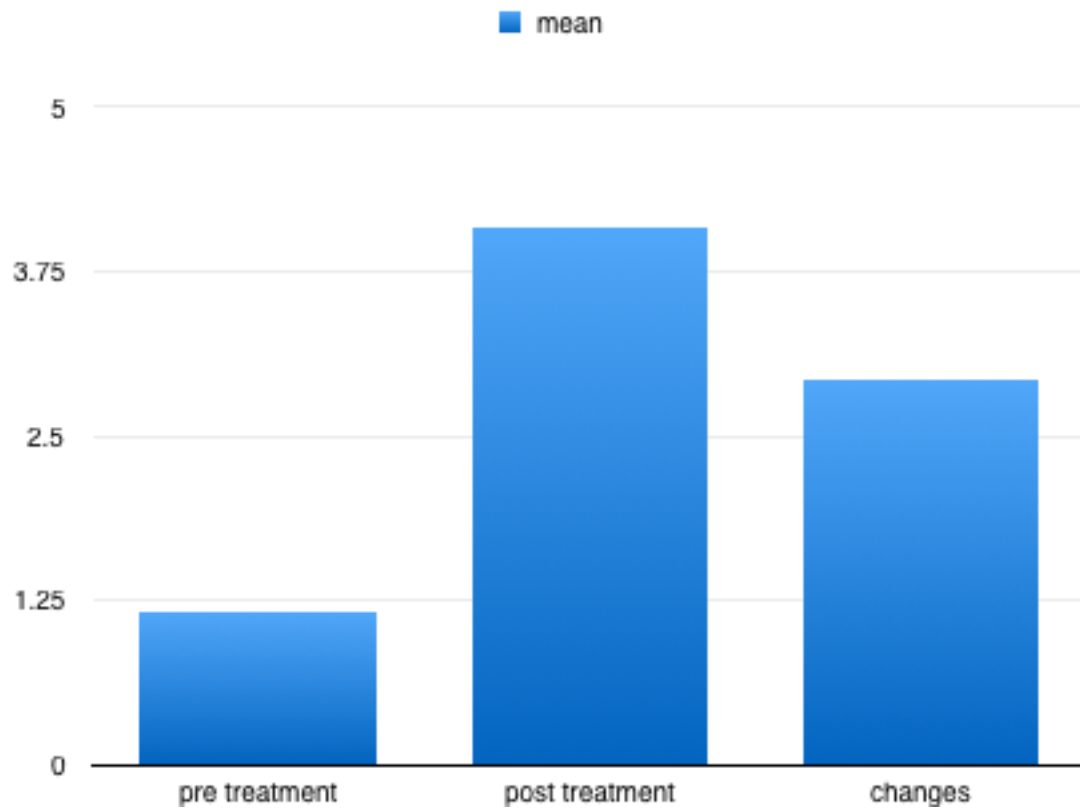
Gestational Age	Term	%
Term	88	88
Preterm	12	12
Total	100	100

Gestational age at delivery:

Among 100 patient studied, 12 % were preterm and 88% term gestation deliveries

Table 8

Reticulocyte count



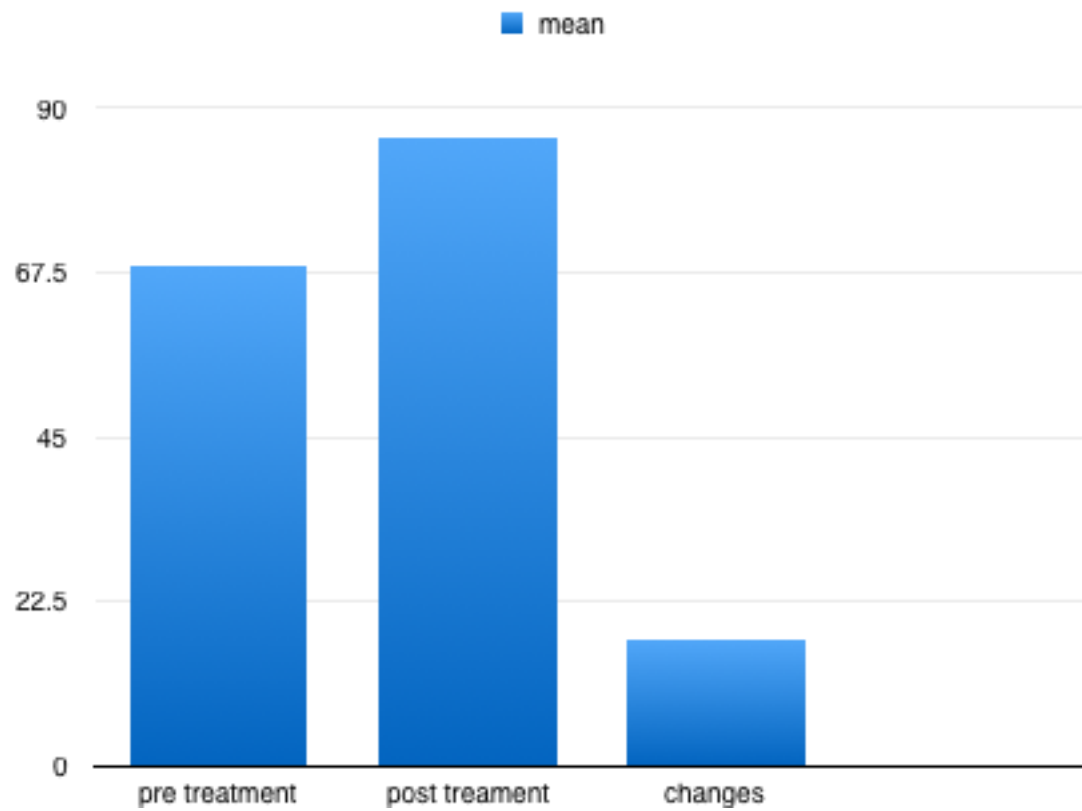
pretreatment reticulocyte count :1.165

posttreatment reticulocyte count:4.098

changes in reticulocyte count:2.93

Table 9

MCV



pretreatment mcv:68.59

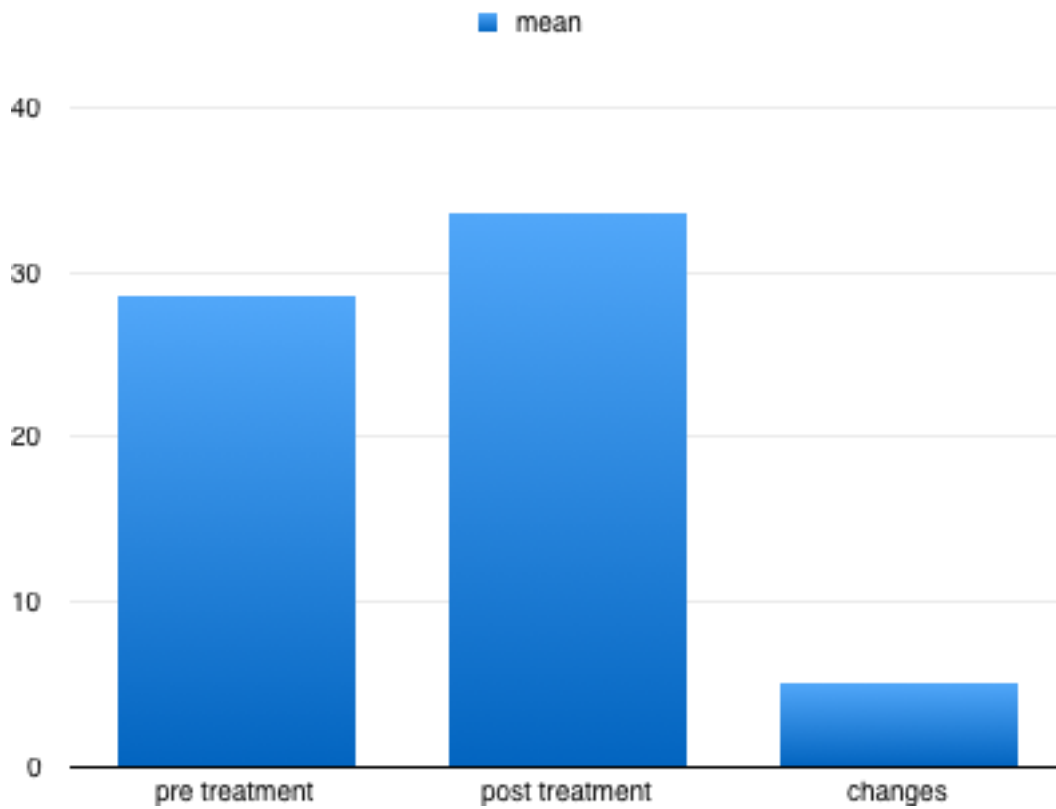
posttreatment mcv:85.94

changes in mcv:17.35

after 3 weeks of therapy rise in mcv of 17.35 is significant

Table 10

Haematocrit



pretreatmenthaematocrit: 23.59

posttreatment hematocrit:33.60

changes:5.01

after 3 weeks of therapy rise in hematocrit 5.01 is significant

RESULTS

Mean age of women was 23.46 ± 3.1 (range 18-30) yrs

Mean parity was 2.

At the beginning, mean Hb was 7.51 ± 0.60 g%..

After completion of therapy, mean Hb raised to 10.9 ± 0.8 g%.

Of the total women. The mean duration to achieve haemoglobin level more than 11 g% was 6.5 ± 2.3 wks

SIDE EFFECTS OF THERPY

Thromobophlebitis

Giddiness and restlessness

Mild fever

There were no major anaphylactic reactions

DISCUSSION:

Iron deficiency anemia is an important health concern for everyone, more so among pregnant women all over the world. The redeeming feature in this anemia is that it has tremendous response to iron supplementation. The factors causing iron deficiency anemia are present even before pregnancy, right from when the female attains menarche. The blood loss occurring during menstruation, inadequate and poor nutrition, poor bioavailability of the dietary iron when added with the requirement of pregnancy can lead on to iron deficiency anemia. It has been postulated that many women are in iron depleted state at the start of their pregnancy²¹.

The iron supplementation is done parenterally when the anemia is severe of oral supplementation is inadequate²². Also parenteral supplementation is required when the woman has defective absorption of oral iron due to various conditions like inflammatory bowel disease, ferrous intolerance²³. In our study population of 100 antenatal patients attending GTMCH OPD between 18-24 weeks of gestation ,clinical features and laboratory parameters were evaluated and results are statistically analysed.of the population studied,majority of them were between 21-25 yrs age group

accounting for 58% followed by 29% below 20yrs and 13% between 26-30yrs of age.

Many studies showed that iron sucrose brought about a faster increase in hemoglobin levels as compared to oral iron supplementation. They also showed that only iron sucrose was capable of improving iron reserves.

The improvement in serum ferritin levels was showed not to be because of administering iron directly intravenously. The mechanism was explained to be due to rapid release of iron from the iron sucrose complex and this enabling the binding of this iron to the transport proteins found in human body. These proteins carry the iron and deposit them in parenchymatous tissues and enable them to be used up at a later date.

Out of 100 patients ,72 ‘percentage of anemic patients were unbooked and 28% were booked in a hospital.of the total study group of 100 mothers,52% were primigravida followed by 40% second gravida,5% third gravid and 3 5 fourthgravida.

Majority of the anemic population belonged to class 5 and class 4 socioeconomic status accounting for 48 and 47 percentage respectively whereas only 3 percent belonged to higher socio economic class.

About 52% of the patients had easy fatigability as their presenting symptom followed by 30% of the patients who were identified by pallor sign and 15% had breathlessness as complaint.

On following these 100 patients, we could observe that about 88% reached term and 22% had preterm delivery.

On observing laboratory investigations, we could conclude that there is a marked rise in reticulocyte count of about 2.093% (pretreatment - 1.165% post treatment-4.098%) following 3 weeks of iron sucrose injections which is statistically proven as significant.

The pretreatment MCV is 68.5 and post treatment MCV 85.94% with changes after three weeks is 17.35% and hematocrit before treatment is 23.59 and post treatment 33.6 with changes 5.01 is analysed as significant statistically.

There was a cent percent improvement of clinical symptoms following iron sucrose therapy.

Only minor adverse reactions caused by iron sucrose. No major reaction

Changes in hemoglobin:

In this study intravenous iron sucrose was administered to women and the result of treatment was verified by estimating the baseline hemoglobin and repeat estimation 3 weeks after the therapy. The pretreatment hemoglobin levels of women participating in this study was 7.51 ± 0.60 g and the repeat hemoglobin values were 10.9 ± 0.81 g.

This was comparable to a study done by Bayomeu et al²⁴ where the results obtained showed rise in hemoglobin values from 9.6 ± 0.7 g to 11.11 ± 1.3 g at 4 weeks of therapy.

Another study was conducted by Westad by randomized controlled trial which reported improvement in postpartum anemia in about 128 women by administering intravenous iron sucrose and showed a rise in hemoglobin from 6.5g before treatment to 11.g after 4 weeks of therapy.

Rosario et al studied the influence of intravenous iron sucrose in women presenting with anemia following childbirth or surgery and found that the rise in hemoglobin was an additional 2.1g/dl following intravenous administration.

Patel et al⁵ studied the influence of iron supplementation both in antenatal and postnatal women and he reported that the rise in hemoglobin was

about 7.9 on day 0 to 9.25 on day 8 and 11.6g on day 15 following therapy.

When administered among postnatal women the rise in hemoglobin was from 7.9g on day 0 to 9.4 on day 8 and 11.2g on day 15 following intravenous iron sucrose.

All these studies show that the administration of iron sucrose plays an important role in improving the hemoglobin status of women both antenatally and postnatally.

changes in hematocrit:

Hematocrit estimation was done in the study 3 weeks after administration of intravenous iron sucrose. This hematocrit is an indicator of improvement of hemoglobin status and in our study time taken for improvement was 3 weeks.

Seid et al studied the effect of iron sucrose in improving hemoglobin by 2,6g/dl and found that the time taken to achieve this improvement was 4 weeks.

Likewise another study was conducted comparing iron sucrose with ferric carboxymaltose and it showed the latter drug brought about a greater

increase in hemoglobin values in shorter duration of time. But carboxymaltose being far more costly than iron sucrose is a big disadvantage.

The study concluded that iron sucrose is a cost effective method to improve hemoglobin and that it is superior to oral iron supplementation for the same purpose.

Bhandal and Russel performed a randomized controlled study to compare oral iron with intravenous iron in management of postpartum anemia. They reported that in the short term intravenous iron provided better improvement of hemoglobin levels as against oral iron supplementation, But this advantage was lost as by day 40, the hemoglobin increase was similar in both groups.

Breymann et al conducted a study involving 129 pregnant women with anemia with hemoglobin values less than 9g/dl and proved that intravenous iron sucrose administration improved the hemoglobin levels by about 2g% and this outcome was evident by 4 weeks of therapy.

Westad et al studied the time taken for rise in hemoglobin and correction of anemia following intravenous iron administration and found that a

target of 11g Hb was achieved in 80% of individuals treated with iron supplementation intravenously.

They also found that iron supplemented got incorporated into hemoglobin after about 3 to 4 weeks and this was why there occurred a delayed increase in hemoglobin following iron therapy.

Al moment et al showed that iron sucrose resulted in greater improvement of hemoglobin values in about 3 weeks duration.

Changes in mcv:

In our study mean mcv value as after 3 weeks showed improvement as rise in mcv

Adverse reactions:

5 % treated with iron sucrose showed minor adverse reaction.

1.giddiness and restlessness.

2.mild fever

3.thrombophlebitis

There were no major anaphylaxis reaction.

Similar reports were also presented by Al moment et al who compared intravenous iron sucrose with oral preparations and found that there was

no incidence of adverse effects when women were administered iron sucrose as against non compliance, gastrointestinal side effects and nausea found in the group treated with oral iron.

Hogine et al performed another study comparing the adverse reactions occurring following iron sucrose and intramuscular iron and found no adverse reactions following iron sucrose but severe pain and hence poor compliance following intramuscular iron administration.

Various factors play an important role in affecting the effects of treatment. In our study the hemoglobin values improved considerably without any difficulty.

Caretti et al study showed that the increase in hemoglobin was inversely dependent on the baseline hemoglobin value. He postulated that low baseline values tend to respond more favourably.

He also mentioned that the improvement was better when used after 7 months of gestation rather than in early second trimester. This effect of period of gestation on anemia correction has been attributed to the influence of physiological hemodilution occurring in second trimester.

All these studies show that when the baseline value is lower and the onset of anemia is at a later period of gestation, the improvement of hemoglobin levels tend to be better with intravenous iron supplementation than oral iron.

Summary

In our study 100 patients with iron deficiency anaemia of GTMCH OP department was followed from June 2015 to July 2016. Patient selected according to inclusion and exclusion criteria already stated.

The result of the study as follows:

1. majority of patients, around belonged to age group 21- 25 yrs
2. unbooked patient received more iron sucrose than booked patients.
3. majority of patients belonged to class 4
4. primigravida affected more than multigravida
5. symptoms like easy fatigability, pallor, breathlessness seen on examination
6. symptomatic improvement seen in 100% of patients
7. Mean rise in Hb seen as with iron sucrose 2.5g%
8. Mean rise in reticulocyte count observed as 2.093%
9. Mean rise in mcv seen with iron sucrose 17.35
10. the adverse effect not observed in all

Conclusion

Intravenous iron sucrose is safe in pregnancy. It corrects anaemia in short duration and replenishes iron stores better than oral iron. As the rate of increase in Hb is faster IV iron sucrose is suitable for treatment of anaemia in 2nd trimester. There was significant difference in ferritin level after treatment with oral & parenteral iron. With iron reserves restored only in the iron sucrose group. It has half life of about six hours. This is an advantage of iv iron sucrose over iron dextran. Anaemia was corrected satisfactorily without the use of weight dependent formula. Mild adverse events noted were Vomiting, giddiness, rashes following first dose. Because there was no serious adverse drug reaction and no anaphylaxis, we feel its safer for treatment of anaemia in pregnancy.

It is accepted that iv iron sucrose therapy gives a rapid erythropoietic response in short duration. The rate of Fe delivery to bone marrow is a major factor for erythropoiesis. It rises the Hb at faster rate. Iron sucrose is definitely the first line of treatment for anemia in pregnancy in view of easy accessibility, safety good efficacy compared to other parenteral iron and blood transfusion.

As compared to western women whose iron stores are sufficient and they need 30-40 mg of elemental iron for anaemia prophylaxis in pregnancy. The stores in Indian women is deficient. And the need 100mg elemental

Fe for prophylaxis, it reduces the need for blood transfusion, and can be given as an outpatient basis.

Intravenous iron sucrose is effective in improving Hb, hematocrit, mcv, reticulocyte count in short duration.

It is safe with no adverse reaction

Thus it is concluded that intravenous iron sucrose is safe, effective, without any adverse reaction.

IV iron sucrose therapy effective to treat moderate anemia in pregnant women .It causes rapid rise in Hb and replacement of stores fast

The image shows a page from a ledger or account book. The page is filled with a grid of columns and rows, typical of a financial record. The text is extremely faint and illegible due to the low resolution and blurriness of the photograph. The columns likely represent different categories of accounts or transactions, and the rows represent individual entries. The page is tilted slightly to the right.

Table 1. Age- and sex-specific mean values of the variables measured in the study.

Age (yr)	Sex	Height (cm)	Weight (kg)	Body mass index (BMI) (kg/m ²)	Waist circumference (cm)	Waist-hip ratio (WHR)	Trunk muscle strength (kg)	Trunk muscle endurance (min)	Trunk muscle power (W)	Trunk muscle endurance power (W)	Trunk muscle endurance power index (W/kg)
18	M	175.2	68.5	39.1	85.2	0.91	10.2	12.5	127.5	12.75	0.35
18	F	162.5	55.2	34.0	78.5	0.88	9.5	11.8	118.2	11.82	0.34
20	M	178.5	75.2	42.1	90.5	0.92	11.5	14.2	146.3	14.63	0.38
20	F	165.2	62.5	37.8	82.2	0.89	10.2	12.8	130.5	13.05	0.36
22	M	182.2	82.5	45.3	95.2	0.93	12.8	15.5	167.8	16.78	0.41
22	F	168.5	68.2	40.5	85.5	0.90	11.2	13.8	149.2	14.92	0.39
24	M	185.5	90.2	48.6	100.2	0.94	14.2	17.2	184.8	18.48	0.44
24	F	172.2	75.5	43.8	90.2	0.91	12.5	15.2	167.2	16.72	0.41
26	M	188.2	98.5	52.3	105.2	0.95	15.5	18.8	202.5	20.25	0.47
26	F	175.5	82.2	46.8	95.2	0.92	13.8	16.5	184.2	18.42	0.44
28	M	192.2	108.5	56.4	110.2	0.96	17.2	21.5	227.2	22.72	0.52
28	F	180.2	90.2	50.1	100.2	0.93	15.2	18.2	195.2	19.52	0.49
30	M	195.2	120.2	61.6	115.2	0.97	19.5	24.2	247.2	24.72	0.58
30	F	185.2	100.2	54.1	105.2	0.94	17.2	20.5	218.2	21.82	0.55
32	M	198.2	130.2	65.7	120.2	0.98	22.2	27.5	275.2	27.52	0.66
32	F	190.2	110.2	58.0	110.2	0.95	19.2	23.2	226.2	22.62	0.62
34	M	202.2	140.2	69.3	125.2	0.99	25.2	30.2	307.2	30.72	0.77
34	F	195.2	120.2	61.6	115.2	0.96	21.2	25.2	263.2	26.32	0.71
36	M	205.2	150.2	73.2	130.2	1.00	28.2	33.2	336.2	33.62	0.89
36	F	198.2	130.2	65.7	120.2	0.97	23.2	27.2	294.2	29.42	0.81
38	M	208.2	160.2	77.0	135.2	1.01	32.2	38.2	391.2	39.12	0.99
38	F	200.2	140.2	70.0	125.2	0.98	27.2	31.2	336.2	33.62	0.91
40	M	212.2	170.2	79.9	140.2	1.02	35.2	42.2	437.2	43.72	1.07
40	F	205.2	150.2	73.2	130.2	0.99	30.2	35.2	357.2	35.72	0.99
42	M	215.2	180.2	83.7	145.2	1.03	38.2	46.2	477.2	47.72	1.15
42	F	208.2	160.2	77.0	135.2	0.99	32.2	37.2	387.2	38.72	1.07
44	M	218.2	190.2	87.2	150.2	1.04	42.2	50.2	507.2	50.72	1.23
44	F	210.2	170.2	81.0	140.2	0.99	35.2	40.2	417.2	41.72	1.15
46	M	222.2	200.2	90.1	155.2	1.05	45.2	54.2	537.2	53.72	1.31
46	F	215.2	180.2	83.7	145.2	0.99	37.2	42.2	437.2	43.72	1.15
48	M	225.2	210.2	93.3	160.2	1.06	48.2	58.2	567.2	56.72	1.39
48	F	218.2	190.2	87.2	150.2	0.99	39.2	44.2	457.2	45.72	1.15
50	M	228.2	220.2	96.4	165.2	1.07	52.2	62.2	597.2	59.72	1.47
50	F	220.2	200.2	90.9	155.2	0.99	41.2	46.2	477.2	47.72	1.15
52	M	232.2	230.2	99.1	170.2	1.08	55.2	66.2	627.2	62.72	1.55
52	F	225.2	210.2	93.3	160.2	0.99	43.2	48.2	497.2	49.72	1.15
54	M	235.2	240.2	102.1	175.2	1.09	58.2	70.2	657.2	65.72	1.63
54	F	228.2	220.2	96.4	165.2	0.99	45.2	50.2	517.2	51.72	1.15
56	M	238.2	250.2	105.0	180.2	1.10	62.2	74.2	687.2	68.72	1.71
56	F	230.2	230.2	100.0	170.2	0.99	47.2	52.2	537.2	53.72	1.15
58	M	242.2	260.2	107.4	185.2	1.11	65.2	78.2	717.2	71.72	1.79
58	F	235.2	240.2	102.1	175.2	0.99	49.2	54.2	557.2	55.72	1.15
60	M	245.2	270.2	110.2	190.2	1.12	68.2	82.2	747.2	74.72	1.87
60	F	238.2	250.2	105.0	180.2	0.99	51.2	56.2	577.2	57.72	1.15
62	M	248.2	280.2	113.0	195.2	1.13	72.2	86.2	777.2	77.72	1.95
62	F	240.2	260.2	108.3	185.2	0.99	53.2	58.2	597.2	59.72	1.15
64	M	252.2	290.2	115.4	200.2	1.14	75.2	90.2	807.2	80.72	2.03
64	F	245.2	270.2	110.2	190.2	0.99	55.2	60.2	617.2	61.72	1.15
66	M	255.2	300.2	117.6	205.2	1.15	78.2	94.2	837.2	83.72	2.11
66	F	248.2	280.2	113.0	195.2	0.99	57.2	62.2	637.2	63.72	1.15
68	M	258.2	310.2	120.1	210.2	1.16	82.2	98.2	867.2	86.72	2.19
68	F	250.2	290.2	116.3	200.2	0.99	59.2	64.2	657.2	65.72	1.15
70	M	262.2	320.2	122.1	215.2	1.17	85.2	102.2	897.2	89.72	2.27
70	F	255.2	300.2	117.6	205.2	0.99	61.2	66.2	677.2	67.72	1.15
72	M	265.2	330.2	124.5	220.2	1.18	88.2	106.2	927.2	92.72	2.35
72	F	258.2	310.2	120.1	210.2	0.99	63.2	68.2	697.2	69.72	1.15
74	M	268.2	340.2	126.8	225.2	1.19	92.2	110.2	957.2	95.72	2.43
74	F	260.2	320.2	123.0	215.2	0.99	65.2	70.2	717.2	71.72	1.15
76	M	272.2	350.2	128.6	230.2	1.20	95.2	114.2	987.2	98.72	2.51
76	F	265.2	330.2	124.5	220.2	0.99	67.2	72.2	737.2	73.72	1.15
78	M	275.2	360.2	131.2	235.2	1.21	98.2	118.2	1017.2	101.72	2.59
78	F	268.2	340.2	126.8	225.2	0.99	69.2	74.2	757.2	75.72	1.15
80	M	278.2	370.2	133.0	240.2	1.22	102.2	122.2	1047.2	104.72	2.67
80	F	270.2	350.2	129.8	230.2	0.99	71.2	76.2	777.2	77.72	1.15
82	M	282.2	380.2	134.7	245.2	1.23	105.2	126.2	1077.2	107.72	2.75
82	F	275.2	360.2	130.9	235.2	0.99	73.2	78.2	797.2	79.72	1.15
84	M	285.2	390.2	136.4	250.2	1.24	108.2	130.2	1107.2	110.72	2.83
84	F	278.2	370.2	133.0	240.2	0.99	75.2	80.2	817.2	81.72	1.15
86	M	288.2	400.2	138.8	255.2	1.25	112.2	134.2	1137.2	113.72	2.91
86	F	280.2	380.2	135.9	245.2	0.99	77.2	82.2	837.2	83.72	1.15
88	M	292.2	410.2	140.4	260.2	1.26	115.2	138.2	1167.2	116.72	2.99
88	F	285.2	390.2	136.8	250.2	0.99	79.2	84.2	857.2	85.72	1.15
90	M	295.2	420.2	142.3	265.2	1.27	118.2	142.2	1197.2	119.72	3.07
90	F	288.2	400.2	138.8	255.2	0.99	81.2	86.2	877.2	87.72	1.15

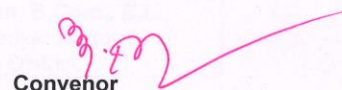
The following Project was approved by the Committee:

Name of the PG	Course	Name of the Project	Remarks
Dr. K. Vahitha Begum	Final Year- M.S. OG., GTMC, Theni	Intravenous iron sucrose therapy for mild to moderate anemia in pregnancy	Approved

Please note that the investigator should adhere the following: He/she should get a detailed informed consent from the Patients/participants and maintain Confidentially.

1. He/she should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution.
2. He/she should inform the Institution Ethical Committee in case of any change of study procedure site and investigation or guide.
3. He/she should not deviate for the area of the work for which applied for Ethical Clearance. He/She should inform the Institution Ethical Committee immediately, in case of any adverse events or any serious adverse reactions.
4. He/she should abide to the rules and regulations of the institution.
5. He/she should complete the work within the specific period and apply for if any extension of time is required. He/she should apply for permission again and do the work.
6. He/she should submit the summary of the research work to the Ethical Committee on completion of the work.
7. He/she should not claim any funds from the institution while doing the work or on completion.
8. He/she should understand that the members of Institutional Ethical Committee have the right to monitor the work with prior intimation.


Chairman


Convenor

To

The above individual – through Head of the Department concerned.

